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The **Nutraceuticals** Landscape

Functional foods, supplements, nutraceuticals properties, regulation, markets

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Summary

Abstract ... 3

1. Overview and state of the art ... 4

2. Classification of Nutraceuticals ... 6

2.1. Traditional Nutraceuticals ... **7**

2.1.1. Chemical Constituents: ... 7

2.1.2. Probiotics and Prebiotics ... 8

2.1.3. Nutraceutical Enzymes ... 9

2.2. Non-Traditional Nutraceuticals ... **9**

2.2.1. Fortified Food ... 9

2.2.2. Recombinant Nutraceuticals ... 10

3. Concerns regarding nutraceutical safety and efficacy ... 10

3.1. Nutraceuticals Toxicity ... **11**

3.1.1. Nutraceutical Contaminants ... 11

3.1.2. Nutraceuticals – Drug Interaction ... 12

3.1.3. Nutraceuticals Advanced Delivery Systems Toxicity ... 13

4. Nutraceuticals' Regulatory pathway overview ... 13

5. Advancing the safety assessment of botanicals and nutraceuticals ... 17

5.1. Why Toxicology Matters More Than Ever in Nutraceuticals ... **17**

5.2. Regulatory Toxicology Testing Expectations ... **18**

5.3. What Makes a Toxicology Assessment Rigorous ... **19**

5.3.1. Hazard Identification ... 19

5.3.2. In Vivo Validation ... 19

5.3.3. Integration of NAMs ... 19

5.3.4. Risk Characterization and Dossier Compilation ... 19

5.4. Strategic Integration of NAMs in Nutraceutical Toxicology ... **20**

5.5. Bridging FDA and EFSA Requirements: A Unified Strategy ... **20**

6. Market overview ... 20

6.2. Market Dynamics and Growth Drivers (2026-2030) ... **21**

6.3. Product Insights ... **22**

6.4. Application Insights ... **22**

6.4.1. Weight management & satiety nutraceuticals ... 22

6.4.2. Men's health nutraceuticals ... 23

6.4.3. Aging population ... 23

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6.4.4. Consumer awareness 23
6.4.5. Increasing cost of healthcare 23
6.5. Distribution Channel Insights 24
6.5.1. Increasing number of distribution channels 24
7. Nutraceutical Key market challenges: 24
7.1. Challenging regulatory environment 25
7.2. Threat of counterfeit dietary supplements 25
7.3. Consumer distrust 25
8. Insights into the global market 25
8.1. North America 26
8.1.1. Geography Analysis 27
8.2. Asia-Pacific 27
8.3. European Union 28
8.3.1. Geography Analysis 29
8.3.2. European Competitive Landscape 30
8.4. Nutraceutical Market Share 30
8.4.1. Nutraceutical Market Companies 31
9. Italy in the Global Nutraceutical Market 32
9.1. Top-Performing Product Segments 32
9.2. Major Consumer Brands 32
9.3. Regulatory Framework and Compliance 33
9.4. The Tuscany Landscape 33
9.4.1. Academic and Scientific Core 33
9.4.2. Tuscan Industrial Ecosystem & CDMOs 35
10. Nutraceuticals Key Market Trends 38
11. Looking to the future of nutraceuticals 38
11.1. Clinical recommendations 38
11.2. Future research recommendations 39
12. Conclusions 39

Abstract

The healthcare, nutrition, and personal care industries have converged to create innovative, cross-functional market segments (nutraceuticals, cosmeceuticals, and nutra-cosmetics) that focus on delivering health and wellness benefits using natural resources like herbs, vitamins, and plant extracts. Nutraceuticals, in a broad sense of the term, encompass functional foods and non-prescription supplements used primarily for disease prevention and pharmacological support, while cosmeceuticals are topical products offering dual aesthetic and therapeutic benefits. Nutra-cosmetics further blur these lines as orally administered cosmetics designed to promote outward beauty from within using active proteins and enzymes; however, across all three categories, medical claims are strictly contingent upon meeting legally mandated criteria.

Driven by an aging global population, rising chronic disease rates, and a shift toward proactive, personalized healthcare, these interconnected industries are experiencing rapid, multi-billion-dollar growth. Modern consumers increasingly demand clean-label, plant-based products tailored to specific needs such as immunity and gut health, yet the sector suffers from fragmented global regulations and a lack of universally established definitions. This minimal oversight has led to a market saturated with unsubstantiated therapeutic claims, highlighting a critical deficit in rigorous clinical evidence regarding product safety and efficacy. To overcome these limitations and differentiate products in a highly competitive space, manufacturers are leveraging novel formulation technologies, integrating advanced biotechnology and nanosystems, such as liposomes, polymeric micelles, nanoparticles, and dendrimers, to significantly enhance bioavailability, safety, and therapeutic activity. This scientific push is further complemented by innovations in consumer-friendly delivery formats and eco-friendly, tamper-proof packaging.

Ultimately, this report synthesizes the scientific evidence and market dynamics within this "nutraceutical multiverse" by evaluating novel formulation strategies, shifting consumer insights, and current industry trends.

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1. Overview and state of the art

There were many historical civilizations, such as ancient Egyptian, Greek, Roman and others that used herbal products and plants in treating and preventing diseases. The oldest written document that included different 12 recipes of herbal medications was discovered on Sumerian clay tablet in Nagpur (around 5000 years ago). Dioscorides, the father of pharmacognosy, wrote "De Materia Medica" book in 77 AD, which included 657 plant originated medicines[1]. Hence, herbal products have always been an interesting area along the human history. There were many plants that were famous for their healing properties over the last millennia. For instance, ginseng had been used in China for treating and preventing different health problems. Moreover, ancient Egyptians used many plants, including garlic, turmeric, thyme, cumin, juniper and others in medicine. Cinnamon represented a great value in both Roman and ancient Egyptian civilizations. The Indian culture also used natural products in treating and preventing several diseases, such as Ayurveda. Finally, honey was considered as one of the most well-known remedies in many ancient civilizations and was mentioned in religious books, such as the Bible and Quran. These findings have triggered a series of studies in nutraceuticals field[2].

There is a significant ongoing controversy regarding the establishment of a specific definition and a unified set of regulations for the so-called nutraceutical compounds, as their exact classification remains poorly established on a global scale[3,4]. Despite this regulatory ambiguity, nutraceuticals are widely recognized as health-enhancing products designed to improve both mental and physical functions while minimizing the risk factors associated with various diseases.

Functioning essentially as a hybrid between conventional foods and pharmaceutical drugs, the broad terminology encompasses a wide range of ingredients, including minerals, vitamins, amino acids, and botanicals, meaning that both dietary supplements and fortified foods can often be classified as nutraceuticals[5]. Historically, the term itself, a combination of "nutrition" and "pharmaceutical", was first coined in 1989 by the Foundation for Innovation in Medicine in New York[6], and was later expanded upon by DeFelice in 1995, who defined a nutraceutical as "a food or parts of food that provide medical or health benefits, including the prevention and/or treatment of disease"[7].

Because a persistent grey area exists between these related categories, numerous attempts have been made to clearly distinguish nutraceuticals from dietary supplements and fortified foods[8]. For instance, it is generally argued that the primary difference lies in the purpose of use: fortified foods are intended to supply the body with essential carbohydrates, proteins, vitamins, and minerals strictly to improve overall health or to prevent and treat anaemia, whereas nutraceuticals are utilized to prevent or support the treatment of a much wider array of diseases[6]. Furthermore, the Dietary Supplement Health and Education Act (DSHEA) of 1994[9] provided a highly specific framework for dietary supplements, defining them as non-tobacco products intended to supplement the diet by increasing the total daily intake of specific dietary ingredients like vitamins, minerals, herbs, or amino acids. DSHEA established strict criteria, mandating that dietary supplements must be represented in specific dosage forms such as capsules, tablets, or liquids, must be explicitly labelled as dietary supplements, and, crucially, cannot be consumed as conventional foods or sole dietary items.

In stark contrast, nutraceuticals are expected to explicitly treat or prevent health problems and can indeed be consumed as conventional everyday foods[6]. This terminological complexity extends beyond ingestible products, prompting the Food and Drug Administration (FDA) to outline specific definitions to resolve confusion among cosmetics, pharmaceutical drugs, and herbal products. Under FDA guidelines, cosmetics are strictly

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defined as articles intended to be rubbed, poured, sprinkled, or sprayed onto the human body for the purposes of cleansing, beautifying, promoting attractiveness, or altering appearance[10]. Conversely, pharmaceutical drugs are defined by the Federal Food, Drug, and Cosmetic Act (FD&C Act) as articles intended for the diagnosis, cure, mitigation, treatment, or prevention of disease, as well as any non-food articles intended to affect the structure or function of the body[10]. Because of these rigid legal definitions, the hybrid terminology of "cosmeceuticals", which describes products widely marketed as a mixture of both cosmetics and drugs, has not yet been officially acknowledged under the law by the FD&C Act[10].

In this report, the term nutraceutical is used in the broadest sense, unless otherwise specified.

The global spread of nutraceutical products has accelerated dramatically in recent years. A primary driver of this market expansion has historically been the less stringent regulatory oversight compared to the strict, government-monitored pharmaceutical industry. Marketed as safe, natural, and effective alternatives to conventional drugs, nutraceuticals appeal to consumers seeking disease prevention and health optimization without the side effects or high out-of-pocket costs often associated with pharmaceuticals. Consequently, the industry has seen exponential growth.

Today, a vast majority of the global population utilizes dietary supplements in some form[11], propelling the global nutraceutical market well beyond USD 400 billion in the early 2020s, with projections continuing to forecast robust annual growth[12].

Despite this widespread usage, the global regulatory landscape remains highly fragmented, even as scrutiny has increased over the last five years. In the United States, there is still no distinct, legally recognized category for "nutraceuticals." Instead, they are largely regulated by the FDA as dietary supplements or food ingredients under the DSHEA[13]. Under this framework, premarket approval is generally not required unless a new dietary ingredient is introduced, meaning enforcement is heavily reliant on post-market surveillance. Furthermore, FDA regulations mandate that marketing labels bear the disclaimer: *"This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease"*.

Conversely, the European Union employs a much stricter framework. The European Food Safety Authority (EFSA) heavily regulates health and nutrition claims, requiring robust scientific substantiation and strict compliance before a product can be marketed with specific functional claims[14].

To better understand and regulate these products, several classification approaches have been adopted. Nutraceuticals can be categorized by their novelty (traditional vs. non-traditional), or by their chemical constituents (nutrients, herbals, dietary supplements, medical foods, and functional foods). They can also be divided into "potential" or "established" nutraceuticals based on the strength of their safety and efficacy profiles. Other classification parameters include structural nature (phytochemicals vs. herbals), bioavailability, and specific therapeutic uses[15].

Despite their popularity, many traditional herbal nutraceuticals suffer from inherent physical and pharmacokinetic limitations. Common drawbacks include poor aqueous solubility, low permeability, ineffective targeting, and rapid metabolism in the body. To overcome these hurdles, researchers have increasingly integrated Novel Drug Delivery Systems (NDDS). NDDS enhance formulation stability by preventing chemical and physical degradation and mitigate plasma concentration fluctuations. They also enable sustained release

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and targeted delivery, thereby reducing potential toxicity and maximizing the therapeutic efficacy of the active constituents[16,17].

