



“The Nutraceutical Amino Acids”- Nature’s Fortification for Robust Health

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ABSTRACT

Nutraceuticals i.e. the product positioned at the interface between food and drugs, are an increasing group of products gaining importance; patients/consumers of drug always have a wish to have no or less side/ toxic effect and also complementary or alternative benefit of the drug products and that’s why nowadays they are using nutraceuticals. In recent years, because of health benefits and an alternative to modern medicine, there is a growing interest in nutraceuticals. Nutrients, functional foods, medicinal food, herbals and dietary supplements are major constituents of nutraceuticals these play an artistic instrumental role in health maintenance, they also show various acts against various disease conditions and thus promote and sustain the quality of life. The article aims to explore and discuss the ability of nutraceuticals to treat or prevent underlying causes of disease; the article outlines nutraceuticals with their therapeutic applications, adverse effects and interaction. Various researches on nutraceutical product are under process which will be integrating and assessing information further.

Keywords: Dietary supplements; functional foods; medicinal food; farmaceuticals.

1. INTRODUCTION

The burden of chronic diseases like cancer, cardiovascular diseases, obesity, and diabetes is demonising worldwide. In 2001, chronic diseases contributed nearly 59% of the 56.5 million total reported deaths in the world and 46% of the global burden of diseases [1]. Customers are intensely concerned about how their health care is administered, managed, and priced. As they are insatiable with the costly, advanced disease treatment approach mainly in current medicine [2]. Soil and nutrition contamination, air and water pollutions, has caused by industrialization as it is hovering over large area of various chemicals, heavy metals, electromagnetic waves, and other potentially harmful man-made items. These problems have led to an increased occurrence of diabetes, obesity, different cancers and vascular diseases, physiological problems, as well as other degenerative diseases. That's why, the cost of medical care have dramatically increased through the raised demands for health care.

The medicines we ingest, inject, and inhale are often complex therapeutic compounds. The drugs are typically mixtures of chemicals prepared from starting materials or drug sources. Depending on the sources from which the drugs were produced, the drugs can be categorized as natural, synthetic, or semi-synthetic [3]. The general stages of synthetic drug discovery are same as those of natural drug discovery. In natural drug discovery, the lead complexes come from natural sources like plants, while in synthetic drug discovery, the lead compounds are typically produced by combinatorial chemistry, a method by which hundreds to millions of molecules are formed from miniature chemical building blocks. Combinatorial chemistry is an efficient way to make many new chemicals but generates molecules that are less structurally intricate than natural compounds. Most of the synthetic drugs show fewer therapeutic effects and cause unacceptable side effects. Consumers are turning massively to food supplements to improve health due to the risk of toxicity or adverse effect of a drug that's by pharmaceutical fails [4].

Today's scenario shows more consent to receive natural drug in comparison to receive synthetic drug. As well as synthetic drug discovery has lower strike-rates via High Throughput Screening (HTS) because the products are not as widely varied as those in natural products. Due to the

disappointment of alternative drug discovery methods to deliver many lead based compounds in key therapeutic areas such as anti-infective, immune suppression and metabolic diseases, the natural product research has been renewed. Natural products research stays to discover diversified lead structures, which can be used as templates for the growth of new drugs by the pharmaceutical industry. Undoubtedly that natural product continues to be central sources of new pharmaceutical compounds [3].

Natural products including animals, plants and minerals have been the basis of treatment of human diseases. Foods play a vital role in normal functioning of the body and are helpful in maintaining the health of the person and in sinking the risk of several diseases [5].

Plants are one of the supreme resources of human foods and medicines. Promptly increasing knowledge on nutrition, medicine, and plant biotechnology has intensely altered the concepts about food, health and agriculture and has brought a revolt on them. The latest developments in medical and nutrition sciences, health endorsing foods, natural products, has received extensive attention from both health professionals and the public. It is very imperative that the nutrients found in foods, fruits and vegetables is accountable for the health benefits [6]. For example, scurvy will happen if vitamin C is absent in the human diet. Similarly, blindness will occur when diets are lacking in vitamin A [7]. Epidemiological and clinical studies have confirmed the relationship between diet and health. It is well known fact that population consuming a large proportion of plant based foods including vegetables, fruits grains and cereals or those with a high consumption of seafood, have a lower occurrence of cardiovascular diseases and certain types of cancer [8]. Therefore, individuals have tried to achieve a better quality of life by eating vegetables, fruits and other plant based foods, taking dietary supplements or nutraceuticals, or using nutritional therapy or phyto-therapy to replace chemotherapy or radiotherapy. Hence due to increase in demands for nutraceuticals, phyto-nutrients and their therapeutic services, manufacturers, marketers, and related licensed professionals have grown-up consequently. Positioned at the interface between food and drugs, a growing body of products is assuming importance as the consumer is focusing for the substitute of useful products and i.e. nowadays they are using nutraceuticals. Progressively,

People are using natural dietary supplements and other forms of nutraceuticals as part of incredible flow to have physiological profits or to afford protection against diseases [2].

2. CONCEPT OF NUTRACEUTICALS

Around 2000 years ago, Hippocrates properly stressed "Let food be your medicine and medicine be your food". In 1989 Stephen De-Felice founder and chairman of the Foundation for Innovation in Medicine (FIM) Cranford, NJ [9] coined the term "nutraceuticals" meaning "nutrition" and "pharmaceutical". Nutraceuticals are medicinal foods that play a significant role in retaining well being, modulating immunity, and improving health thereby preventing as well as treating specific diseases. Nutraceuticals currently getting recognition as being beneficial for various uses as shown in Table 1 like in obesity, coronary heart disease, osteoporosis, cancer, diabetes and other chronic and degenerative diseases such as Parkinson's and Alzheimer's diseases.

Various advantages of nutraceuticals are-

- ✓ Offers low cost and premature control of risk factors for subsequent disease (e.g. heart disease).
- ✓ Offer a protective model for disease prevention than the existing medical model.
- ✓ Offer control of moderately elevated risk factors (e.g. blood cholesterol, triglyceride,

etc.), which existing healthcare system fails to control.

