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Health Supplement Use and Related Adverse Events in Dubai, United Arab Emirates: A Cross-Study

Naseem Mohammed Rafee Abdulla

UAEU

جامعة الإمارات العربية المتحدة
United Arab Emirates University

United Arab Emirates University

College of Medicine and Health Sciences

HEALTH SUPPLEMENT USE AND RELATED ADVERSE EVENTS IN DUBAI, UNITED ARAB EMIRATES: A CROSS-SECTIONAL STUDY

Naseem Mohammed Rafee Abdulla

This dissertation is submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy

Under the Supervision of Dr. Abderrahim Oulhaj

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Declaration of Original Work

I, Naseem Mohammed Rafee Abdulla, the undersigned, a graduate student at the United Arab Emirates University (UAEU), and the author of this dissertation, entitled "*Health Supplement Use and Related Adverse Events in Dubai, United Arab Emirates: A Cross-Sectional Study*", hereby, solemnly declare that this dissertation is my own original research work that has been done and prepared by me under the supervision of Dr. Abderrahim Oulhaj, in the College of Medicine and Health Sciences at UAEU. This work has not previously been presented or published, or formed the basis for the award of any academic degree, diploma or a similar title at this or any other university. Any materials borrowed from other sources (whether published or unpublished) and relied upon or included in my dissertation have been properly cited and acknowledged in accordance with appropriate academic conventions. I further declare that there is no potential conflict of interest with respect to the research, data collection, authorship, presentation and/ or publication of this dissertation.

Student's Signature: _____ Date: 01/05/2018

Advisory Committee

1) Advisor: Dr. Abderrahim Oulhaj

Title: Assistant Professor

Institute of Public Health

College of Medicine and Health Sciences

2) Co-advisor: Dr. Tom Loney

Title: Assistant Professor

Institute of Public Health

College of Medicine and Health Sciences

3) Member: Prof. Michal Grivna

Title: Professor

Institute of Public Health

College of Medicine and Health Sciences

Approval of the Doctorate Dissertation

This Doctorate Dissertation is approved by the following Examining Committee Members:

1) Advisor (Committee Chair): Dr Abderrahim Oulhaj

Title: Assistant Professor

Institute of Public Health

College of Medicine & Health Sciences

Signature _____ Date: 15/04/2018

2) Member: Dr Luai Awad Ahmed

Title: Associate Professor

Institute of Public Health

College of Medicine & Health Sciences

Signature _____ Date: 15.04.2018

3) Member: Professor Abdu Adem

Title: Professor

Department of Pharmacology

College of Medicine & Health Sciences

Signature _____ Date: 15-04-2018

4) Member (External Examiner): Professor Anwar T. Merchant

Title: Professor

Department of Epidemiology and Biostatistics

Institution: University of South Carolina

Signature _____ Date: 4/18/2018

This Doctorate Dissertation was accepted by:

Acting Dean of the College of Medicine and Health Sciences: Professor Ruth Langer

Signature _____ Date 7 May 2018

Dean of the College of Graduate Studies: Professor Nagi T. Wakim

Signature _____ Date 14/5/2018

Copy 9 of 10

Advisory Committee

1) Advisor: Dr. Abderrahim Oulhaj

Title: Assistant Professor

Institute of Public Health

College of Medicine and Health Sciences

2) Co-advisor: Dr. Tom Loney

Title: Assistant Professor

Institute of Public Health

College of Medicine and Health Sciences

3) Member: Prof. Michal Grivna

Title: Professor

Institute of Public Health

College of Medicine and Health Sciences

Abstract

Health supplement products contain ingredients of more than thousand chemicals. Several of these chemicals may adversely affect human health. Previous studies have found that consumers are generally unaware regarding the risks of health supplements and their associated adverse events. In addition, they are unaware of the appropriate reporting process to relevant authorities should adverse events occur. Moreover, many healthcare professionals have inadequate knowledge, attitude and practice in health supplement consumption-related adverse events and their reporting. The purpose of this research was to measure the health supplement consumption in the population of Dubai, the adverse events thereof, and the level of knowledge, attitude, and practice among healthcare professionals about the issue.

This research project comprised two cross-sectional studies. The first was a telephone survey using computer-assisted personal interviewing carried out among the general population. The second study was an on-line survey among healthcare professionals from various private and government healthcare settings in Dubai that sought to assess their knowledge, attitude, and practice (KAP) toward health supplements. Descriptive statistics were used to describe the demographic characteristics of the sample using frequencies and percentages as appropriate. Chi-square, or ANOVA, was used as appropriate to test for statistical differences. Analyses were conducted using STATA version 14.2.

In the first survey, among 1,203 participants, 455 (37.8%) reported either current or previous use of health supplements. Of the 455 users, 389 (85.54%) were knowledgeable about health supplements and 442 (97.14%) had encountered no adverse events. Of the 13 (2.86%) who had encountered adverse events, the degree of severity was either moderate or mild. Most (10, 76.92%) did not know how to report the adverse event to healthcare professionals. Only 3 (23.08%) had ever reported an event.

In the second study, 427 healthcare professionals participated to the online survey. Of these, 78 (18.3%) had a good level of KAP towards health supplements, 166 (38.9%) had a fair level of KAP, while 183 (42.9%) had a poor level. Job experience of over 6 years resulted in a significant difference (P=0.017) in mean KAP scores. No

statistically significant differences in scores were found with gender or educational levels. Significant differences, however, (P=0.001) were found with nationality where non-UAE national participants had a higher level of KAP than UAE nationals. There were also significant differences in mean KAP scores between occupational groups, physicians and pharmacists having higher scores than other healthcare providers.

The findings of this research provide important new knowledge about health supplement use in Dubai. The findings may be used to develop policies and programs on health supplements that will help to minimise the risk of adverse events arising from their use. The results also point out that it is important to institute educational initiatives to assess any risks related to the use of health supplements. Such initiatives will help to raise both awareness and knowledge in both the population and healthcare professionals regarding the use and adverse events of health supplements.

Keywords: Health supplements, Dubai, adverse event, knowledge, attitude, practice.

Title and Abstract (in Arabic)

استهلاك المكملات الصحية والآثار الصحية المرتبة في إمارة دبي – الإمارات العربية المتحدة: دراسة استقصائية

الملخص

كل منتج مكمل صحي في إمارة دبي يحتوي على العديد من المكونات التي تصل إلى أكثر من ألف مادة كيميائية في المجموع. العديد من هذه المواد الكيميائية قد يكون لها بعض الآثار السلبية مما سيؤثر على صحة الإنسان. كثير من الدراسات أثبتت أن المستهلكين بشكل عام لا يدركون عن المخاطر المصاحبة للمكملات الصحية والآثار السلبية المرتبطة بها. كذلك، بعض المستهلكين لا يدركون كيفية تزويد السلطات المعنية في حال وجودها بأي من الأعراض الجانبية التي يتعرضون إليها. وبالإضافة إلى ذلك، فإن العديد من المتخصصين في مجال الرعاية الصحية ليس لديهم المعرفة الكافية، أو التصور على الأعراض السلبية والمصاحبة مع استهلاك المكملات الصحية.

يهدف هذا البحث إلى إجراء مسح سكاني في إمارة دبي لتحديد نسبة استهلاك المكملات الصحية من قبل سكان دبي، والآثار السلبية والمصاحبة مع استهلاك المكملات الصحية (إذا تم تحديدها) ومستوى المعرفة والممارسة بين المتخصصين في مجال الرعاية الصحية حول هذه القضية. لاحقا تم استخدام نتائج البحث لتقييم الأثر الصحي لإنشاء نظام اليقظة للمكملات الصحية في دبي.

أجريت دراسات من خلال توزيع استبيانات للمستهدفين من السكان والمختصين وتم استخدام المعلومات التي تم جمعها في تقييم الأثر الصحي للنظام المراد إنشائه. قام هذا البحث بملء الفجوة المعرفية الحالية في هذا المجال البحثي في دبي كما لا تتوفر أي معلومات سابقة بشأن هذا الموضوع في دولة الإمارات العربية المتحدة.

مفاهيم البحث الرئيسية: المكملات الصحية، دبي، الإمارات العربية المتحدة، الأعراض الضارة، المعرفة، الممارسة، التصور.

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Dedication

To my beloved mother and children

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List of Abbreviations

ADI	Acceptable Daily Intake
ADR	Adverse Drug Reactions
AE	Adverse Events
CAM	Complementary and Alternative Medicine
CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
CGMPs	Current Good Manufacturing Practice
CM	Complementary Medicines
CPSS	Consumer Products Safety Section
DNA	Deoxyribonucleic Acid
DS	Dietary Supplements
DSHEA	Dietary Supplement Health and Education Act
EMA	European Medicines Agency
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FFD&C Act	Federal Food, Drug, and Cosmetic Act
GAP	Good Agriculture Practices
GMP	Good Manufacturing Practice
GVP	Good Pharmacovigilance Practices
HC	Health Canada
HS	Health Supplement
ICSR	Individual Case Safety Report
LOAEL	Lowest Observed Adverse Effect Level
MAH	Marketing Authorisation Holders

NHP	Natural Health Products
NHPD	Natural Health Products Directorate
NHPR	Natural Health Products Regulations
NLEA	Nutrition Labelling and Education Act
NNHPD	Natural and Non-Prescription Health Products Directorate
NOAEL	Non-Observed Adverse Effect Level
OTC	Over the Counter
TGA	Therapeutic Goods Administration
UN	United Nation
UR	Under Reporting
USDSHEA	United States Dietary Supplements Health and Education Act
WHO	World HealthOrganization

Chapter 1: Introduction

1.1 Overview

Within the last two decades, consumption of dietary supplements has increased worldwide, especially in the United States of America (Millen et al., 2004; Slesinski et al., 1995; Wu et al., 2011). This has raised the awareness and interest of regulatory organizations, healthcare professionals and researchers (Al-Ahmad et al., 2012).

The World Health Organization (WHO) and the United States (US) Dietary Supplements Health and Education Act (DSHEA) of 1994 both define dietary supplements as a product (other than tobacco) that is meant to supplement the diet. Both organizations include vitamins, minerals, herbs, botanical products, amino acids, or dietary substances in their definitions. The use of dietary supplements including herbal supplements is gaining popularity in many developed countries (Aina & Ojedokun, 2014).

In the Local Order No. (11) of 2003 concerning Public Health and Safety of the Society in the Emirate of Dubai and its Administrative Resolution No. (30) of 2007, dietary supplements are referred to as health supplements (HS). These supplements are strongly related to human health as about 1,000 different chemicals may be included in the ingredients. These constituents may cause disease or other adverse events by their chemical reactions with the human body. HS products such as minerals and vitamins are widely available over-the-counter and are often purchased by consumers without advice from a healthcare provider. HS products are widely consumed for the purposes of weight reduction and energy enhancement, among several other reasons (CPSS, 2015).

Herbs were the predominant form of healthcare for the world's population before the advent of modern medicine and are still common among many underserved populations (Su & Li, 2011; Rossler et al., 2007). HS products, including herbal supplements, also have the potential for drug interaction (Izzo & Ernst, 2009; Moyad, 2010; Tsai et al., 2013; Van & Bogers, 2012), which necessitates consumer awareness and diligence among healthcare professionals in their daily practice (Kemper et al., 2006; Piening et al., 2012).

HS products play an important role in the general healthcare system of many developing countries and are rapidly gaining popularity in many developed countries (Chitturi & Farrell, 2008). WHO estimates that 80% of Asian and African populations rely on traditional medicine as the primary method to meet their healthcare needs (WHO, 2008). The scenario in developed countries is very similar with 70% to 80% of the population using some form of complementary or alternative medicine. Most of these can be used safely if the public is given the right education and advice (Barnes et al., 2004). Physicians need to be ready to discuss their use with patients or advise patients accordingly (Neergheen-Bhujun, 2013).

As HS products have a wide range of possible actions, their effectiveness and safety for human consumption is of concern. Harmful side effects have been reported following the use of some types of HS products (Tsai et al., 2013). For example, Ginkgo Biloba has been implicated in the occurrence of epileptic seizure, and chronic use of zinc may result in anaemia (Al-Ahmad et al., 2012; Izzo & Ernst, 2009; Shaw & Palmer, 2003).

Adverse events, such as allergy, drug interactions, heavy metal poisoning, reactions to adulterants or contaminants and other toxicities, can arise from the product

itself (Tachjian et al., 2011). When these problems occur, a rational approach to management with resuscitation, symptomatic, and supportive care is essential. Clinical features may give clues about the offending agents. HS products that possess pronounced pharmacological effects or toxic constituents can be inherently poisonous, and physicians should anticipate problems with such toxicities if they encounter patients using these products (MOH, 2011).

Also, potentially hazardous interactions between HS products and some medicines have been reported in the literature including synergistic effects, poisoning, or inactivation of at least one of the substances (Tsai et al., 2013). For example, St. John's Wort is a substance that is used as a HS product to treat mild and moderate depression. St. John's Wort can induce liver enzymes and so has the potential to interact with many narrow therapeutic range medicines that are metabolised through the liver such as anti-depressants (Van & Bogers, 2012). Some other substances such as garlic, ginger, and Ginkgo Biloba can induce the risk of bleeding when administered with anticoagulants (Moyad, 2010).

Many HS products, used singly or in combination, have unknown effects. Under the DSHEA, the U.S. Food and Drug Administration (FDA) does not mandate any efficacy and safety assessments of HS products. This is unlike novel medicines and over-the-counter drugs (USFDA, 2016).

HS products are generally regarded as safe by the USFDA unless proven otherwise through its Adverse Event Reporting System (AERS). Since 2006, all manufacturers, packers, distributors and retailers are responsible for reporting serious adverse events associated with their products, including HS products, to the FDA's MedWatch system (Kailin, 2008).

A study by Frankos et al. (2010) showed that many healthcare professionals fail to report adverse events related to the use of HS products to the appropriate authority, as many of them are unaware of the risks and benefits of HS products. Some researchers have investigated the knowledge, attitudes and practices of physicians in terms of complementary and alternative medicine, but there has been little focus on herbal supplements (Clement et al., 2005).

1.2 Statement of Problem

In the United Arab Emirates (UAE) and particularly in Dubai, dietary supplement products and herbal supplements are combined under a definition called health supplement products (HS). Currently, there are limited data and information on HS products and any related adverse events. In addition, unlike the situation in other developed and some developing countries, in Dubai there is no surveillance or reporting system for adverse events resulting from HS product use. It is probable that there are adverse events associated with the consumption of HS products in Dubai. There is a need, therefore, to investigate the current situation and explore the possibilities of establishing a reporting system.

In many countries, spontaneous reporting or vigilance systems are the main means of detecting safety issues associated with HS products. If suspected adverse events associated with HS products do not reach the system, either through direct patient reporting or through reporting from healthcare professionals, the detection of safety issues may be missed or delayed (Gavaza et al., 2011; Piening et al., 2012). This has important implications for public health protection. It is, therefore, important to identify the extent of the problem and the underlying causes to inform public health policy.

1.3 Research Questions

The following research questions were proposed to achieve the objectives of the research:

1. What are the prevalence and characteristics of HS product consumption in the general population of Dubai?

2. Are the consumers of HS products aware of and able to identify HS product related adverse events?

3. How extensive is consumer knowledge about HS products?

4. Do HS products present any potential risks to human health, and, if so, what is the level of this risk?

5. What are the knowledge, attitude and practice of healthcare professionals in Dubai towards HS product related adverse events and the reporting or notification of such events?

6. What is the level of reporting of suspected HS product related adverse events in Dubai?

1.4 Research Aim

Previous studies have found that consumers are generally unaware of the risks of HS products and associated adverse events. In addition, they are unaware of the appropriate reporting process to the specific authorities in the event of adverse events. Also, many healthcare professionals do not have adequate knowledge, attitude or practice in relation to adverse events related to HS product consumption (Qassim et al., 2014; Ting et al., 2010). In a study among community pharmacists working in the

cities of Ajman and Sharjah, United Arab Emirates, only 4.9% were found to have good knowledge of ADRs (Qassim et al., 2014). In a cross-sectional prospective study conducted among US military physicians, 60% of the physicians observed adverse events associated with HS and only 18% reported these events. Around 70% physicians did not know how or where to report the adverse events associated with HS (Cellini et al., 2013). The prevalence of HS product consumption ranges from 10% to 30% according to Kemper et al. (2006) and around 19% according to Hara et al. (2011). In the case of Dubai, however, there is no information about the prevalence of HS product consumption or any related risks. The main aim of this research, therefore, is to evaluate the public health importance of HS product consumption related adverse events in the Emirate of Dubai.

1.5 Research Objectives

The research objectives of this research are as follows:

a- To assess the knowledge of HS products, levels of consumption and occurrence of adverse events in the population of Dubai.

b- To assess the knowledge, attitude and practice (KAP) of healthcare professionals in Dubai regarding HS products and HS product related adverse events.

c- To assess the reporting level of HS product related adverse events among healthcare professionals in Dubai regarding HS products and HS product related adverse events.

d- To understand the views on the setting up of a surveillance system.

1.6 Research Significance

HS products are imported and distributed in many countries where pre-marketing safety and efficacy assessment is not usually a mandatory requirement (Kailin, 2008). Despite high levels of HS product consumption in many countries, there are low levels of reporting of related adverse events by consumers, manufacturers and healthcare professionals (Al-Ahmad et al., 2012). In a free trading country like the UAE, and especially in Dubai, the availability and consumption of HS products with established harmful effects is an issue of significant public health importance (CPSS, 2016).

Healthcare professionals have a key role in identifying HS product related risks and adverse events, but this role may be underdeveloped because of low levels of knowledge and lack of awareness (Walji et al., 2009). For the first time in the UAE, this research will provide an assessment of HS product awareness and practice among both consumers (the general population) and healthcare professionals alike. It will inform and help policymakers, where necessary, to develop programs for public and professional education, establish new policies and regulations on HS products and an adverse event reporting system (CPSS, 2016).

1.7 Organization of the Remainder of Dissertation

The remainder of this dissertation is structured as follows: chapter two reviews the literature in eleven sections; section one presents introductory statements of the chapter. Section two presents the diverse definitions of HS products. Section three provides a review of the literature on the use and demand of HS products in the world population and discusses the gap in knowledge in the UAE context. Section four

describes the global regulations for HS products including the current codex aimed at harmonising food and food supplement rules among all nations of the world. This section gives an overview of the HS product regulations in the following countries: USA, Canada, Australia, and UAE (Dubai). Section five considers the safety and efficacy of HS products including HS product interactions with other food and/or drugs, or other HS products. This section also discusses the various types of HS product related adverse events. Section six presents the literature on global adverse event monitoring systems for HS products including adverse event reporting systems and post-market surveillance. In addition, it discusses the adverse event monitoring system of HS products in some leading countries.

Section seven discusses patient disclosure of HS product use information to healthcare professionals. Section eight identifies the literature on healthcare professionals' knowledge, attitude and practice of HS product related adverse events. Section nine reviews the current literature on the challenges in adverse event data collection and analysis including the under-reporting of adverse events and the quality of data collection. Section ten discusses the benefits of having an adverse event reporting and monitoring system. The last section of this chapter discusses in summary all related HS concepts in relation to the current research.

Chapter three covers the methods used in this research, namely two cross-sectional studies using questionnaires in four sections. The first section presents introductory statements on the research methods. The second section presents details of the survey of HS product consumption in the population of Dubai including study design, study setting, study participants, sampling, sample size, survey instrument, the actual questionnaire including variables, data management including re-coding and

interpretation of the variables, statistical analysis, data limitation, and ethical approval and safeguarding participants. Section three presents similarly on the knowledge, attitude and practice of HS product related adverse events among healthcare professionals. The last section provides a summary of all related information regarding research methods.

Chapter four presents the results from the analysis of the two cross-sectional studies. Chapter five discusses these findings. It presents a summary for each of the study objectives that have emerged from the findings and review of the literature. This chapter also presents the strengths of the study and reviews the limitations of the research.

Chapter six presents a summary of the previous chapters and the conclusion of the findings. This chapter also presents the lessons and contribution of the study for academics and practitioners and makes recommendations for further research.

Chapter 2: Literature Review

2.1 Introduction

Dietary or health supplements (HS) are widely consumed by people across the world and their availability in the global market has been increasing in recent years. They are readily available without prescription and their regulation is not as stringent as medicines/drugs. Though many HS have a clean safety history, various reports/studies imply potential safety concerns regarding the quality and use of these products. Apart from regulating the manufacture and introduction of HS into the market, it is also important to monitor, collect and analyse the adverse events that may be caused by HS to improve the safety of HS use.

These products are becoming an integral part of diet plans, mostly in developed countries. Increasing awareness of essential nutrients and their importance in maintaining a healthy lifestyle has led to a higher consumption of these supplements to offset a perceived lack of essential nutrients from normal diets. Over the years, increasing numbers of products have entered the markets under the label of HS. Today, HS is an umbrella term used to denote a vast variety of supplements that may include vitamins, minerals, herbs or other plants, amino acids, enzymes, and fibres among other products. They are available in various dosage forms and are meant to be exclusively taken by oral route.

Unlike drugs, for which safety profile is well documented and closely monitored with established mechanisms, HS are thought to be harmless and safe for consumption without undergoing vigorous clinical testing. Even though established regulatory and monitoring policies are in place in many countries, adverse events caused by the

consumption of HS may not be adequately reported. This results in a potential health hazard which may go undetected. Lack of awareness about the potential harmful effects of HS among both consumers and healthcare professionals emphasizes the need for more effective regulatory and monitoring systems.

The prevailing policies in regulating the consumption of HS in various countries together with the mechanisms established to identify the potential health risks caused by HS are discussed here. The limitations of current policies and monitoring systems and the specific areas which could make health supplement surveillance more inclusive are also discussed. Dubai, United Arab Emirates (UAE), has an HS market that is expanding year by year. As a result, there is a need to have proper monitoring and reporting systems. In this thesis, extensive research has been carried out to review the regulation and monitoring of HS, the reporting of adverse events in various countries, the various factors preventing the effectiveness of these systems and the need to improve existing systems with specific focus on Dubai.

In this chapter, a detailed review of available literature on the following essential topics was carried out including HS definitions, use of HS in the world population, global regulations of HS, efficacy, safety and adverse events of HS, global adverse event monitoring systems for HS, disclosure of HS use to healthcare professionals, healthcare professionals' knowledge, attitude and practice on HS related adverse events, challenges in adverse event data collection process and analysis, and the benefits of having an adverse drug reaction reporting and monitoring system.

The research questions played a vital role in the selection of the topics for the literature review.

After finalising the topics, the literature review was written from access to the library of the UAE University and Hamadan Bin Mohammed Smart University. Some of the literature was accessed from the Pubmed on-line library. The literature search was conducted using a set of key words and phrases suitable for the framework, like health supplements, dietary supplements, risks of health supplement, use of health supplement, adverse events of health supplements, global regulation of health supplements, food supplements, etc. The literature and related topics were reviewed. Around 87 publications were shortlisted from a total number of 216 as references for the literature review chapter. This filtration process excluded articles after abstract review, after full article review and after data abstraction due to weak evidence.

2.2 Health Supplement - Definitions

The definition of HS differs from country to country and the products considered as HS also differ. The World Health Organization (WHO) and the United States Dietary Supplements Health and Education Act (DSHEA) of 1994 both define dietary supplements as products (other than tobacco) that are meant to supplement the diet. Both include vitamins, minerals, herbs, botanical products, amino acids, and dietary substances in their definitions (Phua et al., 2009).

The Consumer Products Safety Section (CPSS) of Dubai Municipality defined HS as products (other than tobacco) complementary to the diet that include one or more of any dietary ingredient like vitamin, mineral, herb or other botanical, and/or amino acid ingredients. Additionally, dietary substance is defined as any preparation that is planned for use by any individual to enhance the diet’s nutritional value by amplifying the overall dietary intake and in a concentrated dosage form, a metabolite

preparation, element, extract, or a blend of any of the ingredients mentioned earlier (CPSS, 2015).

Under Canadian federal regulations, natural health products (NHPs) are technically a sub-category of drugs. Any substance naturally found in plants, animals, fungi, algae or microorganisms (regardless of the source used for the supplement) that is used to diagnose, treat or prevent disease and is suitable for self-care use is categorized as an NHP in Canada. This category includes vitamins (regardless of source), minerals, traditional Chinese medicines, Ayurvedic medicines, Native North American medicines, traditional herbal remedies and homeopathic medicines. Biologics such as insulin, tobacco and marijuana are specifically excluded from the NHP definition (Walji et al., 2010).

2.3 Use of Health Supplement in the World Population

The use of HS is increasing worldwide. People around the world consider supplements to be safer and more effective than conventional medicines. Ready availability of HS without prescription and extensive advertisements make them the people's medicine of choice for many ailments. Supplements are preferred over conventional medicines for the treatment of digestive conditions, common respiratory ailments and for weight management (NBJ's Supplement Business Report, 2012). In the United States (US) the use of HS is increasing year by year. Statistics show that 65% of the population in 2009, 66% in 2010 and 69% in 2011 were using HS (Gahche et al., 2011; Council for Responsible Nutrition, 2003).

The demand for HS is also increasing globally. The global HS market was worth $243 billion in 2014 (Jose, 2015). The number of visits to providers of complementary

and alternative medicine (CAM) exceeds those to primary care physicians, for annual out-of-pocket costs of $30 billion. Herbal products constitute the major proportion of these treatments (Tachjian et al., 2010). In the US, sales of HS reached $28.1 billion in 2010, a 4.4% growth over 2009 sales. Top supplement categories included: multivitamins ($4.9 billion), sports nutrition powders and formulae ($2.8 billion), B vitamins ($1.3 billion), calcium ($1.3 billion), and fish/animal oil ($1.1 billion) (NBJ's Supplement Business Report, 2012).

According to recent studies, the use of HS and herbal preparations has also increased in the Middle East (Mamtani et al., 2015). In Dubai, the demand for and sale of HS are increasing year by year. The increasing number of HS premises in Dubai indicates the growing HS market: 690 premises in 2014, 740 premises in 2015, and 800 premises in 2016 (CPSS, 2016). In addition, the increasing number of on-line applications for importing HS to Dubai, as shown in Table 2.1, supports evidence of the growth in the market. The HS consignment statistics in Dubai for the years 2012 to 2015 indicate that the number of consignments containing HS imported to Dubai through Dubai ports increased by 86% from 2012 to 2015 (see Table 2.1 for more details). This probably relates to increased consumption of HS in Dubai as the percentage of non-complied HS in Dubai increased from 55% in 2013 to 63% in 2015. This indicates that a growing number of various, new and non-registered types of HS are being imported and marketed in Dubai (CPSS, 2016).

Table 2.1: Health supplement consignments (number, weight) Dubai 2012–2015

Year	Quantity	Gross Weight (Kg)
2012	2019	2,940,877.89
2013	2448	3,790,542.40
2014	3224	4,702,010.22
2015	3752	4,790,351.00

Table compiled by the author from data from Consumer Products Safety Section Annual Reports 2012-2015.

2.4 Global Regulations of Health Supplements

Despite the belief that HS are safe, these products are pharmacologically active and therefore have inherent risk. Most countries are aware of the need for regulation of HS and have regulatory systems for HS. HS are regulated by different authorities around the world. The policies and procedures of established authorities internationally and in various countries in terms of HS regulation are discussed in the following sections.

2.4.1 Codex: harmonising food and food supplement rules

In 1962, the Codex Alimentarius (food code) Commission (Codex) was created to harmonise health food standards internationally by two United Nation (UN) Organizations, the Food and Agriculture Organization (FAO) and the World Health Organization (WHO). Codex comprises more than 150 member countries and international organizations that meet to exchange information and ideas related to food safety and trade issues. The members of Codex are also members of WHO and FAO. Codex Alimentarius is a collection of standards, codes of practice, guidelines, and other recommendations. It has become the global reference point for consumers, food producers and processors, national food control agencies, and the international food trade. Currently, Codex Alimentarius lists more than 200 standards, encompassing

issues like labelling, additives, methods of analysis and sampling, food import and export inspection and certification, pesticides in foods, and contaminants. The code also deals with nutrition and foods for special dietary uses, which includes dietary supplements. The Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU), hosted by Germany, meets every year to study the nutritional problems referred by the Codex Alimentarius Commission. The committee also considers draft provisions on nutritional aspects for all foods and develops guidelines, general principles, and standards for foods for special dietary uses (Das & Sen, 2014).

The CCNFSDU began discussions on the guidelines for vitamin and mineral food supplements in the 1990s and these were adopted in 2005. The guidelines were limited only to food supplements that contain vitamins and/or minerals, where these products are regulated as foods. Although guidelines address the composition of vitamin and mineral supplements, including sources, safety, purity, and bioavailability, they only provide criteria for establishing maximum amounts of vitamins and minerals per daily portion of supplement consumed rather than setting upper limits for vitamins and minerals in supplements. The packaging and labelling requirements of vitamin and mineral supplements are also addressed in the guidelines (Das & Sen, 2014).

These guidelines unfortunately do not address the broad category of dietary supplements, which includes herbals, amino acids, metabolites, concentrates, and many other non-essential nutrients. The codex in its current form has limited global implementation and individual countries have established more effective regulations on a wider range of food supplements (Das & Sen, 2014).

2.4.2 United States food and drug administration regulations

In the US, products falling under the definition of HS include vitamins, minerals, and herbs addressed as dietary supplements and regulated by the Food and Drug Administration (FDA) within the context of the US Federal Food, Drug, and Cosmetic Act (FFD&C Act). Dietary supplements are considered food, and there are no regulatory categories or regulatory definitions to accommodate them separately from other food ingredients. In respect of dietary supplements, the FDA mainly regulates the labelling (including the label on the product container and accompanying material) of the product. The FFD&C Act was amended by US congress many times in the 1990s. These amendments include the1990 Nutrition Labelling and Education Act (NLEA), the 1994 Dietary Supplement Health and Education Act (DSHEA), and the 1997 Food and Drug Administration Modernisation Act (FDAMA).

The 1994 Dietary Supplement Health and Education Act (DSHEA) regulates various types of health claims and structural/functional claims that may be made about dietary supplements.

Health claims in dietary supplements should characterise a relationship between a food, a food component, or dietary ingredient and the risk of a disease (e.g. adequate calcium throughout life may reduce the risk of osteoporosis). The FDA authorises these types of health claims based on an extensive review of scientific literature. Only NLEA authorised health claims or health claims based on authoritative statements may be used in the labelling of dietary supplements.

Structural/functional claims describe the role of a nutrient or dietary ingredient intended to affect the normal structure or function of the human body, (e.g. calcium builds strong bones). In addition, they may characterise how a nutrient or dietary

ingredient acts to maintain such structure or function, (e.g. fibre maintains bowel regularity, or antioxidants maintain cell integrity). Such claims do not need approval from the FDA, but the manufacturer must have substantiated that the claim is truthful and not misleading and must submit a notification with the text of the claim to the FDA no later than 30 days after marketing the dietary supplement with the claim. If a dietary supplement label includes such a claim, it must state in a disclaimer that the FDA has not evaluated the claim. The disclaimer must also state that the dietary supplement product is not intended to diagnose, treat, cure or prevent any disease. Only a drug can legally make such a claim (Hoadley & Rowlands, 2014).

The FDA established current good manufacturing practice (cGMPs) requirements for dietary supplements in 2003 which specify detailed conditions for the preparation, packing, and storing of dietary supplements, and required that dietary supplements be unadulterated and accurately labelled to meet full safety and sanitation standards. Furthermore, the Dietary Supplement and Non-prescription Drug Consumer Protection Act (Public Law 109-462, effective December 2007) was issued and requires that serious adverse events related to dietary supplements and non-prescription drugs be reported (Fu & Xia, 2014).

2.4.3 Canada regulations

In Canada, dietary supplements are referred to as Natural Health Products (NHPs) and comprise a group of health products that include vitamin and mineral supplements, herbal and other plant-based health products, traditional Chinese and Homeopathic medicines, probiotics and enzymes, and certain personal care products like toothpastes that contain natural ingredients (Health Canada, 2012a). The Natural Health Products Regulations (NHPR) under the Canadian Food and Drugs Act

regulates NHPs. NHPR is implemented by the Natural and Non-prescription Health Products Directorate (NNHPD) (Health Canada, 2012b). NNHPD requires all NHPs sold in Canada to have product licenses and the Canadian sites that manufacture, package, label and import NHPs must have site licenses.

