Usage of biologically active supplements and Politic Study of regulation in Kyrgyzstan and Republic of Korea

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List of Abbreviations

DS	Dietary Supplements
BAS	Biological Active Supplements
HFF	Functional Food
EEU	European Economic Union
WHO	World Health Organization
FAO	Food and Agriculture Organization
NS	Nutrient Supplement
ODS	Office of Dietary Supplements
NNPAS	National Nutrition and Physical Activity Survey
DRI	Dietary Reference Intake
UL	Upper Intake Levels
DDPSSES	Department of Disease Prevention and State Sanitary and Epidemiological Surveillance
GMP	Good Manufacturing Practice
AE	Adverse Events
OTC	Over-The-Counter
NHP	Natural Health Product
MedDRA	Medical Dictionary for Regulatory Activities
SOC	System Organ Class

SAE	Serious Adverse Event
DMAA	Dimethylamylamine
RDA	Recommended Daily Allowance
TR CU	Technical Regulations of the Customs Union
HFFA	Health Functional Food Agency
MDSF	Minsitry of Drug and Safety Food
SES	Socioeconomic status
HCW	Health care workers

Abstract

Introduction: Biologically active supplements (BASs) market is increasing in many countries. However, the data on the consumption of BASs is still limited. In the growing market, the pattern of using BASs increased in the Kyrgyz Republic. Expansion the cases of detection substandard and falsified of BASs in Kyrgyzstan should be noted that crisis in the regulation system of BASs and lack of awareness among the population, like these relevant issues have prompted to study this research. The study aims to identify consumers' attitudes towards BASs and assess BAS's knowledge among the Kyrgyz Republic population, and study Kyrgyzstan's regulation system compared to the Republic of Korea.

Materials and methods: As a general method for this study has been used as a qualitative approach. In achieving the research objectives, the data collected from both primary and secondary sources were used. The study's primary data was collected through an online-questionnaire based on BAS use among consumers and non-consumers of the study population. The total number of participants was 372. The secondary resources used the data and the necessary documents for the research from the Kyrgyzstan government and the Korean government on the regulation system of BASs and health functional food.

Results: Prevalence of use of BASs among the population is high. 72.0% of participants were consumers, and 28.0% were non-consumers. Among them, 69.9% were female, and 30.1% were male. Identified: a statistically significant difference between males and females using BASs, a significant difference in knowledge between BAS consumers and non-consumers, and a strong association between BASs and the government regulation.
The study of regulation on HFFs in the Republic of Korea recommended the appropriate functions for regulating the BAS in Kyrgyzstan.

Conclusion: The current results emphasize the compelling need for spreading public awareness in the Kyrgyz Republic regarding biologically active supplements. Consumers should be advised that BAS products may not always be beneficial and can cause serious side effects; therefore, consulting with healthcare professionals before starting any supplement. All multidisciplinary healthcare structure members should also clearly understand the potential hazards and benefits of BAS therapies.

The government needs to make the biologically active supplement market more transparent and strict regulation system on the registration process and distribution channels.

Keywords: *Biologically active supplements, Heath functional food, regulation, therapy.*

CHAPTER I

INTRODUCTION

1.1. Definition and critical terms of the biologically active supplements (BASs)

Nutrition is one of the most critical factors mediating connecting a person with the external environment and determining general health status.

Biologically active supplements also called vitamin supplements or dietary supplements, is one of the most popular consuming these days in every part of the world. Biologically Active Supplements (BASs) are the products containing nutrient and (or) biologically active substances (their concentrates) of natural or artificial origin (identical to the natural), as well as prebiotic components and probiotic microorganisms, which are meant to be taken at the same time with food for optimization of human ration and which are not the only source of food or dietary nutrition [1].

There are three categories of BAS:

- Nutraceuticals - biologically active food supplements are applied to correct a chemical compound of food. It is an additional source nutrient: fiber, amino acids, fats, carbohydrates, vitamins, mineral substances.
- Parapharmaceutics – substances that contain the raw extracts and the vegetable formulas (phytopreparations). They can be applied to preventive maintenance, auxiliary therapy, and maintenance of functional activity of body systems. For instance, commonly used as organic acids, flavonoids, caffeine, biogenic amines, regulatory di- and oligopeptides, some oligosaccharides and, many others, so-called natural products.
- Probiotics – live sufficient bacteria which restores natural micro flora of the body [2].

The primary function is to “adequate consumption of the BAS that is the daily consumption level of nutrient and biologically active substances, established based on calculated and observed quantities or levels of consumption of, nutrient and biologically active substances by a group/groups of almost healthy people. The “norms of physiological need” is an averaged amount of the necessary intake of nutrients and biologically active substances, which ensure the optimal realization of physiological and

biochemical processes inherent to human genotype.

Foodstuffs shall satisfy human physiological needs in necessary substances and energy, comply with requirements usually set for foodstuffs in terms of organoleptic, physical and chemical indices and conform with the requirements established by normative documents for allowed content of chemical, biologically active substances and their compounds, microorganisms and other organisms posing a danger for the health of present and future generations [1].

The primary purposes for using biologically active supplements are:

- For fast deficiency completion of biologically active substances that do not arrive in sufficient quantities. Their level can be lowered and can cause immunity system weakness. Often our body needs more amino acids, poly-nonsaturated fat acids, vitamins, macrocells and microcells, food fibers, ect.
- For resistibility, increase of an organism. Using BAS, we can decrease the damage to environmental factors. For these purposes is generated phytogenesis products based on ginseng ginger, pink rodiola etc.
- For preventive maintenance of infringement of metabolism processes. BAS can also be used for chronic disease prevention;
- For the restoration of immunity system;
- For deducting of toxins and radionuclides from organism [2].

Effectiveness of using BAS is a very relative question. Many specialists think very skeptically about BAS, but some conduct clinical trials to prove its effectiveness. Some the active forms of vitamins and minerals can substantially benefit health and can often is the distinguishing factor between a mild effect and a profound shift in health.

1.2. Background of the study

Biological active supplements have a long history. In the beginning, used herbal plants as an extract then based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illnesses.

Since that period, the term biologically active supplement used interchangeably with complementary/ alternative/ conventional medicine.

Today no global consensus on how the category of products known variously as removing biologically active supplements (BASs), natural health products (NHPs), complementary medicines, Health Functional Food (HFFs), or food supplements in different countries are defined. For example, a product considered to be a biologically active supplement and regulated as a food in the Kyrgyz Republic, in another jurisdiction may be considered a food supplement or a therapeutic good (complementary medicine or prescription medicine) or potentially even a controlled substance.

The other side is that while all regulatory scientists want to protect consumers from harm, ensure that consumers can make informed choices about the products they use, and do the right thing, the scientific challenges and regulatory systems that have emerged to address them vary significantly to country. Even in countries with similar cultures, legal systems, and economic development levels, the rules applied to dietary supplements vary significantly. Some of these differences are discussed below: in Australia, Canada, and the United States, all English-speaking countries with broadly similar cultures and legal systems, to illustrate this point. In other countries with similar legal systems, such as the United Kingdom, New Zealand, and South Africa, or other countries in the Americas, Europe, Africa, and Asia, often with different cultures, legal systems, and levels of economic development, is left to the discretion of others with a lot of experience and knowledge.

Also, the health products "dietary supplements" are often a very emotional topics that evokes a wide variety of opinions and points of view. While some observers may argue that these products should be treated as common medicines and foods, others believe that a more individual approach is needed. There is often a traditional or historical evidence base, and products often contain multiple ingredients. This situation is becoming increasingly difficult due to the lucrative nature of the global dietary supplement sector,

the increased involvement of the growing industrial sector that produces them, and many new and innovative products to the market.

The Biological active supplement market has become more global and lucrative, so it has the importance of ensuring product quality and it is challenges. In the last decades in Kyrgyzstan, the turnover of BASs is becoming one of the most dynamically developing sectors on the pharmaceutical market, and this market has been developing since 2007. The consumption of BAS is very different by countries. In the U.S., more than 80% of the population consumes BAS and in Europe, it is 50%. In Kyrgyzstan, according to the marketing companies Neman-Pharma, Bimed-Pharm ect. the consumer number around 12%-14% in a year regarding the statistics it is substantial growth. The demand for BAS is growing because they are relatively easy to develop, produce, and register than pharmaceuticals. More progress can be expected because of the growth of pharmacy chains and the government's stricter regulations on the registration process and distribution channels. In the market of BAS products in Kyrgyzstan, import products are more dominant than domestic.

1.3. Statement of the problem and significance of the study

The biologically active suplement as nutritive substances and minor food components is used to ameliorate vitamins in organisms, decrease the risk of debilitating diseases, and improve life quality. It exerts their effect by stimulating universal mechanisms of the adaptation-adjustment response of the body to various external and internal factors. At the same time, quantitative changes of parameters of body system functioning are within their physiological boundaries.

Some dietary supplements are formulated under careful conditions in clean, controlled laboratories and labeled accurately. Others are made less carefully and have been found to contain none of the substances listed on their labels. Furthermore, many supplements contain other substances that are not listed on their labels – fillers, different herbs, or actual drugs that are known to be able to cause harm. Such cases are relevant issues in Kyrgyzstan, and this study summarizes some of the challenges in biological active

supplement science in the Kyrgyz Republic. The main reason for the study: in connection with the expansion of the range of detection substandard and falsified of BASs and the low level of control among regulators including regulating through health, safety legislation, quality of composition, effectiveness and label content requirement using of it. Such as issues proposed to explore this scrutiny by revealing these problems:

- Because of increasing cases of detection substandard and falsified biologically active supplements in Kyrgyzstan should be noted that crisis in the regulation system of BAS;
- Lack of knowledge about BASs among populations because of misusing it by self-treatment method without any doctor's consultation, even for unusual diseases. Such in cases to replace drugs with BASs and also to try to cure the disease cannot be categorically impossible;
- Lack of harmonization of current technical regulations by worked out European Economic Union (EEU-agreement between Russia, Kazakhstan, Armenia, Belarus, and Kyrgyzstan): arising disagreement in the interpretation of concepts and requirements of biologically active supplements in confirmation of conformity.

Since 2017 the Kyrgyz Republic ensures the regulation of BASs that comply with the requirements of the technical regulations, such as: TR CU 021/2011 Article 24 "About Safety of foods"on its territory without presenting additional requirements for BAS and without conducting additional conformity assessment procedures. According to the EEU decree, most the BASs approve based on manufacturing certificates by the Department of Disease Prevention and State Sanitary and Epidemiological Surveillance of the Kyrgyz Republic.

In Kyrgyzstan, a review of the literature indicates limited published consumer research data and no recent studies on manufacturers on active biological supplements. Hence, in an attempt to address this gap, the investigation will undertake to:

1. Determine the current control system of BASs based on registration procedures;
2. Identify the practices and attitudes of selected consumers and non-consumer towards active biological supplements;

3. Comparision of the regulation system in Kyrgyzstan and the Republic of Korea.

Based on the results of the studies will develop recommendations for the population to optimize the use of BASs and will help improve the public health issue in the BAS sector in the Kyrgyz Republic.

1.4. Hypotheses of the study

Set 1: Males and females will differ in the use of the biologically active supplements.

H_0: There is equal use of BAS products among females and males.

H_A: There is a significant difference by gender in the use of BAS.

Set 2: Knowledge of biologically active supplements will differ between users and non-users.

H_0: There is no significant difference BAS knowledge among users and non-users group.

H_A: There is a significant difference BAS knowledge among users and non-users group.

Set 3: There is an association between the use of BAS among the population and the government regulation.

H_0: There is no association between the use of BAS and government regulation.

H_A: There is an association between the use of BAS and the government regulation.

*H_0 - Null Hypothesis

*H_A - Alternative Hypothesis

CHAPTER II

REVIEW OF LITERATURE

2.1. Progress on biologically active supplements in the field of medicine

There was limited scientific research on dietary supplements relatively recently, and so little was known about them [2]. From the immemorial time the plants have been used not only for food but also as a source of biologically active substances. The use of plants for medicinal purposes was documented in Sumerian manuscripts more than 5000 years ago. The substances of plant origin were for long the only source of medical drugs [3]. However, even presently, these substances are extensively used in the health care practice. The discovery and exploration of alkaloids opened the way to obtaining chemically uniform monomolecular medicines of natural origin [4]. Even in the era of combinatory chemistry, more than 25% of new medicinal agents are related to plant origin substance [5]. The rapidly growing application of preparations from sweet wormwood (Artemisia annua L.) in the struggle against malaria [6] is a demonstrative example of herbal medicines effectiveness. Interactions of chemical components in the extracts play an important role in the effectiveness of plant preparations. For instance, an alkaloid triptolide from Tripterygium wilfordii, useful for rheumatoid arthritis therapy is highly toxic for humans in purified form. However, the toxicity of non-purified triptolide in plant extracts is significantly reduced [7]. The effectiveness of non-purified plant preparations, as compared to that of purified ingredients, might involve other mechanisms such as protection of active substance from the attack of “foreign” enzymes, a faster transfer of the active substance across membranes, and circumvention of drug resistance of human organisms. Presently, there is a growing interest in mechanisms underlying plant-derived substances the action on gene activities involved in disease development or vital functions of the organism [8].

According to estimates of the World Health Organization (WHO), about 80% of the developing countries population relies on plant preparations in the therapy of diseases, and the number of Member States regulating herbal medicines increased with national

research institutions [9]. Traditionally, plant preparations are widely used in pharmacopeias of Japan, Korea, the USA, Germany, and other European countries. In Kyrgyzstan, medicinal plant preparations were allowed for registration not long ago; however, most such preparations are widely used among the population. In many countries globally bioactive preparations of natural origin are also widely applied as biologically active supplements (nutraceuticals). According from the Food and Agriculture Organization (FAO) data, more than 50000 plant species are used in traditional folk medicine throughout the world. The highest developing percentage of native flora species used for medication is observed in Southeast Asia countries, such as India (20%) and China (19%). In the United States and Russia, slightly more than 10% of plant species are used for therapeutic purposes.

The chemical diversity of the plant kingdom remains mostly unexplored. Even less is known about the biological activity of chemical substances obtained from plants. Our planet's diverse and unique flora is an enormous source of prospects for biotherapy and improvement of public health care. However, the boosted research and implementation of methods for obtaining medicinal agents from natural raw materials are directly related to biodiversity conservation problem [10]. Because of the changing environmental sphere, it has directly affected natural resources used as herbals for healing in medicine. Through the technological items, diversity of BAS is extensively growing in the world.

2.2. Prevalence use of biologically active supplements around the world

Weiyan Gong et al. investigated the prevalence of the nutrient supplement use among the Chinese population aged 6 years and older in 2010–2012. A stratified multistage cluster sampling method was conducted to recruit participants from 150 surveillance sites through an interview-administrative questionnaire. A total of 74,501 children and adults (excluding the pregnant women) were included in the study (mean age, 35.7 years; male, 47.0%, female, 53.5%). Very few of the participants reported using nutrient supplements in the previous month. Participants aged 6–11 years and above 60 years, female, living in large urban, with higher education levels and higher family

incomes, were more likely to use nutrient supplements than their counterparts. The prevalence of nutrient supplement use increased with age in Chinese adults. The highest usage among the nutrient supplements was multi-vitamins and minerals. More females used single vitamin, multi-mineral, multi-vitamins, and minerals than males. The nutrient supplement use proportion was highest amongst the participants with a health problem. The participants who had no idea about their health conditions were the least likely to use the nutrient supplements ($p < 0.05$). According the results of this study , further research is required to understand the social cognition, usage reasons, dosage and consumption motivation of NS, and the relationships with health effects, to ensure that the nutrient supplements can be appropriately promoted in China [11].

Alissa J. Burnett et al. revealed supplement use among populations in Australia that limited studies examine the characteristics of people who take supplements. Investigated the demographics, lifestyle habits, and health status of supplement users; Adults aged >19 years (n=4895) were included from the 2011–2012 National Nutrition and Physical Activity Survey (NNPAS). A supplement user was defined as anyone who took one or more supplements on two 24-h dietary recalls. Supplement use was reported by 47% of women and 34% of men, and supplement use was higher among older age groups, among those with higher education levels and, areas reflecting the least socioeconomic disadvantaged. An association was found between blood pressure and supplement use and, a substantial proportion of Australians take supplements. The study recommended further investigation into the social, psychological, and economic determinants that motivate the use of supplements is required to ensure the appropriate use of supplements among Australian
adults [12].

S. Schwab et al. investigated patterns, prevalence, and determinants of DS use in aged among population-based face-to-face surveys in Europe. The age-standardized prevalence of DS intake was 54.3% in women and 33.8% in men, respectively. The most commonly supplemented mineral and vitamin, respectively, was magnesium (31.9%) and

vitamin D (21.5%) in women and magnesium (18.0%) and vitamin E (12.0%) in men. Compared to the German Dietary Reference Intakes, the highest were reported for biotin, vitamin B6 and B1. Excessive intakes (equal to or above the European Tolerable Upper Intake Levels (UL)) were observed especially for magnesium and vitamin E. 20.2% of the women and 32.5% of the men who took magnesium supplements regularly exceeded the UL for magnesium. DS use determinants were sex, education, smoking, physical activity, neurological diseases, and stroke. A high proportion of the general population aged 65 years and older in Southern Germany uses DS, especially supplements containing vitamins/minerals. The consumption of vitamin D can be regarded as favorable in this age group, whereas the excessive intake of vitamin E might be a cause of concern. [13].

Marinac J.S. et al. surveyed Americans aged approximately 60 years and older regarding their use of herbal products, dietary supplements and their attitudes and knowledge regarding the safety of these popular substances. A face-to-face, 35-item survey was administered to the population 267 residing in the Kansas City, Mo-metropolitan area. Researchers documented usage patterns for, attitudes about, and knowledge of herbal products and dietary supplements in this population. At that moment, 21% respondents took at least one herbal product or dietary supplement, and the potential for adverse drug reactions was apparent in 19% (2012). Glucosamine, garlic, Echinacea, and Gingko Biloba were the most frequently cited substances used by survey participants. White women with at least some college education were most likely to report taking these products. However, preservation of health was by far the most predictive indicator for use of herbal products and dietary supplements. Subjects were found that substantial misconceptions about herbal products and dietary supplements exist among older Americans. Most individuals in this population are interested in receiving additional information about these products [14].

Mashael A. and Manal A. determined the characteristics and lifestyle choices of dietary supplement users and to assess knowledge, attitude, and practice related to dietary

supplements in the health sciences students versus other individuals in Saudi Arabia by a descriptive cross-sectional method through on online questionnaire-based study including 351 participants (138 were health sciences students and 203 were not). More than half of the participants consumed dietary supplements, 53.6% of the health sciences students versus 56.3% of the other individuals. Multivitamins were the most commonly used supplement in all participants. Both groups believed that people might need dietary supplements more during specific times as pregnancy or recovery from diseases, with a higher percentage in health sciences students than other people (43% versus 38%). A significant difference ($P \leq 0.05$) was found concerning opinion and beliefs related to DSs between the two groups. The users of dietary supplements tend to incorporate these products into their lifestyles as part of a broader focus on healthy living. Many health sciences students do not have accurate information about dietary supplements. It is important to strengthen the health science curriculum concerning this topic, to producing better-informed future professionals [15].