Furthermore, NDDS introduce advanced strategies to optimize the pharmacokinetics, biorecognition, and overall effectiveness of nutraceuticals across various administration routes, including oral, sublingual, transdermal, and transmucosal. Recent advancements rely heavily on nanotechnology and advanced biotechnology, extensively utilizing liposomes, phytosomes, nanoparticles, nanoemulsions[18], microspheres, dendrimers, conjugate systems, and chitosan-based[19] delivery systems to modernize nutraceutical formulations[20,21].

Moving forward, the industry must address several critical challenges. First, the presumed safety and efficacy of many trending nutraceuticals still require rigorous scientific validation. Second, harmonizing global regulations remains a formidable hurdle, leaving gaps in quality control and consumer protection across borders. Finally, there is a persistent scarcity of robust *in vitro*, *in vivo*, and clinical trials substantiating many of the industry's health claims. Conducting high-quality dietary intervention trials is notoriously difficult due to confounding variables, such as placebo expectations, cultural traditions, and the inherent complexities of enforcing strict dietary regimens during clinical studies[22].

2. Classification of Nutraceuticals

The variability of nutraceuticals and their different complex structures resulted in various categorizations. The most common classification of nutraceuticals is based on their novelty[15].

A. <u>Traditional Nutraceuticals</u>

- *i. Chemical constituents*
  - a. Nutrients
  - b. Herbals
  - c. Phytochemicals
  - d. Polyunsaturated Fatty Acids (PUFAs)
- *ii. Probiotics and prebiotics*
- *iii. Nutraceutical enzymes*

B. <u>Non-traditional Nutraceuticals</u>

- *i. Fortified nutraceuticals*
- *ii. Recombinant nutraceuticals*

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2.1. Traditional Nutraceuticals

Traditional nutraceuticals are the foods that are not subjected to any manual change[2]. They include three subcategories[23]. Both lycopene in tomatoes and omega 3 fatty acids in salmon are examples of traditional nutraceuticals[15].

2.1.1. Chemical Constituents:

Nutrients

They were defined in 1996 by The Association of American Feed Control Officials "AAFCO". The definition of AAFCO is "*a feed constituent in a form and at a level that will help support the life of an animal*"[15]. There are many available nutrients, such as minerals, amino acids and fatty acids, but the most commonly used nutrients are vitamins and antioxidants[24].

Herbals

They are the oldest recognized form of nutraceuticals. So-called "Ayruveda" is the oldest written prescription of natural remedies, which was written by Indians[25]. Herbals are the products that consist of a whole, fresh plant or its part, such as dried leaf, fruit, roots, or concentrated extract. Nowadays there is an extensive demand on using herbals as nutraceuticals to promote health[15].

Phytochemicals

Phytochemicals are chemical constituents (secondary metabolites) that are extracted from plants. Phytochemicals exert specific biological effects[26]. They may affect the metabolic activity or exert biochemical reactions[2]. They are classified according to their chemical structures into polyphenols, isoflavonoids, anthocyanidins, phytoestrogens, terpenoids, carotenoids, limonoids, phytosterols, glucosinolates and polysaccharides[24,Errore. Il segnalibro non è definito.]. Phytochemicals affect the body by different mechanisms[23]:

- They act as a substrate for different biochemical reactions.
- They act as a catalyst or cofactor in enzymatic reactions.
- They inhibit enzymatic reactions.
- They improve the absorption and stability of nutrients.
- They act as specific growth factors to improve the growth of beneficial bacteria.
- They inhibit harmful, intestinal bacteria.
- They eliminate toxins.
- They act as ligands that exhibit antagonistic or agonistic effect on cell receptors.

Polyunsaturated Fatty Acids (PUFAs)

Fatty acids have essential beneficial properties for any living organisms. Fats can be classified according to their degree of saturation to saturated fatty acids, monounsaturated fatty acids and polyunsaturated fatty acids. Polyunsaturated Fatty Acids (PUFAs) have been categorized based on the position of the first double bond, located close to the terminal methyl group of the backbone chain. The most common and significant PUFAs are omega-3 and omega-6 PUFAs. Omega-3 PUFAs have been used as supplemental therapy for cardiovascular diseases, bipolar depression, asthma and diabetes. Additionally, omega-3 PUFAs reduce the level of lipid in serum so they have been defined as "essential fatty acids".

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PUFAs have been heavily used as nutraceuticals due to their beneficial effects; however, unfortunately, they have low chemical stability because of the presence of oxygen leading to oxidation. Hence, their efficacy would be reduced along with toxic byproducts generation[27].
Subsequently, different novel delivery systems, such as, nanoemulsion, emulsion, liposomes and nanoparticles have been used to improve their stability[15].

2.1.2. Probiotics and Prebiotics

Both prebiotics and probiotics are classified as nutraceuticals[2,28].
Probiotics are a new term that was originated from the phrase "*for life*". They are live, beneficial microorganisms, which enhance health and prevent diseases[29]. In the 90's, Metchnikoff proposed the idea of a beneficial bacteria for the human and suggested using it as treatment. Metchnikoff used *bifidobacteria* to treat infantile diarrhoea. Afterwards, Havenaar and Huisint Veld introduced the modern definition of probiotics: "*as a viable mono or mixed culture of bacteria which, when applied to animal or man, affects the host beneficially by improving the properties of the indigenous flora*". *Bifidobacterium* and *Lactobacillus* are examples of the most commonly used bacterial species as probiotics[15,28,29].
The intensive research in the probiotics field lead to a discovery of a new field: prebiotics. Prebiotics were defined as nutrients that modify the microbial flora of GIT *via* stimulating the beneficial bacteria growth or inhibiting the deleterious bacterial growth[30,31]. This definition was a subject of a debate because any carbohydrate or fermentable dietary fibre that is ingested by the host is accessible to the normal flora. This led to a new definition by the expert panel, which was defined as: "*a substrate that is selectively utilized by host microorganisms conferring a health benefit*"[31]. Moreover, the most commonly used prebiotics are galactose containing oligosaccharides, xylose-containing oligosaccharides, oligofructose, fructo-oligosaccharides and bifidogenic substrates[29].
Products that contain a combination of prebiotic and probiotic are called symbiotic. Pre- and probiotics can enhance the human health by different mechanisms, such as competing with pathogenic organisms for nutrients, producing antitoxins or antibiotics against invasive pathogens, aiding in neutrophil migration and producing some useful enzymes, such as ß-galactosidase, which helps in alleviating the symptoms of lactose intolerance[15].
Thilakarathna *et al.*[32] described the potential of probiotics and prebiotics in cancer chemoprevention by detailing the various mechanisms through which gut microbiota can inhibit cancer progression. For example, probiotics are highly effective at neutralizing toxins and reducing carcinogen levels in the body. Furthermore, while complex polymerized polyphenols, such as ellagitannins and proanthocyanidins, exhibit strong cancer-preventative properties, their structural complexity severely limits their intestinal absorption. Probiotics address this limitation by catabolizing these heavy molecules, significantly enhancing their bioavailability. As a result, polyphenol-based prebiotics have demonstrated promising outcomes in cancer therapy. Additionally, the authors noted that symbiotic offer substantial therapeutic benefits by improving the survival and colonization rates of probiotics in the gut.

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Damaskos *et al.*[33] reviewed the therapeutic application of prebiotics, probiotics, and symbiotic in managing Inflammatory Bowel Disease (IBD), an idiopathic condition[34]. While the exact aetiology of IBD remains unclear, several underlying causes have been proposed, including genetic susceptibility, immune dysregulation, intestinal barrier dysfunction, and microbiome imbalances. Probiotics help prevent and treat IBD through various mechanisms. For example, *Lactobacillus* species reduce the translocation of normal intestinal flora and inhibit the production of the pro-inflammatory cytokine Interleukin-6 (IL-6). Similarly, *Bifidobacterium* prevents abnormal T-cell activation and upregulates the production of the anti-inflammatory cytokine Interleukin-10 (IL-10)[33].

Conversely, prebiotics, most commonly lactulose, inulin, and lactosucrose, exert their therapeutic effects by regulating the physiology of the colonic mucosa through the production of short-chain fatty acids (SCFAs). To maximize these benefits, symbiotic have been developed to improve clinical efficacy, patient compliance, and cost-effectiveness. Various symbiotic formulations have demonstrated superior outcomes in treating intestinal disorders. For instance, one study highlighted that a targeted combination of *Bifidobacterium breve*, *Lactobacillus casei*, and galacto-oligosaccharides successfully improved bowel function in a paediatric patient with short bowel syndrome[35].

2.1.3. Nutraceutical Enzymes

Enzymes are vital functional proteins that act as biological catalysts, without which basic physiological processes would cease. They are fundamental in regulating metabolic homeostasis and can help alleviate various health conditions, such as hypoglycaemia, hyperglycaemia, digestive disorders, and obesity[26].

2.2. Non-Traditional Nutraceuticals

2.2.1. Fortified Food

In several classification systems, fortified foods are considered a subset of nutraceuticals. These are everyday foods intentionally enriched with essential nutrients, such as vitamins, minerals, and other vital trace elements, to maximize their therapeutic and nutritional efficacy[36]. Historically, the primary objective of food fortification was to combat widespread, population-level nutrient deficiencies[37]. For decades, these public health interventions have successfully prevented diseases and improved general health[15].

The strategic use of fortified foods became particularly crucial during the First and Second World Wars, serving as a primary method to alleviate malnutrition among broader populations. This era catalysed formalized nutritional initiatives, leading to the broader U.S. food fortification programs of the 1940s. A major regulatory milestone was reached in 1941 when the FDA officially introduced the "enriched" label for flour fortified with thiamine, niacin, riboflavin, and iron[38]. Over the following decades, these fortification strategies expanded globally. By the late 1970s, food fortification was introduced to the Middle East, marked by countries such as the Kingdom of Saudi Arabia successfully rolling out enriched flour to its population[37].

According to FDA, food fortification is categorized as either mandatory or discretionary. Mandatory fortified foods must strictly adhere to specific standards of identity established by the FDA[38]. This mandatory classification applies primarily to everyday primary items and is broadly divided into two groups: i) flour, which must be specifically enriched with niacin, iron, riboflavin, thiamine, and folic acid; ii) other staple products,

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including rice, breads, cereals, margarine, and various grain products. The addition of nutrients to these mandatory foods must comply with precise FDA regulatory standards. Conversely, the enrichment of all other food products falls outside these strict requirements and is designated by the FDA as discretionary fortification[38].

Fortified food is the most effective treatment for micronutrient malnutrition for several reasons. First, fortified food can be accessible to large number of populations by choosing the most attractive food form[39]. Secondly, it is socially acceptable because people prefer no change in food characteristics or food habits. Thirdly, fortified food can be introduced quickly, and its benefits are achieved quickly as well. Finally, most of people consider them safe and cost-effective.

Folic acid represents a prominently used fortifying nutrient. Folic acid is essential for DNA synthesis and repair, and its deficiency has been correlated to various human diseases, such as megaloblastic anaemia, neonatal neural tube defect and heart disease[40].

Vitamin D is another broadly used fortifying nutrient. It is a fat-soluble vitamin that is highly sensitive to oxygen, light and high temperature. Vitamin D deficiency has shown high prevalence rates in Europe and considered a pandemic problem[41]. It causes metabolic bone diseases, such as rickets in children and osteomalacia and osteoporosis in adults[42]. Milk, dairy products and beverages that were fortified with vitamin D had a positive influence on the daily intake of vitamin D for adults in USA and Canada[43], however, vitamin D fortification is unsuitable for individuals who suffer from milk allergy or lactose intolerance.