Producers of NNHPs are required to register the product with the NNHPD before launching the product in the market. The NNHPD may issue a license after evaluating the submitted documents including a consideration of the safety of the product. NNHPD follows a three-class system for licensing the product where the review time for the products are dependent on how much is already known about the benefits and risks of the products. This system enables quick reviewing and licensing of products about which there is most knowledge and certainty regarding safety, while complex applications require more detailed evaluation efforts.

Class 1: This class has the highest level of certainty about the product (how much is known about the product) and the lowest potential risk. Seventy five percent of NHPs are in this category. These products are supported by pre-cleared information (PCI) based on previous NHPD decisions and can receive a license within 10 days of submission of the application.

Class 2: This class covers moderate certainty of product and moderate risk. Around 20% to 24% of NHPs are in this class, typically those with at least one claim or ingredient supported by a PCI. For example, a Class 2 product may be an existing authorised product with a new claim related to product use. Products falling into this category will undergo an expedited risk-based review with a target of 30 days.

Class 3: This class covers NHPs with the lowest certainty and highest risk and comprises about one to five percent of NHPs. In this class, there are no ingredients or

claims supported by PCI. For example, if a new product is claimed to prevent rheumatoid arthritis, clinical trial evidence with a full pre-market assessment is the level of review needed. The current review period for this class is 180 days, but companies could reduce this time by revising their claims for the NHP to meet the PCI (Harrison & Nestmann, 2014).

2.4.4 United Arab Emirates - Dubai regulations

HS in Dubai Emirate are controlled by Dubai Municipality through Local Circular No. (11/2003) for the year 2003 and the Health Supplement Circular dated 24 February 2010. The trading companies who are licensed inside the UAE and have business related to HS product trading can do HS business in Dubai, but need to register their product(s) with Dubai Municipality prior to importation or any other business related practice.

The Consumer Products Safety Section (CPSS) of the Health and Safety Department is the responsible regulatory authority at Dubai Municipality for HS products. The CPSS controls HS products in three different areas: HS products registration, HS product consignment release, and HS product monitoring in Dubai Emirate through field inspection.

2.4.4.1 Health supplement registration

Companies may register HS products with the CPSS using an on-line system prior to importation of the product into Dubai. Companies submit documentation for the products including artwork of the product, free-sale certificate, which is a certificate that is issued by a related authority in the country of origin of the product certifying that goods such as food items, cosmetics, biologics, or medical devices are

legally sold or distributed in the open market, freely without restriction, and approved by the regulatory authorities in the country of origin (Web Finance Inc., 2016). Additional documentation includes an ingredient report and an analysis report from the manufacturer, a related test report from an accredited laboratory and other supporting documents. The CPSS team then assesses the product documents and its application. If the product does not raise any concern then the CPSS team will register the product. If there are concerns then these must be rectified by the company before re-applying for registration. The validity of registration is 5 years. The company must renew the registration before the expiry date (CPSS, 2015).

2.4.4.2 Health supplement consignment release

The CPSS team at Dubai ports controls the entry of HS products into Dubai Emirate. Companies apply through an on-line system for the shipment release with shipment details and registration details. Inspectors from CPSS consignment release teams to inspect the shipment and the shipment is released if it meets the required standards which include the quality of the product, the storage condition during the shipment and the registration status of the product (CPSS, 2015).

2.4.4.3 Health supplement field inspection

The field inspection team of CPSS monitors the Dubai market through routine inspections of premises where HS are on sale. Field inspectors inspect the shops and ensure compliance with regulations including label modifications, use of unapproved claims and storage conditions. Random sampling and laboratory testing of the registered products further ensure the quality of the HS products in Dubai (CPSS, 2016).

2.5 Efficacy, Safety and Adverse Events of Health Supplements

2.5.1 Efficacy of health supplements

The efficacy of HS has been established through years of practice and is now one of the essential parts of day to day life. Some HS have proven their efficacy through clinical studies. For example, vitamin D and calcium supplements have been shown to be beneficial in the prevention and treatment of bone loss and osteoporosis (Lanham-New, 2008). Similarly, folic acid has been shown to be effective in preventing certain birth defects such as neural tube defects (Wolff et al., 2009). Glucosamine containing supplement use has a proven effect in improving locomotor function and reducing knee pain in osteoarthritis (Kanzaki et al., 2015). Vitamin B12 along with Omega 3 fatty acid were shown to be beneficial in Alzheimer's disease by slowing the rate of brain shrinkage in patients with Mild cognitive impairment (Oulhaj et al., 2016).

2.5.2 Safety of health supplements

As the definition implies, HS are mainly intended to supplement the diet with one or more dietary ingredients like vitamins, minerals, herbs or other botanical, and/or amino acid ingredients. The use of HS and herbs was thought to be safe in the past, but an excessive intake of any nutrient could result in adverse events. There exists a wide variability in the nature and concentration of the ingredient and the source and purity of raw material, especially in herbal supplements. This, along with variations in methods of preparation and a lack of related safety data for human consumption, highlights the potential safety risks involved in HS consumption. The factors affecting the safety and the risk of consuming the supplement may vary by product and category.

For vitamins and minerals, even if they have been established as safe over years of practice and clinical trials, over-dosage may lead to severe direct toxicity to the consumers.

The risk of consuming vitamins and minerals increases as the consumed dose increases. At low dosage, the risk of compromised health due to deficiency is high. At high dosage, the risk of compromised health due to toxicity is high. As the margins between the essential amounts and toxicity are narrow, a conventional method of risk assessment has been established in an Acceptable Daily Intake (ADI) for vitamins and minerals which is a recommended safe level. This level is established following a consideration of two risk assessment values, the NOAEL and the LOAEL. NOAEL is the non-observed adverse event level, which is the maximum dose in acceptable daily intake. LOAEL is the lowest observed adverse event level. If there are no adequate data demonstrating a NOAEL, then a LOAEL may be used. Where various adverse events (or endpoints) occur for a nutrient, the NOAELs (or LOAELs) for these endpoints will differ. The critical endpoint is the adverse event exhibiting the lowest NOAEL (i.e. the most sensitive indicator of a nutrient's adverse events) which ensures protection against all other possible adverse events (COT, 2003; EFSA, 2006).

NOAEL and LOAEL play a vital role to establish an acceptable daily intake of vitamins and minerals. NOAEL can be calculated by extrapolating LOAEL from the dose response curve (one of the most important concepts in pharmacology which describes the relationship between an effect of a drug and the amount of drug given). The factor of 3 is commonly used when extrapolating from a LOAEL to a NOAEL for data derived from studies in experimental animals. This is because the dose levels used

in such studies are commonly at 3-fold intervals. ADI can be calculated from the below formula.

$$\text{ADI} = \frac{\text{No Observed Adverse Effect Level}}{10\ (\text{inter species variation}) \times 10\ (\text{inter individual variation})}$$

For example, the LOAEL of Vitamin B6 (pyridoxine) is identified as 50 mg/kg bw/day based on studies. Uncertainty factor for LOAEL to NOAEL extrapolation was 3. The NOAEL calculated as 16.66 (LOAEL/3). The ADI calculated for Vitamin B6 (pyridoxine) is 16.7 mg/kg bw/day which is equivalent to 10 mg/day for a 60 kg adult. (COT, 2003).

The referral intake of vitamin C by an adult is in a range of 45-90 mg/d, an amount needed to prevent scurvy. The maximum level of safe intake (NOAEL) is 1 gram (g). The margin of ADI is larger and it is more than 10 times greater than the referral intake. A much larger quantity of vitamin C can cause gastrointestinal events such as osmotic diarrhoea, which occurs at intakes of several grams. In the case of vitamin A, the referral intake is 600-900 microgram (µg), and evidence exists of adverse events on bone health at an intake of 1500 µg. Safety and risk assessment values vary for different vitamins and minerals. A close monitoring of international safety standards and studies is essential in the safe control of vitamins and minerals (Mulholland & Benford, 2007).

The established safe range or ADI may not be applicable to all groups. The ADI may differ with life stage or increased or decreased susceptibility to adverse events. Nutritional requirements vary because of growth and existing conditions like altered renal function. A dose that is beneficial for some sub-groups in the population may

possess potential harmful effects for others. Folate supplementation reduces the incidence of neural tube defects in the foetus, but may mask the anaemia associated with vitamin B12 deficiency in older persons, allowing neuropathy, also associated with the deficiency, to progress undiagnosed.

In terms of herbal supplements, one of the safety issues is heavy metal contamination. Herbal supplements may be contaminated by heavy metals such as lead (Pb), cadmium (Cd) and mercury (Hg). This heavy metal contamination increases the risk for the safe use of herbal supplements. The heavy metal contamination is influenced by several factors such as occupational contamination, bioaccumulation of heavy metals in herbs/plants from atmospheric depositions determined by climatic factors, heavy metal pollutions in soil, contaminated wastewater used for irrigation of soil on which the herbs are grown, and the degree of maturity of the plant at the time of harvest (Bentum et al., 2011; Khan et al., 2008). High doses of heavy metal consumption can cause several diseases. They may be carcinogenic or have adverse reproductive effects, and they may unfavourably impact on nutrition by displacing biologically useful metals such as calcium and zinc (Ejeatuluchukwu et al., 2011; Fasinu & Orisakwe, 2013).

Another safety concern relating to herbal supplements is pesticide residues. These may contaminate the herbal supplement due to excessive use of pesticides during the cultivation of the herb and from lack of good agriculture practices (GAP). Organochlorine pesticide residues have been found in several Chinese herbal plants cultivated in China and sold in Hong Kong (Leung et al., 2005). Even though safety is a concern, the use of HS in daily life is increasing and it demands more attention and control.

Other serious concerns in the consumption of HS are adulteration and contamination by various methods. The adulteration of herbal products with undeclared pharmaceuticals, substitution with exhausted drug and substitution with artificially manufactured substances along with contamination from different sources like pollens, dust, moulds and fungi can cause serious adverse events. A study in Hong Kong published in 2011 shows the severity of the under-recognised problem of adulteration of Chinese herbal anti-diabetic and diabetic products with undeclared pharmaceuticals, including both registered and banned drugs (Ching et al., 2011).

When evaluating the safety of the HS, it is important to consider their use by vulnerable groups. Some groups of the population may be particularly susceptible to adverse events from the ingredient of a HS. Vulnerable groups are defined as a sub-population who are more likely to have adverse events or individuals in whom the specific adverse events identified are more likely serious in comparison with the general population. Characteristics that contribute to this vulnerability may be physiological, disease related, or related to other aspects such as lifestyle or therapeutic interventions. Physiological characteristics include age, genetic predisposition and specific physiological conditions. Some age groups may be more susceptible to adverse events from some HS than others. The capacity of the human body to metabolise the ingredients of HS varies through the life span. HS ingredients that are normally excreted or altered by kidney or liver function may potentially pose greater risk to the elderly than to the younger population. This must be considered in the HS specifically intended for use by the elderly such as HS used for osteoarthritis. Children have a lower metabolic capacity than adults, which for certain supplements may make them more susceptible to adverse events. Physiological conditions like pregnancy also increase the chance of adverse events from HS ingredients. Special concern should be

given to the teratogenic effects of HS ingredients intended for use in pregnancy (Phua et al., 2009). A well-known example is the teratogenic effect of high doses of vitamin A if used in the pre-conception period (Rothman et al., 1996).

In addition to the life stages, disease conditions also alter susceptibility to adverse events. Disease, or pre-existing conditions including hypertension, cardiovascular disease, hepatitis, renal disease and diabetes all require special attention if present in a person contemplating HS use. Hepatitis or renal dysfunction may delay the metabolism and excretion of the ingredient leading to toxic levels which may lead to severe adverse events. In diabetic patients, HS may affect insulin and glucose which could lead to severe metabolic adverse events. All these factors should be taken in to account to ensure the safe use HS (Phua et al., 2009).

One of the major concerns about the safety of HS is the potential for interaction between a supplement and other ingested substances like drugs, other dietary supplements or food. This may result in adverse clinical outcomes due to an increase or decrease in the level of drugs, dietary supplements or food in the body. Some examples of these interactions are discussed below.

Calcium carbonate taken as HS may interact with the antibiotic, tetracycline. This is a direct chemical-to-chemical interaction. The calcium carbonate may bind with the tetracycline and form an insoluble product. This will reduce or even eliminate the effect of tetracycline (NAS, 2005).

The use of herbal products forms the bulk of treatments (particularly by elderly persons who also consume multiple prescription medications for comorbid conditions) which increase the risk of adverse herb-drug-disease interactions (Tachjian et al., 2010). The concomitant use of yohimbine bark with guanabenz acetate, a drug used

for hypertension, may diminish the antihypertensive activity of guanabenz through its opposing pharmacodynamic effect (Grossman et al., 1993). Ginkgo biloba leaf, used as an HS for mental alertness, may have an antagonistic effect on platelet activating factor. If it is ingested with an anti-coagulant like warfarin, it will have an additive action and may lead to bleeding (Spencer, 2004). St. John's Wort, used as an HS for depression, has some proven drug interactions. It may interact with cyclosporine, an immune suppressant drug and thereby reduce the effect of cyclosporine. The level of cyclosporine in the blood is controlled by the MDR1-encoded transporter and the enzyme CYP3A4CYP both of which are affected by St. John's Wort. This will reduce the level of the cyclosporine in the blood and may lead to transplanted organ rejection (Ruschitzka et al., 2000; Borrelli & Izzo, 2009). St. John's Wort may also interact with oral contraceptives. Circulating oestrogen levels following oral contraceptive intake are also regulated in part by the activity of MDR1-encoded transporters so that St. John's Wort may lead to reduced levels of oestrogen in the blood level and a reduced contraceptive effect (Borrelli & Izzo, 2009).

Herbal supplements like cranberry, which is used in blood and digestive disorders, in co-administration with warfarin may affect CYP2C9 and CYP3A4. This may lead to an additive action and bleeding may occur (Ge et al., 2014; Mohammed Abdul et al., 2008). The concomitant use of Echinacea, an HS used as an immune stimulant to prevent infections like the common cold and flu, with etoposide, a cytotoxic drug used in the treatment of lung cancer, may produce an interaction and lead to an increased platelet count. The use of Echinacea is not desirable in patients taking etoposide or any other chemotherapeutic drug (Bossaer & Odle, 2012).

All the above mentioned potential HS interactions with drugs shows a clear need for the consumer to discuss any planned use of HS with their healthcare professionals to avoid possible adverse events.

2.5.3 Adverse events of health supplements

The World Health Organization (WHO) has defined an adverse reaction as a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function (WHO, 2002).

All HS carry risks and benefits. Many of these risks are identified in pre-market testing and can be managed as expected or with tolerable side effects that are outweighed by the product's benefits. Adverse events may occur even when a product is being used as directed. An event may occur within minutes after exposure or it can take years to develop. Adverse events can range from minor irritations, like a skin rash, to serious and life threatening events, such as a heart attack or liver damage. Most often, adverse events are unexpected and are not necessarily indicated on the product label or on any other information provided with the product (Health Canada, 2011a).

Adverse events associated with vitamins and minerals are usually due to over consumption compared to the acceptable daily intake (ADI). In this respect, an important consideration is the dietary pattern of the individual taking the vitamin and mineral supplementation as diet also contributes towards daily intake. As stated above, the safe upper level of vitamin C is 1g per day and this can be provided by a single tablet, 1.69 kilograms (kg) of kiwi fruit or 2.5 litre (L) orange juice. For a person taking

these levels of vitamin C in their diet, even a vitamin C supplement with a dose less than 1g may cause adverse events (EFSA, 2006).

The WHO's Uppsala Monitoring Centre, which pools reports from over 100 countries worldwide, has a database of over four million reports, of which 21,000 involve adverse events caused by herbal and natural products. The complexity of herbal products starts with the method of cultivation and collection of the herbs. Major causes of adverse events are the adulteration of herbal products with undeclared chemicals including potent pharmaceutical substances such as corticosteroids and non-steroidal anti-inflammatory agents. Major causes and sources of adverse events associated with herbal products include mistaken or deliberate use of the wrong species of medicinal plants, incorrect dosing, deliberate over-dosing for a more rapid effect, heavy metal contamination (during cultivation or manufacturing),the presence of agrochemical and pesticide residues, the presence of pathogenic microorganisms, errors in the use of herbal supplements both by healthcare providers and consumers, and interactions with other medicines (WHO, 2004; Phua et al., 2009).

In 2009, a division of the US Food and Drug Administration (FDA), the Internet and Health Fraud Team, conducted an internet survey of HS products intended for sexual enhancement. They found that one third of such supplements that are marketed as dietary supplements to promote sexual performance and treat erectile dysfunction, despite having no disclosure of any medicinal content on the label, nevertheless contained the medicinal ingredient sildenafil, the active ingredient in Viagra (USFDA, 2009).

In Germany, the Deutsches Aerzteblatt International, which is responsible for the approval of HS products, carried out research in March 2009 which found that

certain Chinese slimming products, such as slimming tea and slimming herbal capsules, had been associated with 17 incidents in which the consumer became ill with symptoms and signs that included vomiting, arterial hypertension, headache, malaise, nausea, chest pressure, dyspnea, tachycardia, insomnia and high fever. The herbal products subsequently underwent chemical analysis in which sibutramine, a medicinal slimming ingredient, was found. Every capsule of the herbal product contained twice the recommended daily dose of sibutramine. Sibutramine is now a banned ingredient even in medicinal products due to its potential to cause serious side effects (Müller et al., 2009).

In 2001, the FDA issued warnings and an import alert that herbal products are unsafe if they contain or are suspected to contain aristolochic acid (USFDA, 2001). A cohort study of 105 patientsat a Belgian clinic found that rapidly progressive nephropathy developed after they had been administered an herbal weight-loss product containing aristolochic acid (Nortier et al., 2000). Because of a suspected association between aristolochic acid and urothelial carcinoma, 39 patients with end-stage renal disease underwent prophylactic removal of the kidneys and ureters. Urothelial carcinoma was diagnosed in 18 of them. Aristolochic acid nephropathy has been reported in eight other countries, and associated urinary tract cancer has been reported in two (Arlt et al., 2002). The International Agency for Research on Cancer classifies products containing the aristolochia species as human carcinogens (Heinrich, 2003). The toxicological evidence of the risks associated with aristolochic acid is strong. In 1982, tumours were rapidly induced in rats at low doses (Wang et al., 2011). Aristolochic acid is among the most potent two percent of the carcinogens in the Carcinogenic Potency Database (Gold et al., 2005). It is mutagenic, forms DNA adducts in humans, and is carcinogenic in mice. In rabbits, aristolochic acid induces

nephrotoxic effects, the same DNA adducts in kidney as in humans, and urothelial tumours (Arlt et al., 2002).

Patients are increasingly using herbal products for purportedly preventative and therapeutic purposes. Some products have direct effects on the cardiovascular or homeostatic system, whereas others have indirect effects through interactions with medications that could lead to serious consequences. Common herbal remedies that produce adverse events on the cardiovascular system include St. John's Wort, motherwort, ginseng, gingko biloba, garlic, grapefruit juice, hawthorn, saw palmetto, danshen, echinacea, tetrandrine, aconite, yohimbine, gynura, liquorice, and black cohosh (Tachjian et al., 2010).

In a study conducted in 2012 which evaluated the use of supplements containing ephedra, which has been temporally associated with sudden death, 48 cases of those with known supplement use were compared to 144 age, gender, and socioeconomic-matched controls in a 1:3 case control design. Of the 48 sudden deaths temporally associated with supplement use, the underlying cause of death was fatal atherosclerotic coronary disease in 18 (37.5%), sudden unexplained death in 16 (33.3%), and hypertrophic cardiomyopathy in 6 (12.5%). In subjects ≥35 years of age, and known to be taking supplements, there was a significant increase in mortality due to sudden unexplained death (relative risk = 5.1 [95% confidence interval, 1.4–18.7]). This study concluded that atherosclerotic coronary disease and idiopathic sudden death are common etiologies of death when taking supplements (Appel et al., 2012).

HS products are gaining popularity throughout the world and the expanding HS market in Dubai mirrors this consumption. As previously discussed, the consumption of any pharmacologically active substance may have potentially harmful effects. There

are also the additional dangers of adulteration, contamination, drug-HS or HS-HS interactions to consider as these raise significant health issues. As the consumption of HS products may have potentially deleterious effects on human health, there arises a need for this issue to be duly addressed.

2.6 Global Adverse Event Monitoring Systems for Health Supplements

The following sections present details of various worldwide monitoring systems in use regarding HS product related adverse events.

2.6.1 Adverse event reporting systems and post market surveillance

Some countries have established adverse event monitoring systems for HS. Regardless of the pre-market requirements like notification, registration and pre-market approval, the most effective safety assessment measure is post-market surveillance. Monitoring product performance in the market place through collection and investigations of consumer inquiries, complaints, and adverse reactions is the most effective means of assuring quality and safety.

Adverse event reporting is a system that requires the reporting of adverse events associated with a product to the appropriate authority. This is a regulatory requirement in some countries. Post-market surveillance goes beyond this requirement to ensure the overall quality and consistency of products in addition to managing company liability by monitoring the performance and safety experience for a given product in the market place. Post-market surveillance is a broader field, incorporating the collection and analysis of consumer inquiries and complaints, in addition to adverse events, and using this information to resolve issues and ensure continuous improvement. Some leading companies which carry out post-market surveillance for

their products may be in a better position to provide quality and safety assessments than the regulators (Shao, 2014; Frankos et al., 2010).

Many countries have an established pharmacovigilance system for the identification of the hazards associated with drugs. Spontaneous reporting systems for suspected adverse drug reactions (ADRs) continue to be an essential part of pharmacovigilance. Any information on a new or known adverse event that might be potentially caused by a medicine and that necessitates further investigation is considered as signal. Signals are generated from several sources such as spontaneous reports, clinical studies, and the scientific literature. Signal detection is the process that aims to find, as soon as possible, any indication of an unexpected drug safety problem which may be either new ADRs or a change of the frequency of ADRs that are already known to be associated with the drugs involved. The results of this surveillance exercise tend to arouse suspicions and should always be followed up by thorough investigations.

Causality or relatedness assessment evaluates whether the detected adverse event is probably caused by the specific product. Causality assessment tools can be broadly classified as expert judgment/global introspection, algorithms and probabilistic methods (Bayesian approaches) and comprises, among others, the evaluation of temporal relationships, dechallenge/rechallenge information, association with or lack of association with underlying disease, presence or absence of a more likely cause, and biologic plausibility (DSRU, 2017; EMA, 2014; Agbabiaka et al., 2008). In adverse event reporting systems, the agencies receive reports of adverse events from customers, healthcare professionals or companies. Respective regulatory agencies utilise the information for signal detection, not causality analysis. Regulators

do not individually rate or score individual reported adverse events. Rather, they consider all incidents in totality, in context, to identify signals. Agricultural or manufacturing errors, product contamination, and tampering are examples of issues that can be identified through the collection of adverse events (Shao, 2014).

A robust post-market surveillance system involves comprehensive investigation of quality and adverse reaction incidents. This includes collection, documentation, and categorising of incidents followed by causality analysis and corrective action or risk mitigation efforts, where applicable. This process falls outside the scope of most mandatory adverse event reporting requirements. For the handling and mitigating of consumer complaints related to product quality, some regulatory agencies have incorporated requirements into Good Manufacturing Practice (GMP) regulations. For example, in the United States, the FDA has promulgated requirements for complaint handling in the current GMP regulation published in 2007 (USFDA, 2016).

2.6.2 Adverse event monitoring systems in leading countries

Adverse event monitoring systems for HS vary greatly around the world. In some countries, reporting is practiced voluntarily by some companies and provided by healthcare professionals. Some countries have established specific requirements for adverse event reporting. Adverse event monitoring systems in selected countries are described in the following section.

2.6.2.1 USA monitoring system

In December 2006, the US Congress passed the Dietary Supplement and Non-prescription Drug Consumer Protection Act, requiring manufacturers of dietary supplements and OTC drugs to report to the FDA all serious adverse events they

receive within 15 business days and to maintain records of all adverse events they receive for up to six years. The law defines a serious adverse event as death, a life-threatening experience, an inpatient hospitalisation, a persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an event that requires appropriate medical judgment that may jeopardise the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. In addition, this law mandates that the name and address of a party (e.g., a manufacturer, packer, distributor, or retailer) responsible for collecting information about adverse events should appear on the label of a non-prescription drug (also known as an OTC drug) or a dietary supplement (USFDA, 2016).

An adverse event reporting system has been established called MedWatch. By law, companies must report serious adverse events to the FDA within 15 days through the MedWatch system using form FDA 3500A. The label of the product should be attached with the form. Moreover, if the party learns of any new medical information related to a serious adverse event report submitted in the previous 12 months, it must be passed on to the FDA within 15 business days of receiving that information.

Consumers and healthcare professionals can also report adverse events associated with HS voluntarily through the MedWatch system using the same form. The receipt by the FDA of reports of minor adverse events in this way from consumers may lead to signal generation. In addition, clinicians who may find some interaction of HS with drugs during patient treatment should also report these interactions through Medwatch form 3500A. Reports are assigned with a unique identification number and forwarded to a Centre for Food Safety and Applied Nutrition (CFSAN) reviewer who evaluates the report and characterises the relationship of the dietary supplement to the

reported adverse event. Sometimes even reports of minor adverse events can be a signal that a serious adverse event could arise from using a dietary supplement. The reviewer may contact the person who filed the adverse events to obtain more information and may do a scientific background review of the adverse events, whether it is associated with the HS or not. If the signals of adverse events indicate a relation with the intake of the HS, the FDA will act, including product withdrawal from the market (Frankos et al., 2010).

2.6.2.2 Canada monitoring system

Health Canada requires NHP licensees to report all serious worldwide adverse events (AE) arising from the product within 15 working days (Shao, 2014).

Health Canada assesses NHP for safety, effectiveness and quality before they can be licensed for sale in Canada. Health Canada monitors the safety profile of all health products sold in Canada to ensure that the benefits of using them continue to outweigh the risks that may be associated with their use (Health Canada, 2011b).

NHPD controls NHPs after product approval through post-market activities including the Adverse Reaction (AR) reporting system. Along with other medical device problem reporting reports, the MedEffect Canada website supports the reporting of AR associated with NHPs. Canada has an established post-market surveillance system run jointly by NHPD and the Marketed Health Products Directorate (MHPD) (Harrison & Nestmann, 2014).

Consumers and healthcare professionals may report adverse events of NHP products to the Canadian Vigilance System through MedEffect Canada by telephone, on-line or by mail using a consumer side effect reporting form. HC evaluates the

signals associated with the adverse events and the safety profile of the product and, if needed, may recall the product from the market. The MedEffect Canada system allows consumers, patients and healthcare professionals to report an adverse event or side effect thereby generating new safety information of NHP products. Consumers and healthcare professionals may search for advisories, warnings and recalls in the Recalls and Safety Alerts Database of MedEffect Canada (Health Canada, 2011a).

2.6.2.3 Australia monitoring system

In Australia, HS are categorized as Complementary Medicines (CM) and controlled by the Therapeutic Goods Administration (TGA). Australia has a pharmacovigilance system, Therapeutic Product Vigilance, that requires the reporting of adverse events of CMs in the absence of specific requirements for CMs. TGA mandates by law that the sponsor or manufacturer of the product should report AEs within 15 working days. If it is a critical, significant safety issue, the sponsor should report within 72 hours from the time of awareness of the issue by any personnel of the sponsor. Consumers and healthcare professionals may also report adverse events of CM through an on-line form on the TGA website. Each adverse events report received by the TGA is entered into a database and continually evaluated by TGA staff to identify potential emerging problems for detailed investigation. TGA staff carry out detailed investigation and if they identify a safety concern associated with the product, TGA may take regulatory action including recalling or suspending of the product from the market (TGA, 2016).

2.7 Disclosure of Health Supplement Use to Healthcare Professionals

Patients' disclosure of HS consumption to healthcare professionals is one of the factors contributing to the safe use of HS. Drug/HS interaction may lead to major adverse events and demands the attention of healthcare professionals to avoid this. The disclosure rate of complementary and alternative medicine (CAM), which also includes HS, varies from 23-70% and one of the reasons for this is that practitioners did not need to know about their patients' CAM use, and the fact that the practitioners did not ask (Robinson & McGrail, 2004). One study shows that 69% patients did not inform the physician about their dietary supplement use excluding vitamins (Gardiner et al., 2006). Without specific prompting or questioning, consumers of natural products may not disclose their use of such product to primary healthcare professionals. It is helpful if the healthcare professional adopts a pro-active approach and routinely includes questions about health supplement use, but this does not usually happen (Busse et al., 2005). There is concern about a negative response from healthcare professionals: they do not ask, and the perception is that because healthcare professionals work within a biomedical framework, they have less knowledge of CAM (Robinson & McGrail, 2004). Nutritional supplements are often considered safe and natural, and consumers are not aware of the possibility of HS/drug interactions (Bebeci et al., 2015). The regulatory authorities should pay more attention to educating consumers about the complications of the concomitant use of HS and drugs and the need for disclosure of HS use to healthcare professionals. This could be done through public information campaigns and continuing professional education for healthcare professionals to ensure that both consumer and professional are aware of HS, especially herbal supplements (Samojlik et al., 2013).

2.8 Healthcare Professionals' Knowledge, Attitude and Practice on Health Supplement Related Adverse Event

Herbs and other dietary supplements are among the most commonly used complementary medical therapies. Clinicians, however, generally have limited knowledge and confidence to communicate regarding herbs and dietary supplements. Educational interventions and institutional policies are needed for healthcare professionals in relation to herbs and dietary supplements to improve the quality of patient care (Kemper et al., 2006).

The unprecedented global increase in the use of herbal remedies is set to continue apace well into the foreseeable future. This raises important public health concerns, especially as it relates to safety issues including adverse events and herb/drug interactions. Most Western-trained physicians have very limited knowledge of the risks and benefits of this healthcare modality. Therefore, evaluation of healthcare professional knowledge would identify appropriate intervention strategies to improve physician-patient communication in this area (Clement et al., 2005).

A survey conducted in Maharashtra, India, found that a lack of knowledge prevented healthcare professionals from advising their patients on herbs and herbal preparation in a positive way. The authors recommended that the medical curriculum should include training in the use of scientific and evidence-based research on herbal medicines. Physicians must become more educated about the safe and effective use of herbs. Asking patients about supplement use during an initial medical history should be made a central component of patient care and medication use monitoring (Ghia & Jha, 2013).

In a cross-sectional prospective study of US military physicians, 60% of the physicians observed adverse events associated with HS, but only 18% reported these events. Approximately 70% of physicians did not know how or where to report adverse events associated with health supplements. A gap in information of HS and adverse events reporting is identified in the study. A centralised adverse event reporting system could serve to identify potentially harmful HS for further evaluation. Health professionals need to remain vigilant for adverse events associated with HS use and should be better informed on how to report them (Cellini et al., 2013).

A study carried out among doctors working in a teaching hospital in Lagos, Nigeria underlined the fact that there are gaps between knowledge and ADR reporting. For the long-term improvement of ADR reporting, it is very important that these gaps be filled by improved training in pharmacovigilance and risk perceptions of drugs. Healthcare professionals should be made aware that ADR reporting is considered an integral part of the clinical activities of doctors (Oshikoya & Awobusuyi, 2009).

Another descriptive cross-sectional study conducted among oncology practitioners, including medical and allied medical personnel, in Doha, Qatar drew attention to the need to integrate an educational and training program regarding CAM practices and usage to enhance cancer patient management and ensure a more holistic and efficient cancer treatment for patients (Hassan, 2015).

A survey of attitudes and knowledge of HS among US and Canadian pharmacists recommended that pharmacists need to have additional training in HS, that there should be increased regulation of HS, and that there should be an improvement in the quality of information on HS. In addition, the survey data indicated that pharmacists

do not perceive their knowledge of HS to be adequate and that they do not routinely document, monitor, or inquire about patient use of HS (Kwan et al., 2006).