Kyrgyzstan, the development of research on biologically active supplements has not received due attention. The weak level of development of the quality control system in the regulation leads to erroneous results that significantly affect public health. According to evidence–based medicine experts, the prevalence use of dietary supplements among the population is high because of inaccurate information among the population recorded misusing of these products. It needed research on it and provided reliable and accessible information about the use of biologically active supplements [16].

2.3. Importance of the quality of biologically active supplements

The first step in characterizing supplement products is generally identifying the ingredients [17]. Plant identification is a particular challenge. Even when easily identified whole plants or plant parts are used, unless the chain of custody is tight and the exact manufacturing process is known and well-characterized, the quality of extracts and blends such as those found in many botanical products is difficult to ascertain. Reliable analytical methods to characterize the bioactive components in supplements are helpful,

but even for the nutrients in supplements, specific analytical chemistry methods must be often developed [18]. Quality of botanical products is great uncertainty that consumers, clinicians, regulators, and researchers face, including fundamental quality parameters of dietary supplements such as identity, purity, and content determination. Definitions of quality abound, including specifications for sanitation, adventitious agents (pesticides, metals, weeds), and content of natural chemicals. Because dietary supplements are often complex mixtures, they pose analytical challenges, and method validation may be difficult. In response to product quality concerns and the need for validated and use publicly available methods, analytical standards, and reference materials for DS analysis [19]. The rigorous assessment of dietary supplement ingredients requires accurate, precise, and reliable analytical methods and matching reference materials providing resources for characterization and verification of supplement product content that enhance the reliability and reproducibility of research using these products and support product quality [20].

Biologically active supplements are subject to the Department of Disease Prevention and State Sanitary and Epidemiological Surveillance requirements for acceptable manufacturing practices (cGMP) and quality control in the Kyrgyz Republic. cGMP requires specifications for each ingredient and approves it under the EEU Technical regulations. The main specific parameters are identity, purity, potency, and other requirements for regulatory compliance. Each parameter must be analyzed with a scientifically valid method. Analytical laboratory conducts specific testing on BAS within acceptable limits, harmful contents should be excluded from biological active supplement products.

Table 1. The main indicators and devices for quality control of BAS

Testing Typically testing of BAS	**The main devices for conducting quality control of BAS**
Organoleptic and physical characteristics (visual, color, odor, taste, density, transparency of liquids) Purity (absence of impurities such as moisture, microbiology, pathogens, heavy metals, residual solvents, pesticides) Pathogens (Salmonella, E. Coli, Staph) Labeling and packing	Karl Fischer Ro-tap and particle size analysis Titration Gravimetry High Performance Liquid Chromatography (HPLC) Gas Chromatography with Flame Ionization Detection (GC-FID) Gas Chromatography with Mass Spectrometry (GC-MS) Inductively Coupled Plasma Mass Spectrometry (ICP-MS) Total Aerobic Plate Count

The measurement of BASs for heavy metals is routine and usually utilizes atomic absorption spectroscopy or inductively coupled plasma mass spectrometry. The analysis of pesticide and herbicide residues in botanicals used in the preparation of dietary supplements should be a routine quality assurance step to help ensure human health [21].

Huggett et al. concluded that the presence of these pesticides at levels exceeding 20 ng/g in botanical dietary supplements indicates the potential for hazard to human health depending upon the intake levels. It should be noted that the use of many of these pesticides is either banned or restricted in many countries, including Canada, the United States, and the European Union. Therefore, testing the plant material for pesticide residues before incorporation into dietary supplements or assaying the processed dietary supplement could control or eliminate this hazard if highly contaminated materials were

excluded from use or if the final product contained pesticide levels deemed safe for human consumption at the expected levels of intake [22].

Based on technical regulation TR CU 021-2011 “On food safety” under the regulation of EEU is described the paramount analytical control quality of testing: hygienic requirements for the safety of BAS products in the Kyrgyz Republic. The tests that are checking the quality of BAS products based on: organoleptic, microbiological safety standards (pathogenic); toxicological; radiological; containing herbs – tests for pesticides; authenticity tests that prove the ingredients listed are contain; in some cases – tests on Genetically Modified Ingredients. Despite the importance of some of them Melamine, Nitrates, and Mycotoxins: Aflatoxin M1 are not available to check because of unlimited analytical laboratory resources, also not available documents and competence of personal issues. In the Appendix 7 of that Technical Regulation described lists components of biologically active substances, food components, and products, which can hurt human health when used for the manufacture of biologically active food additives[1]. After analytical procedures of BASs have been free from hazardous contaminants, the next step is to ensure a safe and reliable BAS is standardization. The primary function of standardization is to provide consumers with a product that contains consistent levels of active ingredients (chemical standardization), predictable pharmacological and physiological effects (biological standardization). The BAS’s repair is ensured by preventing accidental over dose due to variation and providing the consumer with predictable physiological and pharmacological efficacy. The quality control of BASs containing mixtures of botanicals is complicated due to the batch-to-batch variation in each botanical, chemical composition used in the product. If the product can be standardized using bioassays instead of chemical assays, this problem might become more manageable. The consumer expects a BAS that is safe for consumption. The essential quality control and quality assurance procedures that the BAS industry should follow to ensure BASs have been described in detail above and summarized in Figure 1 [21].

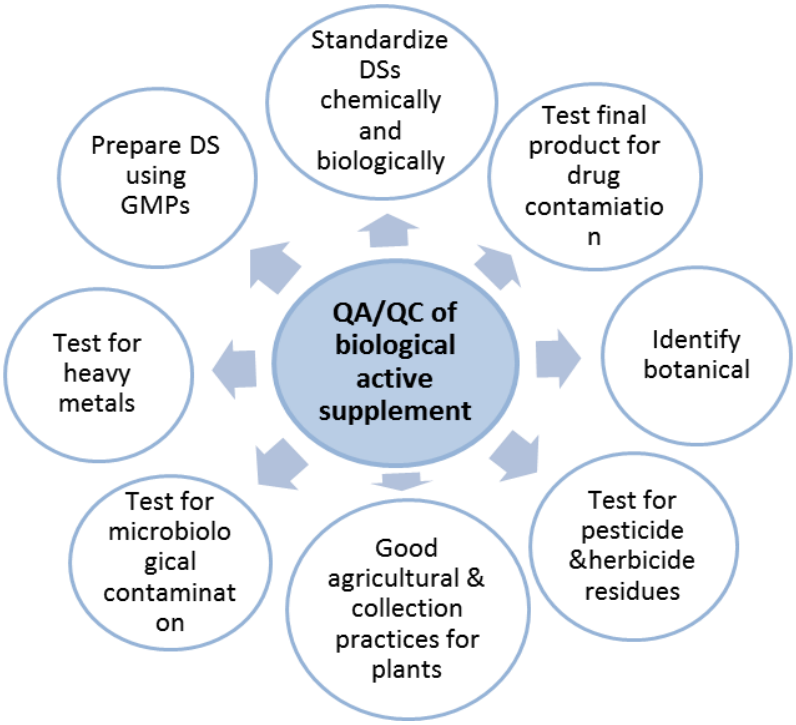

Figure 1. Quality assurance and control of biologically active supplements

Fong et al. and Shiltler et al. described that these procedures include acquiring the botanicals from collectors who use profitable agriculture and collection practices. To be sure that the correct species has been acquired, the material should be authenticated using the macroscopic and microscopic botanical examination. Alternative authentication assays include genetic identification using PCR techniques, immunoassays to identify species-specific proteins or chemical analysis for unique marker compounds. After processing, the botanical dietary supplement should be assayed for hazardous contaminants such as pesticides, herbicides, heavy metals, mycotoxins, and microbes. Besides, pharmaceutical contamination should be ruled out by chromatographic assays designed to detect drugs that might have been added either inadvertently or deliberately during processing. Finally, the botanical dietary supplement should be standardized chemically, based on the concentration of active compoundы, and biologically, based on bioassays for known or desired pharmacological and physiological effects. These final

standardization steps will ensure the consumer of a reproducible and safe product [23, 24].

2.4. Concerns with biologically active supplement use

The manufacture's responsible requirement is to ensure the active biological supplements to the consumer that reaches safe, effective, and acceptable. One of the important parts for the safety of BASs is the Pre and post-market.

1) A pre-market phase with a scientific evaluation of the product dossiers, testing of a sample, and factory inspections to establish a product specification and to document 'Good Manufacturing Practices' (GMP) compliance of the manufacturing source.

2) The post-market surveillance is a key part of identifying safety problems associated with biologically active supplement products. It is conducted in the distribution chain during the surveillance system on it. The market is where products are sold (pharmacies and shops), dispensed (hospitals and clinics), or stored (manufacturers, importers, and wholesalers). Post-market surveillance is often interpreted as having a system for pharmacovigilance to retroactively protect in the future consumers from biologically active supplements that are potentially unsafe. Most developing countries adjust the pre- and –post market system as the main issue. Lack of circulation this system the adverse events happened among consumers of BAS. Rudimentary concerns of biologically active supplements related to product quality, and safety depend largely on dose. This gives rise to health problems. For instance, some dialysis patients receiving substantial doses of calcium and the active form of vitamin D on a chronic basis may exceed the Tolerable Upper Level (UL) and incur adverse effects on health, including calcification of the soft tissues [25].

Very high doses of vitamin D may also cause adverse effects in people with normal kidney function [26]. The most commonly reported reaction-causing supplement is a commercially sold weight loss/energy supplement, including symptoms: abdominal or chest pain and heart problems. Extracts that are used in bodybuilding and weight loss have also been linked to liver injury. This has led to studies of the composition of

different supplements. Causes of liver toxicity from supplements appear to be due to insufficient regulatory authority, inaccurate product labeling, adulterants, and inconsistent sourcing of ingredients [27].

This is evidence of causality from BAS recommend to regulators to take action which pose a hepatotoxicrisk.

Timbo B.B. et al. conducted interviews by telephone from the 2002 American Health and Diet Survey to analyze the prevalence of adverse events related to supplement use. The survey found that 73 % of US noninstitutionalized adults aged 18 years or older and resided in households used a dietary supplement in the previous 12 months, and 4% of them had experienced an adverse event that they thought might be related to dietary supplement use. 85% of supplement users reported taking supplements (i.e., multivitamins plus a singular vitamin/mineral product plus a botanical/herbal product), and 13.3% of adverse events reported to multivitamins/multimineral. Those who reported an adverse event were asked to list the dietary supplements and their symptoms associated with their reaction: abdominal pain, blood pressure problems, nausea, vomiting, allergic reactions, dizziness, itching, and rashes. A higher proportion of supplement users with adverse events than users without adverse events were concurrently taking supplements and prescription drugs or were taking supplements instead of prescription drugs to treat or prevent a health condition. 90% of respondents discontinued taking the products in question after experiencing an adverse event. Just fewer than 50% discussed what they had experienced with a physician, 25% reported their event to a health authority, 12% went to the emergency room, and 9% complained to the manufacturer or retailer. The 74% of users were taking prescription drugs concurrently with DSs.The authors noted that a limitation of the study was that all data were self-reported. It is also difficult to definite an adverse effect to a particular ingredient within a multiple ingredient products or a particular product, especially when multiple supplements are used. The study revealed the lack of knowledge about using DSs. It recommended to food and nutrition professional, and other health care

professionals should take special care to learn about their patients' use of these products [28].

Stephen M.S. et al. aimed to evaluate the characteristics of adverse events (AEs) reported with dietary supplement use, including dietary supplement type and Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) that occurs with reported SAEs. A total of 41,121 unique adverse event cases reported to two large, U.S.-based dietary supplement marketers in 2.5-years (March 1, 2014-August 31, 2016) were assessed for seriousness using established criteria. Each serious adverse event SAE was assigned one or more MedDRA preferred terms and system organ classes (SOC). The types of supplements most responsible for SAEs were assessed. Of the 41,121 AE cases reported, 203 (0.48%) were SAEs. SAEs tended to occur with products marketed for weight loss (69.0%) and glycemic control (19.2%). SAEs occurred most commonly in the cardiovascular, gastrointestinal, and nervous system disorder SOCs. The percentage of SAEs reported to dietary supplement marketers is low, predominantly among consumers of two types of supplements. Further study is needed among a larger cohort of supplement users to determine causal associations between types of supplement products and serious adverse events [29].

The main point of BAS products is not contain what is listed on the label. Still, others contain more or less than the amount of the herb listed on the label. Moreover, many have ingredients that are not listed on the label at all. This problem extends beyond the supplement makers and sellers. Some herbal suppliers (those who grow, harvest, or sell the crops) may mix or even substitute their crops with less expensive or more readily available plants. There is also the problem of accidental contamination when one plant grows in with others, as well as cases of mistaken identity (similarity looks between plants). Given the global market, all of these problems can make it harder for a company to be sure that what they thought they were buying to make supplement is the herb they wanted.

In 2013 researchers in Toronto published a report in which they sampled and analyzed 44 herbal supplements. The supplements were sold in both the US and Canada, and labeled as containing single herbs. Using DNA barcoding analysis, less than half the supplements (48%) contained any of the label's herbs. More than half of the supplements contained something that was not on the label (substitutions or fillers). Even among the samples that contained the herb on the label, many also contained fillers/contaminants [30].

Today, a more severe trend in supplements is extra ingredients or contains prescription drugs or other compounds that are not listed on their labels. For example, some supplement ads are targeted to men as "enhancers" or muscle builders. Certain of these so-called "supplements" have been found to contain substances much like Viagra® or Cialis® and have been recalled. "Prostate health" supplements have been found to contain terazosin, a prescription drug used to treat the symptoms of an enlarged prostate. Other ads target women and tout the supplement as an aid to weight loss. Some of these "weight loss supplements" contained the weight loss drug "sibutramine," which was banned in the United States and other countries because of the risk of heart attack and stroke. The supplement makers recall these only after they have been found to have these illegal additives. Then the FDA can seize these drugs and prosecute the companies who make them [31].

There are also seized that new ingredients with little-known effects are slipped into supplements. In one situation, supplements were labeled as being made from geranium but contained the stimulant drug dimethylamylamine (DMAA), which is harmful to health. This supplement was sold as a "natural stimulant," but it contained DMAA, a human-made drug. The DMAA-containing supplements were exposed after some severe events, including several deaths, leading the FDA to send warning letters to US manufacturers in 2013. Such cases can cause serious health issues for people who take the supplement. Therefore, monitoring supplement use is essential in countries where premarket approval is not required to detect potential adverse reactions. Dietary

indicators are known to be imprecise, and estimates of usual intake lack many nutrients [32]. Deficiency of biochemical indicators is often not well linked with adverse health outcomes that need more attention to be paid to the development of agreed on measures of deficiency and excess ingredients (dose). Safety of Biologically active supplements - the state of food, indicating the absence of unacceptable risks associated with harmful effects on human beings and future generations.

2.5. Regulation of biologically active supplements in the Kyrgyz Republic

In the last decade, the BAS market in Kyrgyzstan has shown substantial growth. Because they are relatively easy to develop, produce, and register, especially when compared to pharmaceuticals. Since 2010 the BAS sales were accomplished via a "black market", but now the government needs to make the BAS market more transparent. More progress can be expected to improve the quality control and safety of the BAS products and the strict regulation system imposed by the government on the registration process and distribution channels. In Kyrgyzstan, in the BAS market are predominantly foreign manufactures from 40 countries, such as India, China, Ukraine, the EAEU and EU countries, the USA, etc. When the Ministry of Health started registering them as a separate group of substances, BAS has been actively promoted on the Kyrgyzstan market. Various distribution channels are selling BAS: • Pharmacies; • Specialty stores; • Internet websites; direct marketing sales. Even though websites' market share was quite substantial in 2007, now most manufacturers prefer to sell their BAS products via pharmacies because consumers trust these stores more than other distribution channels. Evidence-based medicine experts and industry analysts predict that the market will develop in two directions: increased share of regional sales and social consumer group's involvement. Most pharmaceutical firms are interested in the BAS market since the channels of distribution and promotional methods are similar for both BAS and pharmaceuticals. Interest in BAS is growing because of the following two factors:

1. Theoretically, almost all BAS can be advertised. On the contrary, advertising laws on pharmaceuticals are stringent, and accordingly, only Over-the-counter (OTC) drugs can

be advertised. Despite the enormous potential for BAS promotion, there several restrictions imposed for BAS advertising under the Articles 4 and 44 of the Law of the Kyrgyz Republic "On Medicines":

2. The registration procedure most of BAS is relatively simple compared to pharmaceuticals.

Table.2 Comparison special properties between BAS and Pharmaceuticals

Biological active supplements	**Pharmaceuticals**
Only toxicology hygiene and studies	Compulsory clinical and pre-clinical trials
Have only recommendations for usage that allows flexibility in their promotion	Designed for curing particular diseases, so that the promotion for treatment of other illnesses is strictly prohibited
Can be distributed both in pharmacies and other retails stores that have a license for selling food products	Pharmaceuticals can be sold only in pharmacies
Mark-ups for BAS are very high, in some regions they can exceed 50%	Mark-ups for pharmaceuticals (29-30%) have a cap in most regions

According to the law Ministry of Health elaborated decree for BAS regulation:

1. To the heads of republican, region, city, district health organizations, and the Department of Health of Bishkek:

1.1. To prohibit in health organizations the sale and advertising of BAS

1.2. Prohibit to medical workers carrying out the illegal sale and advertising of BAS in healthcare organizations, will take the disciplinary penalty.

2. Pharmaceutical organizations:

2.1. Implement (selling) biologically active supplements only in pharmacies

2.2. To prohibit the implementation of biologically active supplements through the network marketing system (relatively increasing amount of network system in Kyrgyzstan).

In 2017 based on law (Article 4; September 2013) Decree of the Ministry of Health of the Kyrgyz Republic dated September 23, 2013, № 549 that biologically active supplements are not medicinal products and in 2017 has given authority from Department of Drug Provision to the Department of Disease Prevention and State Sanitary and Epidemiological Surveillance under the Ministry of Health to regulate biologically active supplements as food instead of a type of pharmaceutical drug. Currently, perform all regulation procedures of biologically active supplements under the technical regulation document TP TC 021/2011 “On food safety” which is approved between five countries under the Eurasian Economic Union.

