Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Ambiguous Definition of Nutraceuticals: Challenges & Possible Solutions

Priyamvadah Kinth[1, 2]* and Yogesh Suman[1, 2]

[1]CSIR-National Institute of Science, Technology and Development Studies (CSIR-NISTADS), Dr K S Krishnan Marg, New Delhi-110012, India
[2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad-201002, India
*E-mail: bioinformatics.priya@gmail.com
http://doi.org/10.37794/IJSRR.2019.8405

ABSTRACT:

The basic concept behind the emergence of nutraceuticals is an ancient one i.e. disease prevention with food rather than medicine. But this concept has given rise to different terminologies across the globe and different countries have their own set of guidelines and agencies to regulate them and related activities. This review article gives a snapshot of those terminologies, agencies and the regulatory guidelines. The study highlights the key features of the regulatory process with the aim to achieve global harmonization. Special focus has been given to the issues that exist in the new Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016, laid down by FSSAI. The article concludes by highlighting existing issues and possible suggestions that will effectively help in dealing with nutraceuticals without compromising consumers' safety.

KEYWORDS: Nutraceuticals, dietary supplements, food supplement, health foods, regulation

*Corresponding Author:

Priyamvadah Kinth

CSIR-National Institute of Science, Technology and Development Studies (CSIR-NISTADS),

Dr K S Krishnan Marg, New Delhi-110012, India

Academy of Scientific and Innovative Research (AcSIR), Ghaziabad-201002, India

E-mail: bioinformatics.priya@gmail.com

1. INTRODUCTION:

The term nutraceutical is a hybrid or amalgamation of nutrition and pharmaceutical. Reportedly, it was coined in 1989 by Dr. Stephen DeFelice, Chairman of the Foundation for Innovation in Medicine[1]. It is used to describe foods or food components which have the potential to cure specific disease conditions and they exist in different forms like natural diets, herbal products, genetically engineered foods and processed products such as cereals, soups and beverages [2]. It represents the combination of nutrition and pharmaceutical[3]. Nutraceuticals are medicinal foods that enhance health, modulate immunity and help in preventing/curing specific diseases[4]. It may also be defined as "a product (other than tobacco) that is intended to supplement the diet and that bears or contains one or more of dietary ingredients: vitamin, mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract or combinations of these ingredients"[5].

Scholars like Zeisel S H defined nutraceuticals as those diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a nonfood matrix, and used to enhance health in dosages more than what could be obtained from normal food[6]. Another group of scholars described nutraceuticals as pharmaceutical forms (tablets, capsules, powders, etc.) containing bioactive food compounds as active principles[7]. Nutraceuticals have been proven to offer physiologic benefits or to reduce the risk of chronic disease, or both, beyond their basic nutritional functions. Term 'Nutraceuticals' is being, widely adopted as a catchy term to refer to vitamins, minerals, herbs, and various other supplements.

AMBIGUITY IN DEFINITION

Merriam-Webster dictionary defines nutraceuticals as foodstuff (as a fortified food or dietary supplement) that provides health benefits in addition to its basic nutritional value[8] while oxford dictionary referred to it as "another term for functional food". Though several scholars have given different definitions for Nutraceuticals, essence remains the same, and it means "food as medicine". Still ambiguity exists in interpreting differences between Nutraceuticals and different related terminologies like Functional food, Dietary supplements, and Designer food[9, 10]. Some classify functional food as "food fortified with added or concentrated ingredients to functional levels, which improves health or performance while the term nutraceutical is used for anything that is consumed primarily or particularly for health reasons. This will make functional food, a kind of nutraceutical.

According to Health Canada nutraceuticals are a product that is "prepared from foods, but sold in the form of pills or powders (potions), or in other medicinal forms not usually associated with foods and is demonstrated to have a physiological benefit or provide protection against chronic disease." This would mean that nutraceuticals and functional foods are different[11]. Kalra defined nutraceutical as a functional food which aids in the prevention and/or treatment of disease(s) and/or disorder(s) (except anemia) [12]. Lachance and Das also defined nutraceuticals as biologically active phytochemicals that possess health benefits and delivered to the consumer as a dietary supplement and/or as a functional food[13]. Singh R and Geetanjali also defined them in a similar fashion and stated that they have dual role to play: as food and as therapeutic agent. Functional foods also share an overlapping definition with nutraceutical[14]. Any functional food under a given set of circumstances can be treated as dietary supplement, medical food, food for special dietary use or nutraceutical under different circumstances, depending on its ingredients (active components) and the claims reported[15]. Santini & Novellino defined nutraceuticals as extracts from vegetable sources (phytocomplex) or active metabolite complex (of animal origin) and these should be understood as a set of pharmacologically active substances which have inherent therapeutic properties due to the natural active principles of recognized effectiveness which they contain. They are marketed in pharmaceutical form e.g., capsule, tablet, drink, etc.[16]