A study in Gujarat, India, found that community pharmacists' knowledge of the terminology of ADR and awareness of the national pharmacovigilance centre was 65% and 63%, respectively. In addition, 60% of community pharmacists assumed that all herbal products were free from ADRs (Rathod & Panchal, 2014).

In a study among community pharmacists working in the emirates of Ajman and Sharjah, United Arab Emirates, only 4.9% were found to have good knowledge of ADRs. Moreover, the study concluded that knowledge of ADRs and their reporting were also found to be inadequate. Community pharmacists, however, showed a positive attitude towards ADR reporting and felt that they had an important role to play in ADR reporting. Notwithstanding, community pharmacists were unenthusiastic about reporting ADRs that might be caused by over-the-counter drugs (OTC) (Qassim et al., 2014). In a study of the knowledge, attitude and the practice of pharmacovigilance among healthcare professionals in a teaching hospital in north India, fewer than 40% of healthcare professionals knew how to report ADRs (Bajaj & Kumar, 2013).

A cross-sectional survey of community pharmacists in Riyadh, Saudi Arabia discussed the most common hurdles that prevent community pharmacists from discussing the use of HS. These included a lack of time due to other obligations assigned to the community pharmacist (46%), a lack of reliable resources (30.3%), a lack of scientific evidence that supports herbal medicine use (15.2%), and a lack of knowledge of herbal medicines (13.4%). The study also pointed out that further steps must be taken to increase awareness in pharmacists of adverse drug reaction reporting

systems and to improve the curricula and continuous education programs to address herbal products and related issues (Al-Arifi, 2013).

A further survey among pharmacists in Virginia and North Carolina in 1998 concluded that pharmacists with previous continuing education in herbal medications were more knowledgeable of these products (Chang et al., 2007).

In most developing countries, healthcare professionals and, especially, doctors are the principal contributors of adverse event reports (Heinrich, 2003). Usually, a high number of doctors have the correct understanding regarding adverse events and know what should be reported. Nurses, however, know better about where to report adverse events (Rehan et al., 2012). Under-reporting of adverse drug events by prescribers is a common problem. The underreporting of ADRs among health professionals is attributed to various factors including the knowledge and practice of health professionals regarding reporting (Kamtane & Jayawardhani, 2012).

The under-reporting of ADRs, caused by both prescription and OTC drugs, is widespread in both developed and developing countries. The lack of awareness of the available pharmacovigilance systems and insufficient knowledge of ADRs are major reasons. Studies show that increased knowledge correlates to higher ADR reporting (Qassim et al., 2014). Despite health care professionals having the right attitude and willingness to report ADRs, it is mostly the lack of knowledge or unawareness that results in under-reporting. Healthcare professionals need education and formal training in herbal medicines, where to source herbal information and how to evaluate it to makeinformed decisions prior to making recommendations and providing patient information. Continuing education programs, conferences and seminars would assist

healthcare professionals in increasing and updating their knowledge base in herbal medicines (Al-Arifi, 2013).

2.9 Challenges in Adverse Event Data Collection Process and Analysis

The reporting process of adverse events is based on a voluntary system that helps in distinguishing vulnerable groups and generating safety indications. Such a system, however, also has major disadvantages like under-reporting and sub-optimal data quality which limits efforts to establish an effective adverse event monitoring system for HS. Under-reporting may negatively affect signal detection and may result in under-estimation of the size of a problem. The quantity along with the relevance of case reports and the quality of data are important in signal detection (WHO, 2012). The following section briefly discusses the challenges of adverse event data collection.

2.9.1 Under-reporting of adverse event

A study was conducted to evaluate how well the FDA's adverse event reporting system for dietary supplements functions as a consumer protection tool. It estimated that the FDA receives under 1% of reports of all adverse events associated with dietary supplements. The study further suggested that factors that may contribute to under-reporting are many consumers presume supplements to be safe, use these products without the supervision of a healthcare professional, and may be unaware that the FDA regulates them (DHHS, 2001). Under-reporting of adverse events may be for the following reasons. A lack of consumer awareness of the importance of reporting adverse events of HS or even about the unavailability of a reporting system. Even if the reporter is aware of the system, a lack of familiarity with the form or a lack of clarity about the required information might deter submission. Patients are often

reluctant to report the use of alternative treatments to their healthcare providers. Some consumers believe HS are inherently safe since they are natural, and consumers therefore fail to make a connection between the use of a dietary supplement and its adverse events and, as a result, do not report it. Neither is there a clear, common understanding of what constitutes an adverse event. For example, for some, only death or permanent disability qualify, while others include discomfort leading to absence from work or admission to an emergency room for treatment of a symptom such as dehydration. Nor is the recording of the history or asking about HS use a routine part of medical history in either emergency room or follow-up ambulatory visits (Oria, 2008).

Apart from the above-mentioned reasons, the introduction of a dietary supplement, media attention, and the level of educational or regulatory activity recently presented could be other factors that indirectly affect the report rate. There are many psychological and professional issues that contribute to under-reporting. Healthcare professionals fear that ADR reporting may reflect negatively on their competence or even attract litigation. Even although it is essential that all suspected adverse reactions be reported, healthcare professionals are sometimes reluctant to report them because of doubts regarding the causal role of the drug (WHO, 2012). Under-reporting of ADRs is widespread and a remains a daunting challenge in pharmacovigilance (PV). There are patient-related reasons for UR like failure to recognise ADR or the inability to link the ADR with a drug.

2.9.2 Quality of data collected

The quality of information reported depends on the reporter's judgment as well as familiarity with medical reporting, signs, and symptoms. Forms filled by consumers

often include incomplete or inaccurate information about an adverse event. Consumers may lack the information to complete the form with the correct medical terms and standard codes for data entry of adverse event reporting. The form may not collect data about brand name, dose, and other products or medications being taken concomitantly (Oria, 2008).

The 2001 OIG report highlighted the difficulties presented by poor data quality. Adverse event report data were categorised as suboptimal, specifically providing limited medical information, limited information on products and manufacturers, limited information about the consumer, and limited ability to analyse trends. The report found that in 1999, the FDA recorded only 400 adverse events from dietary supplements through MedWatch 3500A forms. Of those, medical records were unavailable in 58% of cases, ingredients could not be determined in 32%, and there was no patient follow-up information available for 27% (DHHS, 2001). The user guidance recently issued on how to fill in the MedWatch 3500A forms improve this situation by helping those reporting adverse events to submit accurate and appropriate information.

These challenges can be overcome by raising the awareness of consumers about the adverse events reporting system. An on-line reporting system could reduce errors with HS associated adverse events reports. If information about the use of HS and adverse events can be collected by healthcare professionals as part of their daily practice and they can report this using correct medical terminology to the adverse events monitoring system, this would raise the quality of reports to the authority and would improve the process of generating signals for the analysis of adverse events (Oria, 2008)

2.10 Benefits of Having Adverse Drug Reaction Reporting System

ADRs have a major impact on public health and are an important cause of hospital admissions. An ongoing ADR monitoring and reporting program can provide benefits to the organization, pharmacists, other healthcare professionals and, more importantly, to patients. These benefits include (but are not limited to) the following: providing an indirect measure of the quality of pharmaceutical care through identification of preventable ADRs and anticipatory surveillance for high-risk drugs or patients, complementing organizational risk management activities and efforts to minimise liability, assessing the safety of drug therapies, especially recently approved drugs, measuring ADR incidence, educating healthcare professionals and patients about drug effects and increasing their level of awareness regarding ADRs, providing quality-assurance screening findings for use in drug-use evaluation programs, and measuring the economic impact of ADR prevention as manifested through reduced hospitalisation, optimal and economical drug use, and minimised organizational liability (ASHP, 1995).

The impact assessment proposal for Directive of the European Parliament and of the Council for the amendment of pharmacovigilance system clearly states the benefits and positive outcomes of having a surveillance or adverse event monitoring system. The document states that 30% of the adverse events associated with drugs and medical substances may be preventable. They assume that they can reduce the health burden by enhancing the European pharmacovigilance system including early detection of fatal adverse reactions, fast implementation of EU-wide decisions on the safety labelling of medicines, clear warnings like not to prescribe a certain medicine to a certain at-risk group of patients, or not to prescribe together two medicines

dangerous in combination, to reach 10% of preventable ADRs in an optimistic scenario and 1% in a conservative scenario (EUROUPA, 2008).

Five percent of total hospital admissions are associated with ADRs and about 5% of hospitalised patients suffer ADR. Another study has highlighted the public health importance of ADRs by estimating that ADRs caused over 100,000 hospital deaths in the United States in 1994 (EUROUPA, 2008).

A proactive and robust pharmacovigilance system could reduce mortality and morbidity, prevent potential disabilities, and improve access to safe and effective medicines for unmet medical needs. The importance of pharmacovigilance/ADR monitoring systems in reducing or preventing drug induced human suffering cannot be understated. Still, the very purpose might be undermined by under-reporting or poor quality of data. The factors contributing to these may vary, but are a potential risk to patient safety and may result in an increased financial burden. Through customer awareness programs and continuing medical education for healthcare professionals, ADR reporting can be made efficient. The establishment of a proactive pharmacovigilance system reduces not only the ADR economic burden but also considerably reduces mortality and morbidity (EUROUPA, 2008; Pirmohamed et al., 2004).

2.11 Summary

This chapter compiled information regarding the consumption of HS and the existing rules and regulations that were exercised in different countries. Various surveys mentioned here implicate the existence of misconceptions about the safety of HS, among both consumers and healthcare professionals. Many developed countries

have various monitoring systems in place to tackle the issue of lack of awareness and under-reporting of adverse events. The quality of data collected is of prime importance and educating healthcare professionals is an important step in this direction. It might be noted that the increasing HS consumption among the Dubai population also significantly increases the potential risks that might be related to HS. The role of CPSS at Dubai Municipality in promoting the safe use of HS through import regulations and field inspections was discussed in this chapter. Apart from the HS import data at CPSS, no studies exist, to date, to establish the extent of HS consumption in Dubai and the occurrence of adverse events, if any, that might be caused by their use. This warrants the need for an extensive study to assess the wide spread use of HS and to educate health professionals and consumers about their safe use. The information collected could be of high significance and could also justify the creation of an ADR reporting system for HS, which in turn could promote the safe use of HS in Dubai.

Chapter 3: Methods

3.1 Introduction

This chapter describes the methodology and research design used in the study. The study aims to evaluate the public health importance of HS product consumption related adverse events in the Emirate of Dubai. The study aims to fulfill the following objectives: measure both healthcare professionals' and the Dubai population's knowledge of HS products, the levels of consumption of HS by the Dubai population, and the incidence of adverse events in the Dubai population. The study additionally aims to identify the level of KAP among Dubai healthcare professionals regarding HS products, any related adverse events, and the reporting of such events.

To find answers to the research questions of the research, the study included the following two cross-sectional surveys: a survey of HS products consumption in the population of Dubai, and a survey of healthcare professionals to assess knowledge, attitude and practice of HS product related adverse events.

3.2 Study 1: Survey of Health Supplement Use in the Dubai Population

3.2.1 Study design

A cross-sectional study design was used to determine the prevalence and characteristics of HS product consumption in Dubai and to study HS product adverse events among consumers. The sampling units were households. A new survey tool was developed based on earlier studies with similar objectives, as shown in Figure 3.1.

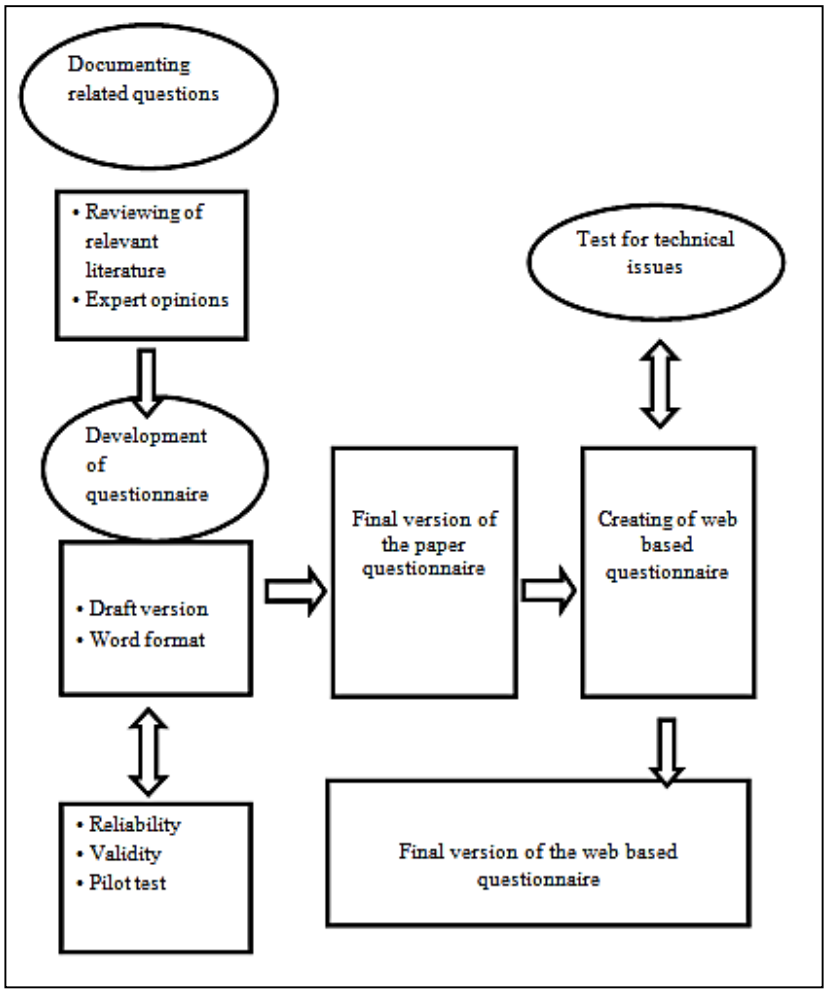

Figure 3.1: Process of questionnaire development

3.2.2 Study setting

This population-based survey included both nationals and non-nationals resident in all areas of Dubai in 2016. The population of Dubai is approximately 2.1 million (DSC, 2014). Dubai Statistic Centre provided the necessary mobile phone numbers for all registered residents in Dubai. Data collection took place between 1 May 2016 and 1 July 2016.

3.2.3 Study participants/population

All residents of Dubai aged 16 and above who were willing to participate were included in the study. In addition, participants had to be willing to disclose their height and weight so that their body mass index (BMI) could be calculated. This was needed to assess HS consumption which is BMI dependent.

3.2.3.1 Population contact database

The co-operation with an established and experienced survey institution was important in this research process as the survey required skilled expertise resources. Dubai Statistical Centre (DSC), a Government of Dubai entity, was selected as the sole official source for the collection, analysis and publication of statistical information and data in the Emirate of Dubai, UAE. Joint meetings with the DSC team were held to clarify the survey objective, questionnaire outline, survey team constitution and timeframe (DSC, 2014).

DSC maintains a regularly updated central database of the contact telephone numbers of all Dubai residents with a fixed landline, and individual mobile telephone numbers.

3.2.4 Sampling

Sampling is one of the most important parts of the survey. A survey is only as good as the quality of its sample. The sample design and the implementation were carried out with the utmost care to avoid possible mistakes. Both nationals and non-nationals were included for a more accurate cross-sectional representation of the Dubai population and, additionally, to maximise generalizability (UN, 2008).

The DSC central database was used in the making of the sampling frame from which geographical areas, households and individuals were selected for sampling purposes. The sample frame covered Dubai geographically and socio-economically (CPSS, 2015) and formed six areas, three in Deira and three in Bur-Dubai.

Stratified sampling was used. Contacts were randomly selected avoiding any duplication that might negatively affect the validity of the result. Pre-survey evaluations, tests and pilot surveys were carried out. Sampling procedure was monitored and the survey was conducted appropriately.

For the purposes of statistical gathering and cost efficiency, the DSC population database was organized geographically and divided into regions. In total, six regions were selected as survey areas for data collection (DM, 2015), three in Deira and three in Bur-Dubai. Area One, Deira, included Al-Qusais and Al-Muhaisina where non-nationals mainly resided. Area Two, Diera, included Mirdif, Al-Mizhar and Al-Warqa where mainly nationals resided. Area Three, Diera, included Hor-Al-Ans and Al-Baraha where both nationals and non-nationals resided. Area Four, Bur-Dubai, included Al-Karama and Satwa where non-nationals mainly resided. Area Five, Bur-Dubai, included Jumeira and Umm-Suqeim where mainly a mixture resided. Area Six, Bur-Dubai, included Al-Quoz and International City where mainly non-nationals lived. The area selection considered the following factors that might influence the survey: the extent and representation of Dubai emirate, Nationals Vs non-nationals in residential areas, and socio-economic status (CPSS, 2015).

The Dubai geographic map constructed by Planning and Survey Departments of Dubai Municipality (DM) was used. Dubai households were divided almost equally into six geographically defined areas. The agreed sample size determined for this study

was 1,200 individuals. The targeted respondents for the survey were Dubai residents, randomly selected from contacts in the DSC database. The database contained necessary information for this survey including name of the house owner, gender, employment status, income range, landline number, house number, several mobile numbers of house residents, area number, and number of residents, etc. (DSC, 2014).The populations of the selected areas were of similar sizes. The sample size per area was proportional to the population of the area. Sampling was completely random within the population of the areas. In each of the six areas, 200 random households were selected using SPSS software, version 20. Each house was registered with mobile numbers ranging from one to maximum 20 different numbers. Mobile numbers for each house were selected randomly. Respondents aged only 16 years or older were included for the purposes of this study. This age detail was not available from the DSC database. Upon enquiry with both Etisalat and Du, the only two mobile phone service operators in the UAE, mobile numbers were not issued to individuals aged under 21 years. Four researchers were therefore hired. They were given random mobile numbers to call, explain the purpose of the survey and ask about ages. Individuals found to be under 16 were subsequently excluded. Another random number from the same house was chosen. About 6,200 mobile numbers were contacted during the three-month period prior to data collection. It would be helpful in future studies if DSC contained this age-related information in their database.

In each selected household, researchers negotiated with respondents regarding their agreement to complete a telephone interview. Interviews were then successfully concluded. Where contact was not made and interviews were not successfully concluded, researchers would call the same number a maximum of three times over

three consecutive days. In the event of failure to contact, another random sample from the same house was selected.

3.2.5 Sample size

As the prevalence of HS product consumption may range from 10% to 30% according to Kemper et al. (2006) and around 19% according to Hara et al. (2011), it was estimated that there may be approximately a 30% prevalence of HS product consumption among both nationals and non-nationals in Dubai.. The required sample size was calculated as alpha=0.05, the desired precision of the confidence interval set to 5%, the population size of nationals and non-nationals in Dubai was 200,000 and 1,900,000, respectively, and the non-response rate to such surveys was estimated to be 12% from previous similar surveys (DSC, 2014).

The sample size was calculated using computer software called OpenEpi. Sample size and power were selected. The size of population was entered as 2,100,000. The expected frequency was entered as an estimate of the true prevalence (30% according to Kemper et al., 2006). The margin of error was set to no more than 3%. The sample size was equal to 1,067 with 95% confidence level. A 12% increase in the sample size was calculated to overcome the non-response rate expected from previous studies in which the total sample size was 1,200.

3.2.6 Survey tool

The survey tool used for this study was a questionnaire. The following describes the process of the survey tool development including the literature/expert review, producing ane-form, reviewing, pilot testing and changes, and the translation of the final questionnaire. This section also presents the questionnaire administration

including the recruitment and training of researchers, the process of the interview, and the ensuring and checking of data quality.

3.2.6.1 Questionnaire development

The process of questionnaire development included some critical stages as illustrated in Figure 3.1.

Literature/expert review: A primary draft version of the questionnaire was developed as a Microsoft Word document based on previous research and input from professionals and experts in the field of HS products. The draft questionnaire was reviewed by PhD Research Committee Members at United Arab Emirates University.

Producing e-form questionnaire: Upon successful review by the UAEU, the draft questionnaire was submitted to the DSC for digital transfer into an electronic version allowing CAPI researchers to conduct telephonic surveys. DSC was a survey partner in this research. The questionnaire was completed by DSC on 17 June 2015.

E-form questionnaire review: The e-form questionnaire was reviewed by a panel of information technology specialists at DSC. Thirty HS specialists from the Consumer Products Safety Section of DM worked with researchers. They checked accessibility, order of questions, and spelling.

Changes in the questionnaire: Upon receiving feedback from information technology specialists, Consumer Products Safety Section HS specialists, and the researchers regardingchanges to the questionnaire, the DSC was asked to modify the numbering of the questions and pages, to replace the field name, Sex, by Gender, replace the term Surveillance by Reporting, add a progress bar at the top of the survey page, show notification if a mandatory question was not answered, change the

formatting, order and context of some questions and answers, and link some questions to each other, and end the questionnaire at certain answers.

Pilot testing: After discussion, the DSC made the required amendments and CAPI was ready to use by 23 July 2015. The pilot study was started on 27 July 2015 aiming to achieve 120 responses. By the 4 August 2015, 74 responses had been received from non-nationals and 60 responses from nationals. This pilot study did not identify any further problems or technical issues with the questionnaire.

Translation: In Dubai, the local language of communication is Arabic, and non-nationals mainly speak English. The questionnaire was therefore produced in both Arabic and English. Translation was carried out to the highest level by the Arab-speaking researcher involved in the survey. The translated questionnaire was proof-checked by language experts at Dubai Municipality. The translated questionnaire was corrected with required changes after proof reading, tests and pilot surveys (UN, 2008).

Questionnaire approval: The final version of the questionnaire was approved and made available for data collection. The questionnaire was subsequently approved by the Social Sciences Research Ethics Committee at UAE University, an authorised agent able to issue approval to students/researchers wishing to conduct social science related research in the UAE.

3.2.6.2 Questionnaire administration

The questionnaire administration process included certain stages such as recruitment and training of researchers, process of the interview, instructions to researchers, and ensuring and checking the data quality.

Recruitment and training of researchers: To ensure the quality of the survey, two teams of researchers/interviewers were hired at DSC for the telephonic survey. One team was Arabic speaking experts and assigned to do the survey for nationals who mainly speak Arabic. The second team was multi-lingual experts who speak both Arabic and English. They were assigned to do the survey for non-nationals. This arrangement increased the quality of communication and helped in clarifying such things as medical terms mentioned in the survey.

One key element of the survey was training. The training process started before the survey and continued during the entire data collection process. During selection of the interviewers, the qualification of a Bachelor degree was listed as a requirement. Training sessions for the interviewers were conducted for supervisors and the coordinators at the DSC to make sure that everyone associated with the survey were clear about their role and the aim of the survey. Training methods included role-play in interviews with various scripts. The training process motivated the interviewers and their practical suggestions were accepted. This training improved the overall quality of the data collection (UN, 2005).

Process of the interview: Survey implementation requires great attention to obtain quality data. The entire survey process was monitored in real time by the writer and problems were addressed as they arose. The supervisor/interviewer ratio was 1:5. Input from the telephonic survey were entered on the specially created Microsoft Excel file during the survey itself (UN, 2005).

A principal concern was how to increase the response rate. It was assumed that unemployed respondents may be more available between 11 AM and 1 PM, and for employed respondents, it was assumed that they may be more available between 3 PM

and 6 PM. This method of approach was successful and increased the response rate in the survey.

Ensuring and checking data quality: The quality of the survey is vital and ensures accuracy, reliability and validity of the results. To ensure quality, World Health Organization (WHO) guidelines were followed using World Health Survey (WHS) (UN, 2005). To achieve the maximum quality, the following principles were adopted: quality standards which need to be adhered to each step of survey, quality assurance procedures ongoing throughout the survey from preparation and sampling through to data collection and data analysis and on to report writing, and evaluation of the quality assurance procedures (UN, 2005).

In the survey procedure, great attention was paid to quality in every respect. Random participants, for example, were re-surveyed to check the quality and veracity of their original answers. Of the 1,200 residents surveyed, 40 were re-surveyed.

The survey was conducted through CAPI and designed such that, if data were missing, interviewers would be alerted, allowing the survey to be completed correctly and with confidence.

The research outcome is entirely based on data from the survey. To ensure the quality of data collected, it was important to obtain accurate data timely. After sampling and before starting the survey, call sheets were provided for each telephone number. The interviewer could make notes related to the survey. These notes might play a vital role in the quality of survey itself. In the event, call sheets did indeed play an important role in the data collection by: recording the status of each telephone number participating in the survey, providing helpful information to the next interviewer like convenient time to call back, seeking attention for feedback and

supervision if needed, and marking the number of attempts with time and response, and recording the outcome of each telephone number enquiry (including completed interviews, refusals etc.) (UN, 2005).

This call sheet worked as a cover page to the questionnaire for each telephone number used in the survey. Upon completion of the questionnaire, data were directly input into the computer using user-friendly software, Epidata. To minimize errors in transferring data, a special data entry team was created from the interviewer team, supervised by one of the supervisors from the survey team.

3.2.7 The questionnaire

The following sections present a summary of the survey tool, its various sections, variables, questions, related scales and coding.

3.2.7.1 Questionnaire sections: summary

A questionnaire (Appendix A) composed of six sections was used to measure HS product consumption and other required variables in the study population. The section, as shown in Table 3.1, asked about demographic information including age, gender, marital status, nationality, occupation, health insurance coverage, income, education, weight and height. All data were nominal except age, height, and weight which were interval. Additionally, income was presented as an ordinal scale. Height and weight were used to present the Body Mass Index (BMI). All data were used to measure the demographic characteristic.

Table 3.1: Population demographic data, scales & variables

Question	Scale	Variables measured
Age	Interval	Demographic - characteristics
Gender	Nominal	
Marital status	Nominal	
Nationality	Nominal	
Occupation	Nominal	
Health insurance coverage	Nominal	
Income	Ordinal	
Education	Nominal	
Weight (kg)	Interval	
Height (cm)	Interval	

The section on health and lifestyle, as shown in Table 3.2, assessed the general health status of the responder including allergies, clinic visits during the previous year, chronic diseases, consumption of drugs and smoking habit. All data were nominal except for clinic visits and smoking habit which were presented as ordinal scale. All data were used to measure health and lifestyle.

Table 3.2: Population health and lifestyle, scales & variables

Question	Scale	Variables measured
Having any allergy	Nominal	Health and life style
Specifying the type of allergy	Nominal	
Frequency of visiting a doctor in the past 12 months	Ordinal	
Whether been diagnosed with chronic medical condition	Nominal	
Whether taken prescription drugs in the past month	Nominal	
Smoking status	Ordinal	

The section, as shown in Table 3.3, focused on HS consumption and comprised questions covering the following points: knowledge of HS, HS consumption including duration, frequency, number and amount, discontinuation of HS consumption, categories, forms and names of HS consumed, ingredients of HS consumed, reason for consuming HS and location of purchasing HS. All data were categorical except for duration of using HS which was presented as ordinal scale. All data were used to measure the HS use except the question - Do you know what HS are?- which was used to measure consumer knowledge regarding HS.

In the section Information about HS Products, as shown in Table 3.4, questions covered the following points: the identity of the person, if any, who recommended HS to the responder, the frequencies of prescribing HS by healthcare professional, HS information source, opinion about information on label including product information and nutritional facts, label information of concern to the responder and, finally, the level of compliance with label recommendations. All data were nominal except for frequency of HS prescribed for the consumer by healthcare practitioner, which was presented as ordinal scale. All data were used to measure consumer knowledge variable on HS.

Table 3.3: Health supplement consumption, scales & variables

Question	Scale	Variables measured
Knowing what HS are	Nominal	Consumer knowledge on HS
Reasons for taking HS	Nominal	Consumption characteristics
Reasons for discontinuing HS	Nominal	
Ever using HS	Nominal	
Duration of using HS	Ordinal	
Frequency of using HS	Nominal	
Which HS categories been using	Nominal	
Which HS forms been used	Nominal	
Which HS ingredient been using	Nominal	
Where purchasing HS	Nominal	
How many HS products been using	Ordinal	
Enter the full name of HS including brand name	Nominal	

Table 3.4: Information about health supplement, scales & variables

Question	Scale	Variables measured
Who advised you to take HS	Nominal	Consumer knowledge on HS
Times HS prescribed by healthcare practitioner	Ordinal	
Where seeking HS product information	Nominal	
Whether finding sufficient information on HS label	Nominal	
Whether nutrition information on HS useful	Nominal	
Which label information concerns you	Nominal	
Whether following recommended label information	Nominal	

The section Adverse Events Related to Health Supplement Consumption, as shown in Table 3.5, asked whether the responder had experienced any adverse event related to HS use. If the respondent answered yes, further questions enquired about the nature, severity, frequency and onset time of the adverse events reported. There are also questions about the exact relation between the adverse event and the HS consumed, and what HS product is confirmed or suspected to have caused the adverse event. Finally, in this section, the responder is asked about the resolution of the adverse event and any period of hospitalisation that was necessary. All data were nominal except for severity of the adverse events, frequency of encountering adverse events, and onset time of adverse events which were presented as ordinal scale. All data were

used to measure the variable of level of experiencing an adverse event, potential deleterious effects on human health in the Dubai population, except for healthcare practitioner investigation on HS consumption at any visiting time, and the resolution of the adverse event.

The section Reporting Adverse Events, as shown in Table 3.6, asked whether the responder had reported an adverse event related to HS and, if so, how this was done. A final question asked for the responder's opinion about establishing a reporting system for any adverse event related to HS.

All data were nominal except for practice of population on establishment of a reporting system of adverse events related to HS consumption, which was presented as ordinal scale. All data were used to measure the reporting of suspected HS-related adverse events, except for establishment of a reporting system of adverse events related to HS consumption, which was used to measure the consumer knowledge on HS variable.

Table 3.5: Adverse event related to health supplement use, scales & variables

Question	Scale	Variables measured
Whether experiencing any AE related to HS use	Nominal	Potential deleterious effects of HS on human health
Which AE of HS use been ever experienced	Nominal	
Severity of the AE	Ordinal	
Frequency of encountering AE due to HS use	Ordinal	
Onset time of AE after consuming HS	Ordinal	
How was the relation between HS consumption and the AE confirmed	Nominal	
Which of the HS you have used was suspected/confirmed to cause the AE	Nominal	
When visiting your healthcare practitioner for any reason, whether asked you about your HS consumption	Nominal	Reporting of suspected HS-related AE
How did the AE resolve	Nominal	

Table 3.6: Reporting adverse event, scales & variables

Question	Scale	Variables measured
Have you ever informed your physician about your HS use	Nominal	Reporting of suspected HS-related AE
Have you ever reported an AE related to HS use	Nominal	
Where did you report the AE	Nominal	
What do you think about the establishment of a reporting system of AE related to HS use	Ordinal	Consumer knowledge on HS

3.2.7.2 Variables

The dependent variables within the population-based survey include consumption rate, consumer knowledge of HS, the level of experiencing adverse event, and the potential deleterious effects on human health in the Dubai population. The independent variables or correlates include: age, gender, marital status, nationality, occupation, health insurance, income, education level, and BMI.

For the three dependent variables, knowledge of HS was defined as an affirmative answer to Q2 - Do you know what HS are? HS use was defined as an affirmative answer to Q23 - Have you ever used HS? and ever having had an HS adverse event was defined as an affirmative answer to Q41 - Have you ever experienced an adverse event from HS?

3.2.8 Data management

Data were managed through SPSS version 20. All data were coded in such a way as to interpret the variables.

3.2.8.1 Re-coding and interpretation of the variables

Some of the variables were re-coded during the analysis. For instance, the nationality category was re-coded as Emirati, Middle East/ North Africa, South Asia, East Asia/ Pacific, Central Asia/ Europe, Africa, Western Europe/ North America/ Australia, and Latin America/ Caribbean. Also, the HS ingredients categories were merged together and re-coded within four different main categories. Moreover, the forms of HS categories of drinks, liquids, caplets, granules, lozenges, and gels were merged and re-coded into one category. Finally, the HS current and past consumption categories were merged into a re-coded ever used category.