Thus, the nutraceuticals can be projected as one of the missing blocks in the health benefit of an individual. It has now been scientifically proved and supported by various research articles that nutraceuticals used as food or part of food, will provide health welfares including prevention or treatment of disease (Fig. 1) [5]. Herbal nutraceuticals are influential in keeping health and act against nutritionally induced acute and chronic diseases by enhancing the optimal health and quality of life [13]. Phytochemicals and Antioxidants are two explicit types of nutraceuticals. Phytochemical help in providing defense against diseases like cancer, diabetes, heart diseases and hypertension e.g. carotenoids found in carrots and antioxidants are helpful in avoiding chronic diseases by preventing oxidative damage in the human body [31]. Over the last 20 years numbers of Nutraceuticals are available for self- medication or for sale [32]. The other side of the coin depict that nutraceutical is a product isolated or purified from foods that are generally sold in medicinal forms not usually associated with foods. When a nutraceutical is validated to have physiological benefits or provide shield against chronic disease, the functional foods are defined broadly as foods that provide more than simple nutrition; they supply additional physiological benefits to the consumer [33]. The concept of Nutraceuticals is shown in Fig. 1 [13].

Table 1. Examples of nutraceuticals and their uses

Nutraceuticals	Uses
Resveratrol [10]	Immune supplement [11].
Flavonones and citrus fruits [12].	Antioxidants, Anti-cancer, beauty drink [12].
Polyols sugar, alcohols [13].	Reduces risk of dental caries [14].
Dietary fibres [15].	Anticancer, helpful in maintaining the digestive tract [16].
Vitamins and trace elements [17]	Nutritional supplement [17]
Terpenoids [18].	Energy drinks [19].
minerals and carbohydrates [7]	Protein supplements [7].
Natural supplement [20]	Neuropathic pain supplement
polysaccharides and Folic acid [21]	Immune supplement [21].
Calcium [22]	Calcium supplement, bone density [22].
Beta –glucan [23].	Immune supplement [24]
Glutamic acid [25].	Amino acid supplement [25]
Peptides [26].	Nutritional supplement, apoptosis, anticancer. [26]
Phytosterol [27]	Daily health supplement [27]
Carbohydrate, amides [7].	Nutrition supplements [7].
Terpenoids , malic acid ,caffeine [28]	Energy drink [29]
Probiotics /prebiotics lactobacilli ,bifida acteria [30]	Maintain gastrointestinal health [30]
Multivitamins [6]	Nutritional supplement [6]

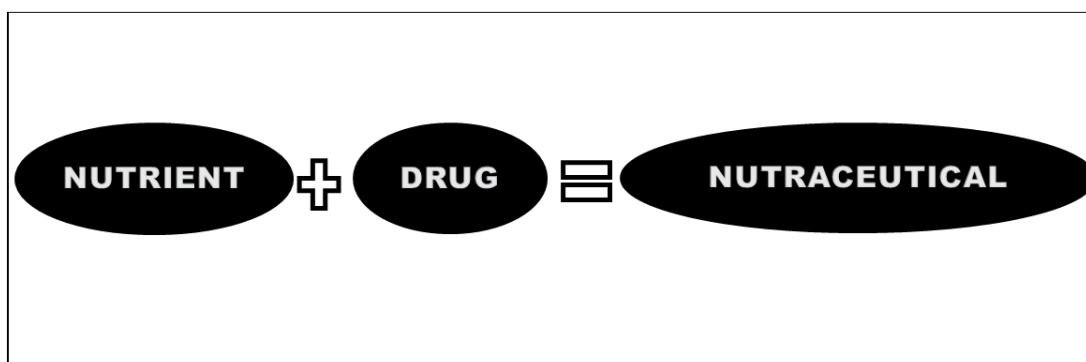


Fig. 1. Concept for Nutraceuticals

There has been a boom in sale of Nutraceuticals because of –

1. Adverse arial properties of pharmaceuticals
2. Increased affinity of patients for self-medication
3. Aging population e.g. – arthritis

3. CLASSIFICATION OF NUTRACEUTICALS

Nutraceuticals is a wide-ranging term used to describe any product derived from food sources that provide more health benefits in addition to the basic nutritional value found in foods. The description of nutraceuticals and linked products often depend on the source. Medical community desire that the term nutraceutical should be more clearly recognized in order to distinguish between the wide diversities of products out there. There are numerous different types of products that may drop underneath the group of nutraceuticals [34].

1. Functional foods
2. Dietary supplements
3. Medicinal foods
4. Farmaceuticals

3.1 Functional Food

Functional food though is totally different from nutraceuticals and might be outlined as food merchandise to be taken as part of the same old diet so as to possess helpful effects [35]. When food is being cooked or prepared using "scientific aptitude" with or without the familiarity of how or why it is being used, then the food is called as "functional food." Thus, useful food provides the body with the specified quantity of vitamins, fats,

proteins, carbohydrates necessary for healthy survival. One useful food which aids within the interference and/or treatment of disease(s)/ disorder(s) apart from deficiency conditions like anemia it is referred to as a "nutraceutical" [36]. Functional food merchandise are a unit milk, cheese and eggs that area unit all enriched with polyunsaturated fatty acid; yoghurt increased with live active cultures (probiotics); fruit juices and drinks with multiplied inhibitor levels; cereals and grains like wheat, oat, barley and fenugreek merchandise with increased amounts of dietary fiber; changed carboxylic acid vegetable oils; and vegetable proteins from soy, canola and hemp, legumes and fruit products [21] e.g. Oats, bran, plantain and lignin's for cardiopathy and carcinoma, prebiotics, oligo fructose for management of microorganism, Omega-3 milk in interference of cardiopathy, oil with down triglycerides for sterol reduction, Stanols (Benecol) in reduction of sterol adsorption [13]. At a similar time, several opportunities for the event of novel dietary merchandise are created with all new fields of study back with newterms. "Nutraceuticals" and "functional foods" area unit two new terms describe health-promoting foods or their extracted elements [37]. Useful foods are a unit designed foods which give enriched foods to client, instead of factory-made dietary supplements in liquid or capsule form [32]. Health North American country defines useful foods as "ordinary food that has elements or ingredients additionally to provide a particular medical or physiological profit, apart from a strictly nutritional effect" [34].

In Japan, all functional foods must meet three established requirements: foods should be

- (1) Should be in their naturally-occurring form,
- (2) Should be an essential part of our daily diet,

(3) Should regulate a biological process in hopes of preventing or controlling disease.