Looking at the classification of nutraceuticals; various scholars have categorized them in different segments and they may range from isolated nutrients, herbal products, dietary supplements and diets to genetically engineered "designer" foods and processed products such as cereals, soups and beverages[17, 18]. Patil C S has grouped nutraceuticals in three categories: nutrients, herbals and dietary supplements[19]. In Das et al. opinion, nutraceuticals mainly comprises dietary fibre, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants, herbal/natural products, dietary supplements and functional foods[20]. A very recent report by ASSOCHAM defined them as food or food products that deliver incremental medical or health benefit, including treatment or prevention of diseases and it covers functional foods, functional beverages and dietary supplements. Probiotics, fortified energy drinks, vitamins and minerals etc. were provided as examples[21]. A very similar classification was also done in the market research report by Frost and Sullivan, 2010 & Bourne Partners, 2013 which classified nutraceuticals in following categories[22, 23]:

1. Dietary supplements

- Botanicals
- Vitamins
- Minerals
- Amino acids
- Enzymes

2. Functional food

- Carotenoids
- Dietary Fibers
- Fatty Acids
- Minerals
- Prebiotics & Probiotics
- Vitamins

3. Functional beverage

- Energy drinks
- Sports drinks
- Functional juices

A lot of literatures have used the terms: nutraceuticals, functional foods, health foods, dietary supplements, health supplements, foods for special dietary uses etc. interchangeably. However, Indian Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016 has specifically defined each of these terms in following ways[24]:

1.1 Health Supplement

It comprises mainly amino acids, enzymes, minerals, proteins, vitamins, other dietary substances, plants or botanicals, prebiotics, probiotics and substances from animal origin or other similar substances with known and established nutritional or beneficial physiological effect and marketed in single use packaging or in dosage forms namely, capsules, tablets, pills, sachets; jelly or gel, semi-solids and other similar forms or any other forms of liquids and powders designed to be taken in measured unit quantities.

1.2Nutraceuticals

Nutraceuticals are the products that provide a physiological benefit and help in maintaining good health. It contains isolates and extracts from food or non food sources and sold in the form of food-format of granules, powder, tablet, capsule, liquid, jelly or gel, semi-solids and other formats and may be packed in sachet, ampoule, bottle, and in any other format as measured unit quantities.

1.3Food for special dietary uses, other than infants and to be taken under medical advice

These are specially processed or formulated to satisfy particular dietary requirements which may exists or arise because of certain physiological or specific health condition like low or high weight, high blood pressure, pregnant or lactating women and geriatric population and celiac disease and other health condition. These should not be used for parenterals use.

1.4Food for specific medical purpose

These foods are specially prepared for weight reduction and intended as total replacement of normal diet. These should not be used for parenterals use and without medical advice. These maybe used for exclusive or partial feeding of persons with a limited, impaired or disturbed capacity to take, digest, absorb, metabolize or excrete ordinary foodstuff.

1.5Specialty food containing plant or botanical ingredients with safe history of usage

These are prepared by using only plant or botanical ingredients specified in the regulation with established history of safe usage in India or in any other country.

2. OBJECTIVE:

This review aims on the following

- To present compiled definitions and regulatory structure of nutraceuticals with special emphasis on the need for a regulatory structure.
- Identify the gaps in the regulatory structure of India that still needs to be addressed.
- Focuses on the need to achieve global harmonization in the regulatory structure to achieve the full potential of this sector keeping in view the interest of the people.

3. METHODOLOGY:

An intensive literature search was conducted to collect the required information. Several academic journals, reports, books, official web pages of relevant regulatory authorities of different countries were searched to collect the required updated information. The bibliographies of all the collected literature was also examined for other potential citations.