Question 29, - HS ingredient have you used? - had a large answer list of 60 different ingredient names. This was re-coded in terms of risk assessment module classification into four main categories of low, medium, high, and extreme ingredients' overall risk estimation.

The risk assessment process for the presence of some ingredients in HS products began with hazard identification, the hazards being the ingredients in the supplement products, as shown in appendix B. Some ingredients can induce certain risks to human health under certain conditions or at certain doses.

The hazard characterisation based on associated risks in response to dose/response relationship and the probability of adverse outcomes include short-term toxicity from reported side effects, long-term toxicity from evidence-based published sources, interactions of food and/or drugs, contamination with toxicants such as heavy metals, and pesticide residue. The risk characterisation within the risk assessment module was calculated as the multiple of the likelihood and severity of the adverse events related to the ingredient. To calculate the risk score, a risk matrix was adopted. The risk matrix had four ranges for severity, as shown in appendix C.

The risk score range was low, medium, high and extreme. As many of the ingredients had several risk factors, either in the impact field or in the probability field, the risk scoring method field was used as a calculation to obtain an overall impact value. This value was then used along with the probability to determine the score used to evaluate project risk. The overall impact value was calculated using average impact. The overall impact was determined by calculating the average of all impact values.

As per above mentioned method, the associated risk(s) with the ingredient in terms of short-term toxicity, long-term toxicity, interactions of food/drugs,

contamination with heavy metals, and pesticide residue are shown in appendix D for each individual ingredient.

Table 3.7 presents a summary of all the above-mentioned ingredients as classified, according to the induced risk, into low, medium, high and extreme risks in which Glandular extract (Hadayer & Schaal, 2016; Gangwar et al., 2015; CPSS, 2015), yohimbe (NIH, 2016; CPSS, 2015; Wongkrajang et al., 2014) was considered as a potential for extreme risk.

Table 3.7: Ingredients overall risk estimation

Level of risk	**Ingredient(s)**
Low	Bilberry, Methylsulfonyl Methane, Garlic, Oxymatrine, Creatine, Folic Acid, Vitamin B6, Potassium, Vitamin B12, Vitamin E, Zinc, Grape Seed Extract, Siberian Ginseng, Lecithin, L-Carnitine, Morinda Citrifolia, Lycopene
Medium	Alfalfa, Saw Palmetto, Tryptophan, Amino Acids, Iron, Spirulina, Calcium, Magnesium, Vitamin C, Caffeine, Echinacea, Chondroitin, Vitamin D, Glucosamine, Cayenne Pepper, Vitamins A & D, Cimicifuga Racemosa, Parsley, Pygeum Africanum, Ginkgo Biloba, Panax Ginseng, L-Cysteine, L-Methionine, Lysine, Chromium, Lutein, Royal Jelly, Bee Pollen, Guarana, Kelp, Fructus Cynosbati, Ginger, Liquorice, Melatonin
High	Gentian, Ephedra, Selenium, Conjugated Linolenic Acid, St. John's Wort, Damiana Folia, Fish Oils
Extreme	Glandular Extract, Yohimbe

3.2.9 Statistical analysis

Data were exported from the computer application as a Microsoft Excel 2010© spreadsheet and analyses were conducted using STATA version 14.2. Data were cleaned prior to analysis. Data were nominal, interval (for age, height, weight, and BMI) or ordinal. Answers to the following questions were ordinal data: Q11 Income, Q17 Frequency of visiting a doctor, Q20 Smoking, Q25 Duration of HS use, Q35 Frequency of HS been prescribed by practitioner, Q43 Severity of adverse events, Q44 Frequency of encountering adverse events, Q45 Onset time of adverse events, Q54 Practice of establishing a reporting system. Descriptive statistics were used to describe the demographic characteristics of the sample using frequencies (percentages) or means (standard deviation) as appropriate. If differences were found between sub-groups of the sample (age, gender, educational status, nationality, etc.), these differences were tested for statistical significance using chi-square test for categorical variables and ANOVA for continuous variables. The distribution of the characteristics of the study population for each of the outcome variables was tabulated. Again, for characteristics that are categorical variables, frequencies and percentages are shown, and for characteristics that are continuous variables, means are shown. Chi-square test or ANOVA was used as appropriate to test for statistical differences. Simple logistic regression analysis was performed to assess the association between HS use (outcome variable) and selected correlates (independent variables). The variables having p value <0.10 were included in a stepwise logistic regression model to identify the independent factors associated with HS use. The confidence interval of 95% and p value <0.05 were used to determine statistical significance.

3.2.10 Data limitations

Bias is the expected difference between an estimated characteristic of a population and that population's true characteristic. Bias may occur in any step of the research. In this research, care was taken to minimise the risk of bias as much as possible.

Information bias: To collect accurate data from the respondents, researchers must be able to understand and identify possible errors in the design of the questionnaire as a research tool. Any errors in the questionnaire design may be considered as information bias and researchers should be able to prevent or minimise this kind of bias.

In the current survey, attention was paid to or even ting any errors arising during the questionnaire preparation stage. Possible biases in the questionnaire were identified like complex questions, double-barrelled questions, and short questions which might not be accurately answered in the population-based survey and an upcoming healthcare professional survey. The questionnaire was limited to the scope of the research questions. In the e-mail survey, respondents tended to choose the first few options from the list (primary bias) and in the telephonic survey, respondents were more likely to answer the later options (recency bias). To minimise this bias, the number of options was reduced and the order of options randomized.

In the population-based survey, the questionnaire was designed in such a way as to afford the interviewer an easy means of conducting it while offering respondents an easy means of responding to questions. The use of technical and complicated clinical terms was kept to a minimum for ease of understanding.

To minimise bias, the questionnaire was evaluated by HS experts at Dubai Municipality. The questionnaire underwent pre-testing and was modified accordingly.

In the population-based survey, stratified sampling was used to minimise the bias associated with sampling. One of the challenging areas in bias was the use of landline phone numbers or mobile phone numbers to conduct the survey. Mobile phones alone were selected for the survey. Many peoplecarry their mobile phones with them for long periods of time daily, and a mobile number may be used as an individual identifier. This minimised the bias associated with a landline phone survey where several people in the same household might use the same number with a resultant difficulty arising in identifying specific individuals.

Interviewer bias: Interviewer bias was considered a concern in telephonic surveys. During the survey, an interviewer might communicate with the respondent in such a way as to obtain a tailored answer. This might lead to unreliable results. Interviewers should have enough knowledge of the questionnaire to be able to communicate with respondents clearly and succinctly to obtain a truthful and accurate answer.

In the telephonic survey for this research, there was a possibility of serious interviewer bias. As interviewers read the questions to the respondent, answer choices were offered. In one question, a large list of answer options was offered. The list was so long that interviewers compromised the question and answer by failing to make all options clear. This was spotted and rectified during the pilot survey. All interviewers were further trained in scientific terminologies included within the survey. This training program improved surveyor skills and minimized the incidence of errors. Interviewers were selected from employees of DSC. They underwent a smart training

program to improve their knowledge of the questionnaire and to enhance their survey skills.

Non-response bias: Non-response bias is the error which may occur due to non-response of contacted individuals. If steps are not taken to prevent non-response bias, the result of the survey may be biased in a way that the opinion of the respondents does not reflect the actual opinion of the source population.

In the population-based survey, care was taken to minimize non-response bias. As discussed in the sampling section, six areas were randomly chosen for sampling. Where there was no response from the respondent, attempts to contact were made over the three following days. Where respondents were unwilling to participate or non-responsive, another random sample was chosen to continue the survey.

To reduce the non-response rate, it was assumed that unemployed people, as shown in DSC directory based on employment status, might be more availablefrom 11 AM to 1 PM, and, similarly, employed people might also be more available from 3 PM to 6 PM. Contact was therefore arranged accordingly for the telephonic survey.

3.2.11 Ethical approval and safeguarding participants

The consent and information details were given to respondents prior to starting the survey.

3.2.11.1 Informed consent

Informed consent, for the purposes of this study, included a participant computer generated dedicated identification number. Informed consent also included the title of the project and the main researcher’s name. It also explained that the study would take

place at the United Arab Emirates University, College of Medicine & Health Sciences, School of Public Health, Al-Ain, UAE, and that participation in the study would take up to 30 minutes: five minutes for set-up/explanation, around 20 minutes for the questionnaire itself, and five minutes for a discussion with the researcher afterwards. In addition, it included the following: an easily understood information sheet dated 5th March 2015 and designed in such a manner as to allow participants to ask questions of the interviewer, an explanation that participation in the survey was voluntary and that participants were free to withdraw at any stage, confirmation that information and opinions provided during the survey would be kept strictly confidential and used only for research purposes, confirmation that names and details would not be linked to this survey and would not be identified in any report/publication, and consent to agree to take part in the study.

This information was provided to the participant verbally, by phone. Participant decision to continue with the survey was deemed consent.

3.2.11.2 Information for participants

The nature and purpose of the survey, as shown in appendix E, were fully explained to participants verbally, by phone. Prospective respondents were cordially invited to take part in the research study. The purpose of the study was comprehensively explained to them. Prospective respondents were given ample time to consider the invitation. A confidentiality code was assigned to each prospective respondent.

3.2.11.3 Ethics review

A Research Ethics Review Form, available at UAE University website, was completed and submitted to Al Ain Medical District Social Sciences Research Ethics Committee at UAE University. Approval to conduct the study was received in June 2015.

3.3 Second study: Knowledge, Attitude and Practice of Health Supplements Related Adverse Event Among Healthcare Professionals

3.3.1 Study design

A cross-sectional study design was also used in the second study to assess knowledge, attitude and practice (KAP) regarding HS products among healthcare professionals including physicians, pharmacists in hospitals and clinics, both public and private, and community pharmacies. To be included in the study, healthcare professionals had to be employed as such for at least three months. A questionnaire was devised for this survey using the same principles adopted in the questionnaire for the population-based study, as shown in Figure 3.1.

3.3.2 Study setting

The survey was carried out in public or private hospitals and pharmacies in Dubai.

3.3.3 Study participants/population

The study population comprised all physicians in all specialties and all pharmacists and assistant pharmacists registered with DHA, with a minimum of three months' experience and who worked in public orprivate hospitals, clinics or healthcare

centres. The inclusion criteria included individuals who were employed in DHA or any other governmental or private health sector who had registration with DHA. Individuals who worked in other free zone health sectors and not registered with DHA were excluded from the study. Additionally, any individual on work probation was excluded.

3.3.4 Sampling

DHA provided the e-mail contact details for all registered physicians and pharmacists working at DHA. Data were collected during the period 2 May 2016 to 23 November 2016. Dubai Municipality additionally provided e-mail contact details for all private pharmacies in Dubai (CPSS, 2015) as well as e-mail contact details for managers at private hospitals and clinics in Dubai. Data for these sectors were collected from 3 May 2016 to 23 November 2016.

3.3.5 Sample size

The latest published numbers of physicians working in public hospitals and clinics in Dubai was 1,096 (DSC, 2012) and the latest published numbers of physicians working inprivate hospitals and clinics in Dubai was 1,288 (DSC, 2012). The number of registered pharmacists in Dubai was 3,155 (DHA, 2014) yielding a total of N= 5,539. All physicians and pharmacists registered with DHA were contacted for this survey. To calculate a sample size for this survey, a pilot study was used. A questionnaire was sent to 85 physicians and pharmacists and 83 replied, producing a response rate of 97%. The questions on which the sample size calculation was based were:

1. Do you know about adverse events of HS?

2. Do you sell/prescribe/dispense any HS at practice site?

3. Do you think it is important to report all adverse events of HS products?

The knowledge of physicians regarding HS products was recorded as 15% according to Clement et al. (2005) and 70% according to Kemper et al. (2006). According to the Dubai pilot study, the levels of knowledge, attitude, and practice (KAP) for healthcare providers towards HS products were 78%, 78%, and 74%. The alpha=0.05 and, as per the results of the pilot study, the level of KAP was estimated as 50%. It was expected that the proportions of respondents answering yes to the above questions 1, 2 and 3 would be around 50%, 50% and 50%. The alpha level is set to 5% and has a 95% confidence interval. The precision (D) of the 95% CI is fixed at 5% so that the width of the 95% CI will be at maximum 10%. According to the assumptions and with 5,000 physicians and pharmacists registered with DHA, a sample size of n=385 was needed to guarantee the desired precision, assuming a non-response rate of around 3%.

3.3.6 Survey tool

In terms of questionnaire development, this survey underwent a similar process as the previous survey. It included the phases of literature/expert review, producing e-form questionnaire, e-form questionnaire review, and changes in the questionnaire. Upon receipt of feedback and comments, DSC made the necessary amendments and activated the survey link on 23 July 2015. The translation process was similar to that used in the first survey.

3.3.6.1 Pilot testing

This pilot study was started on 27 July 2015 in two private hospitals. This was because of a delay in receiving approval to conduct the survey in public healthcare settings. By 4 August 2015, 83 respondents had completed the questionnaire satisfactorily and no problems had been reported. The results of this pilot study were used to calculate the required sample size for the second survey.

3.3.6.2 Questionnaire administration

This survey was designed to be self-completed by respondents through a web-based electronic link sent to respondents'e-mails addresses.

Ensuring and checking data quality: In this e-mail-based survey, the questionnaire was designed to be particularly user-friendly and easily understood. The format was compatible for computer, tablet and mobile phone use.

3.3.7 The questionnaire

The following sections present a summary of the survey tool, its different sections, variables, questions, related scales and coding.

3.3.7.1 Questionnaire sections: summary

A questionnaire composed of four sections was developed to assess healthcare professionals' KAP of HS products, related adverse events and other required variables. This survey was performed electronically by an on-line link sent by e-mail.

The first section, as shown in Table 3.8, asked about demographic information (age, gender, marital status, nationality, employment status, title, years of job

experience, insurance coverage and education). All data were nominal except for age, which was interval. Work experience was presented as ordinal scale. All data were used to measure demographic characteristics.

In the second section, as shown in Table 3.9, a set of questions was developed to measure the level of knowledge of HS products and adverse events. Questions highlighted the following aspects: HS product general information and whether they were harmless or not, whether reporting systems existed, whether there were reporting systems in their workplace, whether respondents knew to whom to report an adverse event, and information on continuous education (articles, training, etc.) related to adverse events of HS products. All data in this section were nominal. The data collected in this section were used to measure the knowledge variable.

Table 3.8: Healthcare professionals' demographic data, scales & variables

Question	**Scale**	**Variables measured**
Age	Interval	Demographic - characteristics
Gender	Nominal	
Marital status	Nominal	
Nationality	Nominal	
Employment status	Nominal	
Title	Nominal	
Work experience	Ordinal	
Insurance coverage	Nominal	
Education	Nominal	

The third section, Practice, as shown in Table 3.10, included the following: types and forms of HS prescribed and/or dispensed, a system to record HS use, discussing

HS use with patients/customers and information sources for these discussions, adverse events encountered in relation to HS consumption, their types and how they are dealt with. All data were nominal except for frequent HS discussion with patients, frequent encountering HS related adverse events and frequent recording HS adverse events, which were presented as ordinal scale. The data collected in this section were used to measure the practice variable.

Table 3.9: Healthcare professionals' knowledge scales & variables

Question	**Scale**	**Variables measured**
Do you know what HS are?	Nominal	**Knowledge**
List as many HS as you can.	Nominal	
Do you agree with the statement that HS are harmless?	Nominal	
Do you know about adverse events of HS?	Nominal	
List as many adverse events of HS as you can.	Nominal	
Do you know what surveillance system is?	Nominal	
Do you know about any existing surveillance system in the UAE?	Nominal	
Do you know about any adverse event reporting system in your organization?	Nominal	
Do you know to whom you can report adverse event?	Nominal	
Have you received continuing education on HS?	Nominal	
Have you read a scientific article related to adverse events of HS in the last 6 months?	Nominal	
Have you ever received training on reporting adverse event?	Nominal	

Table 3.10: Healthcare professionals' practice scales & variables

Question	Scale	Variables measured
Do you sell/prescribe/dispense any HS at practice site?	Nominal	Practice
Which type of HS do you usually prescribe/ dispense?	Nominal	
Which form of HS do you usually prescribe/ dispense?	Nominal	
Do you have a system to record HS use?	Nominal	
How often discussing HS use with patients?	Ordinal	
Topic of discussion about HS use with patients?	Nominal	
Which of HS information sources are helpful for patients?	Nominal	
Barriers limiting discussing HS with patients?	Nominal	
Ever experienced HS related AE in patients?	Nominal	
How frequently encountered AE related to HS use?	Ordinal	
What was the AE?	Nominal	
How often have you recorded HS AE?	Ordinal	
Which authority/personnel you report HS AE?	Nominal	
Is AE reporting form available when you are at the job of prescribing/dispensing medicines to the patients?	Nominal	

In the last section, Attitude, as shown in Table 3.11, questions relate to the reporting of adverse events related to HS. These included reasons for not reporting an adverse event and the importance of reporting such events. For some questions, participants selected their answers from a five-point ordered scale. All data were ordinal except for reason of reporting/not reporting adverse events and the importance of reporting, which were nominal. Data collected in this section were used to measure the attitude variable.

Table 3.11: Healthcare professionals' attitude scales & variables

Question	**Scale**	**Variables measured**
You report HS related adverse events to the higher authority/personnel.	Ordinal	**Attitude**
What is the reason if you don't/wouldn't report an adverse event?	Nominal	
Do you think it is important to report all adverse events of HS?	Nominal	
What do you think about the establishment of a surveillance system of adverse events related to HS consumption?	Ordinal	
Are you concerned about legal problems of reporting an adverse event?	Ordinal	
Do /would you feel confident when reporting an adverse event?	Ordinal	

3.3.7.2 Variables

In this survey, the dependent variables were: healthcare professionals' knowledge of HS adverse events, attitude to HS adverse events, practice related to HS adverse events, and reporting level of adverse events. The independent variables or correlates included: age, gender, marital status, nationality, employment status, job category, work experience, insurance coverage, and educational level.

3.3.8 Statistical analysis

In this study two approaches (descriptive and analytical) were used for data analysis.

Descriptive approach: first of all, the frequencies and percentages for all questions (variables) in the study questionnaire were determined. We reported the percentage of each demographic characteristics, the frequency and the percentage of each question related to healthcare professional's knowledge of HS and the frequency and the percentage of each question related to HS adverse events reported by respondents. We also reported the frequency and the percentage of each question related to healthcare professionals' practice with respect to selling, prescribing or dispensing HS, and types of HS and dosage, record keeping and discussions with patients/consumers. The frequency and the percentage of each question related to respondents' experience of HS adverse events was reported. The second part in statistical analysis plan illustrates the assessment of the knowledge, attitude and practice (KAP) of healthcare providers towards HS. In this regard two measures were calculated: The overall knowledge, attitude and practice score: (knowledge, attitude and practice (KAP) score toward HS related adverse event were assessed by 10-item

questions. A scoring mechanism was used to understand overall KAP level. Each correct answer was given one score, and the range of the score varied between 0 (with no correct answer) to 10 (for all correct answers). Respondents with all correct response get a maximum of 10 points; higher points indicate good knowledge. Based on total score, a score of 70% and above was judged to be good, 50%-69% fair and <50% poor.

Analytical approach: this part of statistical analysis was designed to determine the differences in participants' responses in term of demographic. Before running the comparisons, the normality of our dependent variable (KAP score) among the groups of independent variables were tested by visual inspection of their histogram, Q-Q plot and box plot. The results showed that the data were approximately normally distributed. In total three tests were used to find the associations between KAP scores and selected socio-demographic factors (independent t-test, ANOVA and Pearson correlation).

The independent t-test used when we have one continuous (scale) dependent variable (mean KAP score) and one categorical independent variable with two level (gender, nationality, marital status, employment status, work experience and education). The one way ANOVA used when we have one continuous (scale) dependent variable (mean KAP score) and one categorical independent variable with more than two level (occupation). Pearson correlation used when we have one independent variable (mean KAP score) and one independent variable (age). Here both variables are continuous variable.

3.3.9 Data limitations

In the healthcare professional survey, sampling was done from the total number of pharmacists and physicians registered with Dubai Health Authority (DHA), the local health governing body in Dubai. All pharmacists and physicians working at DHA received an e-mail with a link to a web-based questionnaire from the Head of the Human Resources Department at DHA inviting them to participate in the survey.

Pharmacists and physicians working in the private sector in Dubai received the questionnaire link from their management identified through Dubai Municipality database details of private healthcare providers. This minimised the selection bias related to low response in the healthcare professional survey. There was no incidence of interviewer bias as the survey was completed directly by the respondent without the supervision or help of an interviewer. There was, however, the possibility of a high non-response rate. The tailored design method involving multiple communication with respondents to amplify the response rate was utilised in this research. Reminder e-mails were sent to non-respondents every two weeks from the start of the survey. This reduced the non-response rate.

3.3.10 Ethical approval and safeguarding participants

Every physician and pharmacist registered with DHA was contacted by e-mail by the Head of the Human Resource Department at DHA inviting them to participate in the survey. Healthcare professionals in the private sector were contacted through their managers. The e-mail contained a link to the web-based questionnaire (see Appendix F).

3.3.10.1 Informed consent

The nature and purpose of the study were explained within the first page of the survey and if participants continued to the following page this was taken as their consent to participate in the study.

Around 14 communication e-mails with DHA were made to circulate the survey to government healthcare professionals. The first e-mail was dated 2 May 2016, and the last follow-up reminder e-mail was dated 23 November 2016. DHA circulated the survey link to all government hospitals and medical centres in the Emirate of Dubai by e-mail on 2 May 2016. The on-line survey took a long time to reach completion due to the onerous workloads of the healthcare professionals.

Healthcare professionals in the private sector received the survey link by e-mail from their management sourced from Dubai Municipality database. Contact numbers were issued. Reminder e-mails were sent every month from the start of survey on 3 May 2016 until 23 November 2016. At the end of the survey, a message of thanks was issued to all respondents. No incentives were offered for completing the survey.

Around 15 e-mails were issued to private sector managers, then circulated to pharmacies, clinics and hospitals. The first e-mail was sent on 3 May 2016 and the last follow-up was on 23 November 2016.

A total of 500 pharmacies registered in Dubai Municipality database received a survey link sent by the official e-mail of consumer products safety section at Dubai Municipality. The first e-mail was sent on 4 May 2016 and a reminder e-mail was sent on 23 June 2016.

3.3.10.2 Information for participants

Informed consent contained a dedicated participant identification number. It also included the title of the project, Survey of Healthcare Professionals' Knowledge, Attitude and Practice of Health Supplement Products Related Adverse Events, and the main researcher's name, all as shown in appendix G. It was explained that the study would take place at United Arab Emirates University, College of Medicine & Health Sciences, School of Public Health located in Al-Ain, UAE and that participation in this study would take 15 minutes. In addition, it contained an explanatory information sheet dated 5 March 2015. Participation was voluntary and participants were free to withdraw at any stage. Information provided was strictly confidential. Names and details would not be linked to this survey and would not be identified in any report/publication. It also contained a statement of participant's agreement to take part in the study.

This information was delivered to participants on the first page of the on-line questionnaire. Continuing the survey was deemed agreement to participate and acted as signature of the consent form.

3.3.10.3 Ethics review

Approval to conduct this study was received in June 2015 from the University Student Research Committee at DHA.

3.4 Summary

This chapter discussed the main two surveys used to achieve the objectives of this research. All related sampling and sample size were discussed. Statistical analysis was used to measure dependent variables in the population-based survey including

consumption rate, consumers' knowledge on HS, level of experience of adverse events and to measure the dependent variables of healthcare professional knowledge, attitude, and practice of HS adverse events, and reporting level of adverse events.

Chapter 4: Results

The following section describes the demographic information of the two surveys and display the main results.

4.1 Results of Survey of Health Supplements Consumption in Dubai Population

4.1.1 Participants' demographic characteristics

The demographic information of participants is shown in Table 4.1. A total number of 1,203 participated in the survey. The average age of respondents was 39.2 ± 9.1 SD. The participants were predominantly male (n=1002, or 83.3%). Most of the participants were married (n=1039, or 86.4%). South Asians (n=579, or 48.1%) constituted the largest ethnic group in the study, followed by Middle East/ North Africa (n=301, or 25.0%), UAE (n=142, or 11.8%), Western Europe/ North America/ Australia (n=94, or 7.8%), East Asia/ Pacific (n=41, or 3.4%), Africa (n=32, or 2.7%), Central Asia/ Europe (n=12, or 1.0%), and Latin America/ Caribbean (n=2, or 0.2%). Most of the respondents in the survey were employed (n=1123, or 93.3%) and 41.5% (n=499) had an income in the range of 5,000-<10,000AED, 319 participants (26.5%) earned between10,000-20,000AED, 221 participants (18.4%) had an income higher than 20,000 AED. 164 participants (13.6%) earned less than 5,000 AED.

Educational qualifications of the participants also varied. Nearly half of the participants (48.7%, 586) held graduation certificates, 269 were post graduates (22.4%), 139 were high school education holders (11.5%), 76 non-high school education holders (6.3%), 68 diploma holders (5.7%), 46 higher diploma holders (3.8%), and 19 PhD holders (1.6%). Most participants had health insurance coverage

(n= 1028, or 85.5%). Average height was 171.3 centimetres ±8.9 SD. Average weight was 78.7 kg ±15.3 SD. Average body mass index was 26.8 kg/m^2 ±4.4 SD. There were 546 (45.4%) overweight respondents (25-29.9 kg/m^2), 431 (35.8%) of normal weight (<25 kg/m^2) and 226 (18.8%) were obese (≥30 kg/m^2). 862 participants (71.7%) were non-smokers, 183 were current regular smokers (15.2%), 108 were current occasional smokers (8.9%) and 50 were past smokers (4.2%).

Of the total participants, 115 (9.6%) had an allergy, mainly to aerosols or perfume. Allergy to drugs accounted for 21 participants (1.7%). Allergy to dust accounted for 22 participants (1.8%). 106 had diseases (8.8%), mainly diabetes mellitus (n= 69, or 5.7%) and hypercholesterolemia (n= 31, or 2.6%).

Table 4.1: Characteristics of population based survey participants (N=1203)

Variables	categories	n/Avg	%/SD
Age – years		39.2	±9.1
Gender	Male	1002	83.3
	Female	201	16.7
Marital Status	Married	1039	86.4
	Single	150	12.5
	Divorced	9	0.7
	Widow	5	0.4
Nationality	Emirati	142	11.8
	Middle East/North Africa	301	25.0
	South Asia	579	48.1
	East Asia/Pacific	41	3.4
	Central Asia/Europe	12	1.0
	Africa	32	2.7
	Latin America/Caribbean	2	0.2
	Western Europe/North America/Australia	94	7.8
Occupation	Employed	1123	93.3
	Unemployed	60	5.0
	Student	9	0.7
	Retired	11	0.9
Income (AED)	<5000	164	13.6
	5000-<10000	499	41.5
	1000020000	319	26.5
	>20000	221	18.4
Education	< High school	76	6.3
	High school	139	11.5
	Diploma	68	5.7
	Higher Diploma	46	3.8
	Bachelor	586	48.7
	Master	269	22.4
	PhD	19	1.6
Health insurance coverage		1028	85.5
Height – cm		171.3	±8.9
Weight – kg		78.7	±15.3
Body Mass Index – kg/m2		26.8	±4.4
Body Mass Index – cat kg/m2	Normal (<25)	431	35.8
	Overweight (25-29.9)	546	45.4
	Obese (≥30)	226	18.8
Smoking status	Non-smoker	862	71.7
	Past smoker	50	4.2
	Current occasional	108	8.9
	Current regular	183	15.2
Any allergy		115	9.6
	Drug allergy	21	1.7
	Aerosol & perfume allergy	23	1.9
	Contact allergy	7	0.6
	Dust allergy	22	1.8
	Others	26	2.2
Diseases	Diabetes Mellitus	69	5.7
	High cholesterol levels	31	2.6
	Cardiovascular disease	5	0.4
	Cancer	1	0.1

4.1.2 Use of health supplements among the participants in Dubai population

The use of the HS among participants varied, as shown in Table 4.2. Around 748 (62.2%) participants had never used HS and 455 (37.8%) participants had used HS at least once. Among these 455 participants, 377 were currently using and 138 had consumed HS in the past.

The purpose of HS consumption among the 455 participants who had a history of HS usage was as follows: 301 (66.1%) used HS to improve health, 45 (9.9%) male participants used HS for body building, 11 (2.4%) female participants used HS during pregnancy, 31 (6.8%) used HS to prevent diseases, 27 (5.9%) used HS for diet supplementation, 24 (5.3%) used HS for maintaining weight, 18 (4.0%) used HS for energy boosting and the rest of the participants for other reasons.

The duration of HS usage among the 455 known HS consumers was as follows: 189 (41.5%) used HS for a month, 165 (36.3%) consumed HS anywhere between one to five years, 52 (11.4%) used HS for less than a month, and 45 (9.9%) used HS for more than five years. A breakdown of duration of usage among past and current users was also available. Duration of HS use among the current users varied as follows: 118 (37.2%) used HS for a month, 136 (42.9%) used HS between one to five years, 21 (6.6%) used HS for less than a month, and 40 (12.2%) used HS for more than five years. Among the past users, 71 (51.5%) used HS for a month, 29 (21.0%) used HS for one to five years, 31 (22.5%) used HS for less than a month, and five (3.6%) used HS for more than five years.

Of the 455 participants, 288 (63.3%) were daily users, 116 (25.5%) used HS for one to four times in a week, 22 (4.8%) used HS for one to three times in a month, and 17 (3.7%) consumed seasonally. The number of HS used by the 455 participants

differed. While 388 (85.3%) participants used one to two types of HS, 59 (13.0%) used three to five types, six (1.3%) participants used six to 10 types, and two participants (0.4%) had a history of using more than 10 types of HS.

The reasons for discontinuing HS use were mainly allergy, skin disease, and cost. Participants who used HS (n=455) mainly purchased them from pharmacies (88.3%). The remaining purchase sources were from clinics (9.9%) and nutrition shops (6.7%).

Table 4.2: Use of health supplement among population of Dubai (N=1203)

Variables	N	n (%)
HS use	1203	
Ever used (Including current and past users)		455 (37.8)
Current		317 (26.3)
Past		138 (11.5)
Never		748 (62.2)
Reasons for using HS	455	
To improve health		301 (66.1)
Body building (Male only)		45 (9.9)
Diseases prevention		31 (6.8)
Diet supplementation		27 (5.9)
Weight management		24 (5.3)
Energy		18 (4.0)
Pregnancy (Female only)		11 (2.4)
Immunity booster		8 (1.8)
To prevent cold		8 (1.8)
Ageing		5 (1.1)
Anaemia		4 (0.9)
High blood pressure		3 (0.7)
High cholesterol		5 (1.1)
Digestive		6 (1.3)
Other		8 (1.7)
Reasons for discontinuing HS		
Allergy		4 (0.3)
Skin disease		4 (0.3)
Cost		3 (0.2)
Duration of HS use, overall	455	
Less than a month		52 (11.4)
Month		189 (41.5)
1-5 years		165 (36.3)
More than 5 years		45 (9.9)
Do not know		4 (0.9)
Duration of HS use, Current users	317	
Less than a month		21 (6.6)
Month		118 (37.2)
1-5 years		136 (42.9)
More than 5 years		40 (12.2)
Do not know		2 (0.6)
Duration of HS use, Past users		
Less than a month		31 (22.5)
Month		71 (51.5)
1-5 years		29 (21.0)
More than 5 years		5 (3.6)
Do not know		2 (1.5)
Frequency of HS use	454	
Seasonally		17 (3.7)
<1 a month		9 (2.0)
1-3 times a month		22 (4.8)

Table 4.2: Use of health supplement among population of Dubai (N=1203) (Continued)

Variables	**N**	**n (%)**
1-4 times a week		116 (25.5)
Daily		288 (63.3)
Number of HS use	455	
1-2 supplements		388 (85.3)
3-5 supplements		59 (13.0)
6-10 supplements		6 (1.3)
>10 supplements		2 (0.4)
Purchasing of HS	455	
Pharmacy		402 (88.3)
Clinic		45 (9.9)
Nutrition shop		29 (6.7)
Gym		12 (2.6)
Super market		5 (1.1)
Other		9 (2.0)

4.1.3 Knowledge of consumers on health supplements

The knowledge or source of information about HS among consumers of HS in Dubai is shown in Table 4.3. Among the 455 participants who had ever used HS, 212 (46.6%) were prescribed HS, 204 (44.8%) were self-advised HS, 49 (10.8%) were advised by healthcare professionals, 35 (7.7%) advised by friends and/or relatives, 30 (6.6%) advised from the internet, and 10 (2.2%) from other sources, like advertisements.