The Eurasian Economic Union (EEU) is an international organization of regional economic integration with international legal personality and established by the Treaty on the Eurasian Economic Union signed by the Heads of States of Belarus, Russia, and Kazakhstan in Astana on May 29, 2014. Kyrgyzstan's accession treaty came into effect on 6 August 2015. The objectives of the adoption of the technical regulations are:

- Protection of life and human health;
- Prevention of actions misleading purchasers (consumers);
- Protection of the environment.

Before signature to the agreement of EEU: the regulation system of registration and certification procedures on BAS approved by the Department of Drug Provision and Medical Equipment under the Ministry of Health as a rule of medicine. The establishment of the Eurasian Economic Union (EEU) between five countries and later on the Eurasian Economic Union (EEU) affected the regulatory regime. Developing the technical regulations by these countries must be consistent with each other.

Safety requirements for specialized BAS products following the Technical regulation:

►For use in the production (manufacturing) of BAS are not allowed plants and their products, objects, animal, bacteria, fungi, and biologically active substances hazardous to human life and health and set out in Annex 7 to this technical regulation.

►Biologically active supplements must meet the hygienic requirements of food safety. Contents in a daily dose of BAS derived from plants and (or) their extracts should be in the range of from 10% to 50% of the value of a single therapeutic dose determined with the use of these substances as medicaments [1, 33,34].

2.5.1. Confirmation quality of the biologically active supplement products

The applicant in the confirmation of food products except state control can register by the laws of the State - a member of the Customs Union on its territory a legal entity or person. Confirmation of compliance of food products under the requirement of technical regulations of the Customs Union held in the form:

1) Confirmation (declaration) of conformity of food products;
2) The state registration of a new kind of food;
3) The state registration of specialized food products;
4) Veterinary-sanitary inspection.

The declaration of conformity of food products in the customs territory of the Customs Union, with the exception of unprocessed food products of animal origin, specialized food products, and vinegar. Biologically active supplements are considered a specialized food product; therefore, it is not subject to the declaration of conformity.

The state registration of food products of a new type is carried out at the stage of their manufacturing for the first time in the customs territory of the Customs Union. It is imported into the customs territory of the Customs Union approving its conformity by appropriate state authority. The validity of the state registration of a new kind of food is perpetual. Therefore, such food products are not considered a new type of food product and are not subject to state registration of the applicant. During the registration process of the new kind of food, in case of a new kind of harm, the process may be terminated or suspended, established as a result of state control member of the EEU. The other state registration of the new kind of food follows the state registration of specialized food products. The State registration of specialized food products, including BAS, holds the body authorized by the state of the Department of Disease Prevention and State Sanitary

and Epidemiological Surveillance under the Ministry of Health of the Kyrgyz Republic. In 2016 Ministry of Economic of the Kyrgyz Republic declared a decree for recognition of conformity confirmation results/registration of biologically active supplements:

- Control for biologically active supplements conducted by the technical regulation of the Eurasian Economic Union TR CU 021/2011 “On food safety”;
- State registration of biologically active supplements is carried out at the stage of manufacturing and import to customs territory in the EU;
- Biological active supplements are allowed to be produced (manufactured), stored, transported, and sold after state registration;
- All stages of control of confirmation system of BAS held on Department of Disease Prevention and State Sanitary and Epidemiological Surveillance of the Kyrgyz Republic;
- The state registration of the BAS conducted under the technical regulation document TR CU 021/2011 “On food safety” and it came to effect on August 2017 in the territory of the Kyrgyz Republic;
- Data on the registration of biologically active supplements are entered into the Register of State Registration Certificates and is perpetual;

In Article 53 of the agreement of Eurasian Economic Union about active biological supplements are issued on the territory of the EAEU and provided that it has passed the necessary conformity assessment procedures established by the technical regulations TR CU 021/2011; The applicant has the right to appeal to the decision authority for the registration of BAS products in the courts.

The Kyrgyz Republic ensures the regulation of biologically active supplements that comply with the requirements of the technical regulations TR CU 021/2011 on its territory without presenting additional requirements for BAS and without conducting additional conformity assessment procedures. The Department of Disease Prevention and State Sanitary and Epidemiological Surveillance assess of all comply document packages for the registration BAS product under the list of technical regulation requirements. For instance, the quality of control for BAS should be confirmed by accreditation laboratory

in the territory of EEU. According to the requirements the state registration implemented recognition conformity by state authority. If any non-compliance with these technical regulations, the state registration may be terminated or suspended of registration procedure due to state control or by the decision of the judiciary of the state [1,35].

The regulatory framework of BAS in Kyrgyzstan was carried out in separate stages. All stages of the BAS are regulated by the official documentation that sets out the requirements for BAS composition, the development of their technological process production, registration, storage, transporting, labeling and advertising, handling complaints and recall.

Described at the beginning stage of quality control of testing methods throughout analytical laboratory evidence and conformity the condition of general control mechanism including declaration procedures under the requirement of EEU. According to the specialty of BAS, confirmation procedures used specific TR CU documents, as shown in Table 3.

Table 3.The list of Technical Regulations on BAS

Technical regulation №	**Name of documents**
TR CU 005/2011	"On packing safety"
TR CU 021/2011	Article 24 "About Safety of foods"
TR CU 022/2011	"Food products and labelling"
TR CU 024/2011	"Technical Regulations for Oil-containing products"
TR CU 027/2012	"On safety of particular types of special foodstuff including diet clinical and diet protective nutrition"
TR CU 029/2012	"Requirements of Safety of Food Additives, Fragrances and Technological Additional Products"

It should also be noted that several new regulatory legal acts for improving quality of BAS were prepared and nowadays under the conformation of each five countries. Especially in there was the amendment of some regulation articles which was not appropriate for some countries. For instance, according to the Technical regulation

documents added and changed some articles on the technical regulations of the customs union “On food safety” TR CU 021/2011; The Average Daily Essential Food and Energy Requirements for Fresh Food Labeling which is related to TR CU 022/2011 “On food products and labeling” and TR CU 027/2012 “On safety of particular types of special foodstuff including diet clinical and protective diet nutrition.”

The registration procedure, according to the technical regulation of EEU in the customs territory ensures the same three stages:

1. Analysis of provided documents

2. Analysis of tests such as: organoleptic, microbiological; toxicological; radiological, containing herbs – tests for pesticides (α-β-γ izomers); mycotoxins, DDT and its metabolites; authenticity tests that prove the ingredients listed really contain; in some cases – tests on Genetically Modified Ingredients.

3. Issuance of Certificate of State Registration

Important notification for a manufacturer before applying to the process of registration:

• Not every BAS could be registered in Kyrgyzstan in all registration documents in the country of origin. (The list of allowed BAS’s ingredients is in Addendum 7 in the Technical Regulation: TR CU 021/2011 “About Safety of foods”).

• The full list of proposed medical use approved in the country of origin could be approved only partially by the Kyrgyzstan registration authorities, for instance, labeling assessment under the technical regulation TR CU 022-2011.

• Each biologically active supplement product should have its certificate of registration.

State registration requirements are quite complicated in every country of the EEU. Therefore necessary to amend some articles in the technical regulation documents by requesting of each country.

The procedure of mandatory registration following is the list of documents which the manufacturer or its authorized representative must submit along with an application in order to obtain a certificate of state registration:

1. Copies of the documents approved by appropriate authorities in the country of manufacture also conform that this product is classified as BAS and is not a drug and proves its safety for human beings. These copies must be legalized.

2. Document which is containing a full list of ingredients of the product. BAS is based on herbs - their name in Latin and the method of preparation and explanations of those ingredients commonly used in foods.

3. Standards, references, technical regulations, laws, technological instructions, specifications, recipes used for the manufacturing process of the product.

4. Labeling in the Kyrgyz and Russian languages and a sample of the original label used in the country of manufacture.

5. Usage instructions, annotations in Kyrgyz and Russian languages (not all but necessary information could be placed on the label).

6. Explanation note containing the scientific grounds for BAS compositions; recommendation, contraindications for use and duration, doses, and side effects.

7. Manufacture certificates on toxicological, radiological, hygienic, and biological efficiency and other protocols, if requested.

8. If contained in the BAS live microorganisms, whether need document the type in the Latin language, information about the item (passport, certificate or some other document).

9. Confirmation certificate that BAS does or does not contain genetically modified components.

10. Verifying certificate that this BAS does not contain a drug or psychoactive-related components or other substances.

11. In case a trademark exists, a copy of the trademark certificate by legalized properly.

12. Protocols of tests that are approved by manufacture and trials wherever available.

13. Documents on sample selection procedure indicating the dates of selection, number of the sample, name of the product, manufacture's address, producing date, and the person name who participated in the sample selection process.

14. Power of attorney to get the registration certificate.

15. Brief information on the manufacturing process.

16. BASs for sportsmen and designed to enlarge the muscles - a document from the manufacturer approving that do not contain components attributed to steroids.

17. Certificates of conformity of active ingredients in the BAS product.

18. The main document should be properly legalized, confirming that the manufacturing process for BAS complies with national and international standards, such as GMP, ISO 9000-9002 ect.

19. Copies of invoices for samples that is permitted to "Entry allowed".

20. Usually, samples selected number of 6-8 or 200-300 grams each.

The number of 2, 6, 8, 9, 13, 15, 16 items should be stamped and signed by the manufacturer.

After the completed the whole process of the registration process, a manufacturer/ authorized representative receives the following documents:

►Registration state certificate that is valid perpetual (until some changes occur);

►Expert conclusion of confirmation for safety of the biologically active supplement;

►Conclusions of other laboratories, if during the registration process, extra tests were required [34].

Regarding the labeling of manufactured products and packaging of BASs, the requirements established in the technical regulations of the Customs Union must be observed: TR CU 022/2011 "Food products and labeling" - contains the rules for labeling food products; TR CU 005/2011 "On packing safety" - defines the safety requirements for various types of packaging materials.

The state registration for a new kind of food is held at the manufacturing stage for the first time in the customs territory of the Customs Union, and food products imported into the customs territory of the Customs Union - before its first import into the customs territory of the Customs Union. The state registration for a new kind of food is perpetual,

and in the future, such food product is not considered a new type of food products and is not subject to state registration of the applicant.

It should be noted that currently, the main barriers to the turnover of biologically active supplements in a single economic space are associated with different approaches to regulation in different EEU countries and the lack of a single document in part of the requirements for biologically active supplements. Lack of harmonization of national regulations with the current technical regulations on the critical disagreements in interpreting concepts and requirements during the confirmation its compliance and labeling and advertising differently in the EEU countries. For instance, one of the important procedures on the conformation of the product is "Recognition conformity» for biologically active supplements. This document confirms the quality of biologically active supplements by the manufacturer itself. Some unscrupulous manufacturers can disrupt technology and formulations and put on the market medicines that have not passed the proper tests. Such facts of violations are dangerous to public health. Due to more frequent detection of substandard and falsified biologically active supplements, the crisis in the regulation of biologically active supplements turnover in Kyrgyzstan should be noted. Also, experts of evidence-based medicine regularly identify violations in the sphere of BASs circulation. In Kyrgyzstan, not envisaged clinical trials for the biologically active supplements. Such issues make an obstacle to the control system of the BAS in the country.

The unified register of specialized food products is an integral part of the Unified register of registered food products. It consists of national parts of the unified register of specialized food products, the formation and maintenance of which is provided by the bodies for registration of specialized food products of the Customs Union member state. The primary source of information about the state registration of specialized food products is entered in the unified register of specialized food products, which contains a list of BAS that have passed state the registration in the Kyrgyz Republic. It is an integral part of the Unified register for registering specialized food products of the Customs

Union member state. By this registration, BAS products were registered for 2017 - 2020, 155 names consisted of 95% import BAS products. This is a high indicator that is dominated by foreign products instead of domestic BAS products in the pharmaceutical market. Also, it is indirectly indicating the demand for the BAS needs of the population. To obtain an objective picture of the market for medicinal plants, we studied the dynamics of the registration of biological active supplement products of domestic and foreign production in the Kyrgyz Republic. The data are presented in Figure 2. As shown from this figure, the largest number of biologically active supplements was registered in 2019. In subsequent years, their registration continues in the different dynamics. Because of the reorganizations carried out in the Department of Disease Prevention and State Sanitary and Epidemiological Surveillance and for some other reasons, there were difficulties with accepting BAS products for the registration procedure [1].

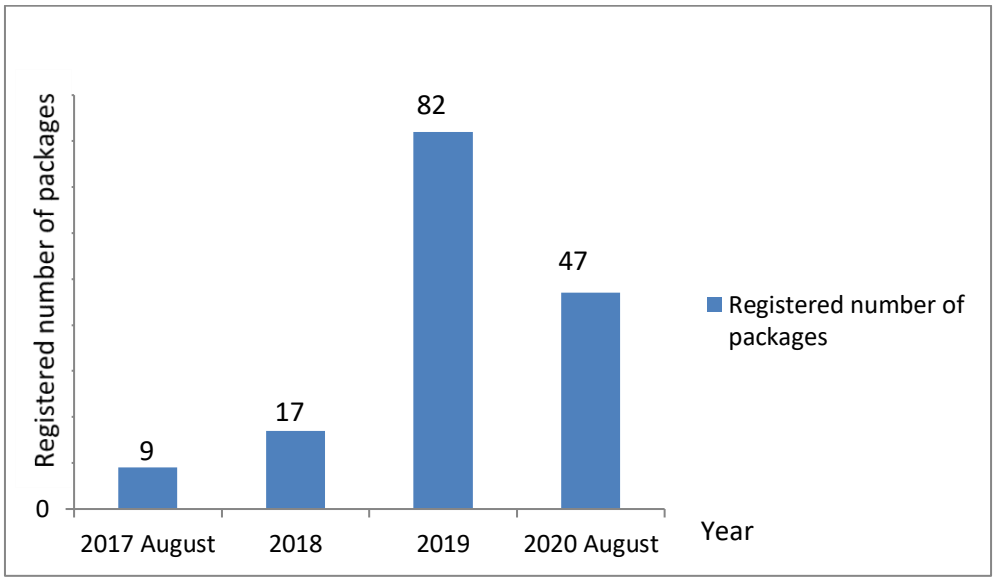

Figure 2. Dynamic's registration of the biologically active supplements for 2017-2020.

Russia adopted a new rule for labeling from 01.01.2019, FZ-488, for the provision of identification means on products. New requirements for the labeling of biologically active

supplements, other food, and non-food products imply that a unique special code is put on the package, a unique sequence of symbols.

The innovation is intended to solve the following urgent problems of technical regulation:

◦ create an automatic product tracking system;

◦ protect consumers from counterfeiting;

◦ fight against unscrupulous companies supplying counterfeit products to the market.

Because of the new rules, the buyer will obtain the maximum information about the BAS by pointing at the unique code of a special scanner installed on a mobile device. It will give information about how and when the goods were produced, through what channels they entered the distribution network [34, 35]. This model successfully practiced almost two years in Russia, contributing to improvement their control system on BAS.

2.5.2. Modern aspects of classification of the biologically active supplements

Nutrition is one of the most critical factors mediating connecting a person with the external environment and determining general health status [36]. A new area of knowledge - pharmaconutriology - is the border line between nutrition science and pharmacology [37]. BASs are one of the main components of a healthy human diet. Problems of ecology, unbalanced nutrition, lack of exercise leads to the fact that dietary supplement becomes practically necessary and vital in our modern life.

The classification is carried out based on theoretical normative legal and scientific and methodological literature, regulatory documents, publications and information manuals, systematization and subsequent logical, structural and comparative analysis.

Nutritional supplements are needed to give the dosage form specific properties, qualities and ensure the safety of the components of the drug. The food supplements related to relative emulsifiers, preservatives, flavorings, and other auxiliary substances [38].

Classifications of dietary supplements are numerous, the main specific area based on biologically active components, physiological action, and functional purpose, methods of obtaining, forms, and other signs [36, 37, and 38].

The dynamic development of biologically active supplements of the pharmaceutical market and their diversity made difficulties creating of a unified classification, therefore, taking valuable parts of it by official normative documents [39].

Nutraceuticals are dietary supplements used to correct human food's chemical composition (additional sources of nutrients: protein, amino acids, fats, carbohydrates, vitamins, minerals, dietary fiber). The functional role of nutraceuticals is shown in Figure 3. The ultimate goal of using nutraceuticals is to improve a person's nutritional status, promote health, and prevent many diseases [40]

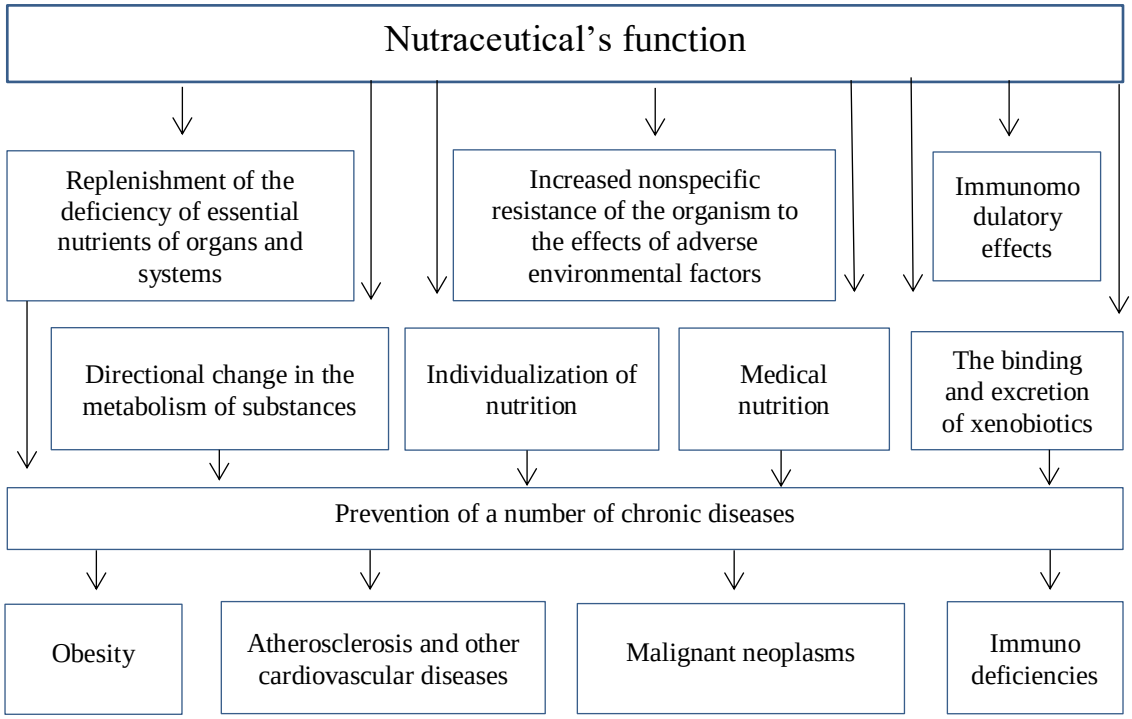

Figure 3.The main functional role of biological active supplements- nutraceuticals

Table 4. Classification by composition and ingredients of biological active supplements

Group	Contents of biological active supplements
1	Mainly based on proteins, amino acids and their complexes
2	Mainly based on animal and vegetable lipids
3	Based on predominantly digestible carbohydrates, including honey with additives of biologically active components, syrups, etc.
4	Based mainly on dietary fiber (cellulose, mercury pectin, gummi, microcrystalline cellulose, bran, fructo-oligosaccharide, chitosan and other polysaccharides)
5	Based on pure substances (vitamins, minerals, organic acids, etc.) or their concentrates (plant extracts, etc.) using various excipients, including dry beverage concentrates
6	Based on natural minerals (zeolites, etc.), including mummy
7	On the base of plants, including flower pollen: dry (teas) and liquid (elixirs, balms, tinctures, etc.)
8	Based on the processing of meat and dairy raw materials, including offal, poultry; arthropods, amphibians, beekeeping products (royal jelly, propolis, etc.)
9	Based on fish, marine invertebrates, crustaceans, mollusks and other seafood, plant marine organisms (algae, etc.)
10	Based on probiotic microorganisms

Parapharmaceuticals are dietary supplements used for prevention, adjuvant therapy, and support within the physiological boundaries of the functional activity of organs and systems. These are natural remedies that have a directed physiological effect, and they are used to prevent various diseases [40].