4. NEED FOR REGULATION:

A lot of factors are reported for the rising demand of nutraceuticals. Rapid industrializations, urbanizations, market globalizations, sedentary lifestyles, nature of work i.e. more technological, strenuous and limited physical activity and various other reasons like increased consumption of fast foods, increasing disposable income etc.; all these factors have had a strong impact on the life style and diets which in turn changed the related disease pattern[25]. This increase in demand has thinned the line between existing pharmaceuticals and food and in turn helps producers to launch new products in the market. New nutraceutical manufacturers are mushrooming and the process of cut-throat competition for survival, the companies may compromise with the quality of product [9, 10]. These products do affect the body functions to an extent but they are not regulated and tested as tightly as pharmaceutical drugs. Thus realizing the fact that most health claims accompanying these products are supported by little or no research, regulators are working on appropriated regulations[26]. According to Santini et al the claims associated with nutraceuticals or functional foods are mainly unsubstantiated due to a lack of studies on possible mechanisms of action and a lack of in vivo research confirming the claimed beneficial health effects on specific pathological conditions. And mostly the literature supporting these claims comes from the studies where the micronutrients have been considered safe for consumption as they come from natural sources[27].

It cannot be assured that “if a little is good, a lot is better” or “it can’t hurt”. Nutraceutical consumption can cause serious problem if it delays the treatment seeking tendency of the consumers. It’s easy to say that a particular nutraceutical product is safe to consume than proving its efficacy. There is a need to generate evidence for the effects of nutraceutical consumption several folds greater than the intended (recommended) dose to establish toxicity data on both short and long term basis. Most importantly, a lack of reported toxicity problems with any nutraceutical should not be interpreted as evidence of safety [28].

5. REGULATORY MECHANISM FOR NUTRACEUTICAL AND SIMILAR PRODUCTS: GLOBAL AND INDIAN SCENARIO

Various countries have their own set of guidelines and agencies to regulate nutraceutical and similar product related activities.

5.1 India

In India, the responsibility of framing and regulating standards for food and related items rests with the Food Safety and Standards Authority of India (FSSAI) as outlined in the Food Safety and Standards Act 2006 which also included nutraceuticals in the section 22 of the act. Earlier there was no regulation which deals specifically with nutraceuticals and they were regulated like any other food item. However in 2016, this authority drafted a new regulation which deals specially with categories like functional foods, nutraceuticals, dietetic products, foods for special dietary uses (FSDU), food or health supplements, foods for special medical purposes (FSMP) and novel foods. This new regulation has given specific definition to nutraceuticals, functional food, dietary supplements and lays the guidelines for the packaging and labeling of these products; nutritional and health claims made, restriction of advertisement avoiding any misleading or false claims, addition of nutritional ingredients within limit; use of additives in nutraceutical formulations; contaminants, toxins and residues and every claim should be backed by valid scientific data. This regulation has also provided a list of nutraceutical ingredients and additives that can be used in the preparation of nutraceuticals [24].

5.2 Canada

In Canada, “Natural health products” (NHPs) exists under the Natural Health Products Regulations, which came into effect on January 1, 2004. They are regulated by Natural and Non-prescription Health Products Directorate (NNHPD), Health Canada. Natural health products (NHPs) are naturally occurring substances that are used to restore or maintain good health and help in the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans; restoring or correcting organic functions in humans; or modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health. Natural health products, often called "complementary" or "alternative" medicines, include: vitamins and minerals; herbal remedies; homeopathic medicines; traditional medicines like traditional Chinese and Ayurvedic (East Indian) medicines; probiotics; other products like amino acids and essential fatty acids. They are often made from plants, but can also be made from animals,

microorganisms and marine sources. They come in a wide variety of forms like tablets, capsules, tinctures, solutions, creams, ointments and drops. To be legally sold in Canada, all natural health products must have a product license, and the Canadian sites that manufacture, package, label and import these products must have site licences. To get product and site licences, specific labeling and packaging requirements must be met, good manufacturing practices (GMP) must be followed, and proper safety and efficacy evidence must be provided. The level of evidence required is also dependent on the claim (disease risk reduction claims require stronger evidence, including clinical studies) [29, 30].