Unfortunately, fortified food has drawbacks and adverse effects associated with its excessive consumption. Excessive intake of fat-soluble vitamins can result in toxicity since there is a risk of metabolism interference (for example, zinc reduces both copper and iron absorption)[38]. It was reported that high intake of calcium causes prostate cancer and hip fracture in men[44] and women[45]. Additionally, it was reported that calcium supplements could lead to heart diseases, especially myocardial infarction[46].

2.2.2. Recombinant Nutraceuticals

Recombinant nutraceuticals were categorized as non-traditional nutraceuticals, which have been formulated by using novel, biotechnological techniques, such as fermentation and genetic engineering[15]. Genetically modified food is useful in controlling certain diseases[47]. However, furthermore, more studies should be done to evaluate the unknown, long-term influence on human body.

3. Concerns regarding nutraceutical safety and efficacy

Nutraceuticals have the potential to partially prevent or co-treat various health conditions. However, there is often a lack of adequate information to properly validate the efficacy, safety, and effectiveness of nutraceuticals, presenting concerns regarding nutraceutical use and there can be issues with how to classify such a product if being used for medicinal purposes.

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Most medicinal or nutritional claims are unverified due to a lack of evidence on possible mechanisms of action and a lack of randomized clinical trials to confirm the claimed beneficial health effects of the specific pathological conditions. Furthermore, *in vitro* data reported in the literature, often focus on single food constituents (micronutrients or secondary metabolites). Such studies assume that the studied micronutrients or secondary metabolites can be generally considered safe as they are derived from commonly used food components; this, however, needs to be validated by rigorous studies.

Therefore, it is crucial to conduct clinical trials to thoroughly study both the efficacy and safety, and to gain a better understanding of the mechanism of action and bioavailability of nutraceuticals. Monitoring the production of nutraceuticals is a critical step that lacks considerable oversight worldwide. Nutraceuticals can be toxic to consumers if they become contaminated with heavy metals, metalloids, mycotoxins, allergens, fertilizers, pesticides or non-product residues from toxic plants during production. The risk of adverse pharmacokinetic or pharmacodynamic interactions between nutraceuticals and therapeutics can occur, which is worrying considering that patients rarely disclose their consumption of supplements to their physicians.

3.1. Nutraceuticals Toxicity

The global consumption of nutraceuticals is dramatically increasing, which is driven by the mistaken assumption that they are safe because they are either a food or food derivative[48]. However, side effects and toxicity have been continuously reported not only due to ingestion of the nutraceutical itself but also owing to the possibility of contamination. Nutraceuticals could be contaminated with pesticides, other toxic plants, metals, fertilizers or even deliberate adulteration with chemical drugs. Additionally, due to the complex nature of herbal products and the presence of many phytochemicals, many studies reported the incidence of drug-herbal interaction after co-administration[49]. Such interaction could result in over exposure to the drugs that elevate the incidence of toxicity and severe side effects. It could also lead to inhibition of the drug efficacy and lower therapeutic outcomes.

A remarkable number of commonly used nutraceuticals are associated with severe adverse effects and toxicity[23]. For example, green tea extracts contain catechins, which have anticancer properties. Green tea extracts are also used to prevent obesity and metabolic disorders[50], but over exposure could result in nephrotoxicity, hepatotoxicity and reproductive toxicity[51]. Moreover, it was reported that the ingestion of caffeine causes anxiety, tachycardia, osteoporosis and reproductive disorders, especially in early adulthood exposure[52].

3.1.1. Nutraceutical Contaminants

The contamination of nutraceuticals represents a critical safety concern, with pesticides posing a particularly severe threat due to their high toxicity upon ingestion. Adverse health effects from pesticide exposure range from mild dermatological rashes to severe respiratory, neurological, and reproductive disorders. Despite these risks, controlled pesticide application remains necessary to maintain the quality and yield of medicinal herbs[53]. Consequently, stringent adherence to maximum residue limits is imperative.

Heavy metals (specifically lead, cadmium, mercury, and arsenic) constitute another major class of nutraceutical contaminants. To mitigate these risks, WHO has established specific guidelines outlining the maximum permissible limits for environmental contaminants in final herbal products[54]. Heavy metal toxicity can occur

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through both acute exposure to high concentrations and chronic exposure to trace levels. The resulting systemic damage can manifest as cardiovascular toxicity, neurological disorders, hepatic and renal dysfunction, and various cancers[55].

In addition to external pollutants, naturally occurring plant secondary metabolites, such as pyrrolizidine alkaloids, pose significant health risks. Animal studies have linked these compounds to developmental toxicity, genotoxicity, carcinogenicity, and hepatotoxicity, with acute exposure primarily resulting in severe liver damage[56]. The toxicity of pyrrolizidine alkaloids stems from their potent alkylating properties, which allow them to bind with cellular proteins and DNA, ultimately causing cellular dysfunction and tissue necrosis[57]. These alkaloids are pervasive, naturally occurring in approximately 6,000 plant species.

Finally, mycotoxins (secondary metabolites produced by fungi during plant cultivation or improper storage) represent a substantial contamination risk[58]. Among the most frequently detected mycotoxins in food supplements are aflatoxins, ochratoxins, and citrinin. The ingestion of mycotoxin-contaminated products can trigger severe adverse health events, including carcinogenic, hepatotoxic, mutagenic, and teratogenic effects.

3.1.2. Nutraceuticals – Drug Interaction

Recently, many studies have reported numerous nutraceutical-drug interactions. The interaction nature may be through interfering with the metabolic pathway of the drug or affecting the drug transporters[59]. Owing to the complex nature and absence of pharmacokinetic, pharmacodynamics and safety studies for nutraceuticals, it is challenging to predict the incidence of nutraceutical-drug interactions[15].

Some of the reported interactions could be serious and life-threatening. For example, aspirin and some non-steroidal anti-inflammatory drugs interact with herbal products containing ginkgo, turmeric, ginger, ginseng, chamomile and garlic. Consequently, these reported interactions could increase the risk of bleeding due to the inhibition of platelet aggregation ability[60].

The cytochrome P450 (CYP) enzymes are one of the mostly expressed metabolic enzymes in the liver and small intestine. Additionally, they are involved in the metabolic pathways of many pharmaceutical drugs. Saint John's Wort herbal extract is among the mostly reported nutraceuticals that induces wide range of CYP, including CYP1A2, CYP2C9, CYP2C19, CYP3A4 and CYP2E1. Induction of these enzymes results in accelerating the metabolism of the consumed drugs. Subsequently, the drug is eliminated from the body rapidly and it loses its activity. It was also reported that Saint John's Wort included treatment failure of anti-depressant drugs and loss of oral contraceptive efficacy[60].

Organic Anion Transporting Polypeptide receptor (OATP) is another key transporter in drug absorption and disposition. Iijima *et al.* conducted a study on 98 medical herbs commonly used in Japan to detect the interaction between some nutraceuticals and pharmaceutical drugs. It was found that 12 herbal species suppressed the function of the intestinal organic anion transporting polypeptide 2B1 (OATP2B1) receptor by less than 20%. Additionally, seven herbal species enhanced the activity of the receptor by more than 150%[61]. Consequently, co-administration of these herbal products dramatically affects the absorption and bioavailability of substrate drugs, including bosentan, benzyl penicillin, aliskiren, fexofenadine, glibenclamide, unaprostone, statins, and other pharmaceutical medications.

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3.1.3. Nutraceuticals Advanced Delivery Systems Toxicity

Recently, the integration of nutraceuticals into nanodelivery systems has rapidly emerged as a pivotal technological advancement. These sophisticated delivery platforms are designed to enhance compound absorption and bioavailability, provide controlled and targeted release profiles, and improve the stability of degradation-prone phytochemicals. Although the unique physicochemical properties achieved through nanonization significantly boost the therapeutic efficacy of these products, these exact same advantageous characteristics are, paradoxically, the principal drivers of potential human toxicity.[62].

Understanding the nanoparticles interaction with the biological systems at the molecular level is essential to predict their mechanism of action and safety.

EFSA suggested an approach to assess the toxicity arising from the incorporation of nanotechnology in the food products and food derivatives. The guidelines titled "*Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain*"[63] recommended a set of physicochemical parameters to be evaluated for nanoparticles.

The EFSA list of parameters includes:

- the identity and chemical of nanoparticles.
- the particle size of nanoparticles.
- the physical properties of nanoparticles.
- the morphology of nanoparticles.
- particle and mass concentration.
- the specific surface area of nanoparticles.
- the surface chemistry of nanoparticles.
- the surface charge of nanoparticles.
- the redox potential of nanoparticles.
- partition and solubility properties.
- dustiness, viscosity, density and pour density.
- the chemical reactivity of nanoparticles.
- the photocatalytic activity of nanoparticles.

4. Nutraceuticals' Regulatory pathway overview

With the increase in health awareness, including lifestyle changes, across the globe, the nutraceutical industry is further anticipated to evolve offering new opportunities for innovative products based on consumer interest in health-enhancing foods. However, this potential for innovation and growth is hindered by a lack of globally harmonized legislation and universally accepted definitions[64,65]. Because the boundaries between nutraceuticals, dietary supplements, and functional foods remain blurred, regulatory oversight is highly inconsistent, with some countries enforcing strict legislation while others leave the sector entirely unregulated. For instance, Japan defines functional foods based exclusively on natural ingredients, whereas the United States permits biotechnology-derived components. Such cross-border discrepancies create significant ambiguity that complicates international distribution.

Despite these varied national approaches, a major milestone for standardizing food safety and efficacy was achieved in 1992 when the United Nations Food and Agriculture Organization (FAO) and the World Health

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[64] http://refhub.elsevier.com/S1043-6618(21)00585-5/sbref1

[65] http://refhub.elsevier.com/S1043-6618(21)00585-5/sbref2

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Organization (WHO) introduced the Codex Alimentarius[66]. Utilized by many nations, these internationally recognized guidelines established foundational rules for the production and marketing of foodstuffs and their derivatives, specifically categorizing health claims into nutrient function, enhanced function, and disease risk reduction.
Globally, there are various standards set among nations and regions as shown in Table 1.

Table 1. Regulatory framework and pertinent policies concerning nutraceuticals in some of the key global markets[67].

Country	Definition	Pertinent acts	Applicable to
Australia	Complementary medicines	The Therapeutics Goods Act, 1989, implemented in 1991; governed by the Department of Health and Ageing.	• herbal medicines • vitamins and minerals • nutritional supplements • homeopathic medicines • aromatherapy products • traditional medicines
Canada	Natural Health Products	The Natural Health Product Regulations (2004) by Health Canada; governed by the Food and Drugs Authority of Canada and the Natural and Non-prescription Health Products Directorate (NNHPD).	• vitamins and minerals • herbal remedies • homeopathic medicines • traditional Chinese medicines, probiotics • amino acids and fatty acids
China	Common foods in standardized dose and method of delivery to improve efficacy and health benefits	No specific act. China's State Food and Drug Administration (CFDA) conducts all affairs relating to health foods. Testing protocol such as complete animal or human clinical study is required for approval. A "blue hat" label is applied to foods deemed functional.	• any common food deemed to be functional
European Union	Food supplements, which are defined as concentrated sources of nutrients and other substances with nutritional benefits	European Food and Safety Authority (EFSA) Directive 2002/ 46/EC	• proteins • vitamins and minerals • other substances with nutritional benefits
India	Foods for special dietary use, specially processed or formulated, to satisfy particular dietary requirements, not including any drug and can only be used for	Food Safety and Standards Act (2006)	• plants or botanicals or their parts in the form of powder concentrate or extract in water, ethyl alcohol or hydro-alcoholic extract, single or combination. • minerals or vitamins or proteins or metals or their compounds or

[66] Archives | CODEXALIMENTARIUS FAO-WHO
[67] Avijeet S. Chopra, et al., The current use and evolving landscape of nutraceuticals, Pharmacological Research, Volume 175, 2022, 106001, https://doi.org/10.1016/j.phrs.2021.106001.