The participants sought information about HS from various sources. Of the 455 participants who had ever used HS, 274 (60.2%) found out information about HS from pharmacies, 145 (31.9%) from the internet, 129 (28.3%) from physicians, 39 (8.6%) from a relative and/or friend, four (0.9%) from other sources and none of them from government centres. Most participants, 355 (78.0%) who had ever used HS, responded in the survey that the labelling information of the HS was very informative, 68 (14.9%)

responded somewhat informative and 28 (6.1%) responded that they did not read the label. Very few responded that it was not informative (0.9%).

Most of the participants were concerned about the labelling information of HS. They checked the labelling information before use. From the labelling information, they were more concerned about of the ingredients, durability, adverse events, indications, precautions and dosing information. Nutrition information on the label was useful for most participants (94.7%). Of the 455 participants who had ever used HS, 334 (73.4%) always and 64 (14.1%) often followed recommended labelling information.

Table 4.3: Knowledge/sources of information about health supplement (N=455)

Variables	**N**	**n (%)**
Who advised to take HS	455	
Self		204 (44.8)
Friend/Relative		35 (7.7)
Advertisement		5 (1.1)
Internet		30 (6.6)
Prescribed		212 (46.6)
Health professional		49 (10.8)
Other		5 (1.1)
From where do you seek HS information	455	
Pharmacy		274 (60.2)
Physician		129 (28.3)
Product helpline		10 (2.2)
Internet		145 (31.9)
Relative/Friend		39 (8.6)
Government centre		0 (0.0)
Other		4 (0.9)
Sufficient information on the label	455	
Do not read the label		28 (6.1)
Not informative		4 (0.9)
Somewhat informative		68 (14.9)
Very informative		355 (78.0)
Type of label information of HS concerns		
Ingredients of supplement		375 (82.4)
Indications of supplement		245 (53.9)
Dosage of supplement		237 (52.1)
Adverse events of supplement		291 (64.0)
Durability of supplement		312 (68.6)
Dietary sources of supplement		226 (49.8)
Claims of supplement		199 (43.7)
Precautions of supplement		233 (51.2)
Dosing instructions of supplement		227 (49.9)
No information concerns		41 (9.1)
Nutrition information on the label is useful		431 (94.7)
Do you follow recommended label information?	455	
Never		22 (4.8)
Sometimes		35 (7.7)
Often		64 (14.1)
Always		334 (73.4)

4.1.4 Forms and ingredients of health supplements

Forms and ingredients of HS used by the participants are shown in Table 4.4. Vitamins were the most commonly used HS among the participants (87.9%). Both minerals and sport nutrition were consumed by 48 participants each (10.5%). Herbal products and dietetic foods were used by nine participants each (2.0%). Five participants (1.1%) used energy drinks and 12 (2.6%) used miscellaneous types. The most widely used dosage form was tablet, at 85.5%. Capsules were taken by 53 participants (11.7%). HS in powder form was used by 46 participants (10.1%) and 16 participants (3.5%) used drinks/ liquids/ caplets/ granules/ gels etc.

Ingredients of HS used by the participants in the survey were as follows: 195 (42.9%) vitamin D, 104 (22.9%) vitamin E, 104 (22.9%) vitamin A & D, 58 (12.7%) calcium & vitamins, 56 (12.3%) vitamin B12, 52 (11.4%) vitamin C, 45 (9.9%) vitamin B6, 27 (5.9%)amino acids, 32 (7.0%) fish oil, 24 (5.3%) calcium & magnesium, 20 (4.4%) vitamin E multi component, 14 (3.1%) zinc.14 (3.1%) were unaware of ingredients. The remainder responded with miscellaneous ingredients.

Table 4.4: Forms and ingredients of health supplement (N=455)

Variables	N	n (%)
Categories of HS	455	
Vitamins		400 (87.9)
Minerals		48 (10.5)
Herbal products		9 (2.0)
Sports nutrition		48 (10.5)
Energy drinks		5 (1.1)
Dietetic food		9 (2.0)
Miscellaneous		12 (2.6)
Forms of HS	455	
Tablets		389 (85.5)
Capsules		53 (11.7)
Powder		46 (10.1)
Drinks/Liquids/Caplets/Granules/Lozenges/Gels		16 (3.5)
Ingredients of HS	455	
Vitamin D		195 (42.9)
Vitamin E		104 (22.9)
Vitamin A & D		104 (22.9)
Calcium & Vitamins		58 (12.7)
Vitamin B12		56 (12.3)
Calcium		52 (11.4)
Vitamin C with/without rose		48 (10.5)
Vitamin B6		45 (9.9)
Fish oil		32 (7.0)
Amino acids		27 (5.9)
Calcium & Magnesium		24 (5.3)
Vitamin E multicomponent		20 (4.4)
Zinc/zinc gluconate		14 (3.1)
Magnesium		7 (1.5)
Folate/Folic acid		6 (1.3)
Potassium		6 (1.3)
Carnitine		5 (1.1)
Alfalfa		1 (0.2)
Chondroitin		2 (0.4)
Creatinine		7 (1.5)
Other		14 (3.1)
Do not know about ingredient		14 (3.1)

4.1.5 Adverse events of health supplements

Adverse events of HS are as shown in Table 4.5. Of the 455 participants who had ever used HS, 442 (97.1%) had experienced no adverse events from HS use. 13 participants (2.9%) had experienced adverse events from HS use. Of these 13 participants, six graded their experience of adverse events as mild (46.1%), five (38.5%) graded their experience of adverse events as moderate, while two (15.4%) graded their experience of adverse events as severe. Additionally, of these 13 participants, two (15.4%) had frequent adverse events, nine (69.2%) experienced adverse events only once and for two (15.4%) adverse events occurred occasionally.

Among these 13 participants, two (15.4%) self-confirmed a co-relation of HS with an adverse event and one (7.7%) confirmed the co-relation by physician. Of these 13 participants, four (30.8%) suspected or confirmed that vitamins had caused the adverse event while one (7.7%) suspected or confirmed slimming tea as the cause. For most of the participants (76.9%), the adverse event resolved after discontinuing supplement intake. Two participants (15.4%) discontinued intake ofthe supplement on medical advice and for one participant (7.7%) intake was discontinued after treatment.

Of these 13 participants, only a few reported the adverse events and only to their physician (23.1%). Regarding the establishment of an adverse event reporting system for HS, 550 (45.7%) participants responded as unsure about any benefit deriving there from, 464 (38.6%) responded as definitely beneficial and 163 (13.5%) responded as somewhat beneficial. These results show that most participants expressed that the establishment of an adverse event reporting system for HS would be beneficial.

Table 4.5:Adverse events of health supplements (N=455)

Variables	N	n (%)
Adverse events from HS	**455**	**13 (2.9)**
Type of AE	13	
Abdominal pain		1 (7.7)
Dermatitis		2 (15.4)
Diarrhoea		2 (15.4)
Constipation		2 (15.4)
Urticaria		3 (23.1)
Other		3 (23.1)
Severity of AE from HS	13	
Mild		6 (46.1)
Moderate		5 (38.5)
Severe		2 (15.4)
Frequency of AE from HS	13	
Once		9 (69.2)
Occasionally		2 (15.4)
Frequently		2 (15.4)
Onset time of AE	13	
< 1 hour		5 (38.5)
1 hour – 1 day		3 (23.1)
> 1 day		6 (46.1)
Relation between HS use and AE confirmed	13	
Self		2 (15.4)
Physician		1 (7.7)
Lab		0 (0.0)
Clinic		0 (0.0)
HS suspected/confirmed to cause AE	13	
Vitamins		4 (30.8)
Slimming tea		1 (7.7)
How did the AE resolve?		
Self-discontinuing the supplement		10 (76.9)
Discontinuing the supplement after medical advise		2 (15.4)
Treatment		1 (7.7)
Ever reported AE	13	3 (23.1)
Where did you report AE	3	
Physician		3 (100.0)
Benefits of establishing AE reporting system	1203	
Definitely not beneficial		15 (1.3)
Not beneficial		11 (0.9)
Unsure		550 (45.7)
Somewhat beneficial		163 (13.5)
Definitely beneficial		464 (38.6)

4.1.6 Factors associated with health supplement use

Table 4.6 shows the bivariate analysis in which HS use dependent variable is tabulated against independent variables. The mean age of the participants who used HS was 38.9 ± 9.0 SD. There was no effect of age on HS use (P=0.307). There was an effect shown of gender on HS use (P<0.001). Females were more likely to be HS users (133 users among 201 respondents, 66.2%) compared to males (322 users out of 1002 respondents, 32.1%). There was no effect of marital status on HS use (P=0.051). Single and divorced/widowed respondents were more likely to report HS use. There was an effect seen of nationality on HS use (P<0.001). Persons of Latin America/ Caribbean/ Western Europe/ North America/ Australia origin were more likely to be users. Persons of South Asian origin were less likely to report use. There was an effect seen of employment status on HS use (P=0.003). There was an effect seen of income on HS use (P<0.001). Those with incomes over 10,000 AED per month were more likely to be users compared to those on lower salaries.

Educational attainment was also significantly associated with HS use (P<0.001). Those educated to higher diploma level and above were more likely to report HS use compared to those of lower educational attainment. Health insurance was significantly associated with HS use (P=0.017). Those with health insurance were more likely to report HS use. Those with an allergy were also more likely to report HS use (P=0.008). Similarly, those who had visited a doctor and those taking medicines were more likely to report HS use. However, body mass index, smoking, and self-reports of medical conditions were not associated with HS use.

Table 4.6: Factors associated with health supplement use

Variables	**All** N	**Users (N=455)** n (%)	**Non-users (N=748)** n (%)	**P Value**
Age – years	1203	38.9±9.0	39.4±9.1	0.307
Gender				
Male	1002	322 (32.1)	680 (66.9)	<0.001
Female	201	133 (66.2)	68 (33.8)	
Marital Status				
Married	1039	379 (36.5)	660 (63.5)	0.051
Single	150	69 (46.0)	81 (54.0)	
Divorced/Widow	14	7 (50.0)	7 (50.0)	
Nationality				
Emirati	142	68 (47.9)	74 (52.1)	<0.001
Middle East/ North Africa	301	144 (47.9)	157 (52.1)	
South Asia	579	141 (24.4)	438 (75.6)	
East Asia/ Pacific/ Central Asia/ Europe	53	28 (52.8)	25 (47.2)	
Africa	32	14 (43.7)	18 (56.3)	
Latin America/ Caribbean/ Western Europe/ North America/ Australia	96	60 (62.5)	36 (37.5)	
Occupation				
Employed	1123	413 (36.8)	710 (63.2)	0.003
Unemployed	60	35 (58.3)	25 (41.7)	
Student/Retired	20	7 (35.0)	13 (65.0)	
Income				
<5000 AED	164	33 (20.1)	131 (79.9)	<0.001
5000-<10000 AED	499	149 (29.9)	350 (70.1)	
10000-20000 AED	319	153 (48.0)	166 (52.0)	
>20000 AED	221	120 (54.3)	101 (45.7)	
Education				
< High school	76	13 (17.1)	63 (82.9)	<0.001
High school	139	39 (28.1)	100 (71.9)	
Diploma	68	18 (26.5)	50 (73.5)	
Higher Diploma	46	22 (47.8)	24 (52.2)	
Bachelor	586	245 (41.8)	341 (58.2)	
Master/ PhD	288	118 (41.0)	170 (59.0)	
Health insurance coverage	1028	403 (39.2)	625 (60.8)	0.017
Body Mass Index – kg/m2	1203	26.9±4.5	26.7±4.3	0.348
Body Mass Index – cat				
Normal (<25 kg/m2)	431	165 (38.3)	266 (61.7)	0.496
Overweight (25-29.9 kg/m2)	546	198 (36.3)	348 (63.7)	
Obese (≥30 kg/m2)	226	92 (40.7)	134 (59.3)	

Table 4.6: Factors associated with health supplement use (Continued)

Variables	**All** N	**Users (N=455)** n (%)	**Non-users (N=748)** n (%)	**P Value**
Smoking status				
Non-smoker	862	326 (37.8)	536 (62.2)	0.059
Past smoker	50	27 (54.0)	23 (46.0)	
Current occasional smoker	108	34 (31.5)	74 (68.5)	
Current regular smoker	183	68 (37.2)	115 (62.8)	
Any allergy	115	57 (49.6)	58 (50.4)	0.008
Drug allergy	20	13 (65.0)	7 (35.0)	0.129
Aerosol & perfume allergy	20	7 (35.0)	13 (65.0)	0.152
Contact allergy	7	2 (28.6)	5 (71.4)	0.252
Dust allergy	23	7 (30.4)	16 (69.6)	0.040
Others	14			
Visited a doctor in last 12 months				
Did not visit doctor in last 12 months	322	79 (24.5)	243 (75.5)	<0.001
Less than monthly	806	342 (42.4)	464 (57.6)	
1-3 times a month/At least once a week	75	34 (45.3)	41 (54.7)	
Diseases				
Diabetes Mellitus	69	25 (36.2)	44 (63.8)	0.779
High cholesterol levels	31	9 (29.0)	22 (71.0)	0.352
Cardiovascular disease	31	14 (45.2)	17 (54.8)	0.393
Medicines	226	115 (50.9)	111 (49.4)	<0.001
Analgesic	41	17 (41.5)	24 (51.5)	0.309
Anti-biotic	28	15 (53.6)	13 (46.4)	
Anti-diabetic	31	17 (54.8)	14 (45.2)	
Anti-hypertensive	14	6 (42.9)	8 (57.1)	
Cholesterol lowering	10	4 (40.0)	6 (60.0)	
Vitamins	12	9 (75.0)	3 (25.0)	
Anti-allergic	8	3 (37.5)	5 (62.5)	
Other	24	16 (66.7)	8 (33.3)	

The association between HS use as an outcome variable and selected population characteristics as independent variables is summarized in Table 4.7. There was positive association of HS use with female gender, higher income, higher educational

level, having health insurance, being a past-smoker, having an allergy, more frequent doctor visits, taking prescribed medications and HS knowledge.

There was a negative association of HS use with being married and Emirati, Middle East/North Africa or South Asian nationality. After adjustment in the multivariate model, the positive association with female gender, higher income, being a past-smoker, having an allergy, more frequent doctor visits, taking prescribed medications and HS knowledge and the negative association with South Asian nationality and Emirati nationality remained (Table 4.8).

Table 4.7: Crude odds ratios for HS use, cross-sectional study of HS use and HS-related adverse events, Dubai, 2015 (N=1203)

Variables		**All**	**Users**	
		N	**N (%)**	**COR (95%CI)**
Age – years		1203	38.9±9.0	0.99 (0.98-1.01)
Gender	Male	1002	322 (32.1)	1
	Female	201	133 (66.2)	4.13 (3.00-5.69)**
Marital Status	Single	150	69 (46.0)	1
	Married	1039	379 (36.5)	0.67 (0.48-0.95)*
	Divorced/ Widow/ Widower	14	7 (50.0)	1.17 (0.39-3.51)
Nationality	Emirati	142	68 (47.9)	0.55 (0.33-0.93)*
	Middle East/ North Africa	301	144 (47.8)	0.55 (0.34-0.88)*
	South Asia	579	141 (24.3)	0.19 (0.12-0.30)**
	East Asia/Pacific/Central Asia/Europe	53	28 (52.8)	0.67 (0.34-1.33)
	Africa	32	14 (43.7)	0.47 (0.21-1.05)
	Latin America/Caribbean/Western Europe/North America/Australia	96	60 (62.5)	1
Occupation	Employed	1123	413 (36.8)	1.08 (0.43-2.73)
	Unemployed	60	35 (58.3)	2.60 (0.91-7.44)
	Student/Retired	20	7 (35.0)	1
Income	<5000 AED	164	33 (20.1)	1
	5000-<10000 AED	499	149 (29.9)	1.69 (1.10-2.59)*
	>10000-20000 AED	319	153 (48.0)	3.66 (2.35-5.68)**
	>20000 AED	221	120 (54.3)	4.72 (2.96-7.50)**
Education	< High school	76	13 (17.1)	1
	High school	139	39 (28.1)	1.89 (0.94-3.81)
	Diploma	68	18 (26.5)	1.74 (0.78-3.90)
	Higher Diploma	46	22 (47.8)	4.44 (1.93-10.20)**
	Bachelor	586	245 (41.8)	3.48 (1.87-6.47)**
	Master/PhD	288	118 (41.0)	3.36 (1.77-6.39)**

Table 4.7: Crude odds ratios for HS use, cross-sectional study of HS use and HS-related adverse events, Dubai, 2015 (N=1203) (Continued)

Variables		**All**	**Users**	
		N	**N (%)**	**COR (95%CI)**
Health insurance	Yes	1028	403 (39.2)	1.53 (1.08-2.16)*
	No	175	52 (29.7)	1
BMI – cat	Normal (<25 kg/m^2)	431	165 (38.3)	1
	Overweight (25-29.9 kg/m^2)	546	198(36.3)	0.92 (0.71-1.19)
	Obese (≥30 kg/m^2)	226	92 (40.7)	1.11 (0.80-1.54)
Smoking status	Non-smoker	862	326 (37.8)	1
	Past smoker	50	27 (54.0)	1.93 ()
	Current occasional smoker	108	34 (31.5)	0.75 (0.49-1.16)
	Current regular smoker	183	68 (37.2)	0.97 (0.70-1.35)
Any allergy	Yes	115	57 (49.6)	1.71 (1.16-2.51)*
	No	1081	395 (36.5)	1
Visited a doctor in last 12 months	Did not visit doctor in last 12 months	322	79 (24.5)	1
	Less than monthly	806	342 (42.4)	2.27 (1.70-3.03)**
	1-3 times a month/ At least once a week	75	34 (45.3)	2.55 (1.51-4.29)**
Diabetes Mellitus	Yes	69	25 (36.2)	0.93 (0.56-1.94)
	No	1134	430 (37.9)	1
High cholesterol	Yes	31	9 (29.0)	0.67 (0.30-1.46)
	No	1172	446 (38.1)	1
Cardiovascular disease	Yes	31	14 (45.2)	1.37 (0.66-2.80)
	No	1172	441 (37.6)	1
Prescribed Medicines	Yes	226	115 (50.9)	1.94 (1.45-2.60)**
	No	977	340 (34.8)	1
Knowledge of HS	No	174	19 (10.9)	1
	Yes	1029	436 (42.7)	6.00 (3.67 – 9.81)**

Notes. *P<.05 **p<.01

Table 4.8: Adjusted odds ratios for HS use, cross-sectional study of HS use and HS-related adverse events, Dubai, 2015 (N=1203)

Variables	**AOR (95%CI)**
Gender	
Male	1
Female	3.26 (2.26-4.70)**
Nationality	
Emirati	0.55 (0.30-1.00)*
Middle East/North Africa	0.66 (0.39-1.12)
South Asia	0.51 (0.28-0.93)*
East Asia/Pacific/Central Asia/Europe	1.16 (0.53-2.52)
Africa	0.50 (0.21-1.22)
Latin America/Caribbean/Western Europe/North America/ Australia	1
Income	
<5000 AED	1
5000-<10000 AED	1.18 (0.71-1.98)
>10000-20000 AED	1.83 (0.98-3.41)
>20000 AED	2.41 (1.20-4.83)*
Allergy	
Yes	1.75 (1.14-2.66)*
No	1
Smoking status	
Non-smoker	1
Past smoker	2.39 (1.27-4.48)**
Current occasional smoker	0.85 (0.52-1.36)
Current regular smoker	0.93 (0.64-1.36)
Visited to a doctor in last 12 months	
Did not visit doctor in last 12 months	1
Less than monthly	1.37 (0.96-1.94)
1-3 times a month/ At least once a week	1.86 (1.02-3.39)*
Prescribed Medicines	
Yes	1.47 (1.04-2.06)*
No	1
Knowledge of HS	
Yes	3.91 (2.26-6.76)**
No	1

Notes. Stepwise regression method was applied to identify significant correlates ($p<0.10$) of HS use *$P<0.05$, **$p<0.01$

4.1.7 Factors associated with adverse events

The factors associated with adverse events of HS are as shown in Table 4.9. The average age of participants who experienced an adverse event was 39.3. There was no effect of age found on the occurrence of an adverse event (P=0.533). Male participants experienced adverse events more than female participants. Of the 322 male participants, 11 (3.4%) experienced adverse events. Of the 133 female participants, only two (1.5%) experienced adverse events. There was no effect of gender on the occurrence of an adverse event (P=0.363).

Of the 379 married participants, only 10 (2.6%) and of the 69 single participants, only three (4.3%) experienced adverse events. Among the seven divorced/ widowed participants, none experienced adverse events. There was no effect of marital status on the occurrence of an adverse event (P=0.538).

In terms of nationality, of the participants, three UAE nationals (4.1%), five Middle East/ North Africa nationals (3.5%), two South Asia nationals (1.4%), one African national (7.1%) and two Latin America/ Caribbean/ Western Europe/ North America/ Australia nationals (3.3%) experienced adverse events. No East Asia/ Pacific/ Central Asia/ Europe national participant experienced adverse events. There was no effect of nationality on the occurrence of an adverse event (P=0.467).

Among 413 employed, 35 unemployed and seven students or retired participants,12 (2.9%) from employed, and one (2.9%) from unemployed participants experienced adverse events. No student or retiree experienced adverse events. There was no effect of occupation on the occurrence of an adverse event (P=1.0).

Participants who had an income greater than 10,000 to 20,000 AED experienced more adverse events: eight participants (5.2%) of 153. Four participants (3.3%) had an income greater than 20,000 AED and one participant (0.7%) had an income of between 5,000 and 10,000 AED experienced adverse events. No participant experienced an adverse event and had an income less than 5,000 AED. There was no effect of income on the occurrence of an adverse event (P=0.088).

In terms of educational level, of the total 13 recorded adverse events, one was experienced by a participant who had a diploma, seven were experienced by participants who had a bachelor's degree, and five were experienced by participants who were of post graduate level. There was no effect of education on the occurrence of an adverse event (P=0.667).

Among the 455 participants who had ever used HS, 403 had insurance cover. Of the 13 participants who experienced adverse events, 12 had insurance coverage. There was no effect of insurance coverage on the occurrence of an adverse event (P=1.0). The adverse events rate was higher in participants with normal body mass index (BMI) (<25 kg/m^2), seven of 165 (4.2%). The BMI mean was 27.1 ± 2.1 SD. BMI showed no effect on the occurrence of an adverse event (P=0.922).

The smoking status of the participant did not play a role in the occurrence of adverse events. Of this group, eight non-smokers (2.5%), two past smokers (7.4%), two current regular smokers (2.9%) and one current occasional smoker (2.9%) experienced adverse events. Smoking status showed no effect on the occurrence of an adverse event (P=0.321).

In terms of allergic status, of the 57 participants who had an allergy, only two experienced an adverse event (3.5%). Of the 455 participants who had ever used HS,

13 were allergic to drugs. Of these, two experienced adverse events (15.4%). There was an effect of drug allergy on the occurrence of an adverse event (P=0.049).

Of the participants who experienced adverse events, nine (2.6%) who had visited a doctor, saw a doctor in a frequency of less than a month. Two (5.9%) who had visited a doctor one to three times a month/ at least once a week, saw a doctor in a frequency of one to three times a month/ at least once a week. Two (2.5%) who did not visit a doctor in the last 12 months, did not see a doctor in the last 12 months. There was no effect of visiting the doctor on the occurrence of an adverse event (P=0.449).

Participants who experienced an adverse event did not suffer from any common major disease like diabetes mellitus, high cholesterol levels or cardiovascular disease. There was no effect of disease on the occurrence of an adverse event (P=1.0). Participants who experienced an adverse event and who were taking medicine numbered five (4.3%). There was no effect of taking medicines on the occurrence of an adverse event (P=0.329).

4.1.8 Factors associated with health supplement knowledge

Table 4.10 shows the association between knowledge of HS and selected socio-demographic and other characteristics of respondents where knowledge is defined by an affirmative answer to the question: Do you know what health supplements are? Overall, 1,029 (86%) respondents knew what HS were. There was a significant positive association between knowledge and female gender. Those of south Asian nationality, on lower income, with lower educational attainment, lacking health insurance and who had not visited a doctor were less likely to report familiarity with HS.

Table 4.9: Factors associated with adverse events

Variables	**All** N	**Adverse events** n (%)	**No adverse events** n (%)	**P Value**
Age – years	455	38.0±5.0	38.9±9.1	0.533
Gender				0.363
Male	322	11 (3.4)	311 (96.6)	
Female	133	2 (1.5)	131 (98.5)	
Marital Status				
Married	379	10 2.6()	369 (97.4)	0.538
Single	69	3 (4.3)	66 (95.6)	
Divorced/Widow/er	7	0 (0.0)	7 (100.0)	
Nationality				0.467
Emirati	68	3(4.1)	65 (95.6)	
Middle East/ North Africa	144	5(3.5)	139 (96.5)	
South Asia	141	2(1.4)	139 (98.6)	
East Asia/ Pacific/ Central Asia/ Europe	28	0(0.0)	28 (100.0)	
Africa	14	1(7.1)	13 (92.9)	
Latin America/Caribbean/Western Europe/North America/Australia	60	2(3.3)	58 (96.7)	
Occupation				1.000
Employed	413	12 (2.9)	401 (97.1)	
Unemployed	35	1 (2.9)	34 (97.1)	
Student/Retired	7	0 (0.0)	7 (100.0)	
Income				0.088
<5000 AED	33	0 (0.0)	33 (100.0)	
5000-<10000 AED	149	1 (0.7)	148 (99.3)	
10000-20000 AED	153	8(5.2)	145(94.8)	
>20000 AED	120	4 (3.3)	116 (96.7)	
Education				0.667
< High school	13	0 (0.0)	13 (100.0)	
High school	39	0 (0.0)	39 (100.0)	
Diploma	18	1 (5.6)	17 (94.4)	
Higher Diploma	22	0 (100.0)	22 (100.0)	
Bachelor	245	7 (2.9)	238 (97.1)	
Master/PhD	118	5 (4.2)	113 (95.8)	
Health insurance coverage				1.00
Yes	403	12 (3.0)	391 (97.0)	
No	52	1 (1.9)	51 (98.1)	
Body Mass Index – kg/m2	1203	27.1±2.1	26.9±0.2	0.922
Body Mass Index – cat				
Normal (<25 kg/m2)	165	7 (4.2)	158 (95.8)	
Overweight (25-29.9 kg/m2)	198	3 (1.5)	195 (98.5)	
Obese (≥30 kg/m2)	92	3 (3.3)	89 (96.7)	
Smoking status				0.321

Table 4.9: Factors associated with adverse events (Continued)

Variables	**All** N	**Adverse events** n (%)	**No adverse events** n (%)	**P Value**
Non-smoker	326	8 (2.5)	318 (97.5)	
Past smoker	27	2 (7.4)	25 (92.6)	
Current occasional smoker	34	1 (2.9)	33 (97.1)	
Current regular smoker	68	2 (2.9)	66 (97.1)	
Any allergy	57	2 (3.5)	55 (96.5)	0.654
Drug allergy	13	2 (15.4)	11 (84.6)	0.049
Aerosol & perfume allergy	7	0 (0.0)	7 (100.0)	1.00
Contact allergy	7	0 (0.0)	2 (100.0)	1.00
Dust allergy	7	0 (0.0)	7 (100.0)	1.00
Visited a doctor in last 12 months				0.449
Did not visit doctor in last 12 months	79	2 (2.5)	77 (97.5)	
Less than monthly	342	9 (2.6)	333 (97.4)	
1-3 times a month/At least once a week	34	2 (5.9)	32 (94.1)	
Diseases				
Diabetes Mellitus	9	0 (0.0)	9 (100.0)	1.00
High cholesterol levels	25	0 (0.0)	25 (100.0)	1.00
Cardiovascular disease	14	0 (0.0)	14 (100.0)	1.00
Medicines	115	5 (4.3)	110 (95.7)	0.329

Table 4.10: Factors associated with health supplement knowledge

Variables	**All (455)**	**Knowledge (n=1029)** n (%)	**No Knowledge (n=174)** n (%)	**P Value**
Age – years	1203	39.3±0.3	38.7±0.7	0.365
Gender				<0.001
Male	1002	837 (83.5)	165 (16.5)	
Female	201	192 (95.5)	9 (4.5)	
Marital Status				0.282
Married	1039	884 (85.1)	155 (14.9)	
Single	150	131 (87.3)	19 (12.7)	
Divorced/Widow/er	14	14 (100.0)	0 (0.0)	
Nationality				<0.001
Emirati	142	131 (92.3)	11 (7.7)	
Middle East/North Africa	301	287 (95.3)	14 (4.7)	
South Asia	579	443 (76.5)	136 (23.5)	
East Asia/Pacific/Central Asia/Europe	53	48 (90.6)	5 (9.4)	
Africa	32	31 (96.9)	1 (3.1)	
America/Caribbean/Western Europe/Australia	96	89 (92.7)	7 (7.3)	
Occupation				0.067
Employed	1123	954 (84.9)	169 (15.1)	
Unemployed	60	57 (95.0)	3 (5.0)	
Student/Retired	20	18 (90.0)	2 (10.0)	
Income				<0.001
<5000 AED	164	85 (51.8)	79 (48.2)	
5000-<10000 AED	499	440 (88.2)	59 (11.8)	
10000-20000 AED	319	296 (92.8)	23 (7.2)	
>20000 AED	221	208 (94.1)	13 (5.9)	
Education				<0.001
< High school	76	26 (34.2)	50 (65.8)	
High school	139	102 (73.4)	37 (26.6)	
Diploma	68	60 (88.2)	8 (11.8)	
Higher Diploma	46	41 (89.1)	5 (10.9)	
Bachelor	586	542 (92.5)	44 (7.5)	
Master/PhD	286	258 (89.6)	30 (10.4)	
Health insurance coverage				<0.001
Yes	1028	897 (87.3)	131 (12.7)	
No	175	132 (75.4)	43 (24.6)	
Body Mass Index – kg/m^2		26.8±0.1	26.3±0.3	0.104
Body Mass Index – cat				0.367
Normal (<25 kg/m^2)	431	362 (84.0)	69 (16.0)	
Overweight (25-29.9 kg/m^2)	546	468 (85.7)	78 (14.3)	
Obese (≥30 kg/m^2)	226	199 (88.1)	27 (11.9)	

Table 4.10: Factors associated with health supplement knowledge (Continued)

Variables	**All (455)**	**Knowledge (n=1029)** n (%)	**No Knowledge (n=174)** n (%)	**P Value**
Smoking status				0.320
Non-smoker	862	733 (85.0)	129 (15.0)	
Past smoker	50	43 (86.0)	7 (14.0)	
Current occasional smoker	108	89 (82.4)	19 (17.6)	
Current regular smoker	183	164 (89.6)	19 (10.4)	
Any allergy				0.323
Yes	115	102 (88.7)	13 (11.3)	
No	1081	922 (85.3)	159 (14.7)	
Visited to a doctor in last 12 months				<0.001
Did not visit doctor in last 12 months	322	230 (71.4)	92 (28.6)	
Less than monthly	806	732 (90.8)	74 (9.2)	
1-3 times a month/At least once a week	75	67 (89.3)	8 (10.7)	
Diseases				
Diabetes Mellitus				0.156
Yes	69	55 (79.7)	14 (20.3)	
No	1134	974 (85.9)	160 (14.1)	
High cholesterol levels				0.299
Yes	31	29 (93.5)	2 (6.5)	
No	1172	1000 (85.3)	172 (14.7)	
Cardiovascular disease				0.073
Yes	31	30 (96.8)	1 (3.2)	
No	1172	999 (85.2)	173 (14.8)	
Medicines				0.233
Yes	226	199 (88.1)	27 (11.9)	
No	977	830 (84.9)	147 (15.1)	

Respondent knowledge of HS stratified by information source (prescription advice) is shown in Table 4.11. The impact of information source on knowledge of HS among different demographic variables was investigated by askingthe participants who had advised them to take HS. A statistically significant difference was found in the knowledge between males and females when the information sources were self-recommendation and prescription (P<0.001), (P=0.004), respectively. A similar pattern of results was observed in employment status (P=0.004), (P=0.001) and

education level (P<0.001), (P<0.001), respectively. Age of the respondents also showed a statistically significant difference in knowledge when the sources of information were relatives and healthcare personnel (P=0.011), (P<0.006), respectively.