3.2 Dietary Supplements

A dietary supplement is a product that comprises nutrients plagiaristic from food products. The "dietary ingredients" existing in these products are: metabolites, vitamins, Minerals, herbs, and amino acids as shown in Tables 2 and 3. The term "bioactive foods" was first defined as "foods, food ingredients or dietary supplements that determine specific health or medical benefits counting the prevention and treatment of disease outside basic nutritional tasks." Why new bioactive foods are important? Bioactive foods are fortified with nutrients to make them more

usable within daily recommended allowances (RDA). These nutrients are rich in vitamins, minerals and nutraceuticals or any food or part of a food that provides health or disease prevention benefits with higher nutrition values [38]. Dietary supplements have also been developed to manage a variety of diseases [21]. Thus, nutraceuticals diverge from dietary supplements in the following phases:

1. Nutraceuticals essentially not only supplements the diet but it should also aid in the prevention and/or treatment of disease and/or disorder.
2. Nutraceuticals are represented for use as a conventional food or as the sole item of meal or diet.

Table 2. Various nutraceuticals amino acid, their sources and uses

S. No.	Source	Amino acid	Uses
1	Protein foods like fish, dairy, eggs and meat [39]	Glutamic acid	Anticancer [40]
2	Plant source: (Legums, Peanuts, Almond, Walnuts, Flaxseeds) Animal source: (Beef, Eggs, Salmon, Shrimp) [41]	Aspartic acid	Immune function, energy production, increases resistance to fatigue [41].
3	Turkey, Light Meat, Wheat Bread, Sweet Chocolate [42]	Tryptophan	Mood and depression, smoking cessation [42].
4	Animal origin: (Meat, Poultry, Fish, Dairy, Cheese) Plant origin: (Lentils, Peanuts, Soy, Mushrooms, Sesame seeds) [43]	Valine.	Muscle metabolism, tissue repair mental vigor, muscle coordination, calm emotions [43]
5	Seafood [44]	Arginine	Anti-inflammatory, migraines, phosphorus helps calcium build bones and teeth. Supports immune system, thyroid function. [45]
6	Eggs [46]	Vitamin A, D E, iron, zinc, arginine	Strong muscles, lower risk of heart disease, healthy eyesight, [47], Weight loss and maintenance [48].
7	Legume [46]	Vitamin A, B, D, calcium,	Breast cancer [49], Allergy [50]
8	Chocolate [36]	Vitamin A, C, E, calcium, cholesterol, arginine	Reduce heart disease risk, stroke [36]
9	Vegetables (spinach, Seaweed, chives, Onion, Soybean, Peppers, leeks, Garlic and Mushroom)	Vitamin B2, K, omega-3 fats, copper	Anticancer [51], Obesity [52], Type 2 diabetes [53]
10	Fruits [46]	Poly phenolic flavonoids, vitamin C, anthocyanins	Antioxidant [51]
11	Nuts (Almonds, peanuts, almonds, cashew nut) [46]	Oleic, palmitoleic acids, carotenes,	Anti-inflammatory [54], Rheumatoid arthritis, Alzheimer's disease[55]

S. No.	Source	Amino acid	Uses
		omega-3 fats	
12	Grain (Breads and pastas) [46]	Dietary fibres, vitamin B, minerals, folate.	Stroke risk reduced, type 2 diabetes risk reduced, heart disease risk reduced & better weight maintenance [16].
13	Beverages (Black tea, Tea, Cocoa, Coffee, Beer and Wine) [56].	Caffeine, arginine	Boost blood flow [57]
14	Dairy products [53]	Arginine	Healthy teeth [58], antihypertensive, cardiovascular disease [59]
15	Soy [60]	Arginine	Cardiovascular benefits, anticancer, hot flashes, bone health, obesity, type 2 diabetes [61].
16	Lentils [62]	Arginine	Weight loss [62].
17	Chickpeas [63]	Arginine	Heart disease, anti-inflammatory, digestion [64].
18	Spirulina [46]	Arginine	Type 2 diabetes, strokes, chronic kidney disease, allergic rhinitis [65]
19	Pumpkin seeds [63]	Arginine	Anti-inflammatory, immune support [63]
20	Chicken [66]	Arginine	Boost sperm production, heart attack, boosting immunity [67].
21	Pork loin [66]	Arginine	Boost immunity, heart health, fat burning, digestion, high blood pressure [68].
22	Turkey breast [69]	Arginine	Body building, diabetics, high cholesterol, gout, insomnia, weight loss [69]
23	Onion, raw [70]	Arginine	Anti-inflammatory, anticancer [70].
24	Garlic, raw [71]	Arginine	Antibacterial, antiviral, anti-cancer [71]
25	Wheat flour, Whole-grain [72]	Arginine	Breast cancer. Heart disease, promote health [72]

3.3 Medicinal Food

Medicinal foods aren't available as an over the counter product to consumers. The FDA considers medical foods to be "formulated to be consumed or administered beneath the direction of a physician, and which is supposed for the specific dietary management of health for which distinctive nutritional requirements, on the basis of recognized scientific principles, are established by medical analysis. Nutraceuticals and supplements do not meet necessities and don't seem to be categorized as Medical Foods. Medical foods can be ingested through the mouth or through tube feeding. Medical foods are always designed to meet certain nutritional requirements for people diagnosed with specific illnesses. Medical foods are regulated by the FDA and will be prescribed/monitored by medical supervision [34] example of medical food, transgenic cows and

lactoferrin for immune improvement, Transgenic plants for oral vaccination against infectious diseases, Health bars with supplementary medications.

3.4 Farmaceuticals

According to a report written for the United States Congress entitled "Agriculture: A gloss of Terms, Programs, and Laws", "(Farmaceuticals) could be a melding of the words farm and pharmaceuticals. It refers to medically valuable compounds created from changed agricultural crops or animals (usually through biotechnology). Proponents believe that victimization crops and presumably even animals as pharmaceutical factories may well be way more value effective than standard strategies. The term Farmaceuticals is additional often associated, in agricultural circles, with a medical application of genetically built crops and animals [86].