5.3 Australia

In Australia, these are referred to as 'complementary medicines' and are regulated as medicines under the Therapeutics Goods Act, 1989, which was implemented in 1991[31]. A complementary medicine is defined in the Therapeutic Goods Regulations 1990 as a therapeutic good consisting principally of one or more designated active ingredients mentioned in Schedule 14 of the Regulations, each of which has a clearly established identity and traditional use. The Australian regulatory guidelines for complementary medicines (ARGCM) provide information for manufacturers, sponsors, healthcare professionals and the general public on the regulation of complementary medicines in Australia [32].

5.4 European Union

The European Food and Safety Authority (EFSA) regulate the food legislation in European Union and these are referred to as food supplements. Food supplements are defined as concentrated sources of nutrients (i.e. mineral and vitamins) or other substances with a nutritional or physiological effect that are marketed in "dose" form (e.g. pills, tablets, capsules, liquids in measured doses). A wide range of nutrients and other ingredients might be present in food supplements, including, but not limited to, vitamins, minerals, amino acids, essential fatty acids, fibre and various plants and herbal extracts. Food supplements are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or to support specific physiological functions. They are not medicinal products and as such cannot exert a pharmacological, immunological or metabolic action. Therefore, their use is not intended to treat or prevent diseases in humans or to modify physiological functions. The European Commission has established harmonized rules to help ensure that food supplements are safe and properly labeled. In the EU, food supplements are regulated as foods and the legislation focuses on vitamins and minerals used as ingredients of food supplements. The Directive 2002/46/EC

of EU legislation is related to food supplements containing vitamins and minerals. The Directive sets out labeling requirements and requires that EU-wide maximum and minimum levels are set for each vitamin and mineral added to supplements [33].

5.5 USA

In USA, Food and Drug Administration (FDA) regulates both finished dietary supplement products and dietary ingredients. FDA regulates dietary supplements under a different set of regulations than those covering "conventional" foods and drug products which is the Dietary Supplement Health and Education Act of 1994 (DSHEA). DSHEA has defined dietary supplements as a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: vitamin, mineral, herb or other botanical, amino acid; dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of the preceding substances. The act maintains that dietary supplements should not be represented for use as a conventional food or as a sole item of a meal or the diet and be labeled as a dietary supplement. Unlike drugs, supplements are not intended to treat, diagnose, prevent, or cure diseases. Claims like these can only legitimately be made for drugs, not dietary supplements.

Under DSHEA, manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing products that are adulterated or misbranded and FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market [34, 35].

5.6 Japan

In Japan, the Ministry of Health, Labor and Welfare (MHLW) regulates health foods as food with health claims (FHC). FHC are foods that are labeled with certain nutritional or health functions and are categorized in two groups. The first group, “Foods with Nutrient Function Claims” refers to all food that is labeled with the nutrient function claims specified by the MHLW and satisfy the standards for the minimum and maximum daily levels of twelve vitamins and five minerals. These foods may be freely manufactured and distributed without any permission from or notification to the national government, provided that it meets the established standards and specifications. The second group is “Foods for Specified Health Uses,” or simply FOSHU. They contain dietary ingredients that are officially approved to claim its beneficial physiological effects and promote health. These are intended to be consumed for the maintenance / promotion of health or special health uses by people

who wish to control health conditions, including blood pressure or blood cholesterol. Every health claim must be approved by MHLW with proven efficacy in human body. MHLW has provided specific labelling requirements and Health Promotion Law has restricted the manufactures to make any health or functional claim in the absence of scientific evidence and also restricted them from making any false or misleading claim [36].

5.7 China

In China, health food is usually defined as food product that have specific health function or supply vitamins and (or) minerals. With the goal of regulating body's function, health food is suitable for specific groups of people. However, it is not used for the purpose of curing disease and causes no acute, sub-acute or chronic health effect to human body. Health food is classified into two groups: nutrition supplement that replenishes the vitamins and (or) minerals but without providing energy or other active ingredients and functional health food labeled with health function claim has physiological effects on the human body. According to the Food Safety Law of the People's Republic of China, companies who plan to place health food in Chinese market shall apply and obtain the health food registration certificate or filing certificate. For domestic health foods produced in China, the registration shall be conducted with China Food and Drug Administration (CFDA), whereas, the filing shall be carried out with Provincial Food and Drug Administration (FDA). For imported health foods produced in overseas factories, both the registration and filing shall be applied with CFDA. Meanwhile, oversea companies shall have a permanent Chinese representative office or appoint a Chinese agent to deal with registration or filing and obtain such certificates [37].