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Country	Definition	Pertinent acts	Applicable to
	oral administration. They can be used as conventional foods, which cannot claim to cure any specific disease, but can claim indirect health benefits.		amino acids in amounts not exceeding the recommended daily allowance for Indians or enzymes (within permissible limits) • substances from animal origin. • dietary substances for use by humans that supplement the diet by increasing total dietary intake.
Japan	Food for Specified Health Uses	The Foods for Specified Health Use (FOSHU) regulatory process	• food with health function (not substantiated on scientific evidence) • food with certain effectiveness, but without established mechanism of the effective element for the function
Latin America (Colombia, Brazil, Argentina)	Functional foods	ANVISA (Agencia Nacional de Vigilancia Sanitaria) in Brazil.INVIMA (The National Food and Drug Surveillance Institute) in Colombia.	• fiber • probiotics • flavonoids • plant sterols • fatty acids.
Russia	Foodstuffs with clinically proven effectiveness that are recommended prophylactically and for the prevention of pharmaceutical therapy induced side-effects and the achievement of complete remission.	Ministry of Healthcare and Social Development's #1898, (1997): The Procedure for the Examination and Health Certification of Active Dietary Supplement regulated under Biologically Active Dietary Supplements (BADS)	• vitamins and minerals • amino acids • dietary fibers • bioflavonoid • alkaloids • essential oils • polysaccharides
United States	Dietary supplements, products (other than tobacco) intended to supplement the diet that contains one or more of the main dietary ingredients.	Dietary Supplement, Health and Education Act (DSHEA) of 1994	Concentrates, metabolites, constituent, extract or combination of: • vitamins and minerals • amino acids • herbs or other botanicals

Current European regulations monitored by the European Food Safety Authority (EFSA) include food supplements but do not officially mention or recognize the term nutraceutical.
There is also no distinction between food supplements and nutraceuticals for the purpose of obtaining a beneficial health claim application on new products. Indeed, medicinal claims for nutraceuticals are required to conform with regulatory requirements (efficacy, safety, and quality testing) of other medicinal products.

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Therefore, nutraceuticals can either be monitored as a food component under Directive 2002/46/EC[68] or a medicinal product under Directive 2004/27/EC[69].

The safety of supplements is monitored under Directive 2002/46/EC by EFSA and the European commission. In an effort to synchronize various legislations in relation to nutrition health claims, Regulation EC 1924/2006 was put into effect[70]. The aim of this regulation was to instil confidence among consumers by providing understandable information and assuring the safety and efficacy of products. Health claims can now only be placed on product labels or packaging if they are compliant with EFSA guidelines[71].

Europe is also home to the European Nutraceutical Association (ENA) since 2005, which serves as a non-profit organization to evaluate emerging evidence in relation to nutraceuticals[72].

In the U.S., FDA is not entirely responsible for nutraceuticals, but they are monitored by the Dietary Supplement Health and Education Act[73] and the Food and Drug Administration Modernization Act of 1997 (FDAMA)[74]. Notably, in the case of a botanical preparation, they do not require clinical testing before marketing, separate from a botanical drug. For a botanical preparation to be considered a drug substance, intended for diagnostic, preventive, or curative purposes, the manufacturer must provide clinical efficacy and safety data for over-the-counter drug review. According to the DSHEA, the manufacturer bears the responsibility to ensure the safety of nutraceuticals.

The nutraceutical intended for marketing should comply with the following criteria: (i) be intended for ingestion in form of pill, capsule, tablet, powder or liquid form, (ii) not be represented for use as a conventional food or as sole item of a meal/diet, and (iii) be labelled as a "dietary supplement". Due to the need to increase surveillance on the growing supplement and nutraceuticals markets, the FDA established the Office of Dietary Supplement Programs (ODSP). However, there is significant concern that these legislations do not provide adequate protection to consumers as the manufacturers are responsible for ensuring a product's safety and efficacy before production and marketing[67]. Manufacturers are not required to seek approval or register their product with the FDA prior to reaching the market. This potentially place the consumer at risk to unsafe on inefficacious prod that lack preclinical and clinical evidence.

On the contrary, in Canada, the regulation of nutraceuticals is governed by the Food and Drugs Authority of Health Canada and is regulated more like a drug than as a food category. The category comprises homeopathic medicines, herbal remedies, vitamins and minerals, traditional Chinese medicines, probiotics, and other products (e.g., amino acids and fatty acids).

Other countries do not have any specific regulations. For example, Indian regulations do not provide any specific legal status to nutraceuticals. The Food Safety and Standards Act (FSSA) established in 2006 does not distinguish between functional foods, nutraceuticals, and dietary supplements[75]. Each of these products is indicated as food for a special dietary application. In India, Ayurveda is an entire field of natural medicinal products that has been practiced for thousands of years and is considered a tested system for supervised administration of natural products[76].

In Asia-Pacific region, Japan, was among the first countries to face the issue of regulating food supplements and foodstuff by their regulatory authority, the Foods for Specified Health Use (FOSHU)[77]. Many other countries, such as Australia or China, regulate nutraceuticals simply as a category of food.

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[68] European Commission, Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements, in 2002/46/EC, E.C.T.E.F.S. Authority, Editor, European Commission: Brussels, Belgium, 2002.

[69] The European Commission, Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use. Official Journal of the European Union, 2004. L136/34–57.

[70] European Commission, Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. 2006 20 Nov 2020.

[71] European Commission, Commission Regulation (EU) No 1047/2012 of 8 November 2012 amending Regulation (EC) No 1924/2006 with regard to the list of nutrition claims Text with EEA relevance. Official Journal of the European Union, 2012.

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For some countries including Colombia, Brazil, and Argentina, a simple registration-based approach to local authority is used, and a notification-based approach is valid in Mexico and Chile. Brazil, China and Taiwan, also have stricter requirements, where prior to registration, a complete animal or human clinical study is required.

The Russian Federation Food Security Doctrine regulates nutraceuticals under Biologically Active Dietary Supplements (BADS)[78]. Nutraceuticals are defined as foodstuffs with clinically proven effectiveness recommended for prophylactic use to prevent side effects induced by pharmaceutical products and the achievement of complete remission. The definition includes vitamins, minerals, amino acids, dietary fibres, and para-pharmaceuticals (bioflavonoid, alkaloids, essential oils, polysaccharides).

The COVID-19 pandemic has highlighted that greater regulatory oversight and enforcement is required for nutraceuticals, dietary supplements, and functional foods internationally. During the pandemic, several products were advertised as prophylactics, therapeutics, and even cures for COVID-19 despite a clear lack of evidence for safety or efficacy. In the U.S. for example, oleandrin was proposed as a supplement, which could have been lethal if consumed[79]. This along with many other examples prompted the FDA and Health Canada to issue several warnings to various companies for false advertising and mislabelling their products, and to prevent harm to consumers[80]. While this shows an example of enforcement of regulatory oversight in action in the U.S. and Canada, there is certainly room for improvement to prevent such products from reaching consumers in the first place.

5. Advancing the safety assessment of botanicals and nutraceuticals

As the global nutraceutical and botanical industry rapidly expands, regulatory bodies, including the FDA, EFSA, and the collaborative Botanical Safety Consortium, are increasing their scrutiny to protect consumers. Despite significant technological advances, serious safety risks persist in the supply chain, such as misidentified plant species, undeclared pharmaceutical ingredients, heavy metal and pesticide contamination, mycotoxins, and product misuse.

A major challenge in addressing these risks is the current lack of globally harmonized evaluation approaches, as already mentioned above. To meet strict regulatory expectations and ensure market integrity, product developers must provide transparent, well-documented, and evidence-based toxicology assessments.

To achieve this, the industry is transitioning away from traditional animal models toward New Approach Methodologies (NAMs). By integrating analytical chemistry, "omics" technologies, high-throughput screening, and artificial intelligence-driven computational toxicology, developers can now accurately predict ingredient behaviour and underlying toxicity mechanisms. These modern, *in silico* tools streamline risk assessments and regulatory submissions while elevating ethical standards, ultimately accelerating innovation, securing market access, and building consumer trust[81].

5.1. Why Toxicology Matters More Than Ever in Nutraceuticals

Nutraceuticals today embrace an ever-growing variety of ingredients including plant extracts, bioactive peptides, fermented products, and novel micronutrients. Many of these are new to the market and lack a substantial history of safe human use, meaning toxicology data becomes a critical aspect of their regulatory dossiers.

In the U.S., ingredients classified as New Dietary Ingredients (NDIs) must be notified to the FDA prior to marketing. This requires

[78] V.A. Tutelyan, et al., Chapter 18 - Russian regulations on nutraceuticals and functional foods, in: D. Bagchi (Ed.), Nutraceutical and Functional Food Regulations in the United States and Around the World, second ed., Academic Press, San Diego, 2014, pp. 309–326.
[79] DiPietro MA, Mondie C. Toxicity of herbal medications suggested as treatment for COVID-19: A narrative review. J Am Coll Emerg Physicians Open. 2021 Mar 31;2(2):e12411. doi: 10.1002/emp2.12411. PMID: 33817690; PMCID: PMC8011616.
[80] Health Canada, Health Product Advertising Incidents Related to COVID-19, 2021
[81] IJNRD2607179.pdf

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- **New Dietary Ingredient (NDI) Notifications:** submission must provide evidence of safety; frequently necessitating toxicology studies tailored to the intended use and population.
- **Generally Recognized As Safe (GRAS) Determinations:** safety must be demonstrated through either scientific procedures or a wellestablished history of safe consumption.
- **Adverse Event Reporting:** mandatory post-market surveillance to identify and manage potential safety signals, ensuring ongoing consumer protection.

In the European Union, the Novel Food Regulation (EU 2015/2283) governs many new nutraceutical components mandating

- **Comprehensive Toxicological Testing:** genotoxicity, sub-chronic toxicity, reproductive and developmental toxicity studies.
- **Exposure and Metabolism Assessments:** analysis of anticipated intake levels, absorption, distribution, metabolism, and excretion (ADME) profiles to inform risk characterization.
- **Qualified Presumption of Safety (QPS):** a streamlined safety assessment applicable to certain microorganisms used in production, reducing data requirements if criteria are met.
- **Scientific Opinions:** EFSA's conclusions derive from peer-reviewed data and thorough risk assessments, forming the basis for regulatory decisions.

For both regions, the quality, relevance, and scientific rigor of toxicology data are critical factors influencing regulatory approval, commercial success, and liability mitigation.

5.2. Regulatory Toxicology Testing Expectations

Meeting FDA and EFSA safety expectations requires targeted toxicological data demonstrating that nutraceutical ingredients are safe under realistic use conditions. **Table 2** lists the core toxicology endpoints, their purpose, and the specific regulatory requirements in both the U.S. and EU.