Table 3. Various marketed sources of arginine

Manufacture	Dosage form/Brands	Uses
Element of health care, USA	L-Arginine plus™ powder	High blood pressure [73] nitric oxide production
Integral Life Sciences	L-Arginine softgel	Reduce menopause symptoms [74]
Zydus nutriva	GRD sugar free (diet protein Powder)	Postprandial glycemia, obesity [75].
Prima force	Agmatine Powder	Enhanced rates of absorption and overall bioavailability [76]
Jarrow formulas	Jarrow formulas arginine tablets	Synthesis of proteins [77] Production of creatine phosphate [78]
Betancourt nutrition	B-NoxAndrorush powder	Boosting your testosterone output, reducing lactic acid accumulation, maximizing muscle cell volumization [79]
Now foods	NOW L- Arginine capsules/powder	Supplement in good stead with athletes and bodybuilders [80].
Olympian Labs	DIM Capsules	Growth and repair of muscle tissues, mobilisation of stored fatty acids. [81]
Gat pharma	Nitraflex powder	Increasing blood NO levels [82]
AI sports nutrition	AI sports nutrition agmatine capsules	Dietary supplement, increased nitric oxide synthesis , promote nutrient delivery , improves body composition , increased endurance [83]
Cellucor	NO3 chrome capsules	Supplement for muscles
Biogreen labs	L Arginine capsules	Reduce blood pressure helps against leg cramping increase blood flow [84]
Source Naturals	L-Arginine L-Citrulline Complex Tablets	Supports liver detoxification, Supports heart function and circulation, Supports muscle metabolism and energy
PacificCoastNutriLabs	L-Arginine platinum capsules	Dietary supplements muscle mass formula [79]
Doctor Recommended	Cardio Heart Health-L-arginine powder supplement	Regulate cholesterol levels, artery function, blood flow [85]

4. DIETARY SUPPLEMENT & HEALTH EDUCATION ACT

Dietary Supplement Health and Education Act (DSHEA) passed in 1994 to control the human nutraceuticals market that doesn't allow federal agency to contemplate a replacement product a "drug" or "food additive" if it falls underneath the definition of a "dietary supplement," which has among different substances any attainable part of the diet yet as concentrates, constituents, extracts or metabolites of those elements [87].

According to the North American country Dietary Supplement Health and Education Act (DSHEA) formally outlined "dietary supplement" as:

1. A dietary supplement may be a product (other than tobacco) that's meant to supplement the diet that bears or contains one or a lot of the dietary ingredients like, a

vitamin, a mineral, a herb or different biological science, an organic compound, a dietary substance to be used by man to supplement the diet by increasing the whole daily intake, or a concentrate, metabolite, constituent, extract, or mixtures of those ingredients.

2. It is meant for consumption in pill, capsule, tablet, or liquid kind.
3. It is not depicted to be used as a traditional food or because the sole item of a meal or diet.
4. It is tagged as a "dietary supplement" [36]
5. Includes product like AN approved new drug, certified antibiotic, or authorized biological that was marketed as a dietary supplement or food before approval, certification, or license (unless the Secretary of Health and Human Services waives this provision).

Under the DSHEA (1994), the manufacturer of a dietary supplement is chargeable for making certain that the dietary supplement is safe before it's marketed [88]. With the passage of the Dietary Supplement Health and Education Act of 1994, the definition of nutraceuticals has been distended to incorporate vitamins, minerals, herbs and different botanicals, amino acids, and any dietary substance to be used by humans to supplement the diet by increasing total dietary intake (for example, enzymes or tissues from organs or glands). Dietary Supplements additionally as well as botanicals, Vitamins, co-enzymes, creatinine, Ginkobilba, Ginseng, Saint John's Wort, Saw palmetto [13] To abide by the laws, a nutraceutical should be tagged as a "dietary supplement" and shall not be depicted to be used as a traditional food or as a sole item of a meal or diet [2]. The Indian Health and Dietary Supplement Association was created to represent pharmaceutical, nutraceuticals, herbal, direct merchandising and different service homeward-bound trade corporations and plans to affiliate with the International Alliance of Dietary Supplement Associations within the close to future. The association is coming up with a scientific conference to bring the trade and government along to share info, expertise and views on the utilization and regulation of dietary supplements [21]. Many European countries have adopted the extremely restrictive CODEX standards for dietary supplements that eliminate the consumer's ability to get dietary supplements in therapeutic or significant preventive dosages. Codex Alimentarius (Latin for "Food Code") is that the United Nation's projected set of international pointers for nutritional supplements, food handling, production, and trade that is step by step being sanctioned in countries round the world, beginning within the EU [37].

The DSHEA permits 3 kinds of claims on labels of dietary supplements [89].

1. Nutrient content (such as "high in calcium"),
2. "Structure-function" or nutrition support (for example, "vitamin C prevents scurvy" or "calcium builds sturdy bones"), and
3. Illness claims

5. FDA MODULATION ACT

The passage of the Food and Drug Administration Modernization Act of 1997 (FDAMA) created further choices out there to the makers of nutraceuticals which results in bringing

a balance in federal agency rules between approving therapeutic products so they will profit patients and protective public health with important changes were conjointly created within the labeling of nutraceuticals [90].

6. WORLD DEMAND OF NUTRACEUTICALS

World demand for nutraceuticals ingredients advanced 5.8% annually to \$15.5 billion in 2010, serving a \$197 billion international nutritional product industry. China and India can emerge as the quickest expanding nutraceuticals markets as strong economic process permits them to upgrade and diversify food, nutrient and drug production capabilities. Herbal, non-herbal extracts has increasing acceptance by customers and medical professionals pushed world demand for herbal and non-herbal extracts up to 6.5% annually to \$1.85 billion in 2010. Nutrients, minerals and vitamins demand reached \$9.5 billion in 2010, up to 6.3% annually from 2005. International demand for nutraceuticals nutrition ingredients rose up to 4.6% annually to \$4.2 billion in 2010. Natural vitamin E formulations and beta carotene (vitamin A) also will fare well in the international marketplace supported effectiveness blessings over artificial ingredients for adult and pediatric nutritional [91]. The worldwide foodstuff growth about the nutraceuticals is shown in Fig. 2.

The nutraceuticals industry lies beneath 3 main segments that embody functional foods, dietary supplements, and herbal/natural products. World nutraceuticals market is estimated as USD 117 billion (INR 5148 billion). In 2007, nutraceuticals sale is projected to achieve \$74.7 billion at an AAGR of 9.9%. This assumes a world economic recovery in 2003 and an end to price competition as shown in Fig. 3 [92].

According to a recent report, the total marketplace for nutraceuticals in India is growing at 21% each year. It presently valued at INR 44bn (€621 m), however might be value quite INR 95bn in four years [91]. As a concept, "Nutraceuticals" continues to be in its stage of infancy in India. But it's been growing much quicker than world rates at CAGR of 18 for the last three years driven by functional food and beverages categories (36). The foremost chop-chop growing segments of the trade were dietary supplements (19.5% per year) and natural/herbal products (11.6% per year).