Various definitions and regulatory agencies monitoring nutraceuticals and similar products across countries have been summarized in Table-1

Table 1: Nomenclature of Nutraceuticals/ Health supplements/Similar health products and Regulatory agencies in India, USA, Canada, Australia, Japan, China and EU

	India	**USA**	**Canada**	**Australia**	**Japan**	**European Union**	**China**
Prevalent nomenclature for nutraceuticals/Health supplements	Nutraceuticals/ Health supplement	Dietary Supplement	Natural health Products	Complementary medicines	Food for Special Health Use (FOSHU)	Food supplements	Health Food
Regulation dealing with nutraceuticals	Food Safety and Standard Regulation	Dietary Supplement Health and Education Act (DSHEA)	Natural Health Product Regulation	Australian regulatory guidelines for complementary medicines (ARGCM)	Food Sanitation Law	Directive 2002/46/EC of Food Legislation	Food Hygiene Law
Year in which regulations came into force	2016	1994	2004	1989	1991	2002	2003
Authority responsible for implementing compliance guidelines for Nutraceuticals	Food Safety and Standard Authority of India (FSSAI)	Food and Drug Administration (FDA)	Natural and Non-prescription Health Products Directorate (NNHPD), Health Canada	Therapeutic Goods Administration (TGA)	Ministry of Health, Labor and Welfare (MHLW)	European Food Safety Authority (EFSA)	China Food and Drug Administration (CFDA)

Regulatory requirements for registration	i) Product evaluation ii) Licenses iii) Health & label Claim	i) Product licensing ii) Evidence requirements for safety & efficacy iii) Labelling iv) Heath claims v) Good manufacturing practices (GMP) vi) Adverse reaction Reporting vii) Clinical trials	i) Product licensing ii) Evidence requirements for Safety & efficacy iii) Labelling iv) Site Licensing v) Good manufacturing practices (GMP) vi) Adverse Reaction reporting vii) Clinical trials	i) Product Application ii) Good manufacturing practices (GMP) iii) Labeling iv) Post-market surveillance	i) Manufacturing process ii) Health claims iii) Product packaging and labels iv) Samples, applicant and manufacturer detail v) Product formula vi) Clinical trials (Human clinical trials compulsory)		i) Manufacturing process ii) Health claims iii) Product packaging and labels iv) Samples, applicant and manufacturer detail v) Product formula vi) Clinical trials
Claims required to be verified	1. Nutritional claim, 2. Health claim a. Nutraceutical ingredient b. A health related benefit c. Other claims	1. Health claims 2. Nutrient claims 3. Structure/ fun-ction claims and related dietary supplement claims	1. Claim by health condition 2. Claim by health effect 3. General Health Claim	1. General Level Health Claim 2. Medium Level Health Claim 3. High Level Health Claim	1. Function Claim	1. Nutritional claim 2. Health claim	1.Structure/function Claim 2. Disease risk reduction claim

(**Source:** Compiled from Draft Regulations – Food Safety and Standards Authority of India; Sharma et al., 2013; Devla et al., 2011; Patel D et al., 2008; Palthur et al., 2010; Patel et al., 2014)[2, 3, 7, 24, 38]

6. EXISTING ISSUES

Nonetheless, different country-specific regulations, safety, and health claim substantiation are the main challenges which the nutraceuticals are experiencing. The bigger challenge is the absence of a shared supra-national regulation for nutraceuticals, which would recognize their potential and possible role as therapeutic tools in some pathological conditions based on assessed safety, known mechanism of action, clinically proven efficacy in both reducing the risk of illness onset and enhancing overall well-being. It seems very crucial for the competent national authorities to ask the manufacturers to provide clinical data that substantiates safety, efficacy, and mechanism of action of any claims attributed to food supplements and nutraceuticals, avoiding any possible source of confusion [16, 27].

If we look at how India's regulatory system has defined nutraceuticals; then there isn't much difference between nutraceuticals and health supplements in terms of definition, marketed forms and health benefits. Moreover, there is a partial overlap between the definitions of nutraceuticals and health supplement as both claim beneficial effects for health; however, while nutraceuticals are made from food or part of a food, food supplements are single substances used alone or in mixtures with the scope of adding micronutrients. And according to the regulation, both the health supplements and nutraceuticals are prohibited to claim that they can help in preventing, treating or curing human diseases. The definition given by Dr. Stephen DeFelice and also the definitions used for nutraceuticals in majority of the literature, they were described as the products that help in treatment and prevention of diseases. If this property of nutraceutical is dissociated from them, then what is the use of having them as a separate entity when we already have health supplements or similar products. Specially talking in Indian context where we have abundant of traditional knowledge and plethora of products coming out of that knowledge, then what is the need of introducing an additional product in the bucket and that too without any outstanding feature.