The nationality of the respondents also showed a statistically significant difference in knowledge when the source of information was self-recommendation (P=0.014), relatives (P=0.029), prescription (P<0.001), and healthcare personnel (P<0.001). Moreover, a statistically significant difference was found in the knowledge of respondents and their monthly income when the information sources were prescription (P=0.010) and healthcare personnel (P=0.026). A similar pattern of results was observed in health insurance coverage variable (P=0.022), (P=0.030), respectively. BMI, as a continuous variable, showed a statistically significant difference in the knowledge of HS when the information source was self-recommendation (P=0.043). Also, when BMI was converted and categorised, a statistically significant difference was found in the knowledge of the respondents when the information source was the internet (P=0.027). In relation to smoking status, respondents showed a significant difference in the knowledge of HS when they obtained their information from the internet (P=0.022).

Regarding visiting the doctor in the last 12 months, respondents showed a statistically significant difference in the knowledge of HS when the source of information towards HS was self-recommendation (P=0.008), internet (P=0.001) and prescription (P=0.014). Among co-morbidities (chronic medical conditions) respondents suffering from only diabetes mellitus showed a statistically significant difference in the knowledge of HS when the source of information towards HS was

prescription (P=0.002). When the respondents were asked about medication history, a statistically significant difference in the knowledge of HS was observed among the respondents when the sources of information towards HS were self-recommendation and prescription (P<0.001), (P<0.001), respectively. Conversely, there was no statistically significant difference in the knowledge of HS in other demographic specifications (marital status, allergy history) and source of information towards HS.

Table 4.11: Knowledge by prescription advice

Variables	All (455)	Self (n=204)	P Value	Relative (n=35)	P Value	Internet (n=30)	P Value	Prescribed (n=212)	P Value	Health professional (n=49)	P Value
		n (%)		n (%)		n (%)		n (%)		n (%)	
Age – years	455	38.9±0.6	0.995	35.1±4.5	0.011	37.3±1.3	0.328	39.2±9.7	0.511	42.2±1.3	0.006
Gender			<0.001		0.445		0.303		0.004		0.373
Male	322	162 (50.3)		27 (8.4)		24 (7.5)		136 (42.2)		32 (9.9)	
Female	133	42 (31.6)		8 (6.0)		6 (4.5)		76 (57.1)		17 (12.8)	
Marital Status			1.00		0.343		0.609		0.266		0.839
Married	379	170 (44.9)		27 (7.1)		26 (6.7)		181 (47.8)		42 (11.1)	
Single/Divorced/Widow/er	69	34 (44.7)		8 (10.5)		4 (5.3)		31 (40.8)		7 (9.1)	
Nationality			0.014		0.029		0.139		<0.001		<0.001
Emirati	68	27 (39.7)		9 (13.2)		4 (5.9)		38 (55.9)		2 (2.9)	
Middle East/North Africa	144	60 (41.7)		12 (8.3)		10 (6.9)		67 (46.5)		24 (16.7)	
South Asia	148	56 (39.7)		4 (2.8)		5 (3.5)		82 (58.2)		3 (2.1)	
East Asia/Pacific/Central Asia/Europe	28	20 (71.4)		4 (14.3)		4 (14.3)		3 (10.7)		4 (14.3)	
Africa	14	8 (57.1)		2 (14.3)		0 (0.0)		4 (28.6)		2 (14.3)	
America/Caribbean/Western Europe/Australia	60	33 (55.0)		4 (6.7)		7 (11.7)		18 (30.0)		14 (23.3)	
Occupation			0.004		0.759		0.097		0.001		1.000
Employed	413	194 (47.0)		33 (8.0)		30 (7.3)		182 (44.1)		45 (10.9)	
Other	42	10 (23.8)		2 (4.8)		0 (0.0)		30(71.4)		4 (9.5)	
Income			0.156		0.701		0.293		0.010		0.026
<5000 AED	33	9 (27.3)		1 (3.0)		2 (6.1)		23 (69.7)		2 (6.1)	

Table 4.11: Knowledge by prescription advice (Continued)

Variables	All (455)	Self (n=204)	P Value	Relative (n=35)	P Value	Internet (n=30)	P Value	Prescribed (n=212)	P Value	Health professional (n=49)	P Value
5000-<10000 AED	149	67 (45.0)		10 (6.7)		7 (4.7)		72 (48.3)		8 (5.4)	
>10000-20000 AED	153	75 (49.0)		13 (8.5)		15 (9.8)		59 (38.6)		22 (14.4)	
>20000 AED	120	53 (44.2)		11 (9.2)		6 (5.0)		58 (48.3)		17 (14.2)	
Education			<0.001		0.123		0.967		<0.001		0.385
≤ Higher Diploma	92	29 (31.5)		11 (12.0)		6 (6.5)		52 (56.5)		11 (12.0)	
Bachelor	245	101 (41.2)		19 (7.8)		17 (6.9)		123 (50.2)		22 (9.0)	
Master/PhD	118	74 (62.7)		5 (4.2)		7 (5.9)		37 (31.4)		16 (13.6)	
Health insurance coverage			0.326		1.00		0.558		0.022		0.030
Yes	403	184 (45.7)		31 (7.7)		28 (6.9)		180 (44.7)		48 (11.9)	
No	52	20 (38.5)		4 (7.7)		2 (3.9)		32 (61.5)		1 (1.9)	
Body Mass Index – kg/m2		27.4±0.3	0.043	25.9±1.0	0.157	25.6±0.8	0.089	26.9±4.4	0.885	26.7±0.6	0.695
Body Mass Index – cat			0.069		0.089		0.027		0.126		0.604
Normal	165	71 (43.0)		19 (11.5)		18 (10.9)		70 (42.4)		21 (12.7)	
Overweight	198	82 (41.4)		11 (5.6)		8 (4.0)		103 (52.0)		20 (10.1)	
Obese	92	51 (55.4)		5 (5.4)		4 (4.3)		39 (42.4)		8 (8.7)	
Smoking status			0.128		0.096		0.022		0.155		0.742
Non-smoker	326	135 (41.4)		21 (6.4)		21 (6.4)		160 (49.1)		36 (11.0)	
Past smoker	27	15 (55.6)		5 (18.5)		5 (18.5)		11 (40.7)		2 (7.4)	
Current occasional smoker	34	19 (55.9)		4 (11.8)		3 (8.8)		10 (29.4)		2 (5.9)	
Current regular smoker	68	35 (51.5)		5 (7.3)		1 (1.5)		31 (45.6)		9 (13.2)	
Any allergy			0.690		1.00		1.000		0.693		1.00
Yes	57	27 (47.4)		31 (7.9)		3 (5.3)		183 (46.3)		6 (10.5)	
No	395	176 (44.6)		4 (7.0)		37 (6.8)		28 (49.1)		43 (10.9)	
Visited to a doctor in last 12 months			0.008		0.062		0.001		0.014		0.137

Table 4.11: Knowledge by prescription advice (Continued)

Variables	All (455)	Self (n=204)	P Value	Relative (n=35)	P Value	Internet (n=30)	P Value	Prescribed (n=212)	P Value	Health professional (n=49)	P Value
Did not visit doctor in last 12 months	79	47 (59.5)		9 (11.4)		13 (16.5)		25 (31.7)		4 (5.1)	
Less than monthly	342	146 (42.7)		21 (6.1)		14 (4.1)		170 (49.7)		40 (11.7)	
1-3 times a month/At least once a week	34	11 (32.3)		5 (14.7)		3 (8.8)		17 (50.0)		5 (14.7)	
Diseases											
Diabetes Mellitus			0.099		0.244		1.000		0.002		0.502
Yes	25	7 (28.0)		0 (0.0)		0 (0.0)		19 (76.0)		1 (4.0)	
No	430	197 (45.8)		35 (8.1)		30 (6.7)		193 (44.9)		48 (11.2)	
High cholesterol levels			0.196		1.00		3.96		0.089		0.606
Yes	9	2 (22.2)		0 (0.0)		0 (0.0)		205 (46.0)		0 (0.0)	
No	446	202 (45.3)		35 (7.9)		30 (7.0)		7 (77.8)		49 (11.0)	
Cardiovascular disease			0.591		0.614		0.613		0.276		0.381
Yes	14	5 (35.7)		0 (0.0)		0 (0.0)		9 (64.3)		0 (0.0)	
No	441	199 (45.1)		35 (7.9)		30 (6.8)		203 (46.0)		49 (11.1)	
Medicines			<0.001		0.156		0.830		<0.001		0.407
Yes	115	35 (30.4)		5 (4.3)		8 (7.0)		73 (63.5)		39 (11.5)	
No	340	169 (49.7)		30 (8.8)		22 (6.5)		139 (40.9)		10 (8.7)	

4.1.9 Risk assessment of health supplement use

Respondents' HS use were assigned a risk score based on the activity of the ingredient and the frequency of use. Scores ranged from one to a maximum of 12. Data were available to assign scores to 408 HS users in this way. Scores were then arranged into three categories or tertiles. Tertile one represented HS use with the lowest risk, tertile two represented HS use with an intermediate risk, while tertile three represented HS use with the highest risk. Overall, 148 (36.3%) of participants consumed HS with ingredients within the lowest risk tertile, 219 (53.7%) of participants consumed HS with ingredients within the intermediate risk tertile, and 41 (10.1%) of participants consumed HS with ingredients within the highest risk tertile. HS use in each risk tertile is shown in Table 4.12 by selected socio-demographic and other characteristics of the respondents.

Gender, income, smoking status, having allergy, having high cholesterol, HS capsule-form consumption, purchasing from clinic are significantly associated with HS risk. Compared to males, females were more likely to consume HS in the intermediate risk tertile. Those earning between 5,000 and 10,000 AED were more likely to be in the higher risk categories. Past smokers, those who consumed their HS in capsule-form and those who obtained their HS from a clinic were more likely to be in the high risk tertile, while those with an allergy or high cholesterol were more likely to be in the low risk tertile, although numbers were small.

Table 4.12: Health supplement risk tertile by characteristics of participants

Variables		Lowest Tertile n%	Middle Tertile n%	Highest Tertile n%	P Value
All		148 (36.3)	219 (53.7)	41 (10.1)	
Age – years		39.0±8.7			
Gender	Male	120 (42.4)	129 (45.6)	34 (12.0)	<0.001
	Female	28 (22.4)	90 (72.0)	7 (5.6)	
Marital Status	Married	131 (38.8)	174 (51.5)	33 (9.8)	0.064
	Other	17 (24.3)	45 (64.3)	8 (11.4)	
Nationality	Emirati	27 (41.5)	35 (53.9)	3 (4.6)	0.239
	Non-Emirati	121 (35.3)	184 (53.6)	38 (11.1)	
Occupation	Employed	134 (36.6)	192 (52.5)	40 (10.9)	0.148
	Other	14 (33.3)	27 (64.3)	1 (2.4)	
Income (AED)	<5000	16 (55.2)	12 (41.4)	1 (3.4)	0.042
	5000-<10000	33 (25.8)	77 (60.2)	18 (14.1)	
	10000-20000	54 (39.1)	71 (51.5)	13 (9.4)	
	>20000	45 (39.8)	59 (52.2)	9 (8.0)	
Education	≤ Higher Diploma	38 (46.9)	35 (43.2)	8 (9.9)	0.093
	Bachelor	80 (35.9)	124 (55.6)	19 (8.5)	
	Master/PhD	30 (28.9)	60 (57.7)	14 (13.5)	
Health insurance coverage	Yes	136 (25.5)	189 (63.8)	36 (10.6)	0.261
	No	12 (37.7)	30 (52.3)	5 (10.0)	
BMI – kg/m2 (cat)	Normal	51 (38.6)	70 (53.0)	11 (8.3)	0.261
	Overweight	62 (32.3)	105 (54.7)	25 (13.0)	
	Obese	35 (41.7)	44 (52.4)	5 (6.0)	
Smoking status	Non-smoker	95 (33.0)	167 (58.0)	26 (9.0)	0.049
	Past smoker	8 (33.0)	10 (41.7)	6 (25.0)	
	Current occasional	15 (50)	12 (40.0)	3 (10.0)	
	Current regular	30 (45.5)	30 (45.5)	6 (9.0)	
Any allergy	Yes (n=53)	29 (54.7)	20 (37.7)	4 (7.5)	0.013
	No (n=352)	117 (33.2)	199 (56.5)	36 (10.2)	
Visited to a doctor in last 12 months	No doctor visits in last 12 months	23 (34.3)	39 (58.2)	5 (7.5)	0.524
	Less than monthly	119 (37.8)	163 (51.7)	33 (10.5)	
	At least once a month/week	6 (23.1)	17 (65.4)	3 (11.5)	

Table 4.12: Health supplement risk tertile by characteristics of participants (Continued)

Variables			Lowest Tertile n%	Middle Tertile n%	Highest Tertile n%	P Value
Diabetes Mellitus		Yes	10 (43.5)	11 (47.8)	2 (8.7)	0.760
		No	138 (35.8)	208 (54.0)	39 (10.1)	
High cholesterol		Yes (n=8)	7 (87.5)	1 (12.5)	0 (0.0)	0.010
		No (n=400)	141 (35.3)	218 (54.4)	41 (10.3)	
Cardiovascular disease		Yes	4 (30.8)	8 (61.5)	1 (7.7)	0.914
		No	144 (36.5)	211 (53.4)	40 (10.1)	
Medicines		Yes (n=109)	32 (29.4)	68 (62.4)	9 (8.3)	0.103
		No (n=299)	116 (38.8)	151 (50.5)	32 (10.7)	
Adverse events		Yes (n=13)	8 (61.5)	5 (38.5)	0 (0.0)	0.144
		No (n=395)	140 (35.4)	214 (54.2)	41 (10.4)	
Forms of HS	Tablet	Yes (n=349)	130 (37.2)	189 (54.1)	30 (8.6)	0.055
		No (n=59)	18 (30.5)	30 (50.9)	11 (18.6)	
	Capsule	Yes (n=47)	10 (21.3)	21 (44.7)	16 (34.0)	<0.001
		No (n=361)	138 (28.2)	198 (54.9)	25 (6.9)	
	Powder	Yes (n=40)	16 (40.0)	22 (55.0)	2 (5.0)	0.588
		No (n=368)	132 (35.9)	197 (53.5)	39 (10.6)	
Purchase of HS	Pharmacy	Yes (n=360)	133 (36.9)	193 (53.6)	34 (9.4)	0.474
		No (n=48)	15 (31.3)	26 (54.2)	7 (14.6)	
	Clinic	Yes (n=43)	16 (37.2)	18 (41.9)	9 (20.9)	0.041
		No (n=365)	132 (36.2)	201 (55.1)	32 (8.8)	
	Nutrition shop	Yes (n=28)	7 (25.0)	17 (60.7)	4 (14.3)	0.366
		No (n=408)	141 (37.1)	202 (53.2)	37 (9.7)	
Advise of using HS	Self	Yes (n=175)	66 (37.7)	87 (49.7)	22 (12.6)	0.222
		No (n=233)	82 (35.2)	132 (56.7)	19 (8.1)	
	Friend/Relative	Yes (n=27)	11 (40.7)	15 (55.6)	1 (3.7)	0.616
		No (n=381)	137 (36.0)	204 (53.4)	40 (10.5)	
	Internet	Yes (n=22)	7 (31.8)	11 (50.0)	4 (18.2)	0.424
		No (n=386)	141 (36.5)	208 (53.9)	37 (9.6)	
	Prescribed	Yes (n=198)	76 (38.4)	106 (53.5)	16 (8.1)	0.381
		No (n=210)	72 (34.3)	113 (53.8)	25 (11.9)	
	Health Professional	Yes (n=45)	13 (28.9)	27 (60.0)	5 (11.1)	0.550
		No (n=363)	135 (37.2)	192 (52.9)	36 (9.9)	

Figure 4.1 shows a flow chart of the total number of participants in the n survey. Among a total of 1203 participants 455 consumed HS of whom 13 experienced adverse events. Of those who experienced adverse events, three visited a healthcare centre which proved the adverse event to be associated with the consumption of HS. All three reported the adverse events.

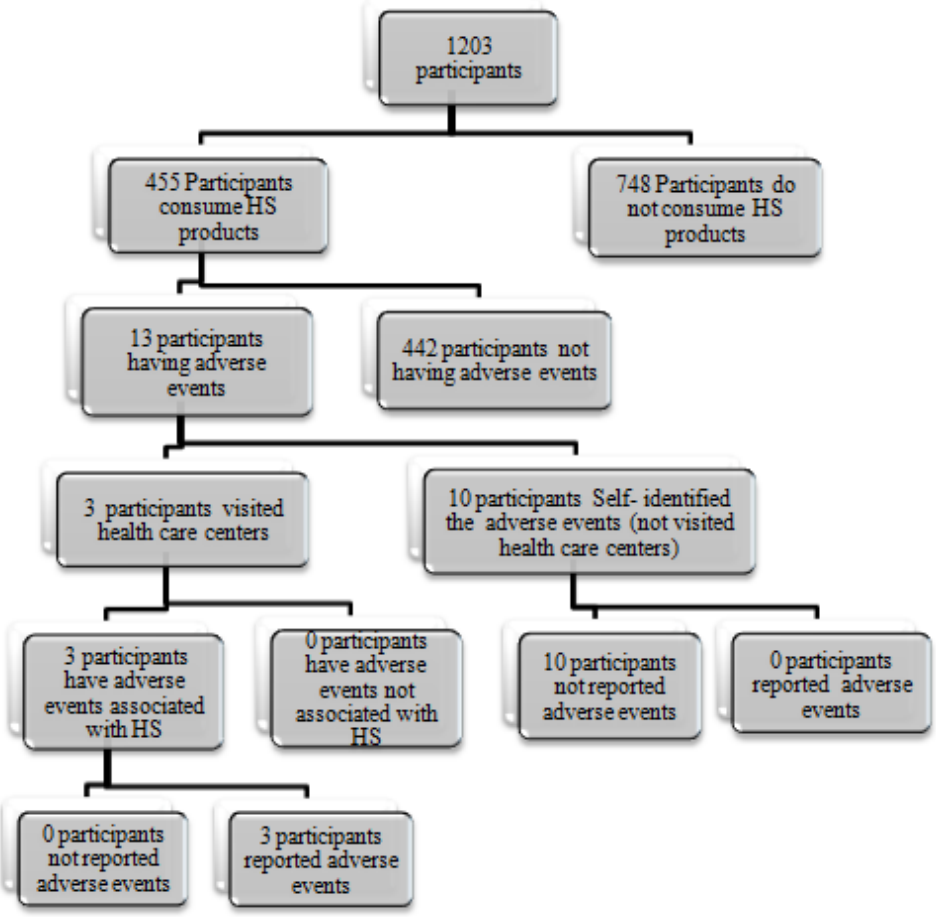

Figure 4.1: Structure of observed outcomes for population survey

4.2 Results of Second Study: Cross-Sectional Study Among Healthcare Professionals

This cross-sectional study was conducted among physicians and pharmacists in Dubai both registered with Dubai Health Authority and those working in the private sector. A total of 427 participants responded to the on-line questionnaire. Of those,

205 (48%) were pharmacists, 49 (11.47%) were physicians and 173 (40.5%) were other healthcare professionals.

4.2.1 Demographic characteristics

Among the 427 respondents, there was a relative equality of numbers in terms of gender: 221 (51.75%) were male and 206 (48.2%) were female. Mean age was 35.43 (SD ±8.43) with a range of 22-67. The socio-demographic characteristics of participants are shown in Table 4.13.

Table 4.13: Demographic characteristics of healthcare professionals

Demographic	N (%)
Age	(22 -67)
Mean age ± S.D	(35.43±8.43)
Gender	
Male	221 (51.75%)
Female	206 (48.2%)
Nationality	
Emirati	69 (16.2%)
Middle East/North Africa	47 (11%)
South Asia	260 (60.8%)
East Asia/Pacific	32 (7.5%)
Central Asia/Europe	1 (0.23%)
Africa	12 (2.8%)
Western Europe/North America/Australia	2 (0.46%)
Not specific	4 (0.93%)
Marital status	
Married	315 (73.77%)
Single	103 (24.12%)
Divorced	6 (1.41%)
Widow	3 (0.7%)
Employment status	
Government	161 (37.7%)
Private	264 (61.8%)
Self-employed	2 (0.5%)
Occupation	
Specialised physician	32 (7.5%)
Physician	17 (4.0%)
Pharmacist	192 (45.0%)
Assistant pharmacist	13 (3%)
Other	173 (40.5)
Work experience	
1-2 years	62 (14.5%)
3-4 years	60 (14.1%)
5-6 years	47 (11.0%)
Less than 1 year	19 (4.4%)
More than 6 years	239 (56.0%)
Insurance coverage	
Yes	405 (94.8%)
No	22 (5.2%)
Education	
Graduate	273 (63.9%)
Post graduate	154 (36.1%)

4.2.2 Knowledge on health supplements

Table 4.14 summarises healthcare professionals' knowledge of HS, HS safety, HS adverse events and adverse event reporting. Of the participants, 352 (82.4%) knew what HS are and 183 (42.9%) believed HS to beharmless. Around half, 192 (45.0%) knew what a reporting system was, but fewer could identify reporting systems either within the UAE or within their organization. Around 40% had attended educational sessions on HS and read journal articles, but only about a quarter knew how to report adverse events or had training on the process.

Table 4.14: Descriptive data on healthcare professional's knowledge

Knowledge on HS	**N (%)**	
Do you know what HS are (n=427)	Yes	352 (82.4%)
	No	75 (17.5%)
Do you agree with the statement that HS are harmless (n=427)	Yes	183(42.9%)
	No	244 (57.1%)
Do you know what reporting system is (n=427)	Yes	192 (45.0%)
	No	235 (55%)
Do you know about any existing reporting system in the UAE (n=192)	Yes	68 (35.4%)
	No	124 (64.6%)
Do you know about any AE reporting system in your organization (n=427)	Yes	96 (22.5%)
	No	331 (77.5%)
Do you know to whom you can report an AE (n=427)	Yes	112 (26.2%)
	No	315 (73.77%)
Have you ever received any continuing education on HS products (n=427)	Yes	191 (44.7%)
	No	236 (55.3%)
Have you read a scientific article related to AE of HS in the last 6 months (n=427)	Yes	189 (44.3%)
	No	238 (55.7%)
Have you ever received training on how to report an AE (n=427)	Yes	108 (25.3%)
	No	319 (74.7%)

Table 4.15 shows that around two-thirds of respondents (277, 65%) reported that they knew of adverse events associated with HS use and could list common adverse events.

Table 4.15: Health supplement adverse events reported by respondents

Adverse events		**N (%)**
Do you know about adverse events of HS (n=427)	Yes	277 (64.9%)
	No	150 (35.1%)
Adverse events (n=277)		
Adverse event	**N (%)**	**Adverse event**	**N (%)**
Abdominal pain	179 (64.6%)	Headache	120 (43.32%)
Anorexia	57 (20.57%)	Hypertension	84 (30.32%)
Anxiety	59 (21.29%)	Hypotension	47 (16.96%)
Chest pain	32 (11.55%)	Muscle cramping	54 (19.49%)
Convulsions	27 (9.74%)	Muscle pain	35 (12.63%)
Dermatitis	65 (23.46%)	Nausea	169 (61.01%)
Diarrhoea	179 (64.6%)	Palpitations	89 (32.12%)
Dizziness	93 (33.57%)	Pyrexia	13 (4.69%)
Dyspnea	25 (9.02%)	Sedation	58 (20.93%)
Edema	45 (16.24%)	Tingling	25 (9.02%)
Fatigue	70 (25.27%)	Urticaria	94 (33.93%)
Hair loss	61 (22.02%)	Vomiting	150 (54.15%)

Among the 191 healthcare professionals who reported that they have received one or more types of continuing education on HS products, 120 (63%) reported that they had official training courses, 118 (62%) reported that had workshops on product orientation, and 108 (56%) reported their continuing education on HS products through electronic learning.

4.2.3 Practice towards health supplements

Table 4.16 summarises healthcare professionals' practice with respect to selling, prescribing and dispensing HS, types of HS and dosage, record keeping and discussions with patients/consumers.

A total of 232 respondents (54.3%) prescribed or dispensed HS. Most commonly these were vitamins, herbal supplements, and minerals. Tablets (n=165, or 71.12%), soft gels (n=160, or 68.96%), capsules (n=151, or 65.08%), chews/gummies (n=128, or 55.17%), chewable tablets (n=126, or 54.31%) and caplets (n=126, or 54.31%) were the most identified formulations. 41.81% of the participants stated that they had a system to record HS use. Most respondents (195, 85%) always or often discuss HS use with their patients/customers and product effect is the most discussed topic. The Internet was the most used source of information on HS. Literacy was cited as the most important barrier limiting discussion between practitioners and patients/customers.

Table 4.16: Descriptive data on healthcare professionals' practice

Practice		N (%)
Sell/prescribe/dispense HS at practice site (n=427)	Yes	232 (54.3%)
	No	195 (45.7%)
Types of HS prescribed (232)	Dietetic	94 (40.50%)
	Herbal	149 (34.9%)
	Vitamin	221 (64.22%)
	Energy drink	46 (19.82%)
	Mineral	132 (30.9%)
	Food	84 (36.2%)
	Sport nutrition	86 (37.01%)
Dosage forms of HS prescribed (n=232)	Caplets	126 (54.31%)
	Chews/ Gummies	128 (55.17%)
	Gel	46 (19.82%)
	Liquid	102 (43.96%)
	Soft gels	160 (68.96%)
	Vegi-caps	112 (48.27%)
	Capsule	151(65.08%)
	Drink	56 (24.13%)
	Gel caps	49 (21.12%)
	Lozenges	52 (22.41%)
	Spray	31 (13.36%)
	Wafers	32 (13.79%)
	Chewable tablets	126 (54.31%)
	Drops	77 (33.18%)
	Granules	54 (23.27%)
	Powder	98 (42.24%)
	Tablet	165 (71.12%)
Availability of a system to record HS use (n=232)	Yes	97 (41.81%)
	No	135 (58.18%)
Discussion with patients/ consumers on HS (n=232)	Always	111 (47.84%)
	Often	86 (37.06%)
	Sometimes	30 (12.93%)
	Never	5 (2.15%)
Discussion topic of HS use with patients/ customers (n=227)	Product effect	208 (91.62%)
	Product AE	99 (43.61%)
	Product quality	165 (72.68%)
	Product price	91 (40.08%)
Information sources of HS (n=227)	Internet	186 (81.93%)
	Printed material	145 (63.87%)
	Multimedia	73 (32.15%)
Barriers limiting discussing HS with patients/ customers (n=227)	Literacy	100 (44.05%)
	Cultural ethics	45 (19.82%)
	Language	84 (37.0%)
	Social level	63 (27.75%)

Table 4.17 summarises respondents' experience of HS adverse events. Of the 232 who had prescribed HS, 55 (23.70%) of their patients/ customers had experienced an adverse event related to HS use. Of these, 39 (70.90%) occasionally or rarely encountered adverse events while 12 (21.8%) reported frequent encounters. Asthenia (weakness, lack of strength) was the commonest reported event followed by gastrointestinal symptoms. Of the 55 respondents who reported experience of patient adverse events, 24 (44%) never reported them. Only 10 (18%) always reported Patient adverse events. Most reports were made internally within the practitioner's organization, usually to a more senior staff-member. Among the 232 who prescribed or dispensed HS, only 58 (25%) said they had access to reporting forms at work.

4.2.4 Attitude towards health supplement

Table 4.18 summarises respondents' attitude towards the reporting of adverse events associated with HS use. Total 369 respondents (91%) agreed or strongly agreed that adverse events associated with HS use should be reported to a higher authority. The most common reasons given for not reporting was not knowing where to report and difficulty in confirming that an adverse event was related to HS use. There was good agreement on the importance of reporting and of the likely benefits of setting up a reporting system. There were concerns about possible legal problems, but most respondents were confident that they would be able to report an adverse event.

Table 4.17: Reported adverse event related to health supplement

Reported AE related to HS			**N%**
Ever experiencing AE related to HS use in patients/customers during practice (232)		Yes	55 (23.70%)
		No	177 (76.29%)
Frequency of encountering AE related to HS use (55)			
Once			16 (29.09%)
Occasionally			39 (70.90%)
AE	**N%**	**AE**	
Abdominal pain	25 (45.45%)	Edema	1 (1.81%)
Alopecia	4 (7.27%)	Headache	14 (25.45%)
Anorexia	5 (9.09%)	Hypotension	2 (3.63%)
Asthenia	55 (100%)	Nausea	22 (40%)
Chest pain	4 (7.27%)	Pain	2 (3.63%)
Convulsion	1 (1.81%)	Pruritus	4 (7.27%)
Dermatitis	7 (12.72%)	Pyrexia	1 (1.81%)
Diarrhea	18 (32.72%)	Sedation	2 (3.63%)
Dizziness	12 (21.81%)	Urticaria	7 (12.72%)
Dyspnea	5 (9.09%)	Vomiting	14 (25.45%)
How often have you recorded HS AE (55)	Always		10 (18.18%)
	Never		24 (43.63%)
	Often		2 (3.63%)
	Sometimes		19 (34.54%)
Which higher authority did you report HS AE (31)	Ministry of Health		3 (9.67%)
	Senior physician		8 (25.80%)
	Pharmacist in-charge		23 (74.19%)
Availability of AE reporting form at the work (232)	Yes		58 (25%)
	No		138 (59.48%)
	Don’t know		36 (15.51%)

Table 4.18: Descriptive data on healthcare professional's attitude

Attitude		N (%)
Reporting HS related AE to the higher authority (n=427)	Strongly disagree	3 (0.7%)
	Disagree	5 (1.2%)
	Neutral	50 (11.7%)
	Agree	182 (42.6%)
	Strongly agree	187 (43.8%)
Reason of not reporting AE (n=427)	It's not important	20 (4.7%)
	Don't know where to report	172 (40.3%)
	Don't know what is AE of HS	78 (18.3%)
	Concerned that the report is a false alert	38 (8.9%)
	Lack of time to investigate the case	76 (17.8%)
	Consider as extra work	12 (2.8%)
	Difficulty in confirming AE	139 (32.6%)
Importance of reporting all AE of HS (n=330)	No	3 (0.90%)
	Only when hospitalisation is needed	23 (6.96%)
	Only when it is life threatening	16 (4.84%)
	Yes (all)	288 (87.27%)
Establishment of AE reporting system related to HS use (n=330)	Definitely beneficial	271(82.12%)
	Not beneficial	1 (0.30%)
	Not sure	24 (7.27%)
	Somewhat beneficial	34 (10.30%)
Concerning about legal problems of reporting AE (n=330)	Definitely	104 (31.51%)
	Definitely not	21 (6.36%)
	Not	33 (10%)
	Not sure	89 (26.96%)
	Somewhat	83 (25.15%)
Feeling confident when reporting AE (n=330)	Definitely	209 (63.33%)
	Definitely not	1 (0.30%)
	Not	5 (1.51%)
	Not sure	31 (9.39%)
	Somewhat	84 (25.45%)

4.2.5 Overall knowledge, attitude and practice

Based on the questions in Table 4.19, a summary score was created for the KAP of respondents. A correct option scored 1, an incorrect response zero. A total score of 10 was obtainable. For all study participants (427), KAP scores were normally distributed (see Figure 4.2) with a mean score of 4.85 (standard deviation ± 1.88). Scores were grouped into three categories: good (≥7), fair (5-6) and poor (0-4).