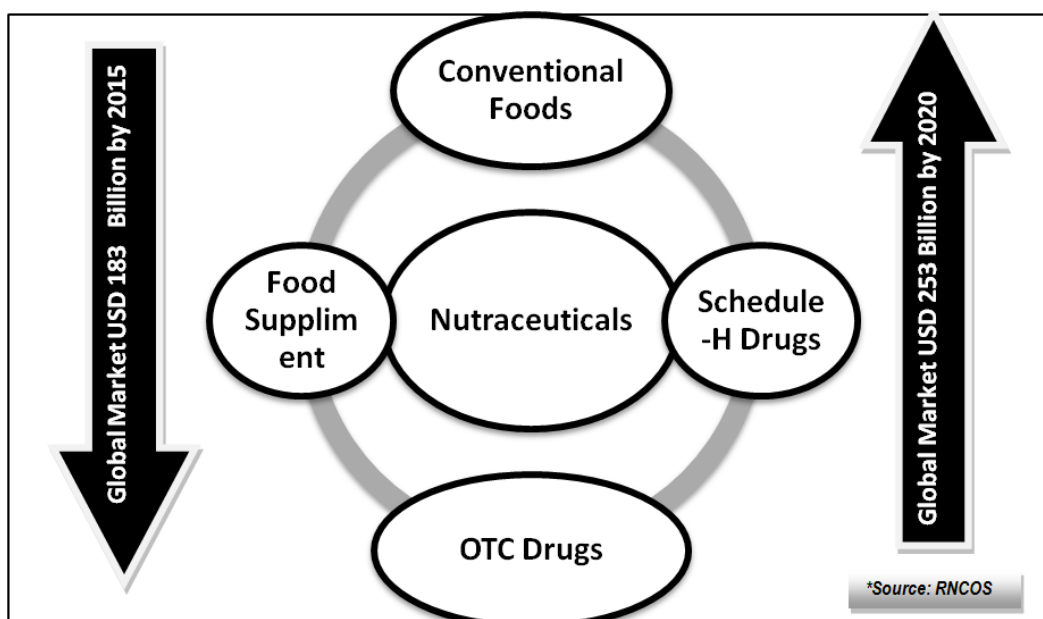


Fig. 2. Compound annual growth rate of nutraceuticals global market

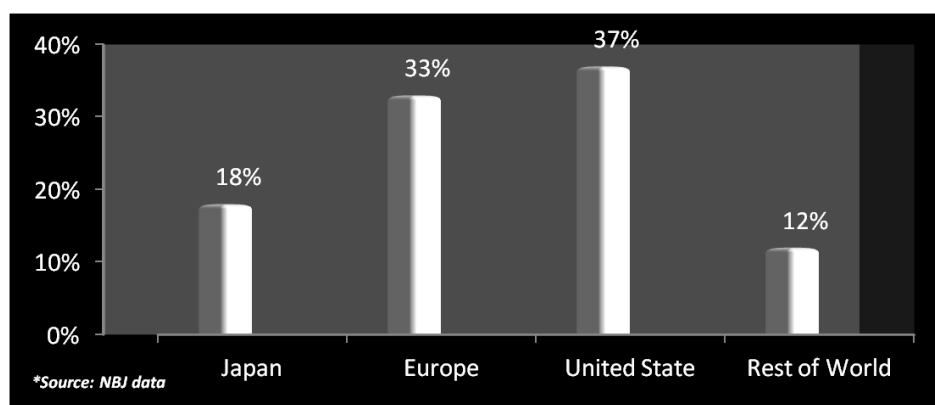


Fig. 3. Global nutraceuticals consumption

In the world market, Nutraceuticals and functional foods has become a multi-billion greenback trade and inside Canada, it is estimated that the Canadian nutraceuticals trade has potential to age to 50 billion US bucks. After US, JAPAN nutraceuticals trade is the second largest market in the world, that features a steady average rate of growth of 9.6% per annum [93]. The total Indian nutraceuticals market is expected to be approximately \$5 billion in 2015.

7. MARKETED NUTRACEUTICALS

There are several nutraceuticals products that are marketed by different factory-made for the

health edges of the creature as shown in Table 4.

8. MARKETED STRUCTURE

The preference for the invention and production of nutraceuticals over pharmaceuticals are well seen in pharmaceutical and biotech firms. a number of the pharmaceutical and biotech firms, that commit major resources to the invention of nutraceuticals embody Monsanto, American Home product, Dupont, Bio Correx, Abbott Laboratories, Warner-Lambert, Johnson & Johnson, Novartis, Metabolex, Scio-tech, Genzyme Transgenic, PPL therapeutics, Unigen,

Table 4. Various marketed nutraceuticals preparation and their uses

Marketed nutraceuticals	Uses	Manufacture
Glowelle®	Antioxidants, Anti-cancer, beauty drink [12].	Nestlé
Muscle Optimeal®	Anticancer, Helpful in maintaining the digestive tract [16].	Jarrow formulas, USA
Weight smart tm	Nutritional supplement [17]	Bayer corporation, Morristown,NL, USA
Rox®	Energy drink [19]	RoxAmerica, Spartanburg, SA, USA
Proteinex®	Protein supplements [7].	Pfizer Ltd., Mumbai, India
PNer plus	Neuropathic pain supplement (Michael D. Stubblefield, 2009)	NeuroHelp, SanAntonio, Texas, USA
Mushroom optimizer	Immune supplement (H. DUREJA,2003)	jarrow formulas, Los Angeles, CA, USA
CalcirolD-3®	Calcium supplement, Bone density [22]	Cadilla healthcare limited, Ahmedabad, India
Betafactor® capsules	Immune supplement [24]	Ameriden® international Inc.,USA
WelLife®	Amino acid supplements [25].	Daesang America Inc., Hackensack, NJ, USA
Pediasure®	Nutritional supplement, Apoptosis, Anticancer [26]	Abbott nutrition
Revital	Daily health supplement [27]	Ranbaxy
Ferradol Food® Powder	Nutrition supplements [7].	Pfizer Limited , India
5-Hour energy®	Energy drink [29]	Living essentials, USA
Beneflora® probiotic	Maintain gastrointestinal health [30]	Nupro, USA
Becadexamine®	Nutritional supplement [6]	Glaxosmith kiln

and Interneuron [94]. The nutraceuticals trade within the United States is about \$86 billion. This figure is slightly higher in Europe and, in Japan, represents just about a quarter of the \$6 billion total annual food sales. Forty seventh of the Japanese population consumes nutraceuticals even without specific monetary figures, business reports continually suggest that the nutraceuticals market is consistently growing. The approach to regulation and promoting nutraceuticals is notably heterogeneous on the world level. This can be for the most part owing to the challenges in classifying this product, absence of an appropriate regulative class for this hybrid product.