Another big challenge is to make people capable of taking informed and educated decision regarding consumption or non-consumption. With so many of similar products available in different prices in market shelves, how the common people are supposed to pick a particular item best suitable to them according to their health in order to get the desired benefit that they expect.

7. DISCUSSION & FUTURE PROSPECTS

Although FSSAI has come up with regulatory guidelines related to health supplements and nutraceuticals but mere introduction will not do any good. It has to come up with stricter norms for claimed health benefits supported by clinical trials. Manufacturing a product from the natural sources which are safe to consume will not guarantee promised health benefit unless supported by proven scientific evidence. Since these products are non-prescription based; two approaches can be used - first is to prove the safety and efficacy of not only ingredients but also the finished product supported by proper human clinical trial prior the market penetration and second is to make people aware about all the aspects of the different categories of food products available like their associated health benefits, the targeted population, any side-effects if any, right amount of dose, its composition, duration of consumption etc. Additionally, health practitioners like doctors and nutritionists also have a crucial role to play in enabling people to make the right choices. Our aim should not be to steer the growth of nutraceutical industry rather it should be to protect our people from consuming any false or misleading or unnecessary product. Efforts should not be scaled up to launch new products in the market and attract consumers but to promote more research to prove the associated health claims and the efficacy of the products. For this purpose, three most important pillars which are regulatory authority, manufacturers and medical practitioners should work together in the interest of the people.

ACKNOWLEDGEMENT

I would like to acknowledge UGC for providing me the fellowship during the course of my study. I would also like to express my gratitude to my guide Dr. Yogesh Suman for his constant guidance and CSIR-National Institute of Science, Technology and Development Studies campus for providing us the facility to carry out this study.

REFERENCES

1. Brower V. Nutraceuticals: poised for a healthy slice of the healthcare market? Nat Biotechnol. 1998; 16:728-731.
2. Devla M N, Acharya S R, Acharya N S and Kumar V. Dietary supplements: a legal status in India & in foreign countries. Int J Pharm Pharm Sci. 2011; 3(3):7-12.
3. Sharma A, Kumar P, Sharma P and Shrivastav B. A Comparative Study of Regulatory Registration Procedure of Nutraceuticals in India, Canada and Australia. International Journal of Pharmaceutical Quality Assurance. 2013; 4(4):61-66.

4. Singh J and Sinha S. Classification, regulatory acts and applications of nutraceuticals for health. Int J Pharm Bio Sci. 2012; 2:177-187.
5. Halsted C H. Dietary supplements and functional foods: 2 sides of a coin? Am J Clin Nutr. 2003; 77 (suppl):1001S-1007S.
6. Zeisel S H. Regulation of nutraceuticals. Science. 1999; 285:1853-1855.
7. Palthur M P, Palthur S S S and Chitta S K. Nutraceutical: concept and regulatory scenario. Int J Pharm Pharm Sci. 2010; 2(2): 14-20.
8. Ahmad M F, Ashraf S A, Ahmad F A et al. Nutraceutical market and its regulation. Am J Food Technol. 2011; 6(5):342-347.
9. Bhowmik D, Gopinath H, Kumar B P, Duraivel S and Kumar K P S. Nutraceutical – A Bright Scope and Opportunity of Indian Healthcare Market. The Pharma Innovation. 2013; 1 (11): 29-41.
10. Gupta S K, Yadav S K and Patil S M M. Nutraceutical – A Bright Scope and Opportunity of Indian Healthcare Market. International Journal of Research and Development in Pharmacy and Life Sciences. 2013; 2(4):478-481.
11. Robert E. C. Wildman. Handbook of Nutraceuticals and Functional Foods. CRC Press, Taylor & Francis, 2007.
12. Kalra E K. Nutraceutical- Definition and introduction. AAPS PharmSciTech. 2003; 5(3): 1-2.
13. Lachance P A and Das Y T. Nutraceuticals. Comprehensive Medicinal Chemistry II. 2007; 1: 449-461.
14. Singh R and Geetanjali. Nutraceuticals: promising health product. International Research Journal of Medical Sciences. 2013; 1(1): 14-17.
15. Borchers A T, Keen C L and Gershwin M E. The basis of structure/function claims of nutraceuticals. Clinical Reviews in Allergy and Immunology. 2016; 51 (3): 370-382.
16. Santini A & Novellino E. To Nutraceuticals and Back: Rethinking a Concept. Foods. 2017; 6 (74): 1-3; doi: 10.3390/foods6090074.
17. Malik A. The potentials of Nutraceuticals. Pharmainfo.net 6. 2008
18. Dureja H, Kaushik D, Kumar V. Developments in nutraceuticals. Indian J Pharmacol. 2003; 35: 363–372.
19. Patil C S. Current trends and future prospective of nutraceuticals in health promotion. BIOINFO Pharmaceutical Biotechnology. 2011; 1(1): 01-07.