(Olowokere et al., 2014). Overall, 78 (18.3%) respondents had good KAP, 166 (39%) had fair KAP, while 166 (40%) had poor KAP.

Table 4.19: Knowledge, attitude, and practice assessment

KAP Items	**N%** Correct answer
Knowing what HS are	352 (82.4%)
Whether HS are harmless	244 (56.7%)
Knowledge about adverse events of HS	277 (64.9%)
Definition of reporting system	192 (45.0%)
Knowing any AE reporting system in organization	96 (22.5%)
Knowing to whom reporting AE	112 (26.2%)
Receiving any continuing education on HS	191 (44.7%)
Reading scientific article related to AE of HS in the last 6 months	189 (44.3%)
Receiving training on how to report an AE	108 (25.3%)
Reporting HS related AE to higher authority/personnel	369 (86.42%)

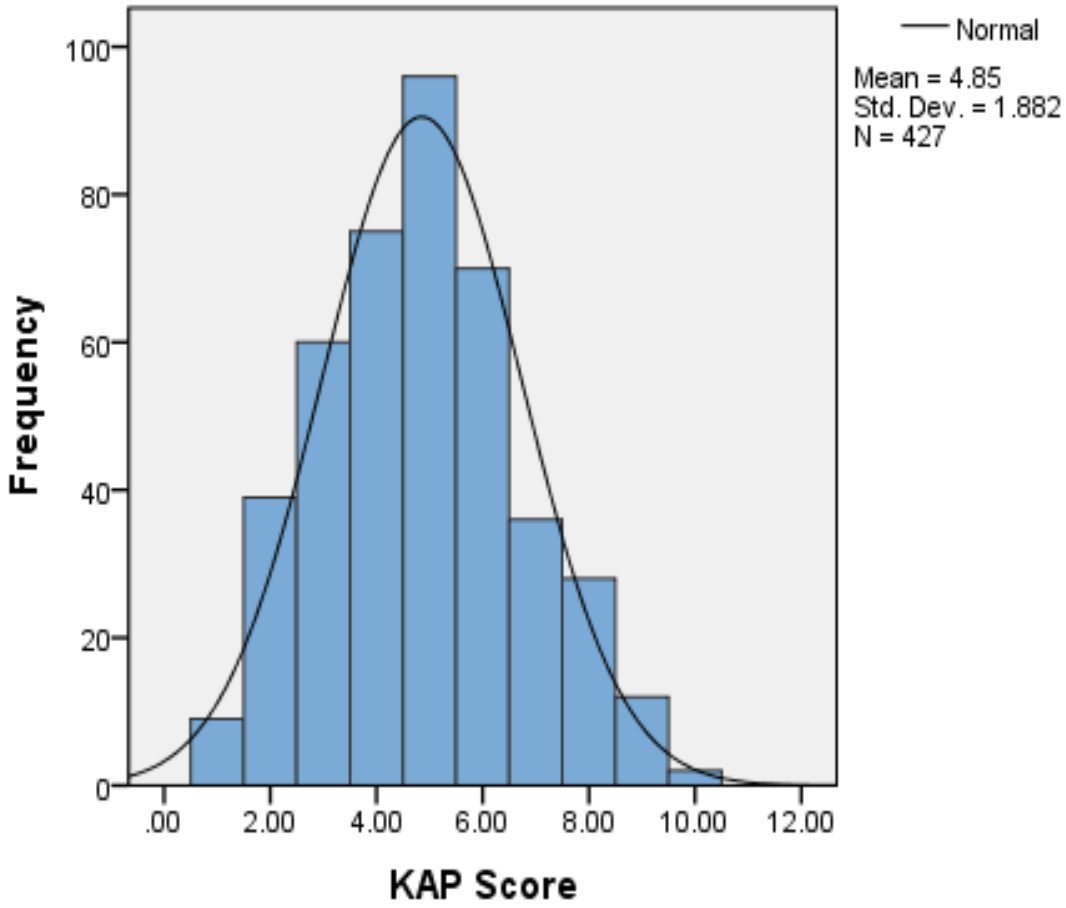

Figure 4.2: Distribution of healthcare professionals' knowledge, attitude and practice score

4.2.6 Factors associated with knowledge, attitude and practice score

Table 4.20 summarises the association between KAP scores and selected socio-demographic factors. Scores were significantly higher among non-UAE nationals compared to UAE nationals, among physicians and pharmacists compared to other healthcare practitioners and among practitioners with six or fewer years of experience compared to those with more than six years of experience. No association was found between KAP scores and age, marital status, government/private employment status or graduate/non-graduate educational level.

Table 4.20: Factors associated with KAP score

KAP Score		
	Mean ± (SD)	**P-Value**
Age	35.43 ±(8.428)	0.113
Gender		
Male	4.9 ±(1.82)	0.352
Female	4.76 ±(1.92)	
Nationality		
UAE national	4.14 ±(2.1)	0.001
Non-UAE national	4.98 ±(1.81)	
Marital status		
Single	4.59 ±(1.81)	0.141
Married	4.91 ±(1.91)	
Employment status		
Government	4.62 ±(2.2)	0.051
Private	4.98 ±(1.7)	
Occupation		
Physicians	5.5 ±(0.264)	0.000
Pharmacists	5.1 ±(0.129)	
Other healthcare	4.4 ±(0.140)	
Work experience		
Six year and less	5.04 ±(1.97)	0.017
More than six years	4.6 ±(1.7)	
Education		
Graduate	4.78 ±(1.83)	0.361
Post Graduate	4.96 ±(1.91)	

4.2.7 Comparisons between occupational groups

Table 4.21 summarises the experience of HS related adverse events among various occupational sub-groups making up the sample. Most of those reporting adverse events (46/55, 84%) were pharmacists. Generally, all occupational groups agreed or strongly agreed that adverse events should be reported.

Table 4.21: Experience of health supplement related adverse events among various occupational sub-groups

	All N=427	**Pharmacist** N=205	**Physician** N= 49	**Others** N= 173
Ever experiencing AE related to HS use in patients/customers during practice	N= 232 55 (23.7%)	N=189 46 (24.3%)	N=18 4 (22.2%)	N=25 5 (20%)
Frequency of encountering AE related to HS use	N=55	N=46	N=4	N=5
Once	16 (29.09%)	13 (28.3%)	0	3 (60%)
Occasionally	39 (70.90%)	33 (71.7%)	4 (100%)	2 (40%)
Frequency of recording HS AE	N=55	N=46	N=4	N=5
Always	10 (18.18%)	7 (15.2%)	1(25%)	2 (40%)
Never	24 (43.63%)	22 (47.8%)	1(25%)	1 (20%)
Often	2 (3.63%)	2 (4.3%)	0	0
Sometimes	19 (34.54%)	15 (32.6%)	2 (50%)	2 (40%)
Reporting HS related AE to higher authority	N= 427	N=205	N=49	N= 173
Strongly disagree	3 (0.7%)	1(0.48%)	0	2 (11.5%)
Disagree	5 (1.2%)	1 (0.48%)	0	4 (2.3%)
Neutral	50 (11.7%)	21 (10.24%)	7 (14.3%)	22(12.7 %
Agree	182 (42.6%)	96 (46.83%)	24 (48.9%)	62(35.8 %
Strongly agree	187 (43.8%)	86 (41.95%)	18 (36.7%)	83(47.9 %

Chapter 5: Discussion

5.1 Introduction

This dissertation reports findings from two large cross-sectional studies that were designed and carried out in Dubai to quantify HS use and any related adverse events. The first study consisted of a computer assisted personal interview conducted by telephone and involved 1,203 Dubai residents. The study investigated HS consumption, knowledge and the reporting of any HS related adverse events. The second study used an on-line questionnaire to assess HS knowledge, HS related adverse event knowledge, as well as knowledge, attitude and practice (KAP) among 427 Dubai healthcare professionals. The stimulus for this research arose from the writer's work with consumer safety in Dubai Municipality, a strongly held belief of the public health importance of HS use in Dubai and the need to raise awareness among healthcare professionals to improve patient safety. It is believed that no similar study has previously been carried out in UAE.

5.2 Key Results

5.2.1 First study: survey among Dubai population

In the general population sample, the prevalence of ever having used HS was 38% and the prevalence of current use was 31%. These levels were similar to findings from studies in other countries. There are few data on HS use and adverse events in the UAE. Although in one study, conducted among university students, the consumption rate of HS was 39%. (Alhomoud et al., 2016). In one recent study conducted among the female college students in Saudi Arabia 76.6% of the participants were using HS (Alfawaz et al., 2017). A cross-sectional household survey,

conducted among Saudi residents of the Riyadh region resulted with 73% of alternative medicines which includes herbal supplements (Al-faris et al., 2008). The consumption rate of HS among students in Qatar was 49.6% (Mamtani et al., 2015) while the rate in the US has been increasing yearly and, in 2009, was 69% (Gahche et al., 2011).

In one of the community based survey study conducted in the rural population of United States, 61% of the HS using participants were aware that HS products were not much regulated by controlling authorities and they were getting information about HS from internet, family / friends, physicians and pharmacists (Owens et al., 2014). In a study conducted among the US army soldiers, 48% of the respondents had knowledge about the HS and they were getting it from the leading magazines, friends/team mates, physicians/ para medical staff or from internet (Tharion et al., 2004). It is difficult to assess overall knowledge and awareness of HS in the sample, but about half of HS users had been prescribed HS while 60% had received information about HS from a pharmacist, suggesting a reasonable level of awareness.

Of the users surveyed, only 13 (3%) reported experiencing adverse events and most were not serious.

The published literatures, identifies a high risk of adverse events associated with HS, especially herbal supplements, as they have a higher risk of contaminations, drug interaction and adulterations. Heavy metal contamination occurs mainly through the substandard cultivation and manufacturing practices. One study identified that the high dose consumption of heavy metals can cause several diseases, they may be carcinogenic or have adverse reproductive effects (Ejeatuluchukwu et al., 2011). Pesticide residue contamination which is occurring due to excessive use of pesticides during the cultivation of the herb and from lack of good agriculture practices (GAP).

Organochlorine pesticide residues which may lead serious health issues if consumed above the limit, have also been found in a number of Chinese herbal plants cultivated in China and sold in Hong Kong (Leung et al., 2005)

A number of studies identified the adverse events associated with intended adulteration of HS for the best result with banned medicinal ingredients or medicinal ingredient which need medical supervision. In 2009, a division of the US Food and Drug Administration (FDA), the Internet and Health Fraud Team conducted an internet survey of HS products intended for sexual enhancement. They found that one third of such supplements which are marketed as dietary supplements to promote sexual activity and treat erectile dysfunction, despite having no disclosure of any medicinal content on the label, nevertheless contained the medicinal ingredient sildenafil, the active ingredient in Viagra (USFDA, 2009). In Germany, a research carried out by the government authority controlling HS products (Deutsches Aerzteblatt International) found 17 incidents of illness with vomiting, arterial hypertension, headache, malaise, nausea, chest pressure, dyspnea, tachycardia, insomnia and high fever associated with consumption of Chinese slimming products, such as slimming tea and slimming herbal capsules which have a banned medical ingredient sibutramine (Muller et al., 2009).

A study conducted in United States by searching the published articles of herb-drug interaction stated that common herbal remedies that produce adverse effects on the cardiovascular system include St. John's wort, motherwort, ginseng, gingko biloba, garlic, grapefruit juice, hawthorn, saw palmetto, danshen, echinacea, tetrandrine, aconite, yohimbine, gynura, licorice, and black cohosh (Tachjian et al., 2010). In 2001, the FDA issued warnings and an import alert that herbal products are unsafe if they contain or are suspected to contain aristolochic acid (USFDA, 2001).

The literature suggests a rate of adverse events with HS consumption of up to 10%. It was somewhat surprising, therefore, that the rate in this study was only 3%. One reason for the lower rate found here may be because of the better monitoring and control of HS availability in the Dubai market-place by the health authorities compared to other countries with higher reported rates. Other reasons may be because consumers are more knowledgeable and/or are using HS under pharmacist supervision.

The findings that adverse events often go unreported is noteworthy and may be linked to the lack of an adverse events monitoring system in Dubai. One FDA-commissioned study estimated that FDA receives less than 1% of all adverse events associated with dietary supplements. The study suggested that the factors that may contribute to under-reporting are that many consumers presume supplements to be safe, use these products without the supervision of a healthcare professional, and may be unaware that FDA regulates them (DHHS, 2001). This strengthens the case for raising awareness among consumers of the importance of reporting adverse events to the appropriate authority and of establishing an HS adverse events monitoring system.

5.2.2 Second study: survey among healthcare professionals

In the healthcare professionals' survey, although most respondents knew what HS were and a fair proportion had participated in HS education or read journal articles about them, the composite knowledge score indicated that only 20% could be described as having good KAP towards HS use while 43% considered that HS were harmless. This low level of knowledge is of concern. The findings reported here are consistent with a study among community pharmacists in Ajman and Sharjah, UAE (Qassim et al., 2014). These results were also similar to findings in the US and Canada

where the knowledge towards HS was reported to be unsatisfactory (Kwan et al., 2006).

Previous studies have likewise obtained results consistent with this view in which poor knowledge about pharmacovigilance and ADRs reporting was reported among community pharmacists (Afifi et al., 2014; Vessal et al., 2009; Toklu & Uysal., 2008; Bawazir, 2006; Li et al., 2004). However, some research findings are contrary to our results and showed good knowledge about how to report ADRs (Evans et al., 2006; Zolezzi & Parsotam, 2005; Green et al., 2001). This difference may be due to different study area, different sample sizes with varied demographic characteristics and scales.

In a further study in Gujarat, India, it was found that 65% of participants were knowledgeable about the terminology of adverse drug reactions (ADR) and 63% knew about the role of the National Pharmacovigilance Centre, but that 60% of community pharmacists considered all herbal products to be free from ADRs (Rathod & Panchal, 2014). Moreover, several research studies have revealed gaps in information on HS and adverse event reporting among healthcare professionals (Cellini et al., 2013; Oshikoya & Awobusuyi, 2009). This poor knowledge about HS may indicate a need for improved education and training both as part of continuing professional development and within the basic curriculum.

Nearly all healthcare professionals in this study agreed that reporting HS related adverse events was necessary, but only 40% said they did not know where to submit any report. The findings of US study (Cellini et al., 2013) reported that 70% of healthcare professionals do not know where to report the adverse events associated with HS.

Regarding the healthcare professionals knowledge about how and where to report ADR, our study showed that 60% of respondents were knowledgeable about the existence of national PV program. This is in accordance with 59.3% of Ting et al., (2010) study and 55.9% of Qassim et al., (2014) study, whereas only 28% of healthcare professionals in SathviK et al., (2014) study were knowledgeable about ADR reporting system in the UAE. However, some research findings are contrary to our results and showed more knowledge and awareness about local PV system (Bawazir, 2006; Van et al., 2002; Green et al., 2001). The implications of this factor results in that ADR go unnoticed and left unreported.

Furthermore, a KAP survey among healthcare professionals in a teaching hospital in India reported that fewer than half (40%) of the respondents knew how to report ADRs (Bajaj & Kumar, 2013). A possible explanation for this negative practice in this study might be due to the fact the most healthcare professionals (77.5%) did not know to whom to report an adverse event. In addition, most of them (74.7%) had no training on how to report adverse events. Further, onerous demands of other work duties coupled within adequate professional conduct compromise the reporting rate of HS related adverse events. This may cause pharmacists to execute their services in too short a time. Therefore, there is an essential need for educational interventions among healthcare professionals to improve their knowledge and increase their reporting rate of HS.

According to a study performed in Ras Al Khaimah, UAE, 18% of participant pharmacists indicated that they reported ADR to different set-ups and 6% of them reported ADR on at least two occasions. Moreover, only 3.6% of community

pharmacists from Ajman and Sharjah have submitted ADR report to Ministry of Health or pharmaceutical companies (Osama & Rana, 2014).

About half of the sample prescribed or supplied HS to patients or consumers and, of these, about a quarter had experience of adverse events in their patients or consumers. These are lower than the results reported by another study conducted among military physicians, where 60% observed adverse events in their patients associated with HS (Cellini et al., 2013). In this study, only about one fifth of those experiencing an adverse event always reported these events.

Experiences towards HS product related adverse events play an important role in the perception of ADR and influence how healthcare professionals will report ADRs. In the sample, the majority reported that they felt confident when reporting an adverse event, similar to findings in a study conducted among community pharmacists that assessed their knowledge and attitude about ADR. It showed a positive attitude towards ADR reporting and that respondents felt that they had an important role to play in ADR reporting (Qassim et al., 2014).

Findings and reports from other studies have shown that a lack of knowledge was one of the important factors that prevented healthcare professionals from advising patients/customers on herbs and herbal preparation use in a positive way (Ghia & Jha, 2013). These findings, however, differ from the findings in this study, where literacy and language were the most commonly identified barriers limiting discussion of HS products. Also, a study carried out in Saudi Arabia among community pharmacists concluded that a lack of time and a lack of reliable resources were the commonly identified barriers (Al-Arifi, 2013). The differences with the study reported here may be due to cultural differences.

5.3 Strengths

An important strength of the first survey was that it used a large random sample of the general population and, therefore, there can be confidence that the findings are generalizable to the whole Dubai population. The sampling frame was a list of households and mobile telephone numbers registered to each of those households. Lists are regularly updated by the Dubai Statistics Centre. Households were randomly sampled from each of six geographical areas in Dubai. Telephone numbers were randomly sampled from each household. The sample obtained mirrors what is known of the population of Dubai in terms of age, gender, nationality, education and income. The sample size was estimated before the start of the study and was considered of adequate power. The questionnaire was adapted from published instruments and revised by experts to ensure content validity. It was accurately translated into Arabic and tested to ensure the clarity of the questions and the respondents' ability to provide accurate answers. Interviewers were trained to increase reliability and reduce interviewer bias. The CAPI telephone interview helped to ensure a good response rate, minimise interviewer effects and provided a good level of anonymity. The use of mobile telephone numbers rather than fixed telephone numbers further minimised selection bias since response was not open to those who just happened to be at home when calls were made. Finally, the entry of data directly into the database reduced the incidence of data entry errors and facilitated rapid data processing and analysis.

The second survey was completed on-line by participants who were invited by e-mail to take part. Although the e-mail lists were complete and included the entire target population, as expected, the response rate was low, selection bias affecting the external validity of the results. Care was taken with the construction of the

questionnaire and anonymity of the respondents was assured so that there could be greater confidence in the internal validity of the results. Despite the lower response rate, the sample obtained still provided adequate power.

5.4 Limitations

There were several limitations to the study. First, as with any cross-sectional design, it is not possible to infer cause and effect or the direction of any associations between dependent and independent variables. While there is reasonable confidence in the generalisability of the results, selection and response bias may affect this. It has not been possible to compare non-responders with responders to investigate further this source of bias. Also, since the study was conducted in Dubai, it will not be directly generalizable to other Emirates. Although based on questionnaires that had been used in other studies, the questionnaires used in this study had not been separately validated.

Chapter 6: Conclusion

This study included two cross-sectional surveys. The firststudy was a population based survey with a cross-sectional design which aimed to measure HS use in Dubai and the incidence of related adverse events. The survey was conducted by telephone with the participation of 1,203 residents of Dubai. The study attempted to gather information on HS consumption, local knowledge of HS, adverse events related to HS consumption, and the reporting habit of adverse events among the population in Dubai.

The consumption of HS products is common in many countries such as the USA. As per the findings of this study, however, this is not the case in Dubai, UAE which has a consumption rate of only 38%. The degree of knowledge of participants about HS may play a vital role in the reduction of adverse events associated with HS use, as 85.54% of participants in this study who had used HS had knowledge about HS.

The second study was a survey based on a cross-sectional descriptive study using an on-line questionnaire to assess the levels of knowledge, attitude and practice (KAP) of Dubai healthcare professionals regarding HS products and any perceived related adverse events. The inspiration for this cross-sectional study came from a belief in the importance of raising the awareness of HS and any related adverse events among healthcare professionals to improve the quality of patient care. Regarding the healthcare professional survey, improper behaviour towards HS was one of the markers of poor knowledge. The present study revealed poor knowledge among healthcare professionals towards HS products and HS product related adverse events.

Health professionals appear to be insufficiently knowledgeable about HS use and any related risks among their patients/consumers. Health professionals should be

attentive to any possible adverse health events from the use of such supplements. It is recommended that physicians and healthcare professionals include questions about the use of HS when acquiring a medical history from patients/consumers. It is further recommended that all HS producers clearly label ingredients and any known side effects of their use. Finally, and importantly, it is recommended that those considering the use of HS in future should have their lifestyle assessed by a healthcare professional prior to any such use.

The overall attitude of healthcare professionals was perceived to be relatively negative. Few included HS in an adverse report to the related authorities as most did not know to whom to report such an event. This reporting behaviour highlights several issues and calls for a safety monitoring system for HS products. In addition, it is possible that consumers fail to tell their physicians or pharmacists about any adverse events arising from their use of HS. This means that the current situation may not reveal many HS-related adverse events. There is, therefore, a need for initiatives to raise awareness among professionals and HS users of an avenue for reporting adverse events. Ad hoc reporting systems are at present a mainstay of detecting signals of safety concerns associated with HS. If a suspected adverse event associated with HS does not reach the appropriate personnel, or if a proper reporting system is not in place, either through direct patient reporting or through reporting from healthcare professionals, then patient safety is at risk with resultant important implications for public health.

6.1 Managerial Implications

It is anticipated that this thesis will make a positive contribution to HS product research and reform debate in the UAE. By assessing the current consumption rate

among the population and the levels of knowledge of such products, by exposing some of the related adverse events and by shedding light on the KAP levels of healthcare professionals in Dubai, it is felt that an important knowledge gap has been filled. The resultant recommendations should help to focus future debate and decision making at the highest level within and among both national and local government departments and health authorities.

6.2 Research Implications

It is hoped that this study will provide a platform for future HS research in the UAE. The study may set the scene for an objective approach to a better understanding of HS products eligible for inclusion in the reporting system. The study also allows researchers to identify challenges through academic research and to make evidence-based policy recommendations that support reporting system reform activities in the UAE. In addition, future research may be presented to policy makers at national and international meetings, seminars and conferences.

In conclusion, this study offers a valuable contribution to HS, KAP, and reporting system research in the UAE, and allows for international comparisons and global benchmarking.

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Appendices

Appendix A: Prints of the Population-based Questionnaire

Section A- Demographic Data				
Age				
Gender	Male □		Female □	
Marital status	Married □	Single □	Divorced □	Widow □
Nationality	UAE national □	Non UAE national □ (Specify ……..)		
Occupation	Student □	Employed □	Non-employed □	Retired □
Health insurance coverage	Yes □		No □	
Income	< 5000 AED □	5000 - < 10000 AED □	10000 - < 20000 AED □	20000 > AED □
Education	Less than high school □	High school □	Graduate □	Post graduate □
Weight (kg)				
Height (cm)				

Section B- Health and Lifestyle	
1	**Do you have any allergy?** Yes □ *(if yes, please choose from below options)* No □ Don't know □ Food □ Drug □ Aerosol □ Contact □ Other □ Specify
2	**How frequently have you visited a doctor in the past 12 months?** At least once a week □ 1-3 times a month □ Less than monthly □ Never □
3	**Have you ever been diagnosed with any chronic medical condition?** *(you can choose more than one answer)* Respiratory disease No □ Yes □ Specify (…) Skin disorder No □ Yes □ Specify (…) Disease of the digestive system No □ Yes □ Specify (…) Diabetes No □ Yes □ Specify (…) Cardiovascular disease No □ Yes □ Specify (…) Cancer No □ Yes □ Specify (…) Other No □ Yes □ Specify (…)
4	**Have you taken prescription drugs in the past month?** Yes □ Specify (……) No □ Don't know □
5	**Do you smoke?** Every day □ Occasionally □ In the past □ Never □

Section C- Health Supplements Consumption

1 **Do you know what health supplements are?**
Yes □ No □

2 **Have you ever used health supplement?** *(if your answer is "Currently", please proceed to question C4, if your answer is "Never", please proceed to the last question of the questionnaire)*
Currently □ In the past □ Never □

3 **Why did you discontinue using any health supplements?** *(you can choose more than one answer)*
Allergic reactions □ Serious skin disorders □ Cost □ Others □ Specify (…)

4 **For how long have you been using / had you used health supplement?**
Less than a month □ More than a month but less than a year □ 1-5 years □ > 5 years □ Don't know □

5 **How frequently do/did you use health supplement?**
Daily or almost daily □ 1-4 times a week □ 1-3 times a month □ Rarer than monthly through the year □ Seasonally □ Don't know □

6 **Which categories of health supplements do /did you use?** *(you can choose more than one answer)*

Vitamin □ Mineral □ Herbal □ Sport nutrition □ Energy drink □ Dietetic food □ Others □ Specify (……)

7 **What is the form of the used product(s)?** *(you can choose more than one answer)*

Tablet □ Capsule □ Wafers □ Powder □ Gel □ Chews/ Gummy □ Drops □ Caplet □ Chewable tablets □
Granules □ Drink □ Spray □ Lozenges □ Soft gels □ Vegicaps □ Gel caps □ Liquid □ Don't know □

8 **Which health supplement ingredient(s) do/did you use?** (you can choose more than one answer)

Alfalfa	□	Amino Acids	□	Bee Pollen	□
Bilberry/Eyebright Combination	□	Caffeine, Multicomponent	□	Calcium	□
Calcium & Magnesium	□	Calcium & Vitamin	□	Cayenne Pepper	□
Chondroitin	□	Chromium (Chromium Picolinate)	□	Cimicifuga Racemosa	□
Conjugated Linolenic Acid	□	Creatine	□	Damiana Folia	□
Don't Know	□	Echinacea	□	Ephedra	□
Fish Oils	□	Folate (Folic Acid)	□	Fructus Cynosbati	□
Garlic	□	Gentian, Multi-Component	□	Ginger	□
Ginkgo Biloba	□	Glandular Extract, Multicomponent	□	Glucosamine	□

	Grape Seed Extract	□	Guarana	□	Herbal Caffeine, Alone	□
	Iron (Ferrous Xxxate)	□	Kelp	□	L-Carnitine	□
	L-Cysteine	□	Lecithin	□	Licorice	□
	L-Methionine	□	Lutein	□	Lycopene	□
	Lysine	□	Magnesium	□	Melatonin	□
	Methylsulfonyl Methane	□	Morinda Citrifolia (Noni)	□	Oxymatrine	□
	Panax Ginseng	□	Parsley	□	Potassium	□
	Pygeum Africanum	□	Royal Jelly	□	Saw Palmetto	□
	Saw Palmetto (Topical)	□	Selenium	□	Siberian Ginseng	□
	Spirulina, Multicomponent	□	St. John's Wort	□	St. John's Wort, Multicomponent	□
	Tryptophan	□	Vitamin B6	□	Vitamin B12	□
	Vitamin C (With Or Without Rose Hips)	□	Vitamin D	□	Vitamin E	□
	Vitamin E, Multicomponent	□	Vitamins A & D	□	Yohimbe, Alone	□
	Yohimbe, Multicomponent	□	Zinc (Zinc Gluconate)	□	Others Specify (…….)	□
9	**For what reason do/did you take health supplements?** *(you can choose more than one answer)*					
	Body building	□	Control aging	□	Control anemia	□
	Control blood pressure	□	Control cholesterol level	□	Detoxify	□
	Digestive	□	Energy booster	□	Hormone therapy	□
	Immune booster	□	Improve overall health	□	Insomnia	□
	Memory improvement	□	Menopausal	□	Mental alertness	□
	Mood alteration	□	Organ health Specify (……..)	□	Pregnancy	□
	Prevent colds	□	Prevent health problems Specify (……..)	□	Supplement my diet	□
	Weight management	□	Others Specify (……..)	□		
10	**Where do/did you purchase health supplement(s)?** *(you can choose more than one answer)* Pharmacy □ Clinic □ Gym □ Nutrition shops □ Supermarket □ Other □ Specify (…….)					
11	**How many health supplement products have you ever used?** 1-2 □ 3-5 □ 6-10 □ > 10 □					
12	**Enter the full name of health supplement(s) you have used, including brand name.** Supplement name(s) (…….) Don't know □					

Section D- Information about Health Supplement Products	
1	**Who advised you to take health supplements?** *(you can choose more than one answer)* Self-recommendation □ Friends/ Relatives □ Advertisement □ Internet □ By prescription □ Health care personnel (nurse, etc.) □ Other □ Specify (……...)
2	**How many times have health supplements been prescribed for you by your health care practitioner?** Once □ Twice □ Several times □ Never □
3	**Where do you seek health supplements product information?** *(you can choose more than one answer)* Pharmacy □ Physician □ Producer helpline □ Internet □ Government call center □ Relatives / Friends □ Other □ Specify (...)
4	**Do you find sufficient information on the label of health supplement products?** Very informative □ Somewhat informative □ Not informative □ Don't read the label □
5	**Do you think nutrition information on health supplement products is useful?** Yes □ No □
6	**Which label information concerns you?** *(you can choose more than one answer)* Ingredients □ Indication □ Prescribed dosages □ Adverse reactions □ Product durability □ Dietary sources of nutrients □ Claims □ Precautions □ Dosing instructions □ None □
7	**Do you follow recommended label information?** Always □ Often □ Sometimes □ Never □

Section E- Adverse Events Related to Health Supplement Consumption	
1	**Have you ever experienced any adverse event related to health supplement use? (***if no, please proceed to the last question of the questionnaire)* Yes □ No □
2	Which adverse event of health supplement use have you ever experienced? (you can choose more than one answer) Abdominal pain □ Anorexia □ Anxiety □ Chest pain □ Convulsions □ Dermatitis □ Diarrhea □ Dizziness □ Dyspnea □ Edema □ Fatigue □ Hair loss □ Headache □ Hypertension □ Hypotension □ Muscle cramping □ Muscle pain □ Nausea □ Palpitations □ Pyrexia □ Sedation □ Tingling □ Urticaria □ Vomiting □ Other □ Specify (……..……...)
3	**What was the severity of the adverse events?** *(you can choose more than one answer)* Mild □ Moderate □ Severe □ Life-threatening □
4	**How frequently have you encountered adverse events due to health supplement consumption?** Once □ Occasionally □ Frequently □
5	**What was the onset time of adverse events after consuming health supplement?** *(you can choose more than one answer)* Less than 1 hour □ 1 hour to 1 day □ More than 1 day □
6	**How was the relation between health supplement consumption and the adverse event confirmed?** *(you can choose more than one answer)* Discontinued use ceased the effect □ Not confirmed/personal opinion □ Physician opinion □ Medical diagnosis without lab confirmation □ Clinical test □
7	**Which of the health supplement(s) you have used was suspected/confirmed to cause the adverse event(s)?** Supplement name(s) (…….) Don't know □
8	**When visiting your health care practitioner for any reason, has he/she ever asked you about your health supplement consumption?** Yes □ No □
9	**How did the adverse event(s) resolve?** *(you can choose more than one answer)* **(***if you answered any but not "Hospitalization", please proceed to question F1)* Discontinued use by personal decision □ Discontinued use by medical advice □ Medical treatment □ Hospitalization □ Resolved spontaneously □ Still persists □ Other □ Specify (……..)
10	**How long have you been hospitalized due to the adverse event(s)?** *(you can choose more than one answer)* Less than a day □ Few days □ More than a week □

Section F- Reporting Adverse Events	
1	**Have you ever informed your physician about your health supplement consumption?** Yes □ No □
2	**Have you ever reported an adverse event related to health supplement consumption? (***if no, please proceed to the last question of the questionnaire)* Yes □ No □
3	**Where did you report the adverse event(s)?** *(you can choose more than one answer)* Pharmacy □ Physician □ Producer helpline □ Internet □ Government call center □ Hospital □ Clinic □ Police □ Others □ Specify (…….)
4	**What do you think about the establishment of a surveillance system of adverse events related to health supplement consumption?** Definitely beneficial □ Somewhat beneficial □ Not sure □ Not beneficial □ Definitely not beneficial□