Table 2. FDA vs EFSA regulatory requirements for safety assessment of nutraceutical ingredients[82].

Endpoint	Purpose in Toxicology Assessment	FDA Requirement	EFSA Requirement
Genotoxicity	Detects potential DNA damage and mutation risk	AMES test and micronucleus test required	AMES and *in vitro* micronucleus tests are initial screens; if positive, follow up with *in vivo* micronucleus, comet assay, or transgenic rodent mutation assay
Sub-chronic Toxicity	Identifies target organ/systemic toxicity; establishes safe intake levels after repeated exposure (28 or 90 days).	28- or 90-day animal studies, duration based on exposure	Mandatory 90-day studies in rodents for most novel foods
ADME Studies	Determines Absorption, Distribution, Metabolism, and Excretion (ADME), crucial for understanding systemic exposure and accumulation	Case-by-case, not always required	Strongly encouraged for novel foods and new ingredients

[82] Rigorous Toxicology Assessments in Nutraceutical Safety: Meeting FDA and EFSA Guidelines - Aragen Life Sciences

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Endpoint	Purpose in Toxicology Assessment	FDA Requirement	EFSA Requirement
Reproductive Toxicity	Evaluates risk to fertility, pregnancy, and offspring development—critical when wide population exposure is possible	Required for broad exposure or sensitive populations	Required when ingredients may be consumed by general/sensitive population
Carcinogenicity	Assesses risk of cancer after long-term or lifetime exposure; informs safe use and labeling	Required based on structural or exposure-based concern	Required for ingredients intended for long-term exposure

A well-designed toxicology program addresses these core endpoints as dictated by regulatory agencies. Satisfying both FDA and EFSA requirements with properly scoped studies and documentation not only enables regulatory approval but also helps build consumer confidence and minimizes post-market risk.

5.3. What Makes a Toxicology Assessment Rigorous

A reliable toxicology assessment is built on traditional methods: hazard identification, risk characterization, and, when appropriate, targeted *in vivo* validation. Besides these, modern assessments like New Approach Methodologies (NAMs) are strategically combined with traditional methods to achieve more human-relevant and efficient safety insights. The use of tiered tests, along with tailored data generation for risk assessment, provides a pragmatic and effective strategy for safety assessment.

5.3.1. Hazard Identification

- Comprehensive literature review to identify existing toxicology and exposure data.
- Use of *in silico* modelling to predict hazards based on chemical structure and biological similarity
- Deployment of *in vitro* screening for genotoxicity, cytotoxicity, and oxidative stress markers.

5.3.2. In Vivo Validation

- Acute toxicity studies to determine immediate health hazards following a single exposure.
- Sub-chronic and chronic studies (typically 28 or 90 days) for identifying cumulative systemic effects.
- Reproductive and developmental toxicity testing, important for broad dietary use cases.
- Carcinogenicity studies in rare cases where structure or usage indicates potential long-term risk.

5.3.3. Integration of NAMs

- Human-relevant *in vitro* tools, including 3D tissue systems, organoids, and organ-on-chip models for target organ toxicity.
- *In silico* algorithms like QSAR or structure activity-based tools (e.g., VEGA QSAR) for predicting genotoxicity and systemic effects.
- Read-across frameworks to apply existing data from similar compounds, enabled by shared chemistry and metabolism.
- Use Threshold of Toxicological Concern (TTC)-derived limits for risk assessment when toxicity data are limited but exposure is expected to be low, following accepted regulatory guidelines.
- Inclusion of existing human data from epidemiological or clinical sources, particularly where post-market surveillance exists.

5.3.4. Risk Characterization and Dossier Compilation

- Estimate realistic human exposures based on proposed dosage form, frequency, and population.
- Define Margins of Exposure (MOE) and NOAELs/LOAELs using derived toxicological dose data.

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- Compile a comprehensive regulatory dossier presenting risk assessments, raw data, method validations, and expert interpretations in formats aligned with U.S. (NDI, GRAS) or EU (Novel Food, EFSA) submission requirements.

5.4. Strategic Integration of NAMs in Nutraceutical Toxicology

Regulators around the world are actively encouraging the use of NAMs where scientifically justified, recognizing their value in improving ethical standards while maintaining rigorous safety evaluation. By thoughtfully integrating NAMs with traditional studies, the toxicology program becomes more efficient, ethical, and scientifically powerful.

Effective use of NAMs are listed

- Improves Relevance: provide mechanistic, often human-specific toxicity insights not available from traditional animal models.
- Increases Efficiency: accelerate safety assessments and reduce development timelines.
- Enhances Ethics: reduce animal usage in line with international principles and regulatory momentum.
- Supports Regulatory Flexibility: enable scientifically justified read across and waivers, reducing duplicative studies and supporting global dossier harmonization.

5.5. Bridging FDA and EFSA Requirements: A Unified Strategy

While safety is the mutual priority, differences in regulatory philosophies drive distinct submission expectations, while FDA typically accepts a broad array of data types and formats, with a pragmatic approach that prioritizes safety and feasibility; EFSA demands strict adherence to internationally recognized standards including OECD test guidelines, GLP compliance, and rigorous documentation.

Given these differences, it is critical to design toxicology programs that satisfy both authorities upfront, facilitating faster global commercialization.

To unlock both U.S. and EU markets efficiently a good strategy could be to i) design studies up front to meet the highest standards (e.g., GLP, OECD, Redbook) to avoid repetition and increase cross-border dossier acceptance; ii) capture multiple toxicological endpoints within individual studies to conserve resources and iii) provide scientific justifications for any non-standard approach, especially NAMs or literature-based read-across. Moreover, early consultation with experienced toxicology and regulatory experts is recommended to tailor study design and data packages accordingly.

6. Market overview[83]

Growing health and fitness awareness among consumers around the world coupled with shift towards preventive healthcare are expected to primarily drive nutraceuticals market growth. The global increase in aging population and rising chronic disease burden are also promoting nutraceuticals consumption. The growth of e-commerce and digital wellness platforms has drastically improved access to nutraceuticals, making product discovery, research, and purchasing easier than ever. Growing distrust in synthetic chemicals and rising preference for transparency in ingredient sourcing are also expected to help bolster the demand for nutraceuticals made from clean label ingredients.

On the contrary, high costs of premium nutraceuticals products, lack of standardization, scientific validation and efficacy challenges, and risk of contamination and adulteration are anticipated to slow down nutraceuticals market penetration across the study period and beyond.

The rise of personalized nutrition is reshaping the nutraceuticals market, driven by advances in genomics, microbiome science, and AI. Consumers increasingly seek supplements tailored to their genetic makeup, lifestyle, and health conditions. Companies are offering DNA-based testing kits that recommend customized supplement regimens based on nutrient deficiencies, allergies, or metabolic profiles.

[83] Nutraceuticals Market Size, Share | Growth Report [2033]

This trend promotes efficacy, consumer trust, and long-term engagement. Startups and wellness platforms integrate data-driven algorithms to offer real-time, personalized plans. As precision healthcare gains momentum, DNA-guided nutraceuticals are emerging as a premium segment, transforming the market from generic products to individualized health solutions with measurable outcomes.

6.1. Nutraceutical Competitive Landscape

The global nutraceuticals industry is characterized by a diverse landscape of players, ranging from established pharmaceutical giants to specialized ingredient manufacturers and innovative startups. Key companies, including Yakult Honsha Co., Ltd., Amway Corp., Herbalife Nutrition Ltd., Nestlé S.A., The Kraft Heinz Company, The Hain Celestial Group, Inc., GlaxoSmithKline plc., General Mills Inc., Danone, and Tyson Foods, Inc., hold significant positions due to their extensive product portfolios, established distribution networks, and strong brand recognition.

These major players often employ strategies such as strategic acquisitions to expand into new product categories or geographies, as seen with Nestlé's growing focus on personalized nutrition through the acquisition of smaller, specialized firms. They also invest heavily in R&D to develop new ingredients and formulations, and to launch new product lines that emphasize natural, organic, and plant-based ingredients to cater to evolving consumer preferences and health concerns. This continuous innovation and expansion contribute to their leading positions within the market, influencing consumer trends and shaping the competitive dynamics. Besides, key industry participants also leverage partnerships and collaborations to access broader distribution channels and gain research capabilities.

Nutraceutical providers should focus on the personalized nutrition trend to boost their sales potential. Focusing on developing plant-based nutraceuticals and incorporation of clean-label ingredients is the best opportunity for companies as per this nutraceuticals market analysis.

Providing nutraceuticals in different delivery formats is expected to be the prime focus of new companies.

6.2. Market Dynamics and Growth Drivers (2026-2030)

The global nutraceuticals market is segmented by product, distribution channel, functional claim, end user.

Based on functional claim, the market is segmented into:

- high/added fibre,
- vitamin/mineral fortified,
- brain health,
- bone health/added calcium,
- weight management,
- cardiovascular health,
- skin/hair/nails,
- added protein,
- and others.

Based on product, the market is segmented into:

- dietary supplements (vitamins, minerals, enzymes, fatty acids, proteins, others),
- functional foods (dairy food, breakfast cereals, snacks, baby food, others), and
- functional beverages (fortified and functional hot drinks, functional carbonates, fortified juices, herbal beverages, fortified and functional energy drinks, fortified water, others).

Based on distribution channels, the market is segmented into:

- supermarkets/hypermarkets,
- convenience stores,
- online retail, others

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Based on end user, the market is segmented into:

- lifestyle users,
- athletes,
- geriatric users,
- fitness enthusiasts,
- and others.

6.3. Product Insights

The dietary supplements segment led the market with the largest revenue share of 32.6% in 2025 and is projected to grow at the fastest CAGR during the forecast period, driven by the increasing consumer focus on preventative healthcare and wellness, with individuals proactively seeking to address nutritional deficiencies and support their overall health through supplementation. The aging global population, particularly in developed nations, is also contributing significantly to demand, as older adults often require specific nutrients to combat age-related health concerns.

Furthermore, the rise of personalized nutrition and the growing availability of tailored supplements catering to specific needs, such as sports performance, weight management, and immune support, are attracting a wider consumer base. Technological advancements in supplement formulation, including enhanced delivery systems like liposomes and nanotechnology, are also boosting efficacy and desirability. Besides, a growing awareness of the link between gut health and overall well-being has driven up the demand for probiotics and prebiotics, further expanding the supplement landscape.

The functional beverages segment is anticipated to grow at a significant CAGR over the forecast period, driven by a consumer shift towards healthier, more convenient alternatives to traditional sugary drinks. A key trend is the desire for natural, "better-for-you" options, driving increased demand for beverages enriched with vitamins, minerals, antioxidants, and plant-based ingredients.

The rise of the fitness culture and the growing popularity of active lifestyles have boosted the demand for sports and performance drinks, including those with electrolytes, protein, and BCAAs. Moreover, the convenience factor plays a significant role, with time-constrained consumers seeking easy-to-consume options that offer specific health benefits, like energy boosts, stress relief, or improved sleep. The proliferation of innovative and diverse flavour profiles, coupled with novel ingredients like adaptogens and nootropics, is driving the consumer product adoption rate.

In addition, increased awareness of the potential health risks associated with excessive sugar consumption has played a significant role in the shift away from traditional sugary drinks towards functional beverage options.