GIA (Global industry Analysts) announces the discharge of a comprehensive world report on Nutraceuticals market. The world nutraceuticals market is projected to exceed US\$243 billion by 2015, attributable to shopper desire for leading a healthy life and increasing scientific proof supporting health foods [95].

India is the home of a large variety of medicinal herbs, spices and tree species that have a well giant domestic market. Totally different scientific

teams likewise as various government agencies inflated the recognition of nutraceuticals and functional foods among the public sector. India encompasses a giant share of the international useful food and nutraceuticals market and exports product to numerous countries. However, India's major export destination is that the USA and Japan [96].

- ✓ An Increase in Public Health Consciousness,
- ✓ An Aging Population,
- ✓ Escalating Health Care Costs,
- ✓ Recent Advances in Research and Technology,
- ✓ Changes in Government Regulations and Accountability,
- ✓ Expansion of the Global Marketplace,
- ✓ A Sympathetic Media,
- ✓ Science-based Evidence is contributing to the Popularity of Functional Foods.

Recognition of variation in functional food and nutraceuticals composition will provide opportunity for the industry to give consumers a variety of new products that can be developed for specialized markets [2].

9. MARKET TREND

The nutraceuticals industries three main segments include functional foods, dietary supplements, and herbal/natural product [97]. Nutrition Business Journal (NBJ) identified an \$80 billion nutraceuticals market in 1995 by considering natural and organic foods (\$6.2 billion), functional foods (\$13.4 billion), certain lesser-evil foods with reduced or no unhealthy ingredients (\$23 billion), dietary supplements (\$8.9 billion), and selected market normal foods (\$28.3 billion). NBJ has begun tracking nutraceuticals industry growth. Since 1995, the trade, as outlined by NBJ, has grown by a mean of seven. 1% p.a. In 1997, trade sales totaled \$91.7 billion (NBJ 1998). The foremost speedily growing segments of the industry were dietary supplements (19.5% per year) and natural/herbal product (11.6% per year) [98,99].

According to BCC analysis - The global nutraceuticals market grew to \$46.7 billion in 2002 at an AAGR of nearly 7%. This assumes a world economic recovery in 2003 and a finish to cost competition (Fig. 4). In 2007 nutraceuticals sale is projected to succeed in \$74.7 billion at an AAGR of 9.9% [100].

Indian nutraceuticals market in 2008 is calculable to be USD 1.0 billion whereas the world market is growing at a CAGR of seven; the Indian market has been growing a lot of quicker at a CAGR of 18 looking forward to the last three years, driven by useful food and beverages classes. However, the latent market in India is two to fourfold of this market size and is between USD two to USD four billion with nearly 148 million potential customers, states the FICC Ernst and Young

study titled 'nutraceuticals- vital supplement for building a healthy India' free at the FICCI and Health Foods and Dietary Supplements Association conference. Of the world nutraceuticals market of USD 117 billion, India has but 1 Chronicles share. Globally, this market is predicted to succeed in USD 177 billion in 2013, growing at a CAGR of seven driven by the quick growing dietary supplements class [86].

The functional beverages market in India is emerging at 24%. The purposeful food and beverages classes consisting of nutrition fortified foods, sports and energy drinks, fortified juices and probiotic foods are growing quicker, driven by wider distribution across FMCG channels likewise as aggressive mass selling. The Indian nutraceuticals market is dominated primarily by pharmaceuticals and FMCG corporations with only a few pure play nutraceuticals corporations. Pharmaceutical and FMCG player's active within the nutraceuticals house have diversified by introducing product extensions and developing variants beneath existing whole names. Several new sectors have declared aggressive investment plans that show in Fig. 5. The Indian nutraceuticals market valued at \$1,480 million in 2011 may grow to \$2,731 million in 2016, a report said nowadays. According to the report by business analysis and consulting company Frost & Sullivan, functional foods are going to be the fastest growing class followed by dietary supplements till 2015. The report claim that at this time the dietary supplements were the biggest class accounting for 64% percent of the nutraceuticals market. This market is driven primarily by the pharmaceutical sector in the form of sustenance and mineral supplements; it added [101].

Table 5. Nutraceuticals with different health claims

Nutraceuticals	Health claim
Potassium	High blood pressure and stroke
Plant sterol and plant sterol esters	Coronary heart disease
Soy protein	Coronary heart disease
Calcium	Osteoporosis
Fiber-containing grain products, fruits and Vegetables	Cancer
Folic acid	Neural tube birth defects
Dietary soluble fiber, such as that found in whole oats and psyllium seed husk	Coronary heart disease
Dietary sugar alcohol	Dental caries (cavities)
Dietary fat	Cancer
Dietary saturated fat and cholesterol	Coronary heart disease
Sodium	High blood pressure

Table 6. Amount of L- Arginine in certain foods [106-7]

S. No.	Source	Weight (g)	Amount (mg)
1	Abalone shell-fish	29.59	1247mg
2	Almonds nuts	5	4986
3	Apple	150	8
4	Apples dried	0.147	148
5	Apricots	114	48
6	Banana	175	54
7	Bluefish	85	1020
8	Buttermilk	245	309
9	Butter	14.1	4
10	Cabbage chinese	70	59
11	Carrot	110	48
12	Cashew nuts	160	470
13	Chocolate milk	250	287
14	Celery	120	24
15	Cheese wing	90	585
16	Chicken brest	181	1870
17	Chicken dark meat	109	1320
18	Chicken drumstick	110	872
19	Chicken legs	231	1890
20	Chicken light meat	116	1470
21	Chicken livers	32	352
22	Cauliflower	100	96
23	Corn	154	200
24	Corn grits	242	114
25	Cucumbers	104	36
26	Dates fruit	83	55
27	Eggs whole	50	147
28	Garlic	3	19
29	Hazelnuts	135	2480
30	Hickory nuts	15	298
31	Mango fruit	300	39
32	Milk, human	246	105
33	Milk, whole	244	291
34	Milk, nonfat	120	1570
35	Oats puffed	28.4	320
36	Onions, green	100	6
37	Orange juice	248	117
38	Plain yogurt	227	237
39	Peanuts	144	5050
40	Pistachios	128	2790
41	Pork leg	454	5530
42	Potatos	150	140
43	Soy bean sprouts	70	266
44	Snail	85	2100
45	Tomato soup	244	61
46	Wheat flakes	33	171