Appendix B: Risk Assessment Module

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Alfalfa	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Low Low Low Low	Low Low High High Low	Low Medium High High Medium	(1+2+2+2+2)/5 = 1.8 Low	(1+1+3+3+1)/5 = 1.8 Medium	Medium
Bilberry/ eyebright	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Low Low Negligible Negligible	Low Low Medium Low Low	Low Medium Medium Low Low	(1+2+2+1+1)/5 = 1.4 Negligible	(1+2+2+1+1)/5 = 1.4 Low	Low
Garlic	Short-term toxicity	Negligible Negligible	Low Medium	Low Low	(1+1+2+1+1)/5 =	(1+1+2+1+1)/5 = 1.2	Low

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Negligible Negligible	Medium Low Low	Medium Low Low	1.2 Negligible	Low	
Ginkgo Biloba	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Low Moderate Low Negligible	Low Medium Medium High Low	Low Medium High High Low	(1+2+3+2+1)/5 = 1.8 Low	(1+2+2+3+1)/5 = 1.8 Medium	Medium
Grape Seed Extract	Short-term side effects Long-term toxicity Interactions of medications Contamination of heavy metals Pesticides residue	Negligible Negligible Low Negligible Low	Low Low Low Low Low	Low Low Medium Low Medium	(1+1+2+1+2)/5 = 1.4 Negligible	(1+1+1+1+1)/5 = 1 Low	Low

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Panax Ginseng	Short-term side effects Long-term side-effects Interactions of medications Contamination of heavy metals Pesticides residue	Low Low Low Low Low	Low Low Medium Low Low	Medium Medium Medium Medium Medium	(2+2+2+2+2)/5 = 2 Low	(1+1+2+1+1)/5 = 1.2 Low	Medium
Siberian Ginseng	Short-term side effects Long-term side effects Interactions of medications Contamination of heavy metals Pesticides residue	Negligible Negligible Moderate Negligible Negligible	Low Low Medium Low Low	Low Low High Low Low	(1+1+3+1+1)/5 = 1.4 Negligible	(1+1+2+1+1)/5 = 1.2 Low	Low
Pygeum Africanum	Short-term toxicity Long-term toxicity	Low Low Negligible Negligible	Low Low Low Low	Medium Medium Low Low	(2+2+1+1+2)/5 = 1.6 Low	(2+2+1+1+2)/5 = 1.6 Medium	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low	Low	Medium			
Saw Palmetto	Short-term side effects Long-term side effects Interactions of medications Contamination of heavy metals Pesticides residue	Low Moderate Moderate Low Low	Low Medium Medium Low Low	Medium High High Medium Medium	(2+3+3+2+2)/5 = 2.4 Low	(1+2+2+1+1)/5 = 1.4 Low	Medium
L-Cysteine	Short-term toxicity Long-term toxicity Interactions of food/drugs, drug sensitivity Contamination with Heavy Metals Pesticide Residue	Negligible Low Moderate Moderate Low	Medium Medium Medium Medium Low	Medium Medium High High Medium	(1+2+3+3+2)/5 = 2.2 Low	(2+2+2+2+1)/5 = 1.8 Medium	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
L-Methionine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants. Pesticides residue	Negligible Moderate Moderate Moderate Low	Low Low Medium Low Low	Low Medium High Medium Medium	(1+3+3+3+2)/5 = 2.4 Low	(1+1+2+1+1)/5 = 1.2 Low	Medium
Lysine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Low Low Low	Low Medium Medium Low Low	Low Medium Medium Medium Medium	(1+2+2+2+2)/5 = 1.8 Low	(1+2+2+2+2)/5 = 1.8 Medium	Medium
Methylsulfonyl Methane	Short-term toxicity Long-term toxicity Interactions of food/drugs	Negligible Negligible Negligible Negligible Negligible	Low Low Low Low Low	Low Low Low Low Low	(1+1+1+1+1)/5 = 1 Negligible	(1+1+1+1+1)/5 = 1 Low	Low

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Contamination with heavy metals Pesticides residue						
Chromium (ChromiumPicolinate)	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Moderate Moderate Moderate Low	Low Medium Low Low Medium	Low High Medium Medium Medium	(1+3+3+3+2)/5 = 2.4 Low	(1+2+1+1+2)/5 = 1.4 Low	Medium
Tryptophan	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Moderate Moderate Moderate Low	Low Medium High High Medium	Low High High High Medium	(1+3+3+3+2)/5 = 2.4 Low	(1+2+3+3+2)/5 = 2.2 Medium	Medium
Vitamin C	Short-term toxicity Long-term toxicity	Negligible Low Low NA	Low High Medium NA	Low High Medium NA	(1+2+2)/3 = 1.67 Low	(1+3+2)/3 = 2 Medium	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Interactions of food/drugs Contamination with toxicants Pesticides residue	NA	NA	NA			
Amino Acids	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Low NA NA	Low Low Medium NA NA	Low Medium Medium NA NA	(1+2+2)/3 = 1.67 Low	(1+1+2)/3 = 1.33 Low	Medium
Caffeine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible High Low NA NA	Low Medium Medium NA NA	Low EXTREME Medium NA NA	(1+4+2)/3 = 2 Low	(1+2+2)/3 = 1.67 Medium	Medium
Creatine	Short-term toxicity	Negligible Negligible	Low Low	Low Low	(1+1+2)/3 = 1.33	(1+1+2)/3 = 1.33	

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Low NA NA	Medium NA NA	Medium NA NA	Negligible	Low	Low
Folate (Folic Acid)	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Negligible Low NA NA	Low Low Medium NA NA	Low Low Medium NA NA	(1+1+2)/3 = 1.33 Negligible	(1+1+2)/3 = 1.33 Low	Low
Gentian	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Moderate Moderate High Moderate High	Medium Medium Medium High Medium	High High High High Extreme	(3+3+4+3+4)/5 = 3.4 Moderate	(2+2+2+3+2)/5 = 2.2 Medium	High

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Lecithin	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Negligible Negligible Low Low	Low Low Low Low Medium	Low Low Low Medium Medium	(1+1+1+2+2)/5 = 1.4 Negligible	(1+1+1+1+2)/5 = 1.2 Low	Low
Lutein	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Low Low Low	Low Low Low Medium Medium	Low Medium Medium Medium Medium	(1+2+2+2+2)/5 = 1.8 Low	(1+1+1+2+2)/5 = 1.4 Low	Medium
Royal Jelly	Short-term toxicity Long-term toxicity Interactions of food/drugs	Negligible Low Low Low Medium	Low Low Medium Low Medium	Low Medium Medium Medium High	(1+2+2+2+3)/5 = 2 Low	(1+1+2+1+2)/5 = 1.4 Low	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Contamination with heavy metals Pesticides residue						
Selenium	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Moderate Moderate Moderate High	Low Medium Medium Medium Medium	Medium High High High Extreme	(2+3+3+3+4)/5 = 3 Moderate	(1+2+2+2+2)/5 = 1.8 Medium	High
Vitamin B6	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Negligible Negligible NA NA	Medium Medium High NA NA	Low Low Medium NA NA	(1+1+1)/3 = 1 Negligible	(2+2+3)/3 = 2.33 Medium	Low
Vitamin D	Short-term toxicity Long-term toxicity	Negligible Negligible Low NA	High High Medium NA	Medium Medium Medium NA	(1+1+2)/3 = 1.33 Negligible	(3+3+2)/3 = 2.67 High	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Interactions of food/drugs Contamination with toxicants Pesticides residue	NA	NA	NA			
Glucosamine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Moderate Negligible Negligible	Medium Medium Medium Medium Medium	Low Medium High Low Low	(1+2+3+1+1)/5 = 1.6 Low	(2+2+2+2+2)/5 = 2 Medium	Medium
L-Carnitine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Negligible Negligible Negligible	High Low Medium Medium Medium	Medium Medium Low Low Low	(1+2+1+1+1)/5 = 1.2 Negligible	(3+1+2+2+2)/5 = 2 Medium	Low
Potassium	Short-term toxicity	Negligible Negligible	Low Medium	Low Low	(1+1+2)/3 = 1.33	(1+2+2)/3 = 1.67	

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Low NA NA	Medium NA NA	Medium NA NA	Negligible	Medium	Low
Vitamin B12	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Negligible Low NA NA	Medium Medium Medium NA NA	Low Low Medium NA NA	(1+1+2)/3 = 1.33 Negligible	(2+2+2)/3 = 2 Medium	Low
Vitamin E	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Negligible Negligible NA NA	Low Medium High NA NA	Low Low Medium NA NA	(1+1+1)/3 = 1 Negligible	(1+2+3)/3 = 2 Medium	Low

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Vitamins A & D	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Low NA NA	Low High Medium NA NA	Low High Medium NA NA	(1+2+2)/3 = 1.67 Low	(1+3+2)/3 = 2 Medium	Medium
Zinc	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with toxicants Pesticides residue	Negligible Low Negligible NA NA	High Medium Medium NA NA	Medium Medium Low NA NA	(1+2+1)/3 = 1.33 Negligible	(2+2+1)/3 = 1.67 Medium	Low
Bee Pollen	Short-term toxicity Long-term toxicity Interactions of food/drugs	Low Negligible Low Low Moderate	Medium Low Low Medium Medium	Medium Low Medium Medium High	(2+1+2+2+3)/5 = 2 Low	(2+1+1+2+2)/5 = 1.6 Medium	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Contamination with heavy metals Pesticides residue						
Spirulina	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Low Low Moderate Low	Low Low Low High Low	Medium Medium Medium High Medium	(2+2+2+3+2)/5 = 2.2 Low	(1+1+1+3+1)/5 = 1.4 Low	Medium
Echinacea	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low High High Low Negligible	Medium Low Low Low Low	Medium High High Medium Low	(2+4+4+2+1)/5 = 2.6 Moderate	(2+1+1+1+1)/5 = 1.2 Low	Medium
Glandular Extract	Short-term toxicity Long-term toxicity	High High High NA	High High Low NA	Extreme Extreme High NA	(4+4+4)/3 = 4 High	(3+3+1)/3 = 2.33 Medium	Extreme

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Interactions of food/drugs Contamination with heavy metals Pesticides residue	NA	NA	NA			
Guarana	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Low Moderate Low Low	Medium Medium Medium Low Low	Medium Medium High Low Low	(2+2+3+2+2)/5 = 2.2 Low	(2+2+2+1+1)/5 = 1.6 Medium	Medium
Kelp	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Moderate Moderate Moderate Low Low	Low Low Low Low Low	Medium Medium Medium Medium Medium	(3+3+3+2+2)/5 = 2.6 Moderate	(1+1+1+1+1)/5 = 1 Low	Medium
Morinda Citrifolia	Short-term toxicity	Negligible Negligible	Low Low	Low Low	(1+1+2+1+2)/5 = 1.4	(1+1+1+1+1)/5 = 1	

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Negligible Low	Low Low Low	Medium Low Medium	Negligible	Low	Low
Parsley	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Negligible Moderate Negligible Moderate	Low Low Low Low Low	Low Low Medium Low Medium	(1+1+3+1+3)/5 = 1.8 Low	(1+1+1+1+1)/5 = 1 Low	Medium
St. John's Wort	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Moderate Moderate High Low Low	Medium Medium High Low Low	High High Extreme Medium Medium	(3+3+4+2+2)/5 = 2.8 Moderate	(2+2+3+1+1)/5 = 1.8 Medium	High

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Cayenne Pepper	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low High Moderate Low Negligible	Medium Low Medium Low Low	Medium High High Medium Low	(2+4+3+2+1)/5 = 2.4 Low	(2+1+2+1+1)/5 = 1.4 Low	Medium
Cimicifuga Racemosa	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low High High Low Negligible	Low Low Medium Low Low	Medium High Extreme Medium Low	(2+4+4+2+1)/5 = 3 Moderate	(1+1+2+1+1)/5 = 1.2 Low	Medium
Damiana Folia	Short-term toxicity Long-term toxicity Interactions of food/drugs	Low High Moderate Moderate Low	Medium Low Medium Medium Low	Medium High High High Medium	(2+4+3+3+2)/5 = 2.8 Moderate	(2+1+2+2+1)/5 = 1.6 Medium	High

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Contamination with heavy metals Pesticides residue						
Ephedra	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low High High High Low	Medium Medium Medium Medium Low	Medium Extreme Extreme Extreme Medium	(2+4+4+4+2)/5 = 3.2 Moderate	(2+2+2+2+1)/5 = 1.8 Medium	High
Fructus Cynosbati	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Moderate Moderate Moderate Low	Medium Low Medium Low Low	Low Medium High Medium Medium	(1+3+3+3+2)/5 = 2.4 Low	(2+1+2+1+1)/5 = 1.4 Low	Medium
Ginger	Short-term toxicity Long-term toxicity	Negligible Low Moderate Negligible	Low Low Low Low	Low Medium Medium Low	(1+2+3+1+2)/5 = 1.6 Low	(1+1+1+1+1)/5 = 1 Low	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low	Low	Medium			
Licorice	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Negligible Low Moderate Negligible	Low Low Medium Medium Low	Low Low Medium High Low	(1+1+2+3+1)/5 = 1.6 Low	(1+1+2+2+1)/5 = 1.4 Low	Medium
Lycopene	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Negligible Low Negligible Negligible	Low Low Medium Low Low	Low Low Medium Low Low	(1+1+2+1+1)/5 = 1.2 Negligible	(1+1+2+1+1)/5 = 1.2 Low	Low
Melatonin	Short-term toxicity	Low Low	Low High	Medium High	(2+2+3)/3 = 2.33	(1+3+2)/3 = 2	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Moderate NA NA	Medium NA NA	High NA NA	Low	Medium	
Oxymatrine	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Negligible Negligible Negligible Negligible	Medium Low Low Low Low	Medium Low Low Low Low	(2+1+1+1+1)/5 = 1.2 Negligible	(2+1+1+1+1)/5 = 1.2 Low	Low
Yohimbe	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	High High High Moderate Moderate	High High High Medium Medium	Extreme Extreme Extreme High High	(4+4+4+3+3)/5 = 3.6 High	(3+3+3+2+2)/5 = 2.6 High	Extreme

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Calcium	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Low Moderate NA NA	Low Low Medium NA NA	Low Medium High NA NA	(1+2+3)/3 = 2 Low	(1+1+2)/3 = 1.33 Low	Medium
Magnesium	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Low Moderate NA NA	Low Low Medium NA NA	Low Medium High NA NA	(1+2+3)/3 = 2 Low	(1+1+2)/3 = 1.33 Low	Medium
Chondroitin	Short-term toxicity Long-term toxicity Interactions of food/drugs	Negligible Low Low Moderate NA	Low Low Low Low NA	Low Medium Medium Medium NA	(1+2+2+3)/4 = 2 Low	(1+1+1+1)/4 = 1 Low	Medium

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
	Contamination with heavy metals Pesticides residue						
Conjugated Linolenic Acid	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low Moderate Moderate Low NA	Medium Low Medium Low NA	Medium Medium High Medium NA	(2+3+3+2)/4 = 2.5 Moderate	(2+1+2+1)/4 = 1.5 Medium	High
Fish Oils	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Negligible Moderate Moderate Moderate Moderate	Medium Low Medium Medium Medium	Low Medium High High High	(1+3+3+3+3)/5 = 2.6 Moderate	(2+1+2+2+2)/5 = 1.8 Medium	High

Name of the chemical hazard (Ingredient)	Associated Risk(s) with the ingredient	Severity (Level of impact on the Human Health)	Probability (The chances of that risk happening)	Risk Score (Risk score, found by combining impact and probability on the risk matrix)	Average impact SUM (Risk Impact values)/ number of risks in same category	Average probability SUM (Risk Probability values)/ number of risks in same category	Risk Score (Risk score, found by combining average impact and average probability on the risk matrix)
Iron	Short-term toxicity Long-term toxicity Interactions of food/drugs Contamination with heavy metals Pesticides residue	Low High Moderate Low Negligible	Medium Low Medium Medium Low	Medium High High Medium Low	(2+4+3+2+1)/5 = 2.4 Low	(2+1+2+2+1)/5 = 1.6 Medium	Medium

Appendix C: Risk Assessment Matrix

		Severity			
		NEGLIGIBLE 1 small/unimportant not likely to have a major effect on Human Health	LOW 2 minimal importance has an effect on Human and impact on health	MODERATE 3 serious/important will affect the human health significantly/suffers serious injuries/requires immediate action	HIGH 4 maximum importance could result in disaster/death/serious injuries or toxicity
Probability	LOW 1 risk has rarely been a problem	LOW 1	MEDIUM 2	MEDIUM 3	HIGH 4
	MEDIUM 2 risk most likely occurs with this ingredient	LOW 2	MEDIUM 4	HIGH 6	EXTREME 8
	HIGH 3 risk will occur and associated with the use of this ingredient	MEDIUM 3	HIGH 6	HIGH 9	EXTREME 12

Negligible coded as (1) for small/unimportant that not likely to have a major effect on human health, Low coded as (2) for an effect on human and impact on the health/requires medical treatment, Moderate coded as (3) for serious/important that will affect the human health significantly/suffers serious injuries requires immediate action, High coded as (4) for maximum importance that could result in disaster/death/serious injuries or toxicity.

The probability of the risk matrix was ranging from Low coded as (1) for risk has rarely been a problem, Medium coded as (2) for This risk will most likely occur with this ingredient, and High coded as (3) for the risk will occur and associated with the use of this ingredient/possibly multiple times, and has occurred in the past.

Appendix D: Individual Ingredient Overall Risk Score

Alfalfa scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Soto-Zarazúa et al., 2016; CPSS, 2015). The final score was medium.

Bilberry/ eyebright scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Rouhi-Boroujeni et al., 2015; CPSS 2015). The final score was low.

Garlic scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (EMA, 2016; Nethathe & Russell, 2014; CPSS, 2015). The final score was low.

Ginkgo Biloba scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Edwards et al., 2015; Diamond & Bailey, 2013; Nethathe & Russell, 2014; CPSS, 2015). The final score was medium.

Grape Seed Extract scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (UMMC, 2015; Nieto-García et al, 2014; CPSS, 2015). The final score was low.

Panax Ginseng scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Lee et al., 2012; Kiefer & Pantuso, 2003; Popovich et al., 2011; Nethathe & Russell, 2014; CPSS, 2015). The final score was medium.

Siberian Ginseng scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level

of chances of that risk happening (Cicero et al., 2004; Kiefer & Pantuso, 2003; CPSS, 2015). The final score was low.

Pygeum Africanum scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Moyad, 2014; CPSS, 2015). The final score was medium.

Saw Palmetto scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Avins et al., 2013; CPSS, 2015). The final score was medium.

L-Cysteine scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (McGavigan et al., 2015; CPSS, 2015). The final score was medium.

L-Methionine scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Tapia-Rojas et al., 2015; CPSS, 2015). The final score was medium.

Lysine scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Huang et al., 2016; CPSS, 2015). The final score was medium.

Methylsulfonyl Methane scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Johansson et al., 1998; CPSS, 2015). The final score was low.

Chromium (Chromium Picolinate) scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability

level of chances of that risk happening (Thompson et al., 2013; Sun et al., 2015; CPSS, 2015). The final score was medium.

Tryptophan scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Oketch-Rabah et al., 2016; CPSS, 2015). The final score was medium.

Vitamin C scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (NIH, 2016; Costa et al., 2015; Jemaa et al., 2017; Nađpal et al., 2016; NIH, 2016; CPSS, 2015). The final score was medium.

Amino Acids scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Zhenyukh et al., 2017; CPSS, 2015). The final score was medium.

Caffeine scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Gurley et al., 2015; Campana, 2014; Jabbar & Hanly, 2013; CPSS, 2015). The final score was medium.

Creatine scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Dickinson et al., 2014; CPSS, 2015). The final score was low.

Folate (Folic Acid) scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Manshadi et al., 2014; Zhao et al., 2014; CPSS, 2015). The final score was low.

Gentian scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances

of that risk happening (Akileshwari et al., 2012; Huang et al., 2015; CPSS, 2015). The final score was high.

Lecithin scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Chen et al., 2015; CPSS, 2015). The final score was low.

Lutein scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Olmedilla-Alonso et al., 2014; CPSS, 2015). The final score was medium.

Royal Jelly scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Karaca et al., 2010; CPSS, 2015). The final score was medium.

Selenium scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Yang & Jia, 2014; CPSS, 2015). The final score was high.

Vitamin B6 scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Zhang et al., 2013; CPSS, 2015). The final score was low.

Vitamin D scored negligible as an average score of severity level of impact on the human health, and scored high as an average score of probability level of chances of that risk happening (Reis et al., 2009; CPSS, 2015). The final score was medium.

Glucosamine scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Jacobs et al., 2013; CPSS, 2015). The final score was medium.

L-Carnitine scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Serban et al., 2016; CPSS, 2015). The final score was low.

Potassium scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Chatterjee et al., 2010; CPSS, 2015). The final score was low.

Vitamin B12 scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Gröber et al., 2013; CPSS, 2015). The final score was low.

Vitamin E scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Ledesma et al., 2011; CPSS, 2015). The final score was low.

Vitamins A & D scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Ergin et al., 2013; CPSS, 2015). The final score was medium.

Zinc scored negligible as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Plum et al., 2010; CPSS, 2015). The final score was low.

Bee Pollen scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Petersen, 1977; CPSS, 2015). The final score was medium.

Spirulina scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Pilkington & CAM-Cancer Consortium, 2015; Karkos et al., 2010; UMMC, 2013; CPSS, 2015). The final score was medium.

Echinacea scored moderate as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Karsch-Völk et al., 2014; Lawrenson et al., 2014; CPSS, 2015). The final score was medium.

Glandular Extract scored high as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Hadayer & Schaal, 2016; Gangwar et al., 2015; CPSS, 2015). The final score was extreme.

Guarana scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (da Costa Krewer et al., 2014; CPSS, 2015). The final score was medium.

Kelp scored moderate as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Barton & McLean, 2013; Rosen et al., 2014; CPSS, 2015). The final score was medium.

Morinda Citrifolia scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Assi et al., 2015; CPSS, 2015). The final score was low.

Parsley scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Khosravan et al., 2017; CPSS, 2015). The final score was medium.

St. John's Wort scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Knuppel & Linde, 2004; Cui & Zheng, 2016; Hohmann et al., 2016; CPSS, 2015). The final score was high.

Cayenne Pepper scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Nantakornsuttanan et al., 2016; CPSS, 2015). The final score was medium.

Cimicifuga Racemosa scored moderate as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Wuttke & Seidlová-Wuttke, 2015; CPSS, 2015). The final score was medium.

Damiana Folia scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Avelino-Flores et al., 2015; CPSS, 2015). The final score was high.

Ephedra scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Council for Responsible Nutrition, 2003; CPSS, 2015). The final score was high.

Fructus Cynosbati scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Andersson et al., 2012; CPSS 2015). The final score was medium.

Ginger scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Kafeshani, 2015; CPSS, 2015). The final score was medium.

Licorice scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Qiao et al., 2014; Hruby et al., 2013; CPSS, 2015). The final score was medium.

Lycopene scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Selvan et al., 2014; Viuda-Martos et al., 2014; CPSS, 2015). The final score was low.

Melatonin scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Hartz et al., 2015; CPSS, 2015). The final score was medium.

Oxymatrine scored negligible as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Lu et al., 2015; CPSS, 2015). The final score was low.

Yohimbe scored high as an average score of severity level of impact on the human health, and scored high as an average score of probability level of chances of that risk happening (NIH, 2016; Wongkrajang et al., 2014; CPSS, 2015). The final score was extreme.

Calcium scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Quinn et al., 2013; CPSS, 2015). The final score was medium.

Magnesium scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (Hruby et al., 2013; CPSS, 2015). The final score was medium.

Chondroitin scored low as an average score of severity level of impact on the human health, and scored low as an average score of probability level of chances of that risk happening (UMMC, 2015; CPSS, 2015). The final score was medium.

Conjugated Linolenic Acid scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Koba & Yanagita, 2014; CPSS, 2015). The final score was high.

Fish Oils Acid scored moderate as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Mason & Sherratt, 2016; CPSS, 2015). The final score was high.

Iron scored low as an average score of severity level of impact on the human health, and scored medium as an average score of probability level of chances of that risk happening (Aigner et al., 2015; CPSS, 2015). The final score was medium.

Appendix E: Information Sheet A

Title of project: Health supplement use and related adverse events in Dubai

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide if you wish to take part.

Several of several chemicals within the content of health supplement products (HS) may affect human health by inducing certain adverse events. Previous studies found that consumers are generally unaware regarding HS risks, its associated adverse events and proper reporting process to concerned authorities. This study aims to conduct a population based cross-sectional survey to identify the prevalence of HS consumption in the population of Dubai and the adverse events related to HS consumption. It is up to you to decide to take part or not. If you decide to take part you are still free to withdraw at any time and without giving a reason. The information and opinions you provide will be kept strictly confidential and used only for research purposes. Your name and details cannot be linked to this survey and will not be identified in any report/publication. The completion and submission of the electronic questionnaire indicates the agreement for participation and acts as signature of the consent form.

The study is sponsored by the College of Medicine and Health Sciences of the United Arab Emirates University as well as Dubai Municipality and reviewed by the Al Ain Medical District Human Research Ethics Committee.

For any further information regarding the study, please contact:

Naseem M. R. Abdulla
Tel: +971 45035554
E-mail: nmrafee@gmail.com
5 March 2015
Thank you very much for participating in the study.

Appendix F: Prints of the healthcare professionals questionnaire

Section A. Demographic Data				
Age				
Gender	Male	□	Female	□
Marital status	Married □	Single □	Divorced □	Widow □
Nationality	Drop down list in on-line questionnaire			
Employment status	Government □	Private □	Self-employed □	
Title	Physician □ Specialized physician □ Pharmacist □ Assistant pharmacist □ Other □ Specify (……...…)			
Work experience	Less than 1 year □ 1-2 years □ 3-4 years □ 5-6 years □ More than 6 years □			
Insurance coverage	Yes □ No □			
Education	Graduate □ Post graduate □			

Section B. Knowledge		
1	Do you know what health supplements are?	Yes □ No □ Don't know □
2	Please, list as many health supplements as you can.	(……..)
3	Do you agree with the statement that health supplements are harmless?	Yes □ No □ D on't know □
4	Do you know about adverse events of health supplements?	Yes □ No □ D on't know □
5	Please, list as many adverse events of health supplements as you can.	(……..)
6	Do you know what surveillance system is?	Yes □ No □ Don't know □
7	Do you know about any existing surveillance system in the UAE?	Yes □ Specify (……) No □
8	Do you know about any adverse event reporting system in your institution/organization?	Yes □ Specify (……) No □
9	Do you know to whom you can report an adverse event?	Yes □ No □
10	Have you ever received any continuing education on health supplement products?	No □ Electronic learning □ Product orientation (Principle) □ Official training courses □ Other □ Specify (…)
11	Have you read a scientific article related to adverse events of health supplements in the last 6 months?	Yes □ No □
12	Have you ever received training on how to report an adverse event?	Yes □ No □

Section C. Practice		
1	Do you sell/prescribe/dispense any health supplements at practice site? (if your answer is "No", please proceed to section D)	Yes □ No □
2	Which type of health supplements do you usually prescribe/advice/dispense? (you can choose more than one answer)	Dietetic □ Energy drink □ Food □ Herbal □ Mineral □ Sport nutrition □ Vitamin □ Other □ Specify (…….)
3	Which form of health supplements do you usually prescribe/advice/dispense? (you can choose more than one answer)	Caplets □ Capsule □ Chewable tablets □ Chews/ Gummy □ Drink □ Drops □ Gel □ Gel caps □ Granule □ Liquid □ Lozenges □ Powder □ Soft gels □ Spray □ Tablet □ Vegicaps □ Wafers □ Don't know □
4	Do you have a system to record health supplements use?	Yes □ No □
5	How often do you discuss health supplement products use with your patients/customers? (if your answer is "Never", please proceed to question C9)	Always □ Often □ Sometimes □ Never □
6	What is the topic of discussion about health supplement products use with your patients/customers? (you can choose more than one answer)	Product effect □ Product adverse event □ Product quality □ Product price □ Other □ Specify (……)
7	Which of the following health supplement products information sources are helpful in caring for your patients/customers? (you can choose more than one answer)	Internet □ Printed material □ Multimedia □ Other □ Specify (……)
8	What are the barriers that limit discussing health supplement	Literacy □ Cultural ethics □

	products with your patients/customers? (you can choose more than one answer)	Language □ Social level □ Other □ Specify (……..…)
9	Have you ever experienced an adverse event related to health supplement consumption in patients/customers during your practice? (if your answer is "No", please proceed to question C14)	Yes □ No □
10	How frequently have you encountered adverse events related to health supplement consumption?	Once □ Occasionally (monthly or rarer) □ Frequently (every week) □
11	What was the adverse event? (you can choose more than one answer)	Abdominal pain □ Alopecia □ Anorexia □ Asthenia □ Chest pain □ Convulsion □ Dermatitis □ Diarrhea □ Dizzines □ Dyspnea □ Edema □ Headach □ Hypotensi on □ Nausea □ Pain □ Pruritus □ Pyrexia □ Sedation □ Urticaria □ Vomiting □
12	How often have you recorded health supplements adverse events? (if your answer is "Never", please proceed to question C14)	Always □ Often □ Sometimes □ Never □
13	To which higher authority/ personnel did you report health supplement adverse events? (you can choose more than 1 answer)	Ministry of Health □ Senior physician □ Pharmacist in-charge □ Other □ Specify (……)
14	Is adverse event reporting form available when you are at the job of prescribing/dispensing medicines to the patients/customers?	Yes □ No □ Don't Know□

Section D. Attitude		
1	You report health supplements related adverse events to the higher authority/personnel.	Strongly agree □ Agree □ Neutral □ Disagree □ Strongly disagree □
2	What is the reason if you don't/wouldn't report an adverse event? (you can choose more than one answer)	It's not important □ Don't know where to report □ Don't know what is adverse event of health supplement □ Concerned that the report is a false alert □ Lack of time to investigate the case at work □ Consider as extra work (not your concern) □ Difficulty in confirming/distinguishing the adverse event □ Other Specify (…..……) □
3	Do you think it is important to report all adverse events of health supplement products?	Yes (all) □ Only when hospitalisation is needed □ Only when it is life threatening □ No □
4	What do you think about the establishment of a surveillance system of adverse events related to health supplement consumption?	Definitely beneficial □ Somewhat beneficial □ Not sure □ Not beneficial □ Definitely not beneficial □
5	Are you concerned about legal problems of reporting an adverse event?	Definitely □ Somewhat □ Not sure □ Not □ Definitely not □
6	Do/would you feel confident when reporting an adverse event?	Definitely □ Somewhat □ Not sure □ Not □ Definitely not □

Appendix G: Information Sheet B

Title of project: Healthcare Professionals' Knowledge, Attitude and Practice of Health Supplement Products Related Adverse Events

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide if you wish to take part. Several chemicals within the content of health supplement product (HS) may affect human health by inducing certain adverse events. Previous studies found that consumers are generally unaware regarding HS risks, its associated adverse events and proper reporting process to concerned authorities. More, many healthcare professionals have inadequate knowledge, attitude and practice (KAP) on the issue. This study aims to conduct a cross-sectional survey to identify the level of KAP among healthcare professionals in the Emirate of Dubai.

It is up to you to decide if to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. The information and opinions you provide will be kept strictly confidential and used only for research purposes. Your name and details cannot be linked to this survey and will not be identified in any report/publication. The completion and submission of the electronic questionnaire indicates the agreement for participation and acts as signature of the consent form.

The study is sponsored by the College of Medicine and Health Sciences of the United Arab Emirates University as well as Dubai Municipality and reviewed by the Al Ain Medical District Human Research Ethics Committee.

For any further information regarding the study, please contact:

Naseem M. R. Abdulla
Tel: +971 45035554
E-mail: nmrafee@gmail.com

March 2015

Thank you very much for participating in this study.