20. Das L, Bhaumik E, Raychaudhuri U and Chakraborty R. Role of nutraceuticals in human health. J Food Sci Technol. 2012; 49 (2): 173-183.
21. Indian Nutraceuticals Industry: Current Scenario & Future Trends. The Associated Chambers of Commerce and Industry of India (ASSOCHAM India). 2017
22. Frost and Sullivan. Global nutraceutical industry: Investing in healthy living, FICCI. 2010
23. An Overview of Global Regulatory Trends in the Nutraceutical Industry – April 2013. Bourne Partners. https://bournepartners.wordpress.com/2013/04/22/an-overview-of-global-regulatory-trends-in-the-nutraceutical-industry-april-2013/. Accessed 20 October 2014
24. Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016. FSSAI, Ministry of Health & Family Welfare. https://www.fssai.gov.in/home/fss-legislation/fss-regulations.html
25. Sharma M and Garg S. Functional foods: marketing 'health' to modern India. International journal of Innovative Research and Development. 2013; 2(5): 721-739.
26. Brower V. A nutraceutical a day may keep the doctor away. European Molecular Biology Organization. 2005; 6(8): 708-711.
27. Santini A, Cammarata S M, Capone G et al. Nutraceuticals: opening the debate for a regulatory framework. British Journal of Clinical Pharmacology. 2018; 84:659-672.
28. Crandell K and Duren S. Nutraceuticals: What are they and do they work? Kentucky Equine Research, Inc., Versailles, KY, 29-35. (http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.569.9335&rep=rep1&type=pdf)
29. Health Canada. https://www.canada.ca/en/health-canada.html
30. Malla S, Hobbs J and Sogah E K. Functional foods and natural health products Regulations in Canada and around the world: Nutrition labels and health claims. Report prepared for the Canadian Agricultural Innovation and Regulation Network (CAIRN). 2013. Accessed 8 September 2014.
31. Varghese T and Mishal P. Scrutinizing the term 'nutraceutical' - a global regulatory perspective. Nutraceutical Business Review. 2014. https://www.nutraceuticalbusinessreview.com/technical/article_page/Scrutinising_the_term_nutraceutical__a_global_regulatory_perspective/100047. Accessed 15 October 2014

32. Australian regulatory guidelines for complementary medicines. Therapeutic Goods Administration. https://www.tga.gov.au/publication/australian-regulatory-guidelines-complementary-medicines-argcm. Accessed 24 November 2014.
33. Food supplements. European Food Safety Authority. http://www.efsa.europa.eu/en/topics/topic/supplements.htm. Accessed 24 November 2014.
34. Dietary Supplements. US Food and Drug Administration. http://www.fda.gov/Food/DietarySupplements/default.htm. Accessed 15 December 2014.
35. Dietary supplement health and education act of 1994, public law 103-417, 103rd congress. NIH, Office of Dietary supplements. https://ods.od.nih.gov/About/DSHEA_Wording.aspx
36. Food safety information, Ministry of Health, Labour and welfare. https://www.mhlw.go.jp/english/topics/foodsafety/fhc/index.html
37. China Health Food Registration and Filing, CIRS. http://www.cirs-reach.com/news-and-articles/health-food-registration-and-filing.html
38. Patel H, Shah D and Maheshwari D. A short review on comparative study of regulation of nutraceuticals in USA and India. International Journal for Pharmaceutical Research Scholars. 2014; 3(1): 736-741.