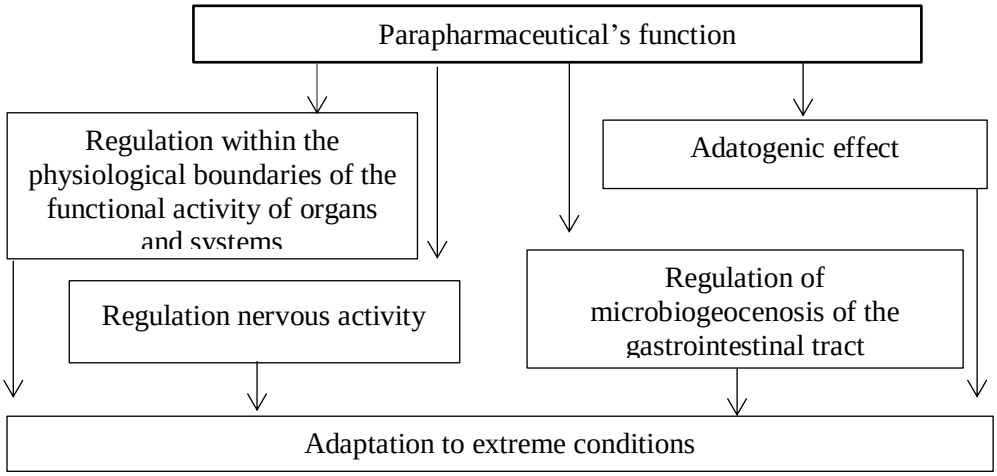

Figure 4. The main functional role of BAS- parapharmaceuticals

Table 5. Classification on the physiological effect on the body of BAS

№	**The name of group**
1	BAS acting on the digestive system
2	BAS acting on the hematopoietic system
3	BAS to maintain the functions of the cardiovascular system
4	BAS used to eliminate various problems with skin and hair
5	BAS affecting the reproductive system
6	BAS that affect the function of the endocrine glands
7	BAS that support the function of the immune system
8	BAS used for viral, bacterial and fungal diseases
9	BAS used in diseases of the skeletal system
10	BAS that affect the functions of the central nervous system
11	BAS used in diseases of the respiratory system

12	BAS acting on the sentiments
13	BAS used for poisoning and intoxication
14	BAS acting on the urinary system
15	BAS acting on the body as a whole
16	BAS for losing weight and body cleansing

Table 6. Classification by contents of BAS

№	**The name of groups**
1	Balms, teas, explosions, fees
2	Proteins, amino acids and their derivatives
3	Vitamin and mineral complexes
4	Vitamins, vitamin-like substances and coenzymes
5	Natural metabolites
6	Fats, fat-like substances and their derivatives
7	Macro and micro elements
8	Polyphenolic compounds
9	Prebiotics and probiotics
10	Beekeeping products
11	Products of plant, animal or mineral origin
12	Carbohydrates and their processed products
13	Enzymes of plant or microbial origin
14	Raw materials for BAS

The creation of a unified classification of biologically active supplements will help to the regulation system on it. Improving the regulation of BASs turnover is one of the state's top priority tasks in this area of research.

2.6. Regulation statement of health/functional food in the Republic of Korea

2.6.1. Key term of health/functional food (HFF)

The term, biologically active supplements, considered in Korea as "health/functional foods." It was defined in the Korean Health/Functional Food Act refers to foods manufactured or processed with functional raw materials or ingredients useful for modification of physiological functions, maintenance of homeostasis, or improvement of specific physiological parameters. The term "functionality" means utilizing nutrients to affect the human body's physiological functions or providing beneficial effects for hygiene purposes, including psychological benefits. Thus, the definition of the functional ingredient is a substance providing health benefits and falls under any of the following subgroups: elaborated raw material originated from an animal, plant, or microorganism; extract or purified substance of any ingredients; synthetic duplicate of the purified substance of any ingredient; or combination of any ingredients which are described above.

The Korean Health and Welfare Committee of the National Assembly proposed the HFFA in November 2000. In August 2002, the HFFA was enacted as a new regulatory framework for the safety, efficacy, and labeling of HFFs, and it came into effect in January 2004. The Act's main goal was to enhance public health by ensuring the safety of new bioactive ingredients. In 2004, the law defined HFFs as "food supplements such as pills, tablets, capsules, powder, and liquids"; in other words, conventional foods were not permitted to make any such claims. However, with increasing pressure from the food industry, after 2008, the definition of HFF was broadly expanded to encompass all types of processed foods. The standardization, safety, and efficacy of a new active ingredient are reviewed by the Ministry of Food and Drug Safety to receive approval as a product-

specific HFF. This authority also makes manufacturers or distributors responsible for submitting all evidence to substantiate their products claims. Conforming to international standards and protecting public health requires constant upgrading of the Health/Functional Food Act [41].

Now, HFFs are defined as "food manufactured or processed with ingredients or components that possess functionality useful for the human body." However, foods for special dietary usage remain under different regulations according to food hygiene laws. Relevant laws and regulations which are used for regulation of the HFFs:

- Food Hygiene Act
- Health/Functional Foods Act
- Enforcement Rule of Health/Functional Foods Act
- Health/Functional Food Code
- Regulation on Approval of Functional Ingredients for Health/Functional Foods
- Labeling Standard for Health/Functional Foods
- Regulations on Recognition of Raw Materials or Ingredients of HFFs
- Regulations on Imported HFF Notification and Inspection Procedure
- Prohibited Ingredients for Korea's Health Functional Food

2.6.2. Classification of health/functional foods

Health/functional foods in Korea are divided into two subcategories: generic and product-specific. Generic HFFs are defined as products with functional ingredients listed by the Ministry of Food and Drug Safety (MFDS). These products include vitamins, minerals, and various other functional compounds. All new ingredients that are not generic HFFs are subjected to efficacy evaluation before marketing based on their ingredients or physiologically active components to ensure the accuracy of the health claims. Authorization is granted on a product-by-product basis by issuing a certificate without regulatory amendments. The MFDS has the exclusive authority to evaluate the safety and efficacy of HFFs before their introduction to the market, and it also keeps manufacturers and distributors responsible for providing all evidence regarding the

advertised claims of their products by developing a system for substantiation of claims or relying on existing information. Under the HFFA, claims regarding nutritive and other functions and reductions in disease risk that are compatible with those adopted by the Codex Alimentarius Commission in 2004 [42], can be used for labeling and advertising of HFFs. Each claim type is defined as follows:

•Nutrient-function claims: These claims indicate the nutrient's physiological role in the development, growth and normal functions of the body. Such claims apply to the nutrients, which have their own Recommended Daily Allowance (RDA) and must be based on the current level of nutrition as a source of evidence.

• Reduction of disease risk claims: It describes the relationship between the consumption of HFFs and the reduced risk of developing a disease or health-related condition.

• Other function claims: These claims are related to specific beneficial effects of HFFs in the context of the total diet on normal functions of the body. Such claims help to positive contributions toward health, the specific improvement of a function, or the modification or preservation of health.

2.6.3. Generic health functional foods

Table 7 indicated that in 2004, the Health/functional Food Act references 37 generic HFFs, including 14 vitamins, 11 minerals, essential amino acids, proteins, dietary fiber (which is a collective term for non-digestible fiber) available as nutritional supplements and as 55 functional ingredients, including ginseng, green tea extracts, and various fibers [43]. The MFDS considered these generic HFFs into an HFF code and divided them as categories: nutritional supplements, health supplements, and ginseng products. According to these categories, the MFDS re-evaluated 37 generic HFFs for scientific substantiation of their claims from 2003 to 2007. As a result, several generic HFFs, including royal jelly, yeast, bee pollen, digestive enzymes, turtles, and eels, were eliminated from the HFF category. These products are re-categorized as conventional food, which is not able to bear health claims [44].

Because of several ambiguous expressions in several claims were changed into “enhanced function” claims. Dietary fibers were listed separately according to their raw materials and were regarded as separate functional ingredients.
In Korea, it is required that anyone selling HFFs should get government approval. Also, to expand the number of generic HFFs covered in the HFF code, new principles for the addition of generic HFFs among product-specific HFFs were introduced.

The functional ingredients estimated by the Regulation on Approval of Functional Ingredients for HFF which is permitted to add to the Code according these cases: “if the item passed from the date of the manufacturing report or the import report , or three or more business persons file the item manufacturing report; or in cases where the person who has obtained the recognition under the provision of Article 14 (2) of the Health Functional Food Act then the item recognized as a functional ingredient and requests the adding (provided three or more persons obtain the recognition). However, sometimes after being recognized as a functional ingredient, the applicant requests data protection concerning their manufacturing processes, human studies on functionality, and toxicology studies. In these cases, adding the functional ingredient can be postponed for up to 5 years from the date of the item manufacturing report or import report, dependent upon the requested validity. For generic HFFs, nutrient-function claims can only be made for vitamin and mineral supplements, which have their own recommended dietary allowances (RDAs).

Table 7. Generic health functional food in HFF Code

Nutrients			
Vitamins		Minerals	
Vitamin A Vitamin D Vitamin E Vitamin K Vitamin B1 Vitamin B2 Vitamin B6 Vitamin B12	β-Carotene Niacin Pantothenic acid Folic acid Biotin Essential fatty acids Dietary fiber Vitamin C	Calcium Iron Copper Iodine Molybdenum Chrome Protein	Magnesium Zinc Manganese Potassium Selenium
Functional Ingredients			
Ginseng	Red ginseng	Plants containing/ chlorophyll	Chlorella/spirulina
Green tea extracts	Aloe whole leaves	Propolis extracts	Coenzyme Q10
Soybean isoflavone	Omega-3 fatty acids	γ-Linoleic acid	Lecithin
Squalene	Phytosterol/-ester	Alkoxyglycerol	Octacosanol
Japanese apricot	CLA	Garcinia cambogia	Lutein
Haematococcus extract	Saw palmetto extract	Glucosamine Mucopolysaccharide	Gingko leaf extract
N-acetylglucosamine	Guava leaf Extract	Banaba leaf extract	Aloe gel
Milk thistle extract	Phosphatidylserine	Primroseseed extract	Red yeast rice
Ganoderma lucidum fruit body	Chitosan/ oligosaccharide	Probiotics	
Fructo oligosaccharide	L-Theanine	Soybean protein	
Functional Dietary Fiber			
Guar gum/ hydrolysates Soy fiber Arabic gum Polydextrose	Glucomannan Tree ear Corn bran Fenugreek seed	Indigestible maltodextrin Wheat fiber Inulin	Oat fiber Barley fiber Psylliu husk

2.6.4. Product-specific health functional foods

If manufacturers or distributors want to market HFFs that are not included in the list of generic HFFs (and hence is regarded as new), they must apply a product-specific HFF. In that case, manufacturers or distributors must provide the MFDS with evidence of the standardization, safety, and efficacy of the product [45].

The MFDS then performs a pre-market review within 120 days of receiving the application, focusing on the origin and nature of the ingredients, the content of functional components (or index components), processing methods, information on the methods and validation for analysis of functional components, stability data, and purity (in terms of the content of microbial, heavy metals, pesticides, etc.), as well as scientific evidence for the safety and efficacy of the HFF.

The evaluation by the MFDS starts once the applicant has submitted the relevant documents. The MFDS first determines whether the standardization has been performed adequately and then evaluates the safety, efficacy, and specifications.

Standardization: The manufacturer submits data on the specific characteristics of the functional ingredient (such as cases of an unclear functional ingredient or an index ingredient for identifying raw materials and states change in the content of functional or index component) arising from the primary manufacturing process, and then the MFDS evaluates the adequacy of these data.

Safety evaluation: The safety of the active ingredient is assessed by the MFDS, which is responsible for reviewing the submitted data, including detailed descriptions on the history of use, manufacturing processes, the quantity for consumption, results of toxicity tests, results of human studies, and results of nutritional evaluation and bioavailability.

The safety of the active ingredient must be validated scientifically according to the preparation of safety data by three categories: (1) cannot be used as a raw ingredient for an HFF; (2) scientific data or historical use describing its manufacturing process, usage, and the amount of intake, database searches of the side effects, toxicity, and evaluating

the amount to be consumed; and (3) evaluating the nutritional effects, toxicity data, and other data relevant for proof of safety.

Efficacy evaluation: The evaluation of HFF efficacy is different from the medicines, as the target consumers of HFFs are: healthy individuals or individuals in the preliminary stage of a disease or borderline condition in an at-risk group. Therefore, efficacy requirements are less distinct for HFFs than for drugs marketed to patients with a medical condition. Currently, no formula exists for the extent of studies required to substantiate a claim regarding HFFs, with the MFDS applying a generalized standard of "competent and reliable scientific evidence," which provides manufacturers and distributors with some degree of flexibility in the type of evidence while contributing to the maintenance of consumer confidence in HFFs. To evaluate whether the submitted information constitutes competent and reliable scientific evidence, each study is reviewed independently, considering the total body of evidence.

Specification: The applicant must also submit samples of the product with documentation regarding the analytical method used for analyzing the functional component to the MFDS, which validates the selectivity, precision, accuracy, linearity, and range of the method. The MFDS then determines the contents of the functional component. If the decision is made to approve the product as an HFF, confirms the period of conformity and hygiene specifications.

2.6.5. Registration prosedure

1) Business License - A locally registered partner with a corresponding business license is necessary in order to register a health functional food; this requires that the local entity is eligible for a business license, complies with national standards, and notifies its intended activities to the local Guide (Article 4-13 Health Functional Food Code).

2) Declaration - If the applicant wants to import HFF, file a declaration with the MFDS (Article 8 Health Functional Food Code). According to the list of the Health Functional Food Code, a distinction is made for products containing substances - subject to simple notification - and substances that have not been approved which are registration needs.

3) Approval of functional ingredients - The approval of new functional ingredients is further elaborated upon in the Regulation on Approval of Functional Ingredient for Health Functional Food [46].

Article 4 of the Regulation requires (i) that the food complies with the Health Functional Food Act, and (ii) that the safety and functionality shall be ensured and scientifically proven.

The applicant should complete the provided form together with the following files:

i. Two copies of the required documentation (including an original copy)

ii. A CD containing the documentation

iii. A sample of the product and the standard of function component

iv. Result of examination issued by a domestic HFF examination of laboratory analysis.

The documentation part is only in the case of new functional foods/substances; data needs to be submitted. Suppose manufacturers or distributors want to market health/functional food that are not included in the list of generic health/functional food. In that case, they have to apply for approval as a product-specific health/functional food. Before the official review, enterprises must submit documents according to Article 12 of the Regulation on Approval of Functional Ingredient for HFF lists the following stages [47]:

i. Executive summary of all submitted documents

ii. Origin information: developing history, current history of approval, and use in domestic or foreign countries, etc.

iii. Manufacturing methods and related data

iv. Characteristics of the ingredients: documents to explain the feature and quality of this active ingredient

v. Materials of the active ingredient’s specification, test method, and test result

vi. Specification, test method, and test result of harmful substances

vii. Materials to substantiate the safety

viii. Materials to substantiate its functional efficacy

ix. Documents related to the intake dosage, intake method, consumption precautions, etc.

x. Confirmation data that the ingredients are not identical with or similar to medicine: distinguish the product from medicines, etc.

A detailed description per an aspect of required documentation follows by article 13 of the Regulation. The Regulation also establishes the formal requirements that the documents are marked with a table of contents, index number, and document number according to their sequence per section. In case one of the required documents cannot be provided, the reasons should be stated and included in the relevant section.

An original copy and executive summary shall be submitted together with a Korean translation of the documents. The provided documents will be treated confidentially.

For the main labeling requirements of the HFFs used Article 17 of the Health Functional Food Act.The names of all ingredients and all imported food products are required to be labeled with the necessary information in Korean without additional stickers on packages.

The outcome and timeline of the procedure for the approval of functional ingredients will take 120 days from the application. The FDA may however, request additional information, in which case a supplementary period will be determined. In case the product cannot be approved, or no additional documentation is submitted, the reasons for denial will be stated, and the dossier will be returned to the applicant (articles 6-10).

If approved, the Commissioner of the MFDS will issue a ´Certificate of Functional Ingredient for HFF.' The certificate can provide for exclusive use of the substance for 5 years.If any modifications need in the Certificate contents may be amended through an "Application of Modification on Certificate of Functional Ingredient for HFF."

To help develop the healthy functional food industry, on Nov. 6th, 2019, MFDS released a guideline introducing a new consultation service to help enterprises expedite approval of functional foods. The MFDS maintains advisory committees for HFFs comprising 30 experts with nutrition, food science, medicines, and consumer unions. These committees comprise six subcommittees that advise the MFDS about regulations, acceptable manufacturing practices, importing and exporting, new active ingredients, standards and specifications, and labeling and advertisements.

CHAPTER III

METHODOLOGY

3.1. Study design

A descriptive cross-sectional, online questionnaire-based study was conducted on 391 participants from August to September 2020 among the population in the Kyrgyz Republic within age above 18years old, including healthcare professionals: doctors, pharmacists, and nurses. A structured self-administered questionnaire was formed based on adequate use of the biologically active supplement and evaluation of its status. It included three parts:

- Sociodemographic data and health status, with supplement users and non-users
- Practices of participants concerning the use of vitamins, minerals, herbals, and other dietary supplements with detailed information about the type, form consumption frequency, and duration
- Safety, quality, availability, accessibility, effectiveness, benefits, side effects, existing regulatory system in the country
- Labeling, packing, composition and finally knowledge and opinion regarding biologically active supplements in all participants. The independent variables knowledge of BASs and gender were compared with the dependent variable of users and non-users. Logistic regression was used to reveal BAS use with occupation, income, education, and government regulation on BASs.