The expanding nutraceutical product market is further reinforcing the growth of functional beverages, as consumers increasingly seek holistic health solutions that combine nutrition, convenience, and targeted wellness benefits. This convergence is driving brands to formulate beverages that deliver functional outcomes similar to supplements, such as immunity enhancement, digestive support, and cognitive performance. As consumers favour clean-label formulations and transparent ingredient lists, companies are innovating with scientifically supported actives and sustainable sourcing practices to strengthen trust and differentiate in a crowded marketplace.

6.4. Application Insights

6.4.1. Weight management & satiety nutraceuticals

The weight management & satiety nutraceuticals segment led the market with the largest revenue share of 16.2% in 2025, driven by the rising global prevalence of obesity and associated health concerns, which are prompting consumers to actively seek convenient, natural solutions beyond traditional dieting. This is fuelling demand for products that promote satiety, regulate appetite, and support fat burning, with a particular emphasis on plant-based ingredients, fibre-rich formulations, and those backed by scientific research. Furthermore, the wellness movement is shifting the focus from mere weight loss to holistic health, leading to increased interest in nutraceuticals that support healthy metabolism, gut health, and balanced energy levels,

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indicating a desire for sustainable solutions rather than quick fixes. The convenience of ready-to-drink shakes, bars, and powders is also a key factor influencing consumer choices in this category, as they make it easy to integrate into busy lifestyles.

6.4.2. Men's health nutraceuticals

The men's health nutraceuticals segment is estimated to grow at the fastest CAGR of 13.7% from 2026 to 2033. Key demand drivers include a growing awareness of preventative healthcare and an increased understanding of how nutrition impacts performance, vitality, and long-term health. This translates to rising demand for supplements targeting areas such as prostate health, muscle development and strength, energy levels, and hormonal balance, especially as men age. Furthermore, the stigma surrounding discussing men's health issues is gradually diminishing, making it more acceptable to seek out supplements that address concerns like erectile dysfunction and stress management. The influence of fitness culture and the desire to maintain an active lifestyle are also contributing factors, leading to increased interest in products that support athletic performance, recovery, and overall vitality.

The growth of this segment is also strongly supported by broader developments in the nutraceutical supplements market, where innovation and personalization are becoming key competitive drivers. Brands are increasingly formulating targeted solutions using clinically studied ingredients to address men's unique needs, from testosterone support and heart health to mental clarity and stress reduction. Rising interest in clean-label, plant-based, and scientifically validated products further accelerates adoption, as men seek reliable, effective, and convenient ways to optimize daily performance and long-term health.

6.4.3. Aging population

Aging represents a natural biological process that results in certain ostensible chronic medical conditions, such as Alzheimer's disease, dementia, respiratory problems, hypertension, CVD, osteoporosis, and cataracts. Due to the increasing growth of elderly populations, many healthcare systems will struggle to maintain a healthy lifespan for their elderly citizens. However, healthy aging can be greatly aided mainly by consuming a healthy and nutritious diet, along with an active and correct lifestyle. Nutraceuticals have the potential to protect against aging and stress. In fact, they have shown to be beneficial in prevention of age-related chronic conditions, thereby promoting longevity and overall well-being for the elderly population[84].

6.4.4. Consumer awareness

This growth is being driven by an increase in consumer awareness of health; including awareness for the benefits of a nutritional diet, improved lifestyles, education programs, and accelerated health awareness information disseminated through social media. Indeed, consumer awareness has also driven the growth of "wellness" products[85]. This area of the nutraceutical market for the US and Canada is anticipated to grow steadily as consumers show increased interest in improving their lifestyles. In the Asia-Pacific region, the growth in nutraceuticals market is also attributed to rise in disposable income and middle-class consumers, urbanization, and increase in incidence of lifestyle-related diseases such as hypertension, diabetes, and cardiovascular diseases[86]. Consumer awareness is largely what drove the increased growth of the nutraceutical market at the beginning of the COVID-19 pandemic.

6.4.5. Increasing cost of healthcare

Changes in the healthcare industry, along with increasing healthcare and drug costs are also triggering the growth of the nutraceuticals market. Consumers are increasingly inclined to look towards nutraceuticals not only to improve their health, but also to save money on expensive over the counter and prescription drugs. In this sense, a substantial increase in the nutraceutical market has been seen in the U.S. and Canada, followed by Asia-Pacific and Mexico[67].

[84] C. Gupta, D. Prakash, Nutraceuticals for geriatrics, J. Tradit. Complement. Med. 5 (1) (2015) 5–14.
[85] D. Cardenas, V. Fuchs-Tarlovsky, Is multi-level marketing of nutrition supplements a legal and an ethical practice? Clin. Nutr. ESPEN 25 (2018) 133–138.
[86] Nutraceuticals World, Consumer Health Awareness Propels the Global Nutraceuticals Market, 2016

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6.5. Distribution Channel Insights

The offline segment led the market with the largest revenue share of 78.4% in 2025. The offline channel, such as pharmacies, supermarkets & hypermarkets, specialty stores, and grocery stores, remains a significant opportunity for nutraceutical sales. Consumers often prefer the tactile experience of physically selecting products and interacting with informed staff who can provide personalized recommendations. Pharmacies[87], in particular, are trusted sources of supplements due to their association with health and wellness solutions. Supermarkets & hypermarkets offer a broader reach with a wider selection of products, catering to more casual consumers. However, this channel's growth can be limited by geographical constraints and by e-commerce competition, requiring offline retailers to focus on creating engaging in-store experiences and building strong customer relationships to maintain their market share.

The online segment is projected to grow at the fastest CAGR of 10.6% from 2026 to 2033. E-commerce platforms offer convenience, accessibility, and a wider selection of products compared to traditional retail. Consumers can easily research and compare products, read reviews, and often find lower prices online. The COVID-19 pandemic significantly accelerated the adoption of online shopping, and this trend is expected to continue. Moreover, direct-to-consumer online brands are gaining prominence, allowing manufacturers to bypass intermediaries and foster direct customer engagement.

6.5.1. Increasing number of distribution channels

The use of different distribution channels provides opportunities for targeting different market segments and increasing nutraceutical sales. Different distribution channels currently being used include online selling, direct marketing, and business-to-business (B2B) channels and business-to-consumer (B2C) channels. The growth of online sales of nutraceutical products can be attributed to the growing number of internet users and growing interest of many of them in online shopping, even in case of health products due to convenience. Based on the Euromonitor International Research report[88], the global vitamin and supplement market accounted for about EUR 60.2 Bn in internet sales contributing a substantial share in the growth of supplement demand. About 44% of the consumers purchase nutraceuticals online globally. Similar sales trends online are anticipated for India, being the second largest growing online population. Some companies use direct marketing approaches with specialized retail stores for consumers. These specialized retail stores are positively perceived by consumers, and they often tend to buy food and health supplements from a specialized store rather than from medical or other stores. For example, Himalaya, an Indian company, successfully used this approach for its nutraceutical products. Digital marketing such as email marketing, social media, apps, e-marketing, websites, virtual sales representatives, and closed platforms are becoming powerful tools for marketing nutraceuticals and nutritional supplements.

These strategies enable the marketers to target and track various aspects of marketing, tailoring the market strategy based on consumer needs. In recent years, multi-level marketing of supplements and nutraceuticals has dramatically increased[67]. Multi-level marketing is a strategy whereby independent distributors sell products directly to the consumer from their own home, online, or via telecommunications. Distributors can be both rewarded for their sales and if they can recruit additional individuals to become distributors. However, while not illegal, this form of supplement distribution is highly unethical and some of the products may be unsafe or simply unnecessary.

7. Nutraceutical Key market challenges:

Major market challenges are represented by: (i) regulatory environment, (ii) threat of counterfeit dietary supplements and (iii) consumer distrust stemming from misleading marketing activities.

[87] Pharmacy Market Size, Share And Trends Report, 2026-2033
[88] Explore reports - Euromonitor.com

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7.1. Challenging regulatory environment

The growth in the global dietary supplements market brings about a greater need for governmental intervention and strengthening of regulations relating to: (i) the production, distribution, safety testing, and (ii) claims regarding the effectiveness of dietary supplements.

The nutraceuticals industry is subject to a wide range of regulations in terms of definitions, quality standards, and labelling requirements across regions. This inconsistency leads to consumer confusion and complicates international trade and compliance. Without strict enforcement, low-quality or unverified products may reach the market, undermining consumer trust. These challenges restrict the market's full potential, especially for smaller players attempting cross-border expansion.

The absence of consistent scientific evidence supporting health claims of nutraceuticals is a major restraint for market development. Many products are launched with minimal clinical data, leading to scepticism about their actual efficacy. Without stringent clinical trials, it becomes difficult to establish credibility and distinguish high-quality formulations from pseudoscientific offerings.

7.2. Threat of counterfeit dietary supplements

The increase in the consumption of dietary supplements has simultaneously led to an increase in the influx of counterfeit and fake supplements into the market. Counterfeiting refers to the branding and sale of non-authorized products and represents a major challenge for the genuine vendors of dietary supplements. Counterfeit dietary supplements are manufactured using low-cost non-standard materials and are not tested or approved by regulatory authorities; therefore, they are unfit for human consumption.

7.3. Consumer distrust

The use of deceptive advertising and communication strategies by some companies, aimed at claiming the health benefits of taking supplements, has led to a growing distrust of consumers towards the entire sector, which is placing challenges for producers both in terms of reputation and in terms of regulatory requirements from the point of view of communicating the effects of products.

8. Insights into the global market

The nutraceutical industry is flourishing and diversifying rapidly. The current market trends in healthcare are inclined towards preventive health care strategies, rather than treatment and disease management. This trend is anticipated to grow as healthcare costs increase in both developing and developed countries. Increasing occurrence of chronic diseases coupled with the high cost of healthcare interventions is creating a demand for personalized nutrition, along with a boost in demand for nutraceuticals. Additionally, there is a shift in consumer preference from synthetic pharmaceutical preparations to natural and organic nutraceutical ingredients[89].

According to recent market research, the global nutraceuticals market was valued at USD 500.62 Bn in 2025[90], although estimates vary with the scope of products included, between USD 646.6 and 671.8 Bn[91]. Forecasts for the coming decade up to 2034 also differ considerably, between USD 1.124 Bn and 1.400 Bn at 5-9% CAGR[91,92].

The nutraceutical industry now represents approximately 29–37% of the value of the pharmaceutical industry, based on the 2025 nutraceutical estimates above.

[89] Ghosh, Dilip, and R. B. Smarta. *Pharmaceuticals to nutraceuticals: A shift in disease prevention*. CRC press, 2016.
[90] Fortune Business Insights (2026). *Nutraceuticals Market Size, Share & Industry Analysis, Regional Forecast 2026–2034*. https://www.fortunebusinessinsights.com/nutraceuticals-market-102530.
[91] Straits Research (2026). *Nutraceutical Products Market Size, Share, Growth, Analysis, 2034*. https://straitsresearch.com/report/nutraceutical-products-market. Zion Market Research (2025). *Nutraceuticals Market Size, Industry Analysis, Share, Forecast 2034*. https://www.zionmarketresearch.com/report/nutraceuticals-market
[92] Fortune Business Insights (2026). *Nutraceuticals Market Size, Share & Industry Analysis, Regional Forecast 2026–2034*. https://www.fortunebusinessinsights.com/nutraceuticals-market-102530.