10. SAFETY AND CLAIM IN NUTRACEUTICALS

Health claims on nutraceuticals that they serve to alert customers as a part of associate overall healthy diet, which can scale back the danger of certain diseases. The FDA at the start licensed

seven health claims in 1993 as half of the 1990 Nutrition Labeling and Education Act (NLEA). Since 1993, the FDA has licensed six additional claims. In an endeavor to accelerate this info to customers, the Food and Drug Administration Modernization Act of 1997 enclosed a provision intended to speed up the method that establishes the scientific basis for health claims. In 2005, the National Academies Institute of medication associated National analysis Council created a superior committee to make an improved framework for the Federal Food and Drug Administration to judge dietary supplements. Though the improved framework fails to differentiate between "nutraceuticals" and "dietary supplements" with the continuing use of a broad definition and lacking bigger distinction, a cheap and scientifically based framework was required to judge the security of "dietary supplements" as well as those shopper product recognized internationally as "nutraceuticals" [37]. FDA regulated dietary supplements as foods to make sure that they were safe and wholesome whose labeling was truthful and not dishonorable. In 2006, the Indian government passed Food Safety and commonplace Act to integrate and streamline many rules covering nutraceuticals, foods, and dietary supplements. The act involves the creation of the Food Safety and Standards Authority (FSSA) [92]. Although food makers could use health claims to market their product, results in profit customers by providing information on healthful consumption patterns that will facilitate to scale back the risk of heart disease, cancer, pathology, high blood pressure, dental cavities or certain birth defects. Health claims are different from structure/function claims that additionally could appear on standard food or dietary supplement labels. Not like health claims, structure/function claims don't deal with disease-risk reduction. Also, the FDA doesn't pre-approve or authorize structure/function claims. Rather, once the manufacturer uses a structure/function claim, the corporate is liable for making sure the claim is truthful and not dishonorable. Several educational, scientific and restrictive organizations are considering ways in which to determine the scientific basis to support claims (other than health claims) for the practical components of nutraceuticals. These are the five types of health-related statements allowed on food and dietary supplement labels:

- Nutrient-content claims indicate the presence of a specific nutrient at a certain level.

- Structure and function claims describe the effect of dietary components on the normal structure or function of the body.
- Dietary-guidance claims describe the health benefits of broad categories of foods.
- Qualified health claims convey a developing relationship between components in the diet and risk of disease, as approved by the FDA and supported by the weight of credible scientific evidence available.
- Health claims confirm a relationship between components in the diet and risk of disease or health condition, as approved by FDA and supported by significant scientific agreement [102].

The following are the FDA-approved health claims as shown in Table 5 a positive relationship between a certain compound and reduced risk of specific disease(s).

Health claims are among the various types of claims allowed in food labeling. They show a

relationship between a nutrient (and other substances in a food) and a disease or health-related condition. Although one should remember that all essential amino acids cannot be delivered completely from natural sources [103].

10.1 Arginine

Arginine an ergogenic (i.e., performance-enhancing) supplement, most notably in the “nitric oxide” (NO) class of supplements is a semi-essential amino acid involved in multiple areas of human physiology and metabolism. NO produced from it improves outcomes in various diseases [104]. L-arginine is readily available over the counter and is popular as a nutritional supplement to increase muscle mass. More recently, L-arginine has been tested as a potential therapeutic in numerous acute and chronic disease states, including sickle cell chest crisis, pulmonary artery hypertension, coronary heart disease, pre-eclampsia and myocardial infarction, because of its bronchodilator and vasodilator actions [105].