Then this research has analyzed a comparative study based on regulation system on BAS between the studied countries Kyrgyzstan and Republic of Korea.

3.2. Study site

This is a study carried out in Kyrgyzstan among healthcare workers from the Infection disease Department of International School of Medicine in Bishkek; National Center for Infection Control; Family Hospital №7; Department of Drug Provision and

Medical equipment; Department of Disease Prevention and State Sanitary and Epidemiological Surveillance; and including pharmacists.

Population: mostly in Bishkek (capital) and from other cities, regions, and villages. Bishkek is the most populated city in Kyrgyzstan (1,012,500 population est.2019) and is situated in the north part of Kyrgyzstan. The city's territory is 169.6 square kilometers and is administered separately and not part of any region. There are predominantly Kyrgyz residents around 66% while European people make up less than 20% of the population and other international populations.

3.3. Study participants and sampling

The target populations were users and non-users of the biologically active supplements among government employees, private entrepreneurs, doctors, nurses, pharmacists, pensioners, and non-employers within age above 18 years old in the Kyrgyz Republic. To determine the sample size, used the Cochran equation calculating sample for proportions of large populations:

$n=p(1-p)(Z/E)^2$

In the formula n is the sample size, Z^2 is the abscissa of the normal curve that cuts off an area α at the tails (1 - α equals the desired 95% confidence level (Z=1.96), E is the desired ±5% level of precision (E=0.05), p is the estimated proportion in the study population and q is $1- p$(p=0.05), a sample of size 385 was needed:

$$n = 0.5(1-0.5)\left(\frac{Z}{E}\right)^2 = 0.5(0.5)\left(\frac{1.96}{0.05}\right)^2 = 384.2$$

Figure 5. Model for determination of appropriate sample size

The sample randomly selected 391 participants by sending a “link” questionaries’ form to the respondent’s telephone number. Trained interviewers collected data during August and September months in 2020 in all study areas. Among the 391 selected respondents, 372 responded to the adjusted survey to accommodate an expected 95% response rate.

3.4. Study variables

Respondents were asked about taking the BAS in the present. Biologically active supplement was defined as a product consumed in tablets, syrup, ointment, powder, herbal preparations, gel, ointment, liquid forms, or capsules etc. intended to supplement the diet to maintain health.

Typical examples would be vitamins, minerals, herbs, Energizers (activators), Proteins, Vitamins, Minerals, Sport drink, Phytopreparations. The motivation of the population regarding use of BAS products for different reasons such as toning the body, improving muscle mass and sports performance, improving brain performance, losing weight, keeping weight, striving for longevity and beauty, and preventing disease, self-medication of a previously diagnosed disease.

Independent study variables were categorized into sociodemographic status, socioeconomic status, health status, and BAS fundamental knowledge. Education, income, and occupation were used to determine socioeconomic status. Educational background was classified into three categories: primary education, specialized secondary graduate, and high graduate education. The definition for each category is education university degree or higher, respectively. Income was also classified into three levels: low, middle, and high. Definition for each level is lower-income quartile, second and third income quartile, and upper-income quartile, respectively. The occupation was labeled either as a group: the first group involved government employers and private entrepreneurs; in the second group health professionals: doctors, nurses, pharmacists, and third group considered as no occupation involved any jobs, housemakers, and pensioners unemployed.

As a health status questioned how participants viewed their health and asked participants to

score from one to three, where three was healthy and two wasnormal and their score was considered as unhealthy.

Other variables of the socio-demographic characteristics as covariates included age, gender, and geographical location. Geographical location was determined as a group: urban and rural residents. Adult, defined between ages 19-29, were grouped into as young adults, and between ages 30-59 were considered working adults, and aged over 60 were considered elderly, respectively.

Last part of the survey described independent/dependent variables related to basic information about BAS including information sources, purchase location, and side effects; taking a course of BAS; difference BAS from medicines; attitude, and knowledge towards biologically active supplement use: safety, quality, effectiveness, accessibility, availability, affordability, and regulation of BAS and assessment of network system on BAS in the Kyrgyz Republic. Definition of each independent/dependent variables represented in Appendix 1. The primary consumption on the practical-theory of BASs according to the respondent's survey interpreted as a model in figure 6.

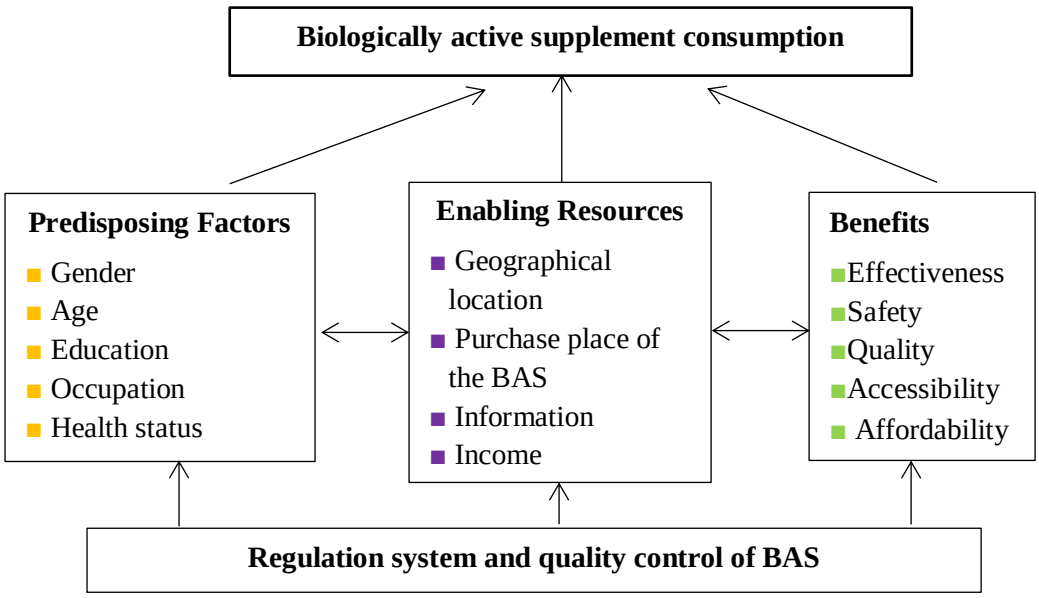

Figure 6. Structure model on the basis of questionnaire/survey on BAS

Based on this model developed three hypotheses of the study to answer the research question under the variables: first by gender; the second through knowledge among consumer and non-consumer as a dependent variable, and third is identifying association government regulation use of BAS in the Kyrgyz Republic. Each hypothesis elucidated the research question.

3.5. Data collection

In achieving the objectives of the research, a qualitative approach has been used as a general research method. To answer the research questions, the data collected from both primary and secondary sources were used in the statistical analysis of the BAS use among population in the Kyrgyz Republic and the textual analysis of the regulation system between two countries Kyrgyz Republic and Republic of Korea.

The primary study's main focus was the use of biologically active supplements and assessed knowledge on the basic terms of biologically active supplements among the study population and the function of the government on the regulation of BASs products.

The study's primary data was used a cross-sectional online survey design to gather information regarding BAS use, attitudes, and regulation system among the population of the Kyrgyz Republic. The survey was administered by interviewing participants anonymously in person using a structured questionnaire between August and September of this year. The questionnaire was prepared in English, translated into Kyrgyz and Russian languages, and back- translated into English to check for consistency. It was pretested on 7 people in Government Family hospital №7, Naryn province in Kochkor region. The questionnaire structure was in four parts, according the dependent and independent variables: First, the interviews described the purpose of the study and confidentiality of their answers and asked respondents whether they consented to participate. The second part was a sociodemographic and socioeconomic profile of the respondent: gender, age, geographical location, educational level, occupation, and income. The third part was described consumption patterns: use of vitamins, minerals, food supplements, herbal

products; composition and form of BAS; reliable information source and purchase places, side effects; duration use of BAS; difference BAS from medicines; attitude, and knowledge towards BAS use: safety, quality, effective, accessibility, availability, affordability and part 4 was about regulation of BAS and the respondent assess to network system on BAS in the Kyrgyz Republic.

At the end of the questionnaire form respondents, indicated their suggestion for improvement of the biologically active supplement sector in the Kyrgyz Republic.

In secondary data of this research has used the documents based on regulation procedures of the BAS as a comparative study between the studied countries Kyrgyz Republic, Department of Disease Prevention and State Sanitary and Epidemiological Surveillance and Republic of Korea, Ministry of Drug and Safety Food. Interwieved employees from the Department of Disease Prevention and State Sanitary and Epidemiological Surveillance of the Kyrgyz Republic and the necessary information from official websites of state bodies of the Kyrgyz Republic and Republic of Korea were also used as secondary data. The purpose of this comparative study improve the regulation system in Kyrgyzstan compared to the Republic of Korea.

3.6. Inclusion and exclusion criteria

The data of this study included 391 respondents aged over 18. Aged under 18 did not answer questions relevant to adults, such as fundamental assessment of biologically active supplements. Those who did not provide an answer or answered as unknown to a specific question on biologically active supplement were excluded from the study. Moreover, those with missing responses in other variables were also excluded. In the end, there were 372 participants for the study analysis, as showed in figure 7.

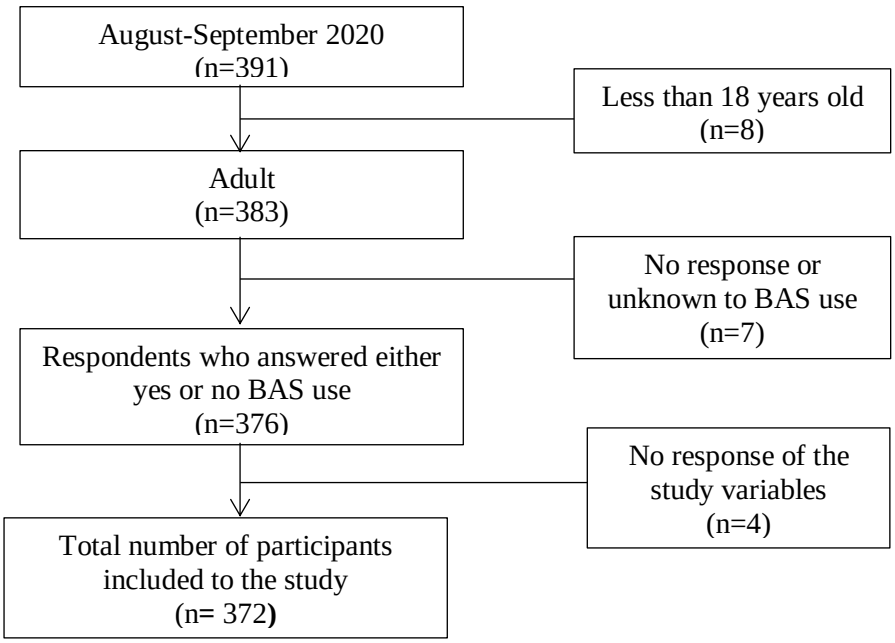

Figure 7. Inclusion and exclusion criteria of the study

3.7. Statistical method

The results of the respondent's data were analyzed and performed with the statistical method (package SPSS, version 25.0). Using a two-tailered test, p values < 0.05 were statistically significant. Described the sociodemographic characteristics by categorical variables except for age and income as a continuous variable. For comparison, the means of two independent groups were used two-sample t-test to determine the statistical evidence that is significantly difference in population means. Concerning categorical variables, the frequencies and proportions were calculated by Cross tabulation. Pearson chi-squared analyses were used to compare the social characteristics, practice, knowledge, and attitudes difference between consumer and non-consumer groups in the study population. Logistic regression analyses were performed to determine the association of each sociodemographic variable, including age, gender, income, geographical location, health status, with the prevalence of BAS use among the study population. The odds ratio (OR) with 95% confidence interval (CI) and p-value have represented the logistic regression analysis

result. Thus, logistic regression was used as a dependent variable as binary, 1=biologically active supplement consumer and 2=biologically active supplement non-consumer, where χ represents each variable also as a binary variant indicated in Figure 8.

$y = ln\left(\frac{P}{1-P}\right) = \beta_0 + \beta_1\chi_1 + \beta_2\chi_2 + \beta_3\chi_3 + \beta_3\chi_3 + \beta_4\chi_4 + \beta_5\chi_5 + \beta_6\chi_6 + \beta_7\chi_7 + \beta_8\chi_8 + \beta_9\chi_9 + \beta_{10}\chi_{10} + \beta_{11}\chi_{11}$
y = BAS consumer=1; BAS non-consumer=2, χ_1 = Education (secondary, high graduate) χ_2 = Income (low, high) χ_3 = Occupation (Unemployed, employed) χ_4 = Health status (Unhealthy, healthy) χ_5 = Age (young adult, elderly) χ_6 = Gender (male, female) χ_7 = Government regulation (yes, no) χ_8 = Knowledge on BAS (yes, no) χ_9 = Safety (yes, no) χ_{10}=Effectiveness (yes, no) χ_{11} =Availability (yes, no)

Figure 8. Logistic regression model

The model revealed the third hypothesis, which was identifying association government regulation use of BAS. For performing statistical method, the variables: education, income, occupation, health status, age were recoded as a binary like others: gender, government, knowledge, safety, effectiveness, and availability. Thus, conducted a bivariant analysis to determine research questions through logistic regression of the study.

CHAPTER IV

STUDY RESULTS

4.1. Discriptive statistics

Description sociodemographic characteristics of the study on biologically active supplement use among the population in the Kyrgyz Republic present in table 8. It is shown percentages of the variables as the weighted frequency with statistical significance at 5%. This study population involved 268 (72%) BAS consumers and 104 (28%) non-consumers. Mainly proportion of consumers taking BAS products like a course in a year (53.7%) compare to less population taking more one course in a year (35.4%), and fewer of the proportion sometimes use due to their income. The population geographical location mainly proportion 78.7% of urban residents in the consumer group and only 21.3% amount of portion in rural residents in non-consumer group. Most consumers were female 75.0% (male 25.0%) compare than non-consumer group female 56.7%. Among consumers the majority age was medium between 30-59 years, 81.8% and the young age 19-29 was 8.6%, and elderly above 60 years was 9.7%. Moreover, in the non-consumer group, there is less aged group than in the consumer group (5.8% and 9.7%, respectively). However, they are significantly more in the consumer group medium-aged population 81.8% than the non-consumer 71.2%. While consumers: 51.5% had high education, 42.9% college graduate education, and 5.6% primary/secondary school graduate education. More than half of the consumers were in middle-income class (55.2%) compare other between low and high classes (35.1% and 9.7%, respectively) were allocated not equally. While 65.4% of non-consumers were from the middle-income population.

Almost similar frequencies were consumers: government employers and private entrepreneurs 22.5% and 23.4%, respectively, while health professionals were 31.7% (14% doctors, 12.9% pharmacists, and 4.8% nurses) and the unemployed population were 22.4%. Primarily in both groups had a permanent job presented as 59.6% in non-consumer group and 45.9% in the consumer group.

As described in the previous part, the statistically significant difference between consumer and non-consumer groups for all independent study variables was p value=0.05. The consumer groups had more people with higher education, higher income, and were government employers and private entrepreneurs. Almost half of the consumers appraised themselves as relatively usual 47.0%, while 36.2% viewed themselves as healthy and 16.8% perceived unhealthy. According to this statement: two-fold less healthy and two times unhealthier population in consumer groups than non-consumer groups. For instance, non-consumer group, 63.5% had the healthy population, and only 7.7% had an unhealthy, while in the consumer group, 16.8% had the unhealthy population and 36.2% had a healthy population.

Attitude towards BAS in the consumer group's population was relatively 79.1% in positive opinion and 62.5% population in the non-consumer group in an unfavorable position for using BAS. Regarding distinguish of BASs from medicines in consumer group, 90.3% population can differentiate, according to this statement, 45.5% of consumers using BAS parallel with medicines. Relatively 55.8% of the non-consumer group cannot determine BAS difference from medicines; therefore, 78.8% of the population in that group indicated no parallel use.

During the taking of BAS, the central part of the consumers group was taking effect. To avoid harmful effects, the BAS products must meet the hygienic requirements of food safety. According to this term included safety of BAS products in this study. 67.2% of the consumer group indicated the safety of their taking BAS products; however, were happened 20.9% of adverse events in this group during the taking BAS products and 52.8% of them individually took action with their harmful effects, and 12.7% of the affected population helped by healthcare workers. Also, 74.0% of the non-consumer groups any idea about the safety of BAS products. Such as cases government should ensure control of quality and safety of BAS products for public health. Therefore, this measure was used to assess awareness of the country's government regulation system among the study

population. Half of the non-consumer and consumer groups were no information about regulation on BAS products (50.0% and 41.0%). Almost the study population in both groups demanded a control system for the BAS sector in the Kyrgyz Republic. The proportion of the assessment network system in Kyrgyzstan, which scored from 0 to 10 was the medium in both groups, presented as a 5-7 level.

Due to mostly BAS products imported from other countries in Kyrgyzstan, their price was more expensive than domestic. Consequently, affordability the primary function play for using BAS products and, it's directly related to the population's income of the. For instance, in both groups, showed more than half the population was in low-income: affordability (82.7% of non-consumer and 57.9% consumer). A small number of percentages showed both groups as high-income affordability (1.0% and 6.0%). Substantially part of consumers had benefited from taking BAS products (89.6%), and 50.0% of the proportion in the non-consumer groups did not notice the beneficence taking of BAS products. Mainly proportions of consumer groups were satisfied for their taking of BAS products (81.3%) and generally 60.6% in the non-consumer group indicated dissatisfaction for the BAS products.

Table 8 showed no significant difference regarding education, geographical location, income, and side-effects among consumer and non-consumer groups with different characteristics (p value=0.275, 0.705, 0.169 and 0.275). The other variables indicated statistically significant there was enough evidence to reject the null hypothesis and significant evidence to support the alternative hypothesis of each variable on BAS among consumer and non-consumers groups.