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North America remains the largest regional market, accounting for 37.2% of the nutraceutical products market. The U.S. alone was valued at USD 176.6 Bn in 2025[93], with a projected CAGR of 5.2% for 2026–2034. Asia Pacific is the leading region in the nutraceutical supplements segment, with a 38.2% share of revenue in 2025 and a projected CAGR of 8.4% through 2034[94].

8.1. North America[95]

The North America Nutraceuticals Market size was valued at USD 191.1 billion in 2025, increased to USD 198 billion in 2026, and is projected to reach USD 236.6 billion by 2031, growing at a CAGR of 3.62% during 2026–2031. This growth reflects a continued shift toward preventive healthcare and proactive wellness management across the region. Increasing awareness of lifestyle-related chronic diseases underscores the importance of nutrition-based interventions in reducing health risks before they escalate into medical conditions. Furthermore, rising demand for clean-label, plant-based, and scientifically validated formulations is driving product innovation and premiumization. Advances in nutritional science and ingredient bioavailability are also improving perceived efficacy. Additionally, stricter regulatory oversight is enhancing product credibility and consumer trust, contributing to the market's long-term stability.

Dietary supplements accounted for 49.87% of the North America nutraceuticals market in 2025, driven by their integration into preventive health practices and long-term wellness strategies. According to the Penn State College of Medicine, approximately 59 million Americans regularly used vitamins or supplements in 2024, highlighting the widespread adoption and strong penetration of this category. This trend reflects a shift toward self-directed healthcare, where consumers proactively maintain immunity, support cardiovascular and metabolic health, enhance cognitive performance, and promote healthy aging, reducing reliance on medical interventions. The segment's growth is further supported by increased awareness of micronutrient deficiencies, concerns over lifestyle-related disorders, and growing trust in scientifically validated ingredients.

The North America nutraceuticals market demonstrates moderate concentration, featuring a mix of global food and pharmaceutical conglomerates alongside specialized nutrition companies. Key players include Nestlé S.A., PepsiCo Inc., Abbott Laboratories, Herbalife Nutrition Ltd., and Amway Corp. These companies maintain their market positions through extensive distribution networks, diversified product portfolios, strong research and development (R&D) capabilities, and established brand equity. Their competitive advantages stem from vertical integration, regulatory expertise, clinical validation of select products, and scalability across supermarkets, pharmacies, specialty stores, and digital platforms. Meanwhile, private-label offerings and mid-sized nutraceutical firms heighten competition by delivering targeted, niche formulations.

The competitive dynamics are evolving rapidly with the emergence of digitally native, direct-to-consumer (DTC) brands. New entrants are incorporating AI-driven dosing algorithms, biomarker tracking, personalized nutrition assessments, and subscription-based replenishment models to appeal to younger, tech-savvy consumers willing to pay premiums for customized formulations. This shift toward personalization is transforming purchasing behaviour, moving the focus from generalized supplementation to tailored wellness programs. In response, established players are increasingly investing in digital transformation, enhancing e-commerce capabilities, forming strategic partnerships with health-tech firms, or acquiring high-growth disruptor brands to remain competitive and engage digitally active consumer segments.

The competitive edge in the market is increasingly favouring brands that can demonstrate measurable health outcomes. Companies investing in peer-reviewed clinical trials, ingredient traceability, third-party certifications, and transparent labelling practices are gaining stronger consumer trust and differentiation. Scientific substantiation, regulatory compliance, and quality assurance are becoming central to brand positioning rather than secondary marketing claims. In an environment characterized by rising consumer scepticism and regulatory scrutiny, the ability to validate efficacy and safety through credible evidence is emerging as a critical factor for achieving long-term competitive advantage in the North American nutraceuticals market.

[93] Market Data Forecast (2026). U.S. Nutraceuticals Market Size, Share & Growth, 2034. https://www.marketdataforecast.com/market-reports/united-states-nutraceuticals-market.

[94] Dataintelo (2025). *Global Nutraceutical Supplements Market Research Report 2034*. https://dataintelo.com/report/global-nutraceutical-supplements-market.

[95] North America Nutraceutical Industry - Companies & Revenue

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8.1.1. Geography Analysis

United States Nutraceuticals Market

The United States accounted for 68.1% of the North American Nutraceuticals Market in 2025, driven by its established supplement culture, advanced product innovation ecosystem, and strong consumer focus on preventive healthcare. The country benefits from widespread awareness of lifestyle-related health issues, high adoption rates of dietary supplements, and a well-developed retail and digital distribution network. The presence of leading nutraceutical manufacturers, ongoing product development in areas such as immunity, cognitive health, sports nutrition, and healthy aging, along with intense marketing and brand competition, further solidifies the United States' leading position in the regional market.

Mexico Nutraceuticals Market

Mexico is expected to grow at a CAGR of 4.8% through 2031, positioning itself as one of the fastest-growing nutraceutical markets in North America. This growth is primarily driven by increasing awareness of preventive health, rising demand for immunity-boosting and metabolic health products, and greater availability of supplements through pharmacies and modern retail channels. Health-conscious consumers, motivated by concerns over obesity and lifestyle-related conditions, are increasingly adopting nutritional supplements. Additionally, the growing penetration of organized retail and digital commerce platforms is enhancing product accessibility in urban areas, supporting sustained market expansion during the forecast period.

Canada Nutraceuticals Market

Canada's nutraceutical market is defined by high per-capita supplement consumption, strong e-commerce adoption, and a structured regulatory framework that bolsters consumer confidence. Canadian consumers show a strong preference for natural health products, clean-label formulations, and plant-based ingredients. Regulatory oversight ensures product quality, transparent labelling, and safety compliance, fostering trust in nutraceutical products. Furthermore, Canada's digitally engaged population and widespread integration of online retail channels contribute to steady growth in direct-to-consumer sales.

8.2. Asia-Pacific[96]

The Asia Pacific Nutraceuticals Market comprises products that provide health benefits beyond basic nutrition, including functional foods, functional beverages, dietary supplements, and personal-care or pharmaceutical-grade nutraceuticals. The market scope covers formulation, manufacturing, distribution, and retail of these products across all Asia Pacific economies. Its significance lies in the region's rapidly aging populations, rising chronic-disease prevalence, and increasing consumer awareness about preventive health, driving demand for products that support immunity, digestion, weight control, beauty, and athletic performance.

The market demonstrates a consistent upward trajectory, driven by rising awareness of wellness benefits, a preference for natural and clean-label products, and fortified supplement variants appealing to health-conscious consumers throughout the region.

By 2030, the market is forecasted to reach USD 149.5 billion, reflecting steady growth through the first half of the decade. The absolute dollar growth between 2025 and 2035 is expected to be around USD 99.7 billion, indicating robust and reliable expansion. Market growth is considered backloaded, with greater adoption of nutraceutical products in dietary supplements, functional foods, and personal care anticipated in the latter half of the timeline.

Leading companies such as Herbalife International of America Inc., General Mills Inc., PepsiCo Inc., Abbott Nutrition, and Amway Corp (Alticor) are consolidating their positions by expanding product portfolios and investing in innovative formulations. Their focus includes high-quality extracts, plant-based ingredients, and fortified health supplements, enabling stronger penetration into health-conscious and premium consumer segments.

[96] Asia Pacific Nutraceuticals Market

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The Asia Pacific nutraceutical market is experiencing robust, sustained growth, largely driven by rising disposable incomes, evolving wellness trends, and a proactive consumer approach to chronic disease management. Currently capturing over 49% of the dietary supplements sector, these science-backed, natural ingredients are proving highly versatile, expanding steadily into functional food formulations and personal care products.

This growing demand is reinforced by the region's massive population of 4.8 billion as of 2024, coupled with increasing household expenditure on preventive wellness, immunity, digestive health, healthy aging, and performance nutrition. Consumers are exhibiting a strong preference for clean-label, organic, gluten-free, and plant-based formulations, spurred by both health awareness and sustainability concerns. The market is also seeing a surge in specialized categories, such as "beauty-from-within" products that boost the anti-aging segment, alongside zero-sugar functional beverages infused with adaptogens. Furthermore, high-income markets like Japan, South Korea, and Australia are taking customization a step further by leveraging AI and genetic testing to deliver digitally enabled, personalized nutrition.

To meet these more complex demands, the industry is heavily investing in advanced extraction and formulation technologies that significantly improve product purity and efficacy, thereby strengthening consumer trust. Capitalizing on these innovations, companies are broadening their specialty portfolios and forming strategic partnerships with healthcare brands, retailers, and online platforms to secure their ingredients as preferred components in the premium natural health space.

Geographically, China anchors the region as the primary engine for production, consumption, and digital distribution, while Japan, India, and South Korea serve as essential innovation and premiumization clusters. With an urban population surpassing 2.2 billion in 2025, market demand is highly concentrated around metropolitan pharmacies, supermarkets, clinics, gyms, and robust e-commerce fulfilment networks. This dense urban infrastructure dramatically optimizes customer acquisition economics, allowing scalable brands to efficiently reach their target audiences and drive long-term regional growth, establishing an expansive outlook across the 2025 to 2035 forecast period[97].

8.3. European Union[98]

The European nutraceutical market size was valued at USD 88.5 billion in 2025 and estimated to grow from USD 92.8 billion in 2026 to reach USD 117.7 billion by 2031, at a CAGR of 4.9% during the forecast period (2026-2031). This growth is driven by increasing spending on preventive healthcare, supportive policies for functional nutrition. Rising obesity rates and the related economic costs are pushing the market toward evidence-based solutions to delay the onset of chronic diseases.

Among product types, functional foods held the largest market share, while dietary supplements are expected to grow the fastest. In terms of source, plant-based ingredients generated the highest revenue in 2025, while microbial-based alternatives are expected to grow rapidly. In terms of distribution channels, supermarkets/hypermarkets accounted for the largest market share, but online retail stores are projected to grow significantly. In terms of geography, Germany led the market, while the United Kingdom is expected to record the highest CAGR by 2031. The market remains fragmented, with agile companies using direct-to-consumer models to target specific health needs, while established food and pharmaceutical companies such as Glanbia PLC, Amway Corp., and others expand their clinical-claim portfolios to maintain their market position.

The European nutraceutical market is growing as more people focus on preventive health and wellness. This shift has increased demand for products that help prevent chronic diseases and support overall health. Consumers are looking for supplements and functional foods that boost immunity, improve digestion, increase energy, and promote well-being. According to the World Health Organization, by 2025, 8.9 million more people in Germany are expected to experience better health, reflecting a broader trend of health awareness across Europe. At Vitafoods Europe 2024, a leading industry event, companies showcased innovative products to meet these needs. For example, Evonik launched AvailOm, an omega-3 powder with Boswellia extract for joint

[97] Asia Pacific Nutraceutical Market - analysis of key trends, regional growth, top players, and a 10-year forecast from 2025 to 2035.
[98] Nutraceutical in Europe Market - Share & Revenue

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health, and IN VIVO BIOTICS, a synbiotic solution to enhance gut health and immunity. These developments highlight the market's focus on creating effective and convenient nutraceutical products that align with the growing interest in preventive health.

Consumers in Europe are increasingly looking for clean-label and natural nutraceutical products due to growing awareness about ingredient transparency and a preference for healthier, minimally processed options. They want products without artificial additives, preservatives, or synthetic ingredients, choosing those with simple, natural components that fit a healthy lifestyle. This shift has pushed manufacturers to update existing products and create new ones that highlight organic certifications, natural extracts, and eco-friendly packaging. For instance, at Vitafoods Europe 2024, companies launched clean-label products like Naturacare's Vital Extend, a bilayer tablet with natural energy-boosting ingredients, and SIRIO Pharma's PureOrganix™ range, which includes organic gummies made with ingredients like evening primrose oil and flaxseed oil, catering to the growing demand for natural and transparent formulations.