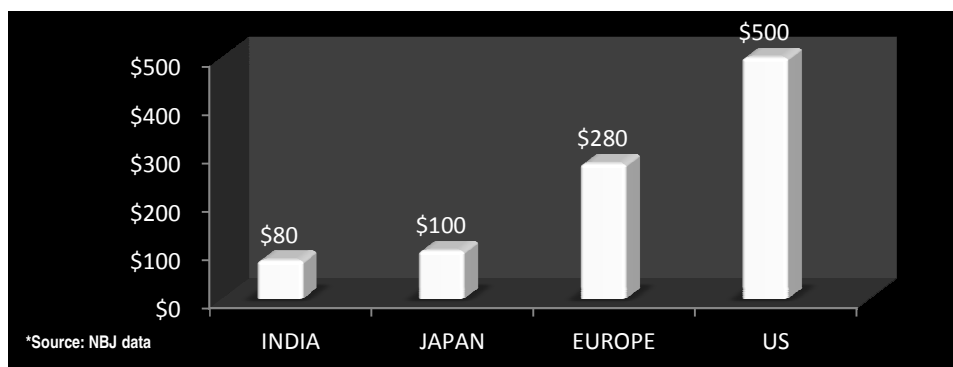


Fig. 4. Nutraceuticals market in different countries

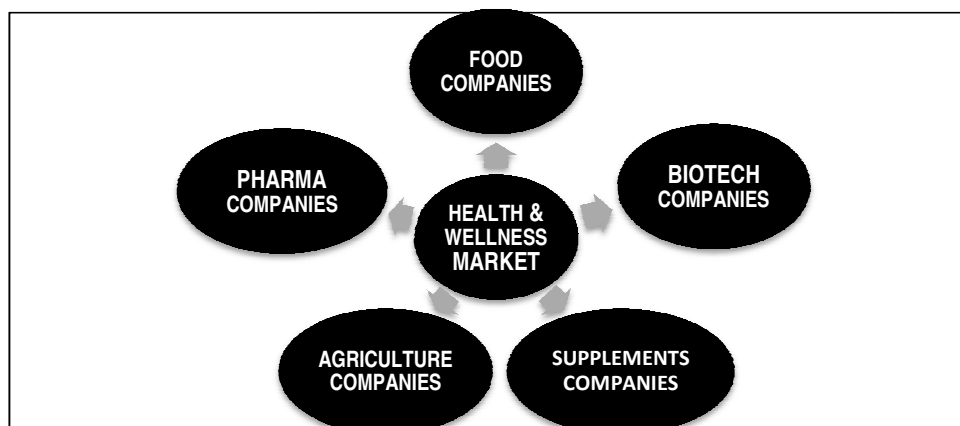


Fig. 5. Chief competitors in the growing market of nutraceuticals

Table 7. Potential effects of L-arginine

Disease	Potential effects
Human Immuno-deficiency Virus (HIV)	Immune status was also improved as evident by an increase in CD3 and CD8 cells and a decrease in the HIV viral load with HMB/Arg/Gln supplementation [108].
Angina pectoris	Administration of L-arginine has been shown to control ischemic injury by producing nitric oxide which dilates the vessels and thus maintains proper blood flow to the myocardium [109].
Congestive heart failure	Nitric oxide inhalation increased pulmonary capillary wedge pressure. L-arginine decreased heart rate mean systemic arterial pressure and systemic vascular resistance. L-arginine increased right atrial pressure, cardiac output, and stroke volume [110].
Atherosclerosis and coronary heart disease	The effect of arginine is largely due to its metabolism to Nitric Oxide. The accumulated data suggest that enhancement of the Nitric Oxide Synthase pathway may be a novel therapeutic strategy in the treatment of atherosclerosis [111].
Hypertension	As a substrate for NO synthase, L-arginine may exhibit antihypertensive activities by augmenting the production of NO in endothelium and improving its bioavailability in vascular smooth muscle cells, which are essential to maintain vascular homeostasis [112].
Intermittent claudication	L-Arginine treatment elevated the plasma L-arginine/ADMA ratio and increased urinary nitrate and cyclic GMP excretion rates, indicating normalized endogenous NO formation. Restoring NO formation and endothelium-dependent vasodilation by L-arginine improves the clinical symptoms of intermittent claudication in patients with peripheral arterial occlusive disease [113].
Preeclampsia	Availability of the substrate for nitric oxide synthesis (L-arginine) prolongs the latency to development of pre-eclampsia in a high risk population of women taking the amino acid supplement in the presence of antioxidant vitamins in a medicinal food. This relatively simple and low cost intervention may have value in reducing the risk of pre-eclampsia and associated preterm birth [114].
Growth hormone secretion	In rats, NO stimulates secretion of GH-releasing hormone (GHRH) and thus increases secretion of GH. However, it has also been observed that GHRH, in turn, increases production of NO in somatotroph cells, which subsequently blunts GH secretion. In humans, L-arginine stimulates pituitary GH release, but the mechanism is not fully clarified. Most studies suggest that an inhibition of somatostatin secretion is responsible for the effect [115].
Ergogenic potential	There is some evidence that L-arginine infusion increases glucose uptake during prolonged exercise and reduces lipolysis. It is possible that these effects are due to increases in NO production but more research is required to confirm this. There is also some evidence that oral L-arginine supplementation can interact with exercise training to increase the beneficial effects of exercise on capillary growth and insulin sensitivity. Further studies are required to elucidate the potential ergogenic and therapeutic potential of L-arginine [116].
Burns and critical trauma	Total parenteral nutrition increased arginine-to-ornithine conversion and proportionally increased irreversible arginine oxidation. The elevated arginine oxidation, with limited net de novo synthesis from its immediate precursors, further implies that arginine is a conditionally indispensable amino acid in severely burned patients [117].
Cancer	NO was first identified in endothelial cells, it is now recognized to be generated by a variety of cell types, including several tumor cell lines and solid human tumors. Unfortunately, the precise role of NO in cancer is poorly understood but it may influence tumor initiation, promotion, and progression, tumor-cell adhesion, apoptosis angiogenesis, differentiation, chemosensitivity, radiosensitivity, and tumor-induced immunosuppression [118].
Gastritis and ulcer	L-Arginine accelerated the ulcer healing and increased gastric blood flow at the ulcer margin, and angiogenesis, whereas treatment with NG-nitro-L-Arginine had an opposite effect. L-Arginine added to NG-nitro-L-Arginine restored the ulcer healing, hyperemia, and angiogenesis [119].

Disease	Potential effects
Gastro-esophageal Reflux Disease (GERD)	The results confirmed an essential role for acid and pepsin in the pathogenesis of acid reflux esophagitis in the rat model and further suggested that various amino acids affect the severity of esophagitis in different ways, due to yet unidentified mechanisms; L-alanine and L-glutamine exert a deleterious effect on the esophagitis, while L-arginine and glycine are highly protective, independent of endogenous prostaglandins and nitric oxide [120].
Erectile dysfunction	Improved sexual performance had an initially low urinary NO _x , and this level had doubled at the end of the study [121].
Infertility	NO is involved in the physiology, biology & pathophysiology of the reproductive system may have great clinical implications in developing therapeutic strategies to prevent NO-related reproductive disorders [122].
Interstitial cystitis	Interstitial cystitis symptom relief is associated with a significant increase in urinary nitric oxide synthase activity as well as in cyclic guanosine monophosphate level [123].
Perioperative nutrition	Arginine supplementation increases serum insulin-like growth factor (IGF-I) levels. Arginine supplementation further increased collagen deposition into subcutaneous catheters as reflected by increased levels of hydroxyproline [124].
Pre-term labour and delivery	L-Arginine significantly reduced the number of contractions, together with an increase of both serum growth hormone and nitrates levels [125].

11. CONCLUSION

Now a day's variety of sickness like obesity, diabetes, metabolic syndromes that are life style sickness as they happens due to amendment within the life style they may be simply counteracted by changes within the diet i.e. by nutraceuticals so nutraceuticals are presently receiving recognition as being helpful in variety of sickness Nutraceuticals provides energy and nutrient supplements to body, that are needed for maintaining optimum health. At present, nutraceuticals are capturing pharmaceutical industry because these are helpful to human health with further advantage of nutrition with least or no side effect. Due to its wide scope, nutraceuticals became product of interest for numerous industries like food industry, biotech industry, agriculture industry as well as pharmaceutical industry. The future of nutraceuticals in Republic of India is bright because they need wealthy sources of raw materials, ease of availability economically available and don't have any or least aspect effects however still lots of labor has to be done on the nutraceuticals.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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