Table 8. Overall characteristics of study population among user and non-user groups

Item		Overall	Consumer	Non-consumer	Chi-square	*P*-value
		n=372	n=268 (72%)	n=104 (28%)		
		n %	n %	n %		
Variables: SES						
Gender	Male	112 (30.1)	67 (25.0)	45 (43.3)	11.88	0.001*
	Female	260 (69.9)	201 (75.0)	59 (56.7)		
Education	Primary/Sec.	19 (5.1)	15 (5.6)	4 (3.8)	2.58	0.275
	College grad.	152 (40.9)	115 (42.9)	37 (35.6)		
	High graduat.	201 (54.0)	138 (51.5)	63 (60.6)		
Geograph.location	Urban	291 (78.2)	211 (78.7)	80 (76.9)	0.14	0.705
	Rural	81(21.8)	57 (21.3)	24 (23.1)		
Age	Young	47 (12.6)	23 (8.6)	24 (23.1)	26.03	0.001*
	Medium	293 (78.7)	219 (81.8)	74 (71.2)		
	Elderly	32 (8.6)	26 (9.7)	6 (5.8)		
Income	Low	124 (33.3)	94 (35.1)	30 (28.8)	3.55	0.169
	Middle	216 (58.1)	148 (55.2)	68 (65.4)		
	High	32 (8.6)	26 (9.7)	6 (5.8)		
Occupation	Govern/priv.	185 (49.7)	123 (45.9)	62 (59.6)	9.35	0.009*
	HCWs	117 (31.5)	85 (31.7)	32 (30.8)		
	Unemployed	70 (18.8)	60 (22.4)	10 (9.6)		
Health status	Unhealthy	53 (14.2)	45 (16.8)	8 (7.7)	22.69	0.001*
	Normal	156 (41.9)	126 (47.0)	30 (28.8)		
	Healthy	163 (43.8)	97 (36.2)	66 (63.5)		
Employment	Permanent	283 (76.1)	194 (72.4)	89 (85.6)	7.16	0.028*
	Doesn’t work	54 (14.5)	45 (16.8)	9 (8.7)		
	Temporary work	35 (9.4)	29 (10.8)	6 (5.8)		

Continued to the next page

Table 8 (continued)

Variables: attitude to BAS

Attitude to BAS	Positive Neutral Negative	240 (64.5) 11 (3.0) 121 (32.5)	212 (79.1) 0 (0.0) 56 (20.9)	28 (26.9) 11 (10.6) 65 (62.5)	99.84	0.001*
Difference BAS from medicines	Yes No Unknown	300 (80.6) 23 (6.2) 49 (13.2)	242 (90.3) 6 (2.2) 20 (7.5)	17 (16.3) 58 (55.8) 29 (27.9)	58.91	0.001*
Parallel using with medicine	Yes No Sometimes	130 (34.9) 175 (47.0) 67 (18.0)	122 (45.5) 93 (34.7) 53 (19.8)	8 (7.7) 82 (78.8) 14 (13.5)	63.37	0.001*
Duration of taking BAS	One course More than 1course I don't use Sometimes	156 (41.9) 98 (26.3) 86 (23.1) 32 (8.6)	144 (53.7) 95 (35.4) 6 (2.2) 23 (8.6)	12 (11.5) 3 (2.9) 80 (76.9) 9 (8.7)	242.7	0.001*
Effectiveness	Yes No Never used	252 (67.7) 63 (16.9) 57 (15.4)	235 (87.7) 25 (9.3) --- ---	17 (16.3) 38 (36.5) --- ---	200.9	0.001*
Safety	Yes No Unknown	198 (53.2) 51 (13.7) 123 (33.1)	180 (67.2) 42 (15.7) 46 (17.2)	18 (17.3) 9 (8.7) 77 (74.0)	110.9	0.001*
Side-effects	Yes No	72 (19.5) 297 (80.5)	56 (20.9) 212 (79.1)	16 (15.8) 85 (84.2)	1.193	0.275
Deal with side-effects	By myself HCWs Unknown	173 (47.0) 60 (16.3) 139 (36.7)	141 (52.8) 34 (12.7) 98 (34.5)	32 (31.7) 26 (25.7) 41(42.0)	20.61	0.001*
Government regulation	Yes No Unknown	126 (33.9) 157 (42.2) 89 (23.9)	110 (41.0) 105 (39.2) 53 (19.8)	16 (15.4) 52 (50.0) 36 (34.6)	23.54	0.001*

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Table 8 (continued)

Affordability	Low Medium High	235 (64.6) 112 (30.8) 17 (4.7)	154 (57.9) 96 (36.1) 16 (6.0)	81 (82.7) 16 (16.3) 1 (1.0)	30.61	0.001*
Benefit	Yes No Unknown	268 (72.0) 19 (5.1) 85 (22.8)	233 (86.9) 2 (0.7) 33 (12.3)	35 (33.7) 17 (16.3) 52 (50.0)	111.8	0.001*
Satisfaction	Yes No	259 (69.6) 113 (30.4)	218 (81.3) 50 (18.7)	41 (39.1) 63 (60.6)	62.25	0.001*

*-Statistically significant

4.2. Use of biologically active supplement by gender

In Table 9 shown the widespread use of BAS products between females and males and the allocation among them quite different. Female consumers more (77.3%) than males (59.8%) while male non-consumers were 40.2%. An independent samples t-test was conducted to examine the gender difference in the use of BAS products. Levene's Test for Equality variances showed no violations, p=0.001. Results indicate that males (M=1.40, SD=0.492) used more than females (M=1.23, SD=0.420) ranks on BAS products, t(370)=3.49, p< .001, Cohen's D=0.37. According to this result, we can conclude that BAS use in males was significantly higher than in females. Therefore, hypothesis 1 was rejected and accepted alternative hypothesis that males and females will differ in the use of biologically active supplement products.

Table 10 illustrates for females and Table 11 for males. The total number 260 were female, and 112 were male. Evenly distributed consumer and non-consumer in female groups (77.3%, 22.7% respectively) while consisting of male consumers were (59.8%). The main parts of both group's consumer's ages were similar from 30-59 (80.7% female and male 85.0%), consumers female and male groups were in middle income (47.3% and 79.1%) and by geographical location substantially consumers in both groups from urban

residents. Female group consumers mostly had college and high level of education (48.8%, 44.3%) while non-consumers were more highly educated people (50.8%). Mostly part of female consumers had jobs in government/private 49.8%, and male group consumers were HCWs 56.7%, while non-consumers of the male had a job in government/private (62.2%). The majority in both: female and male groups had normal subjective health status (45.8%, 50.7%). The majority of male group consumers were familiar with government regulation on the BAS (53.7%) than female group consumers (36.8%), while numerous consumers in the female group (62.3%) and non-consumers in the male group (86.6%) did not know about this subject. Substantially part of consumers in the female groups have checked packaging, labeling, and content of BAS before purchasing (82.1%). In reverse, consumers in the male groups have not checked the BAS package before buying it (70.6%). This is a common prevalence issue is checking the package, label, and content of BAS products before purchasing or using it. It should comply with labeling health claims.

BAS products are safe to use because they come from "natural sources" however, in fact, it is different. For instance, BAS products for 66.2% of consumers in the female group were safe while 84.4% of non-consumers in males were unsafe or doubt say that was safe. Furthermore, mostly non-consumers in both groups did not notice that it was safe. Significantly, consumers in the female group (91.5%) were effective while consumers in the male group (66.1%) didn't have effective from BAS products. Even substantially part in both groups consumers, combines used with medicines. Distinguish BAS from medicines in both group consumers can differentiate (82.0%F, 85.1%M); however the non-consumers in the male group did not know the difference of BAS from medicines (53.4%).

Attitude to BAS majority of both groups' consumers was positive while half of non-consumers in the male group were negative. Significantly satisfied in female and male groups consumers (82%, 49.3%) while male group non-consumers not satisfied (75.6%). Notwithstanding the satisfaction in both group consumers, they got adverse events during the taking of BAS products (15.4% F, 37.3% M).

Accordingly in non-consumers of female and male groups had side-effects before (92.9%, 73.3%). Regarding the income, education, geographical location, occupation, packing of BAS, and side-effects from taking BAS, there was no statistically significant difference by a female between the two groups: consumer and non-consumer (p value=0.118, 0.232, 0.662, 0.106, 0.065 and 0.110, respectively), as mentioned in table 10.

Regarding income, geographical location, education, and side-effects, there were no statistically significant differences by a male between consumer and non-consumer groups (p value=0.233, 0.656, 0.709, and 0.240, respectively), as shown in table 11.

Table 9. Biologically active supplement among consumers and non-consumers by gender

Item		**Use of BAS**		**Mean**	**SD**	***P*-value**
		Yes	No			
Gender group	Male	67 (59.8%)	45 (40.2%)	1.40	0.492	0.001*
	Female	201 (77.3%)	59 (22.7%)	1.23	0.420	

Table 10. Biological active supplement use among female

Item		Consumer	Non-consumer	*P*-value
		n=201 (77.3%) n %	n=59 (22.7%) n %	
Independent Variables SES				
Income	Low	88 (43.8)	21 (35.6)	0.118
	Middle	95 (47.3)	36 (61.0)	
	High	18 (9.0)	2 (3.4)	
Age	Young	22 (10.9)	17 (28.8)	0.001*
	Middle	162 (80.7)	42 (67.8)	
	Elder	17 (8.5)	2 (3.4)	
Geographical location	Urban	155 (77.1)	41 (65.9)	0.232
	Rural	46 (22.9)	18 (30.5)	
Education	Prim/Second.	14 (7.0)	4 (6.8)	0.662
	College	98 (48.8)	25 (42.4)	
	High grad.	89 (44.3)	30 (50.8)	
Occupation	Govern/priv	100 (49.8)	34 (57.6)	0.106
	HCWs	47 (23.4)	17 (28.8)	
	Unemployed	54 (26.9)	8 (13.6)	
Health status	Unhealthy	42 (20.9)	6 (10.2)	0.003*
	Normal	92 (45.8)	19 (32.2)	
	Healthy	67 (33.3)	34 (57.6)	
Independent Variable: attitude to BAS				
Government regulation	Yes	74 (36.8)	10 (16.9)	0.007*
	No	85 (42.3)	28 (47.5)	
	Diff.answer	42 (20.9)	21 (35.6)	
Packaging, labeling and composition of the BAS	Yes	165 (82.1)	43 (72.9)	0.065
	No	8 (4.0)	7 (11.9)	
	Sometimes	28 (13.9)	9 (15.3)	

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Table 10. (Continued)

Safety	Yes No Diff.answer	133 (66.2) 38 (18.9) 30 (14.9)	11 (18.6) 7 (11.9) 41 (69.5)	0.001*
Effectiveness	Yes No Don't know Never used	184 (91.5) 14 (7.0) 2 (0.5) 1 (1.0)	12 (20.3) 11 (18.6) 2 (57.6) 34 (3.4)	0.001*
Parallel use with medicines	Yes No Sometimes	98 (48.8) 60 (29.9) 43 (21.4)	3 (5.1) 47 (79.7) 9 (15.3)	0.001*
Difference BAS from medicines	Yes No Dif. answer	185 (92.0) 3 (1.5) 13 (6.5)	37 (62.7) 9 (15.3) 13 (22.0)	0.001*
Attitude to BAS	Positive Neutral Negative	161 (80.1) 0 (0.0) 40 (19.9)	17 (28.8) 3 (5.1) 39 (66.1)	0.001*
Satisfaction	Satisfied Dissatisfied	185 (92.0) 16 (8.0)	30 (50.8) 29 (49.2)	0.001*
Side-effects	Yes No	31 (15.4) 170 (84.6)	4 (7.1) 52 (92.9)	0.110

*- Statistically significant

Table 11. Biological active supplement use among male

Item		Consumer n=67 (59.8%) n %	Non-consumer n=45 (40.2%) n %	*P*-value
Independent Variables: SES				
Income	Low Meddle High	6 (9.0) 53 (79.1) 8 (11.9)	9 (20.0) 32 (71.1) 4 (8.9)	0.233
Age	Young Middle Elder	1 (1.5) 57 (85.0) 9 (13.4)	7 (16.5) 34 (75.5) 4 (8.9)	0.022*
Geographical location	Urban Rural	56 (83.6) 11 (16.4)	39 (86.7) 6 (13.3)	0.656
Education	Prim/Second. College High grad.	1 (1.5) 17 (25.4) 49 (73.1)	0 (0.0) 12 (26.7) 33 (73.3)	0.709
Occupation	Govern/privat HCWs Unemployed	23 (34.3) 38 (56.7) 6 (9.0)	28 (62.2) 15 (33.3) 2 (4.4)	0.014*
Health status	Unhealthy Normal Healthy	9 (4.5) 34 (50.7) 30 (44.8)	2 (4.4) 11 (24.4) 32 (71.1)	0.018*
Independent Variable: attitude to BAS				
Government regulation	Yes No Diff.answer	36 (53.7) 20 (29.9) 11 (16.4)	6 (13.3) 24 (53.3) 15 (33.3)	0.001*
Packaging, labeling and composition of the BAS	Yes No Sometimes	6 (19.0) 54 (70.6) 7 (10.4)	26 (57.8) 8 (17.8) 11 (24.4)	0.031*
Safety	Yes No Diff.answer	47 (70.1) 4 (6.0) 16 (23.9)	7 (15.6) 2 (4.4) 36 (80.0)	0.001*
Effectiveness	Yes No Never used Don’t know	12 (26.4) 41 (66.1) 0 (0.0) 5 (7.5)	5 (11.1) 27 (60.0) 11 (24.4) 2 (4.4)	0.001*

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Table 11. (Continued)

Parallel use with medicines	Yes No Sometimes	24 (35.8) 33 (49.3) 10 (14.9)	5 (11.1) 35 (77.8) 5 (11.1)	0.006*
Difference BAS from medicines	Yes No Dif. answer	57 (85.1) 3 (4.5) 7 (10.4)	21 (46.7) 8 (17.8) 16 (35.6)	0.001*
Attitude to BAS	Positive Neutral Negative	51 (76.1) 0 (0.0) 16 (23.9)	11 (24.4) 8 (17.8) 26 (57.8)	0.001*
Side-effects	Yes No	25 (37.3) 42 (62.7)	12 (26.7) 33 (73.3)	0.240
Satisfaction	Satisfied Dissatisfied	33 (49.3) 34 (50.7)	11 (24.4) 34 (75.6)	0.008*

*-Statistically significant

4.3. Knowledge, Attitudes towards BAS among consumers and non-consumers

Table 12 described the difference in knowledge of biologically active supplements among consumer and non-consumer groups. The first line of the table indicated that overall knowledge of consumer and non-consumer groups responded to overall knowledge questions with statistically significant differences between the two groups: consumers and non-consumer. In table 12 the result shown that an equal variances *t*-test applied to reveal a statistically reliable difference between the mean number of consumer group (M = 1.42, SD=0.815) and non-consumer group (M = 2.36, SD=0.880), t(370) = 9.74, p = 0.001, α = 0.05. Since p < .001 is less than our chosen significance level α = 0.05, we reject the second null hypothesis, thus accepted the alternative hypothesis that there was a significant difference in knowledge of BAS among consumers and non-consumers group. Accordingly, when looked knowledge questions in the detail, among questions the other response: “Importance government control for BAS products” was shown the different meaning that there was no significant difference between two statements: that the p=0.944 are greater than 0.05, that means no significant difference in importance of government control for BAS products among consumers and non-consumers. The other statements were statistically significant, that means it was difference in knowledge of BAS among consumer and

nonconsumer groups regarding to variables: Distinguish BAS products from medicines (p=0.001); Benefits after taking BAS products (p=0.001); Combine use of BAS products with medicines (p=0.001); Effectiveness (p=0.001); Safety (p=0.001); Comply labeling health claims (p=0.01); The government regulation on BAS and Consumer satisfaction (p=0.001).

Table 12. Assessment of BAS knowledge in consumer and non-consumer groups

Subject	**BAS users and non-users**		**Mean**	**Std. Deviation**	***P*-value**
Overall knowledge on BAS	Yes	268	1.42	0.815	0.001*
	No	104	2.36	0.880	
Detailed knowledge on BAS:					
Whether to distinguish BAS products from medicines	Yes	268	1.17	0.541	0.001*
	No	104	1.72	0.875	
It has benefit after taking BAS products	Yes	268	1.25	0.661	0.001*
	No	104	2.16	0.904	
BAS products can be dangerous when combined with prescription medicines	Yes	268	1.74	0.767	0.001*
	No	104	2.06	0.459	
Taking BAS products effective for health	Yes	268	1.18	0.559	0.001*
	No	104	2.35	0.798	
BAS products are safe to use	Yes	268	1.50	0.772	0.001*
	No	104	2.57	0.773	
BAS products should comply labeling health claims	Yes	268	1.31	0.691	0.010*
	No	104	1.53	0.800	
The government regulates the quality of BAS	Yes	268	1.79	0.752	0.001*
	No	104	2.19	0.684	
Importance government control for BAS products	Yes	268	1.16	0.368	0.944
	No	104	1.16	0.372	
Whether the quality of BAS is sufficient to make consumer satisfaction	Yes	268	1.19	0.390	0.001*
	No	104	1.61	0.491	

*-Statistically significant

4.4. The primary concept attitude towards BAS among the study population

One the BAS products critical property was its form, knowledge awareness the term of biologically active supplements among population, and motivation to consume. During the research, the study population measured the BAS products structure knowledge awareness on BAS among the population, composition, and motivating factors to consume BAS. Knowledge awareness the term of BASs as described in the previous part that the term is kind of food supplement used according to the chemical, biological and natural contains three categories. A result of the study shown that in the study population majority of people understood the term BAS products as a food supplement - 43.5%, vitamin complex - 41.4%, and as vitamins-9.4%. A few people considered as a kind of medicine and usual chemistry. Most parts of the population prefer the composition of the BAS as vitamin and minerals (48.4%), proteins (23.7%), energizers (18.8%), and a small amount of the population choose as herbal and phytopreparations. Based on a study of BAS's assortment of the population used or preferred in the form of capsules, tablets, syrup etc. For instance, the largest number of BAS products was presented in capsules, whose percentage is 42.7%. Tables presented slightly smaller portions - 18.5%, the herbal preparations, and syrup - 14.2%, 13.2%, respectively, as in figure 9 shown kind of forms and motivation factors in percentage.

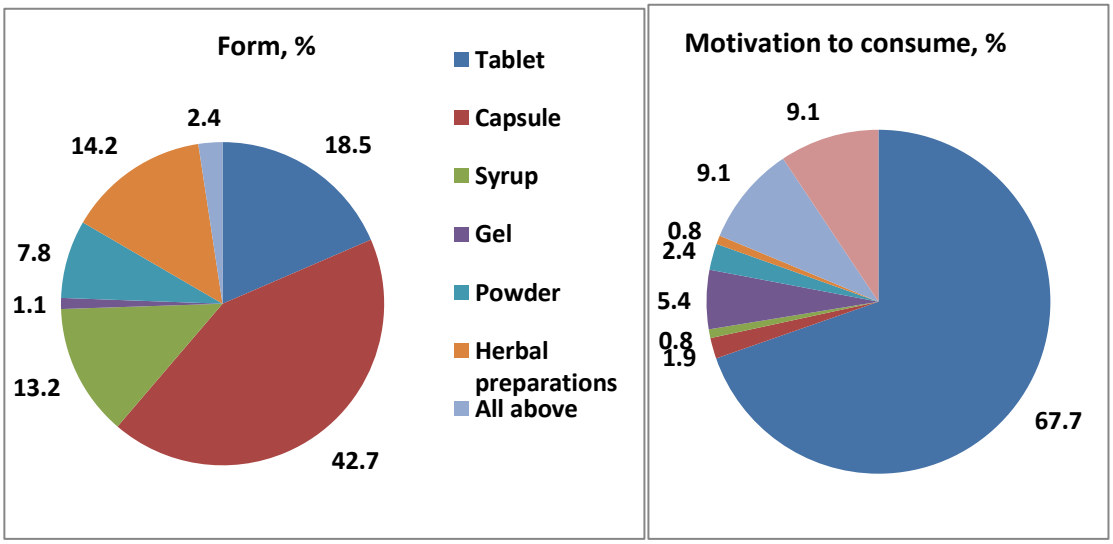

Figure 9. Assortment structure of the BAS by selected population and motivation factors

Figure 9 shows the distribution of the motivating factors on consuming the BAS products among the study population. People were used the BAS in different motivating factors. For instance, most of the population (67.7%) used as toning the body and 9.1% to prevent of diseases, striving for longevity and beauty. Other factors for improving brain performance (5.4%), losing weight (2.4%), improving muscle mass (1.9%), and self-medication of a previously diagnosed disease (0.8%).

Health professionals and experts on medicines maintain that most of the population freely chooses the motivation statements without doctor consultation. In Kyrgyzstan, almost 90% of the BAS products are imported. For that reason, 72.8% of the study population chooses imported BAS products. On the other hand, domestic products have a few BAS products assortments compared to imported products.

4.5. Importance of information sources on the biologically active supplement

In table 13 show the primary information sources which were essential to use in the study population. 40.3% of the study population purchased the BAS products in pharmacy, and 21.5% throughout distributors, 18% in particular stores on BAS products and mostly urban residents obtained via online internet shop. At the moment of purchase, the main crucial component is checking the BAS products packing, labeling, and content. Some BAS products do not match labeling, packaging, and contents. As a consequence of this scrutiny that mostly the population checked the package before purchasing. The other source of purchase is choosing by factors; for instance, 43% of the population preferred by the brand of BAS products, 36.6% - by the country of origin, 12.1% by prices, and 5.1% by the quality of the BAS. BAS products primary importance is an information source that should be reliable and effective for the population. Moreover, the population openly chooses whatever sources they want. This scrutiny revealed that 52.2% of the study population appreciated the doctors' advice and 20.4% specified that they have followed the family, friend's recommendation for using BAS and 14.0% used according to the positive feedback on the internet.

Table 13. Information sources of biologically active supplement in the population

Independent variables		**Frequency**	**Percent**
Purchase place	Pharmacy	150	40.3
	Special store	67	18.0
	Healthy food store	19	5.1
	Online store	43	11.6
	Fitness club	3	0.8
	Distributors	80	21.5
	Total	362	97.3
Important factor for purchase	Brand	160	43.0
	Price	45	12.1
	Country of origin	136	36.6
	Advertising	12	3.2
	Quality	19	5.1
	Total	372	100.0
Information source	Doctor recommendation	194	52.2
	Family recommendation	22	5.9
	Friends recommendation	76	20.4
	Positive feedback on the internet	52	14.0
	Advertising on TV/Inter	14	3.8
	Advertising on public place	5	1.3
	Fitness trainer recom.	4	1.1
	Cosmetologist recom	3	0.8
	Total	370	99.5

4.6. Biologically active supplement usage patterns among the study population

Odd ration (OR) with 95% Confidence interval (CI) measured according to the variables: education, health status, government regulation, the safety of taking BAS, availability, effectiveness, attitude to BAS and in the results showed association BAS consumption with these variables are presented in Table 14. Results showed that BAS use different from on sociodemographic of the study population. For instance age (OR 0.602, 95% CI 0.485 to 0.747) and occupation (OR 0.527, 95% CI 0.312 to 0.891) was associated lower rate of BAS use and statistically significant (p value=0.001 and 0.017, respectively). Income (OR 0.763, 95% CI 0.385 to 1.510), gender (OR 0.706, 95% CI 0.351 to 1.422) both these groups were associated lower rate of BAS use and not statistically significant. Between Education (OR 1.291, 95% CI 0.694 to 2.401), Availability (OR 1.078, 95% CI 0.711 to 1.634) and Government regulation (OR 1.190, 95% CI 0.731-1.936), there was a trend for higher BAS use and strong association use of BAS with education, availability to BAS products and government regulation on BAS. On the other hand, no statistically significant differences between these variables regards the use of BAS, as shown in Table 14
(p value=0.419, 0.725, 0.484, respectively).

People with health status (OR 1.686, 95% CI 1.019 to 2.791), Safety of BAS products (OR 1.661, 95% CI 1.078 to 2.559), and Attitude to BAS (OR 1.862, 95% CI 1.264 to 2.744) were also more likely to consume BAS and strong associated with use of BAS. There was statistically significant (p value=0.042, 0.021 and 0.002. Effectiveness was also associated with BAS consumption with odds of OR 4.146 and 95% CI (2.711 to 6.342).

Table 14. Logistic regression for usage of BAS in specific variables

Variables	OR	95% CI	*P*-Value
Age	0.602	0.485-0.747	0.001*
Education	1.291	0.694-2.401	0.419
Income	0.763	0.385-1.510	0.437
Occupation	0.527	0.312-0.891	0.017*
Health status	1.686	1.019-2.791	0.042*
Gender	0.706	0.351-1.422	0.330
Government regulation	1.190	0.731-1.936	0.484
Safety	1.661	1.078-2.559	0.021*
Effectivness	4.146	2.711-6.342	0.001*
Availability	1.078	0.711-1.634	0.725
Attitude to BAS	1.862	1.264-2.744	0.002*

*-Statistically significant

4.7. Comparative study on regulations of biologically active supplement (BAS) in Kyrgyzstan and health functional food (HFF) in Republic of Korea

The BAS regulations in Kyrgyzstan and HFF in Republic of Korea have a difference according to their functionality and law on food safety in each country. This is research reveals distinguish of the BAS and HFF between the two countries. The use of these product's functionality among two population is similar, the difference of their regulation system. The research study concludes that in Korea, the regulation on HFF well-adjusted regulation system than Kyrgyzstan. Compare to Korea the BAS sector in Kyrgyzstan is one of the emerging industries. Significantly, for the last 10 years is drastically growing, the BAS market in Kyrgyzstan through the networking market system. Regarding this market respectively requests regulation on it. Therefore in Kyrgyzstan BAS sector demand enact appropriate to act on its regulation system from experienced countries profile such as the Korea. In table 15 indicated the differences in the BAS and HFF on specific characteristics between two countries.

Table 15. Difference of regulation on BAS in Kyrgyzstan and HFF in Republic of Korea

Kyrgyzstan	**Republic of Korea**
1. Term: Biologically active supplement	**1.** Term: Health Functional Food
2. Decree of the Ministry of Health of the Kyrgyz Republic dated September 23, 2013 № 549 that BAS are not medicinal products and it came into effect regulation on it in 2017 by given authority to DPSSES	**2.** In August 2002, the HFFA was enacted as a new regulatory framework for the safety, efficacy, and labeling of HFFs, and it came into effect in January 2004. Currently regulated by MFDS
3. The objectives of the adoption of the TR: • Protection of human health; • Prevention of actions misleading consumers; • Protection of the environment	**3.** The ultimate goal of the Act was to enhance public health by ensuring the safety of new bioactive ingredients
4. 1) Confirmation (declaration) of conformity of food products; 2) The state registration of a new kind of food; 3) The state registration of specialized food products (included BAS); 4) Veterinary-sanitary inspection	**4.** Health/functional foods in Korea divided into two subcategories: generic and product-specific. Generic HFFs are defined as products having functional ingredients as listed by the MFDS. If are not included in the list of generic HFFs, they must lodge an application for a product-specific HFF
5. Not every BAS could be registered in Kyrgyzstan in cases of all registration documents in the country of origin	**5.** Every HFF should check it quality according the MFDS with evidence of the standardization, safety, and efficacy

Kyrgyzstan	Republic of Korea
6. The new type of BAS is carried out at the stage of their manufacturing for the first time in the customs territory, and conform by appropriate state authority	**6.** The functional ingredients recognized under the Regulation on Approval of Functional Ingredients for HFF were permitted to be added to the Code
7. Pre-market checks on analysis of provided documents: Analysis of tests such as: organoleptic, microbiological; toxicological; radiological, containing herbs – tests for pesticides (α-β-γ izomers); micotoxins, in some cases – tests on Generally Modified Ingredients	**7.** Pre-market focusing on the origin and nature of the ingredients, content of functional components, methods, validation methods for analysis, stability data, and purity (microbial, heavy metals, pesticides, etc.), scientific evidence for the safety and efficacy
8. BAS registration comply with the requirements of the TR CU 021/2011 on its territory without presenting additional requirements for BAS and without conducting additional conformity	**8.** Registration of HFF followed: 1) Business License 2) Declaration with the MFDS 3) Approvement ingredients
9. The DPSSES has limited authority to evaluate safety and efficacy of the BAS products, also regulating manufacturers and distributers products	**9.** The MFDS the exclusive authority to evaluate the safety and efficacy of HFFs prior to their introduction of the market, and it also keeps manufacturers and distributors responsible for their products
10. Valid of registration certificate is perpetual	**10.** Registration certificate provide for 5 years

CHAPTER V

DISCUSSION

The study's primary purpose was to scrutinize the selected consumer and non-consumer population attitudes towards biologically active supplements: safety, quality, availability, effectiveness, and knowledge. According to the results of the study, the hypothesis indicated:

1) Null hypothesis was rejected and accepted alternative hypothesis that there was a significant difference between males and females using biologically active supplements.

2) The same stage, the null hypothesis was rejected, thus accepted the alternative hypothesis that there was a statistically significant difference in knowledge between biologically active supplement consumers and non-consumers.

3) In this stage, the null hypothesis was failed to reject. Thus, the null hypothesis was accepted that indicated a strong association between the use of BAS and government regulation.

5.1 Descriptive statistics of study population

This study examined the regulation and association of sociodemographics, health status, socioeconomics and fundamental subject on biologically active supplement use among study populations. According to these statements, data stratified by gender, knowledge as independent variables, and using BAS as dependent variables to access the study's purpose. Each variable and respondents' answers were tabulated between consumer and non-consumer groups then recorded in percentage/frequencies. The total number of participants in this study were 372, and the questionnaire rate was 95%. Among them were 30.1% males and two times more females were 69.9%. This result is quite similar to the result of studies in the Lebanese population [48].

Mostly part of the consumers was female consumers (72.0%) than male (28%). This high proportion of consumers being females may be due to the higher percentage of females participated in the study. The same indicator had shown in this study [49].

In Australia, using BAS proportion among the population was female 43.2%, and males were 20.1% in 2014–2015 [50]. The BAS use proportion was 44.53% among the South

Korean population in 2015 compared to women who were more likely to use BAS than men by 38.9% [51].

According to the American Community Survey data source, by 2016, BAS's use in the US was 68.0%, and the consumer confidence interval was high, with 84.0% [52]. Using BAS was more prevalent in developed countries due to the legal protection for the BAS population [53] and the high economic level of countries guiding to BAS's high use.

The age ranged from 30 to 59 years, and the mean age was 30.9. The majority part of the consumers had high education, and those were urban residents. This is characteristics also comparable to this study [48].

This study participated 31.7% HCWs, mostly doctors and pharmacists. Their opinion attitude towards BAS was positive, and more than half of them were consumers. They were strongly associated between BAS and HCWs with OR=2.09, 95% CI 0.68 to 5.82, and a trend for higher dietary supplement use. This finding indicated that HCWs could influence the regulation of the BAS sector in the Kyrgyz Republic.

Consumers group allocated people with higher education, middle income, and a medium level of workers. Their income can freely consume BAS products, which promote health; this is similar to studies [51]. People's attitude towards BAS is positive. However, non-consumers were insufficient knowledge regarding BAS products and were in negative opinion to use BAS. The BAS use percentage has highest among the study population with regular health, where the participants who know their health conditions were the least likely to use BAS.

Substantially part of consumers had benefited from taking of BAS and satisfied. Reversely non-consumers were dissatisfied with the BAS products. Most consumers parallel used BAS with medicines, whereas particularly have had side effects from BAS. In such cases, they individually took action as usual. One research reported that consumers used BAS because they believed in the health benefits, even if scientific evidence indicated no effects [54]. Thus, BAS, including herbs, can be dangerous when combined with medicines.

Due to the study results in Kyrgyzstan, BAS's quality does not meet the hygienic

requirements of food safety. The research revealed that almost all study populations not familiar with existing government regulations on BAS in the Kyrgyz Republic. The population also suggested having control on quality, safety, effective and knowledge awareness on BAS products. Insufficient government regulation of the BAS products marketing may result in an inaccurate recommendation to BAS consumers [55].

In Kyrgyzstan, BAS is not recommended for the general population because the public did not have enough knowledge and the proper attitude toward BAS. Besides, false and exaggerated propaganda leads consumers to distrust the BAS. Therefore, the government regulators and scientific academy should strengthen the BAS quality control, industry sector, and BAS products marketing system to lead the consumers to correct way use of BAS products. Also, BAS-related information sources should be under the government's control (widely public advertising by various publicity channels) to avoid false and exaggerated propaganda and help people better understand BAS. The same research finding among the Chinese population in 2012 [56].

In Kyrgyzstan 90% of BAS products are imported from other countries, respectively, their price more expensive than domestic. Consequently, affordability the primary function play for using BAS products, and it is directly related to the income of the population. The study showed that population affordability to BAS was at a low-income level.

BAS usage varies by age, gender, geographical location, education, income, and health status. For instance, the results showed that widespread use of BAS products by gender males ($M=1.40$, $SD=0.492$) used more than females ($M=1.23$, $SD=0.420$) BAS products, $t(370)=3.49$, $p< .001$, Cohen's $D=0.37$. According to this result, we can compare the differential of using BAS between males and females that BAS use in males was significantly higher than in females. Cohen's effect size represents a 'medium' effect size between two groups that differ by 0.37. This result was consistent with the other researcher's results [51]. Also, females living in urban areas and with a higher education level and middle income were more likely to use BAS products. Consistent with other surveys [57].

Demographic characteristics between males and females were significantly related to the

overall prevalence of BAS use. For instance, both female and male groups had unhealthy subjective, and they may have more health consciousness and more health problems, resulting in higher BAS use. Urban residents with higher income have more accessibility for purchasing BAS products.

Finding results indicated different use of BAS by gender. Mostly females pay more attention to packages than males; it means that BAS should comply with labeling, packing, and composition on health claims. More males familiar with government regulation on BAS. Both groups of consumers were satisfied with taking BAS products, while males do not use BAS were not satisfied and disagree. However, both groups experienced adverse events from taking it. It is directly related to the quality control of BAS products throughout the government regulation system. According to finding between females and males, statistical was significantly different using BAS and insufficient knowledge using BAS products.

This study revealed misperceptions and misconceptions regarding the safety of BAS among the population in the Kyrgyz Republic. Most respondents falsely believed that BAS is safe to use because the ingredients are "natural sources" and no risk to the general population, and they must be safe to be sold in Kyrgyzstan. Similar research conducted in the USA population and the same beliefs revealed that BAS products are harmless [58].

The study results showed that BAS consumers frequently received information from the medical doctors and relatives' advice and families through the internet. Other sources are followed by friends' recommendations, advertising on TV/public places, fitness trainers, and cosmetologist recommendations. The majority of respondents purchase BAS products in pharmacies, particular stores, and online stores. In Kyrgyzstan's overall distributed network market, distributors play the leading role in selling BAS products. Most distributors are non-professionals who should take responsibility for public health. Therefore side-effects and misusing BAS products were relevant issues among the population. Mainly part of consumers chosen the BAS products based on its brands and country of origin.

During the survey, the majority population expressed in this study wanted to know more about the quality, safety, and efficacy of the BAS products. These findings underscore the

need to raise public awareness regarding BAS use. Also evaluated knowledge of physicians, pharmacists, and nurses through a questionnaire regarding BAS products gave a low level of knowledge on BAS mechanisms of action, interactions, safety, and overall herbal medicines [59]. Therefore, healthcare professionals involving physicians, pharmacists, dietitians, and other HCWs need to improve their professional skills consequently the public regarding the safety, quality, and efficacy of BAS in specific conditions as potential interactions with pharmacologic treatments.

5.2. Knowledge, Attitudes towards BAS among consumers and non-consumers

The study defined statistical significance between consumer and non-consumer groups using BAS products and overall knowledge. Thus, the null hypothesis rejected a difference in knowledge and using BAS products among consumer and non-consumer groups. Reversely, interesting research was found. For instance, 73,38% of the study population consumers do not know about supplementation, and 58.59% of the non-consumer group knows about supplementation. This research was designated in a study among the European population using biologically active supplements regarding knowledge [60].

The other regarding knowledge statements were also statistically significant, that means it was a difference of using BAS between: "Distinguish BAS products from medicines (p=0.001); Benefits after taking BAS products (p=0.001); Combine the use of BAS products with medicines (p=0.001); Effectiveness (p=0.001); Safety use of BAS among consumers and non-consumers (p=0,001); Comply labeling health claims (p=0.01); The government regulation on BAS and Consumer satisfaction (p=0.001)".

When conducting the questions based on knowledge, consumers indicated better knowledge of BAS effectiveness and regulation than non-consumers. For distinguishing BAS products from medicines, most consumers answered that item correctly as being yes. Mainly more users correctly answered "no" to labeling and packing BAS products should comply with label health claims.

The other question like benefits after taking BAS products the majority of users correctly answered yes than non-users. Moreover, the other statements, like combining BAS products

with medicines and safety to use BAS products, mostly respond among consumers and non-consumers, were made not know or never used. This defined that both consumer and non-consumer were unclear about the proven combined use of BAS and safety of BAS products. The statement "The quality of BAS products sufficient to make consumer satisfaction in the Kyrgyz Republic" mostly replied "yes." All statements of responses were designated statistically significant at $p>0.05$.

5.3. The main concept attitude towards on BAS among the study population

The central concept of the study has to assess specific characteristics regarding BAS products. For instance, BAS products, awareness of BASs, prevalence type of BAS, and reason to consume or motivating factors. The definitions and categorization of biologically active supplements are not standardized [61]. Therefore, lack of standardization makes it difficult to compare prevalence estimates between populations. This study represented an assessment regarding BAS products' definition among the population that majority of people understood the term of BAS products as a food supplement and a few people considered as a kind of medicine and usual chemistry.

According to the notion based on BAS, the population has chosen the type of the BAS as vitamin and minerals (48.4%), proteins (23.7%), energizers (18.8%), and a few proportions of the population prefer to use as herbal and Phyto preparations. Interestingly, a study conducted by US researchers estimated the study population based on the consumption of single dietary supplement type by category and was statistically significant frequency difference between male and female. It has been implied that more females preferred vitamins and complexes of vitamins/minerals than males. However, the type of energizers preferred more males than females. The other types of BAS products as herbal and phyto preparations fewer people have chosen. These research findings underscore the use type of BAS by gender [62].

Most people used or preferred BAS products in capsules, tablets, herbal preparation, and syrup. The indicated consumption reason for the BAS products among the population and people were used in different motivating factors. For instance, most of the population

(67.7%) used as toning the body and 9.1% to prevent diseases, striving for longevity and beauty. This study showed statistically significant ($p<0.05$) reason for BAS consumption between males and females that underscore different consumption reasons used by gender: for instance, Improving Sport performance for males and health improvement (41.6%) for females. Moreover, both groups were used high prevalence in toning of the body (45.5%F and 29.2%M). Comparison of these studies indicated that BAS consumption was used in a specific way, which was more useful for the population [63].

5.4. Biologically active supplement usage patterns among study population

A significant proportion of the study on BAS showed that BAS use among the study population has been consistent with particular sociodemographic characteristics like females, a higher education level, and income. For instance, women were more likely to use BAS than men [64]. According to the study results, sociodemographic characteristics did not show any association between BAS use and demographic characteristics like gender, age, occupation, and income. However, people with higher education tend to have an occupation that provides higher income. Other research work indicated that the lowest social class tends to have less balanced and less healthy diets [58]. Like this, lower social class may not accommodate the necessary things in life, such as using biologically active supplements.

Between education, Availability, and Government regulation, there was a rending for higher BAS use in those who had education, availability to BAS products and government regulation on BAS. Education was a more robust social determinant of diet than availability and government regulation. Thus, people with higher education tend to have availability, which provides government regulation on BAS products.

People with health status, Safety of BAS products,and Attitude towards BAS were associated with BAS consumption and statistically significant. Effectiveness of BAS products was also strongly associated with BAS consumption. Findings of this association, each of these characteristics with BAS products' consumption, indicated contribution marginally to BASs among consumers to be good health. They believed to ensure a positive effect on health and well-being. These findings were mostly consistent across education

level, regulation, availability, safety, attitude towards BAS, and health status. Other variables showed less likelihood to consume dietary supplements.

5.5. Limitation of the study

There were several limitations in this study. The main limitation of this study is that survey data was self-reported, thus responses may be dishonest. Respondents may have misunderstood the content of the survey on BAS. Firstly, general questions were asked regarding BASs in the questionnaire, not detailed information, such as subcategories of multivitamins and multiminerals ect. Secondly, for the consumer during the previous month may not represent the practices use of BAS, which may underestimate BAS use. In addition, unlike other studies examining BAS, this study did not cover health conditions, such as diabetic, cancer ect. The information that was used in this study could have been useful to help populations use safety BAS in appropriate ways and avoid negative health effects from BAS.

CHAPTER VI

CONCLUSION AND RECOMMEDNATION

This study's objective was to look at selected consumers and non-consumer towards BAS and its regulatory system in the Kyrgyz Republic. Conducted comparative study of the regulation system in Kyrgyzstan and the Republic of Korea. According to the research statement, the conclusion and recommendation consist of two parts:

I. Regarding the questionnaire survey, scrutiny results showed that the use of biologically active supplements is prevalent (72%). It was aged between 40 and 59 years, and the central part of consumers was female (69.9%). BAS use is associated with health status, education, government regulation, safety, and effectiveness. Especially people with higher education level and having a healthier more likely to consume BAS in an appropriate way. The current results emphasize the compelling need for spreading public awareness in the Kyrgyz Republic regarding BAS products. Consumers should be advised that BAS products may not always be beneficial and can cause serious side effects; therefore, consulting with healthcare professionals before starting any supplement. All multidisciplinary healthcare structure members should also clearly understand the potential hazards and benefits of BAS therapies and encourage consumers' disclosure of alternative medicine.

A collaborative effort of governmental structure, health educational institutions is recommended to educate, regulate, and promote the appropriate and safe use of biologically active supplement products.

II. In the second part about a political study on BAS and HFF in Kyrgyzstan and the Republic of Korea, we studied to distinguish the difference between the two countries and determine the appropriate functions for regulating the BAS in Kyrgyzstan.

The regulation system on BAS in the Kyrgyz Republic is not well adjusted; the government needs to make the BAS market more transparent. Also, conformity of confirmation for quality of BAS product procedures does not reply to the international requirement's BAS demands. These findings recommend to the Ministry of Health following the points:

1) The registration of the BAS products in the country suggests establishing new BAS labeling requirements that imply a unique code on the package, a sequence of symbols. This unique system will be single and intended to solve technical regulation's following urgent problems: - create an automatic product tracking system; - protect consumers from counterfeiting; - fight against unscrupulous companies supplying counterfeit products to the market. It will allow the buyer to obtain the BAS's full information by pointing at a special scanner's unique code on a mobile device. It will give information about the product by whom and when the goods were produced, through what channels they entered the distribution network
2) In Korea, the MFDS has given authority to keep manufacturers and distributors responsible for providing all evidence regarding their products' advertised claims by developing a system to substantiate claims. This priority can be a help to regulate counterfeit substances and the quality of BAS in Kyrgyzstan.
3) In Korea regulation system on HFF provided health claims under the HFFA regarding nutrition, reductions in disease risk, and other functions. It helps to control the relationship between the consumption of HFFs and the reduced risk of developing a disease or health-related condition in Kyrgyzstan.
4) In Korea, the safety evaluation is checked very carefully following these criteria: quantity of HFF for consumption, human studies' results, and results of nutritional evaluation and bioavailability. This is an essential factor that can be used as these criteria for safety on food procedures in the Kyrgyz Republic system.

Progress can be expected to improve the BAS products' quality control and safety and the government's strict regulation system on the registration process and distribution channels.

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VIII. APPENDIX

1. Description of variables to explain usage of BASs in Kyrgyz Republic.

Variables: **Soico-economic status**	**Explanation**	**Measurement**
Gender	Whether respondent is male or female	1= male 2= female
Age	How old (in years) the respondents are	A continuous quantitative measure
Geographical location	Measures whether a respondent is resident in an urban or rural area	1=Urban 2=Rural
Education	Whether the respondent had formal education	1= Primary/secondary school 2=Professional,technical college 3= High graduate
Employment	Whether the respondent has work or not	1=Working 2=Not working 3=Temporary not working
Health status	Health condition of respondents	1= Unhealthy 2= Normal 3= Healthy
Occupation	Whether the respondent specialized	1=Doctors, nurses, pharmacists 2=Government employers and private entrepreneurs 3=Housewives, pensioners and students
Income	Relation income and using of BAS	A continuous quantitative measure
Variables: based on BAS		
Attitude to BAS	Respondent's attitude to use of BAS products	1=Positive 2=Neutral 3=Negative
Type of BAS	The respondent that used of prefer the type of BAS	1=Food supplement 2= Vitamins 3=Usual chemnisty 4=Vitamin complex 5=Kind of medicine 6=I don't know

Origin of BAS	Assessment the quality of domestic and import products by repondents	1=Domestic 2=Import
Understanding difference of BAS from medicines	Whether the respondent know difference	1=Yes 2=No
Use of BAS	Whether the respondent use of BAS or not	1=Yes 2=No
Duration of taking BAS	To know how long the respondent is using BAS (for a year)	1=One course 2=More than one course 3=Other
Benefits from using BAS	The respondent take benefit from using BAS	1=Yes 2=No 3=Difficult to answer
BAS composition	Which kind of BAS composition the respondent use or prefer	1= Energizers 2=Proteins 3=Vitamins 4=Minerals 5=Vitamin+Minerals 6=Sport drink 7=Herbal 8=Phytopreparations
Form	Form of BAS that the respondent use or prefer	1=Tablet 2=Capsule 3=Syrup 4=Ointment 5=Gel 6=Powder 7= Herbal preparations 8= All above

Motivation to consume of BAS	Whether the respondent has purpose for using BAS	1=Toning the body 2=Improving muscle mass 3=Improving Sport performance 4=Improving Brain performance 5=Losing Weight 6=Keeping Weight 7=Striving for longevity and beauty 8=Prevention of disease 9=Self-medication of diagnosed diseas 10=Meal Replacement Equivalent 11=Malaise
Use BAS with medicines (parallel)	BAS products can be dangerous when combined with prescription medicines	1=Yes 2=No 3=Sometimes
Effectiveness	Whether the respondent take benefits from BAS	1=Yes 2=No 3=Never used
Safety	BAS products are safe to use	1=Yes 2=No 3=Difficult to answer
Availability and accessibility	Whether the respondent have difficulties to access of BAS	1=Yes 2=No 3=Sometimes
Packaging, labeling and content of the BAS	BAS should comply labeling health claims	1=Yes 2=No 3=sometimes
Information source	Importance information source that people can trust	1=Doctor recommendation 2=Family recommendation 3=Friends recommend. 4=Positive feedback on the internet 5=Advertising on TV/Inter 6=Advertises on public place 7=Fitness trainer recomm. 8=Cosmetologyst recom.

Affordability	Willing to spend money for BAS in som	A continuous quantitative measure
Purhcase place	Place that is reliable for consumers	1=Pharmacy 2=Special store 3=Beaty salon 4=Healthy food store 5=Online store 6=Fitness club 7=Distributors
Government regulation	The government regulates the BAS	1=Yes 2=No 3=Difficult to answer
Importancce of government regulation	Need the regulation for BAS in the country	1=Yes 2=No 3=Difficult to answer
Side effects	Experience of adverse event after taking BAS	1=Yes 2=No
Adverse events	If got adverse events, how deal with it	1=By HCWs 2=By myself 3=Other
Satisfaction with quality of BAS	The respondent satisfied with the quality of BAS	1=Satified 2= Dissatisfied
Important factor for choosing BAS	The respondent can choose BAS according the factors	1=Brand of company 2=Price 3=Country of origin 4=Advertising 5=Quality
Assessment for network marketing system in KG	The respondent assess the network system in Kyrgyzstan	Scored from one (weak) to ten (very high)

2. Ethical Authorization

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과제승인번호	Y-2020-0124

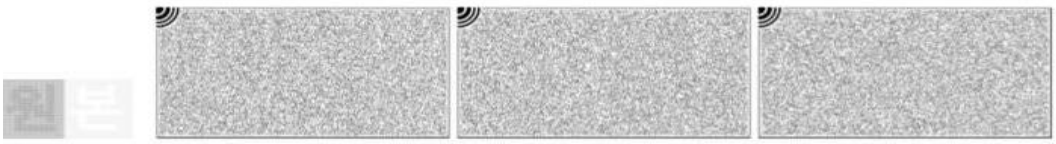
연세의료원 연구심의위원회의 심의 결과를 다음과 같이 알려 드립니다.

Protocol No.	
연 구 제 목	키르기스스탄과 대한민국의 생물학적 활성 보충제 사용 및 규제에 대한 정치적 연구
연 구 책 임 자	Ainur / Yonsei University Yonsei University
의 뢰 자	(학)연세대학교
연구예정기간	2020.09.15 ~ 2021.03.14
지속심의 빈도	12개월마다
과 제 승 인 일	2020.09.15
위 험 수 준	Level I 최소위험
심 의 방 법	신속
심 의 유 형	계획변경
심 의 내 용	- [변경전] 연구제목(국문) : 키르기스 공화국 인구의 생물학적 활동 보충제의 현재 상태 및 사용. [변경후] 연구제목(국문) : 키르기스스탄과 대한민국의 생물학적 활성 보충제 사용 및 규제에 대한 정치적 연구 - [변경전] 연구제목(영문) : Current condition and using of biological activities supplements among population in Kyrgyz Republic [변경후] 연구제목(영문) : Usage of Biologically Active Supplement and Politic study of regulation in Kyrgyzstan and Republic of Korea - [변경후] 임상 연구계획서(국문) : Ainur Kydyralieva-Study-Proposal-Ver-1.1_YUHC-IRB_2020.8.doc 삭제 - [변경후] 임상 연구계획서(국문) : Ainur Kydyralieva-Study-Proposal-Ver-1.1_YUHC-IRB_2020.8(1).doc 추가
심 의 위 원 회	연세의료원 IRB
참 석 위 원	연세의료원 IRB 신속심의자
심 의 결 과	승인

심 의 의 견 -

※ 연세의료원 연구심의위원회는 생명윤리 및 안전에 관한 법률을 준수합니다.
연구책임자 및 연구담당자가 IRB 위원인 경우, 해당 위원은 위 연구의 심의과정에 참여하지 않았습니다.

연세의료원
연구심의위원회
위원장



*** 유의사항 ***

1. 연세의료원 연구심의위원회 규정 준수

연구책임자께서는 모든 연구관련자들이 규정을 이행할 수 있도록 협조하여 주시기 바랍니다.

2. 이의신청

연구자는 심의결과에 이의가 있을 경우 이의신청을 통해 심의관련 의견제시가 가능합니다.
관련 질의에 대한 의견과 충분한 근거를 제출하여 주시기 바라며, 자료 미흡 또는 근거가 불충분할 경우 연구자에게 추가 자료를 요청할 수 있습니다.

3. 질의답변

승인 통보받지 않은 과제는 연구를 진행할 수 없습니다. 시정승인 또는 보완 결과를 받은 과제는 관련 질의에 대한 답변서와 그에 따른 변경 및 수정된 자료를 심의일로부터 6개월 이내에 제출하여야 합니다.

4. 대상자 동의

IRB 승인을 받은 동의서를 사용하여야 하며, 강제 혹은 부당한 영향이 없는 상태에서 충분한 설명에 근거하여 동의절차가 진행되어야 합니다. 또한, 대상자에게 연구참여여부를 고려할 수 있도록 충분한 시간을 제공하여야 합니다.
대상자 모집공고문을 사용하는 경우에는 모집공고문과 게시방법에 대해 IRB의 사전 승인을 받아야 합니다.

5. 중간보고

관련 법령에 따라 연구의 승인 유효기간은 최대 1년을 넘을 수 없습니다.
IRB가 결정한 심의 빈도에 따라 승인 만료일 최소 6주전에 중간보고를 제출하여 승인 유효기간을 갱신하셔야 합니다.

6. 계획변경

연구진행 시, 대상자 보호를 위해 불가피한 경우를 제외하고 연구절차, 대상자 수 등 IRB로부터 승인받은 내용에 변경이 있을 경우에는 반드시 IRB의 승인을 득한 이후에 적용할 수 있으며, 대상자 보호를 위해 취해진 응급상황에서의 변경도 즉시 IRB에 보고하여 주시기 바랍니다.

7. 안전성 정보 보고

대상자의 안전이나 임상연구에 부정적인 영향을 미칠 수 있는 새로운 정보에 대해 신속히 IRB에 보고하여야 합니다.

8. 종료보고

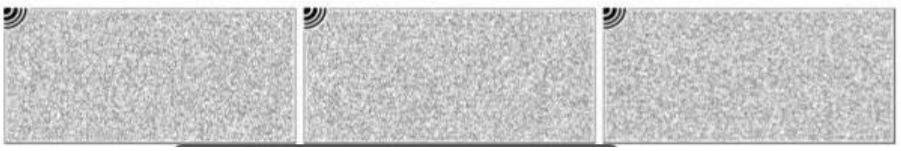
대상자의 관찰이 종료되고 자료 수집이 완료된 후 20일 이내에 보고하여야 합니다.

9. 결과보고

종료보고 이후, 자료분석 결과에 대해 보고하여야 합니다.

10. 내부점검 시 협조 요청

대상자 보호와 계획서 및 관련 규정 준수를 확인하기 위해 점검을 실시하는 경우, 원활한 점검절차 진행을 위해 연구진행과 관련된 서류를 준비하고 협조하여 주시기 바랍니다.



국문 초록

도입: 많은 나라에서 생물학적 활성 보충제 시장이 성장하고 있다. 그러나 생물학적 활성 보충제의 소비에 대한 데이터는 여전히 제한적이다.

관련 시장에서 키르기즈 인구의 생물학적 활성 보충제 사용이 증가하고 검출 기준 미달 및 위조, 변조 사례가 확대되는 것은 생물학적 활성 보충제에 관한 규제 시스템의 위기와 인식 부족 등이며. 이런 문제들이 이 연구에 흥미를 갖게 해주어 연구하게 되었다.

이번 연구는 키르기즈 인구 중 생물학적 활성 보충제에 대한 소비자의 태도를 파악하고 BAS에 대한 지식을 평가하며, 키르기즈의 규제 체계를 대한민국과 비교 연구하기 위한 것이다.

연구소재와 연구방법: 이 연구의 일반적인 방법은 정성적 접근법을 사용해 왔다. 연구 목표를 달성함에 있어 1차 및 2차 연구 소재로 수집된 데이터가 사용되었다. 연구 모집단의 소비자 및 비소비자 간의 생물학적 활성 보충제 사용에 기초한 온라인 설문지를 통해 수집된 1차 설문의 주요 참가 인원은 총 372명이었다. 2차 연구 소재로는 BAS와 HFF의 규제 시스템에 대한 키르기즈과 한국 정부의 연구 자료와 필요한 문서를 사용했다.

결과: 인구대비 생물학적 활성 보충제 사용의 유병률이 높은 것으로 조사되었고 참가자의 72.0%는 소비자였고 28.0%는 비소비자였다. 이 중 여성은 69.9%, 남성은 30.1%로 나타났다.

확인: 생물학적 활성 보충제를 사용하는 남성과 여성은 통계적으로 유의미한 차이가 있고, 소비자와 비소비자 간의 유의미한 지식 차이, 그리고 생물학적 활성 보충제 사용에 대한 정부 규제와 강한 연관성이 있는 것으로 보인다. 한국의 HFF 규제 연구는 키르기즈의 BAS 규제를 위한 적절한 기능을 권고한다.

결론: 키르기즈 공화국에서 생물학적 활성 보충제에 대한 대중의 인식을 확산시킬 필요가 있다는 것이 강조된다. BAS 제품이 항상 이롭지 않을 수 있고 심각한 부작용을 일으킬 수 있으므로, 소비자들은 사용하기 전에 의료 전문가와 상담해야 한다. 모든 다분야 의료 구조 구성원은 BAS 치료의 잠재적 위험과 이익을 명확하게 이해해야 한다. 또한 정부는 생물학적 활성 보충제 시장에 대한 등록 절차와 유통 경로를 보다 투명하게 하고 엄격한 규제 체계를 만들 필요가 있다.

키워드: *생물학적 활성 보충제, 건강 기능성 식품, 규제, 치료제.*