Functional Foods lead the European nutraceutical market in 2025, holding a 36.1% share. The popularity of fortified cereals, probiotic dairy drinks, and protein-enriched bakery products drives this dominance. These items benefit from strong visibility in supermarkets, reduced sugar content, and high consumer loyalty. Fiber-fortified breakfast items and slow-digesting proteins remain household staples, while confectionery brands include plant sterols and omega-3s to cater to healthier snacking trends. Lactose-free specialty dairy drinks with probiotics further strengthen their position by addressing digestive health needs across all age groups.

Dietary Supplements are expected to grow the fastest, with a 6.7% CAGR through 2031, significantly contributing to the European nutraceutical market size during the forecast period. This growth is fuelled by precise dosing, tele-nutrition services, and condition-specific products like enzyme blends for digestion or botanicals for menopause relief. Personalized daily sachets improve adherence and customer retention, while clean-label sports-nutrition capsules attract a broader audience beyond athletes. As e-pharmacy regulations tighten in the region, brands offering clinically backed products in convenient formats are well-positioned to gain market share in both physical and online stores.

Plant-based ingredients made up 54% of the European nutraceutical market share in 2025, driven by the region's strong history with botanical extracts, herbal remedies, and fruit-based antioxidants. Consumers associate plant-based products with safety and sustainability, encouraging retailers to highlight eco-friendly labels and farm-to-table stories. Established suppliers use vertical integration and fair-trade certifications to ensure a steady supply of raw materials, while manufacturers combine different botanicals to create products targeting immunity, sleep, and metabolism. Examples like collagen from citrus peel and fermented soy isoflavones show how even traditionally animal-based or synthetic ingredients are shifting to plant-based options, helping maintain their leading position.

Microbial-based production is expected to grow at the fastest rate, with a 6.9% CAGR by 2031, making precision fermentation a key driver of the European nutraceutical market growth. Fermentation-based ingredients like riboflavin, resveratrol, and new postbiotic peptides avoid agricultural challenges, meet clean-label requirements, and reduce carbon footprints, appealing to environmentally conscious consumers. Collaborations between ingredient manufacturers and biotech startups have cut production costs compared to traditional methods, making these products more affordable. EFSA approvals for fermented bioactives further validate this approach, attracting investments for developing new strains and boosting their use in supplements and fortified foods.

8.3.1. Geography Analysis

Germany Nutraceutical Market

In 2025, Germany accounted for 19.2% of the European nutraceutical market share, driven by its strong focus on clinical testing and adherence to strict quality standards. These factors make German products highly appealing to health-conscious and cautious consumers. The country also complies with rigorous EFSA requirements, ensuring product safety and reliability. German companies actively collaborate with partners

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across Europe, sharing research and expertise. This commitment to quality and innovation has built a strong reputation for Germany, positioning it as a key leader in the European nutraceutical market.

United Kingdom Nutraceutical Market

The United Kingdom is the fastest-growing market, with a projected CAGR of 7.4% through 2031. Since Brexit, the United Kingdom has been quicker to approve new foods and adapt labelling regulations, giving it an advantage in the market. Local brands are focusing on innovative products like gummies for cognitive health and beverages for stress relief, which align with growing consumer interest in mental and physical well-being. This adaptability and focus on evolving health needs have positioned the United Kingdom as a dynamic and rapidly expanding market for nutraceuticals.

Southern Europe Nutraceutical Market

Southern Europe offers diverse growth opportunities in the nutraceutical market. Italy leads in per-capita supplement spending, driving demand for premium anti-aging products. Spain incorporates functional foods into its Mediterranean diet, promoting items like olive-oil-based spreads and fibre-enriched gazpacho. France combines its culinary traditions with expertise in beauty products, boosting the popularity of nutricosmetics such as collagen supplements for skin health. These regional trends highlight the unique consumer preferences and growth potential across Southern Europe.

8.3.2. European Competitive Landscape

The European nutraceutical market is highly competitive, with no single company dominating the industry. Leading companies like Nestlé SA, Glanbia PLC, and Herbalife Nutrition Ltd. are working to expand their operations across the value chain, from sourcing raw materials to delivering finished products. Despite their efforts, their combined market share remains below 30%, leaving significant opportunities for smaller and innovative companies to enter and grow. This competitive environment encourages innovation and allows new players to focus on specific consumer needs. Smaller companies often succeed by offering unique products or targeting niche segments, which helps them carve out a space in the market.

Technology is becoming a key factor in driving growth and innovation in the nutraceutical market. For instance, Danone's acquisition of The Akkermansia Company has enhanced its expertise in microbiome research, enabling the development of advanced gut-health products. These advancements are helping companies meet the growing demand for tailored and effective health products, which health-conscious consumers increasingly seek. Technology is also enabling companies to create more personalized solutions, which appeal to consumers looking for products that address their specific health needs.

Collaborations between companies are also playing a significant role in shaping the market by fostering innovation and improving efficiency. For example, Arla has partnered with Volac to establish a high-protein production hub in Wales, while AstaReal and Polaris are working together to create algae-based astaxanthin combined with plant omega-3s for athletic recovery. Startups are using regulatory technology to simplify compliance with European Food Safety Authority (EFSA) requirements, enabling faster market entry or licensing opportunities. These partnerships and advancements are helping companies remain competitive while addressing increasing regulatory challenges.

8.4. Nutraceutical Market Share

The top 5 companies in the nutraceutical industry include Nestlé S.A., Abbott Laboratories, Danone S.A., Herbalife Nutrition, Amway Corporation[99]. These are prominent companies operating in their respective regions covering 10.2% of the market share. These companies hold strong positions globally due to their experience in market. Their diverse product portfolios, backed by robust production capabilities and distribution networks, enable them to meet the rising demand across various regions.

[99] Nutraceutical Market Size, Share & Forecast 2034

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- Nestlé is the strong global player in the nutraceutical industry, with a product range covering vitamins, minerals, and functional foods. Besides a strong brand, Nestlé s competitive advantage is thus derived from a very extensive distribution network and focus on innovation. Nestlé emphasizes health and wellness in its investments in R&D to continue developing fundamentally obtained science-backed products.
- Abott is a vibrant player in the nutraceutical market space, particularly in health-related dietary supplements and functional foods. Abbott could be differentiated from other companies by focusing on how depending on scientific evidence proves product efficacy and quality. Building on very strong consumer confidence, that consumer trust about Abbott strengthens rigorous clinical research, investments in personalized nutrition, and digital health solutions.
- Danone is an important player in functional foods, particularly in the area of probiotics and nutraceuticals based on dairy. Danone has adopted consumers' trends in product lines that are health and wellness oriented. Danone's R&D, sustainability initiatives, combined with a regional focus on emerging markets, support its growth. The company's reputation is one of quality and innovation.
- Herbalife Ltd. is a specialist in weight management, nutrition & skin care products following a direct selling model that encourages an individual, personalized approach to customers. Its presence strength in brand equity, and global presence create a competitive advantage in the area of weight management. The company's network marketing scheme allows fast multiplication although it is under fire of scrutiny and presents regulatory challenges in some countries.
- Amway operates as a direct-selling model in which it sells various dietary supplements and functional foods. This, combined with an extensive distribution network and a diversified portfolio of products, provides a competitive edge because of the personal approach toward customers. In addition to this expanding and varied portfolio of products, Amway employs strong brand loyalty and an emphasis on quality to perpetuate its presence in the market.

8.4.1. Nutraceutical Market Companies

Major players operating in the nutraceutical industry include:

- Abbott Laboratories
- Amway Corporation
- Athletic Greens (AG1)
- Blackmores Limited
- Dabur India Limited
- Danone S.A.
- Garden of Life LLC
- Glanbia plc
- Herbalife Nutrition Ltd.
- Nature’s Bounty Co.
- Nestlé S.A.
- Otsuka Holdings Co., Ltd.
- Persona Nutrition
- Swisse Wellness Pty Ltd

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9. Italy in the Global Nutraceutical Market

The Italian dietary supplement and nutraceutical market stands as the undisputed leader in Europe, capturing over 25% of the total European market share. Valued at approximately USD 8.9 billion in 2025, the sector is projected to expand at a compound annual growth rate (CAGR) of 8.6% through 2033. This robust growth is fuelled by a unique combination of demographic shifts, consumer behaviour (an estimated 8 out of 10 Italians consume vitamins and dietary supplements), and a strong tradition of scientific and pharmaceutical excellence[100].

Italy features one of the world's oldest populations, with a median age exceeding 48 years and over 24% of citizens aged 65 and above. This fuels a structural demand for products targeting healthy aging, joint longevity, cardiovascular care, and cognitive maintenance.

In addition, unlike markets where supplement purchasing is a self-directed process, Italian consumers rely heavily on professional medical guidance. Purchasing decisions are primarily anchored by the advice of doctors, paediatricians, and pharmacists, driving demand for clinically proven, scientifically sound formulations

The reliance on professional consultation is starkly reflected in the distribution of sales across the country.

Distribution Channel	Market Share	Key Characteristics
Pharmacies	77.9%	The absolute dominant channel, heavily driven by pharmacist recommendations.
Mass Retail	7.7%	Primarily focused on lower-cost, generic vitamins and basic minerals.
Parapharmacies	7.6%	Offers over-the-counter wellness choices combined with professional oversight.
Online Retail (E-commerce)	6.9%	Rapidly growing among younger demographics, though still small compared to retail pharmacies.

9.1. Top-Performing Product Segments

- **Probiotics & Gut Health:** the most profitable niche in Italian pharmacies, accounting for over €537 million in sales.
- **Vitamins and Minerals:** traditional staples for immune support and daily vitality.
- **Proteins & Amino Acids:** the fastest-growing ingredient segment, driven by sports nutrition and senior muscle-mass preservation.
- **Clean-Label & Plant-Based:** a massive consumer shift away from synthetic multivitamins toward organic, personalized, and DNA-based or condition-specific botanical formulations.

9.2. Major Consumer Brands

- *Aboca* (Sansepolcro, AR): the European leader in 100% natural dietary supplements and medical devices based on molecular complexes[101].
- *PharmaNutra* (Pisa, PI): renowned for patented active ingredient absorption technologies, specifically sucrosomial iron (SiderAL)[102].

[100] digitalmarketingfarmaceutico.it
[101] Aboca - Per la salute di oggi e di domani
[102] Home - pharmanutra.it

- *Alfasigma* (Bologna, BO): a pharmaceutical giant formed by Alfa Wassermann and Sigma-Tau, with a strong focus on gastrointestinal and vascular supplements[103].
- *Menarini* (Florence, FI): Italy's largest pharmaceutical group, which operates a dedicated and highly successful nutraceutical division[104].
- *ESI* (Albisola, SV): produces food supplements, herbal remedies and natural cosmetics, with products distributed in more than 50 countries[105].
- *Unifarco* (Santa Giustina, BL): develops and produces supplement and cosmetic lines tailored for a vast European pharmacy network[106].
- *Laborest* (Milan, MI): part of the Uriach group, specializing in supplements for the musculoskeletal system and neurological well-being[107].

9.3. Regulatory Framework and Compliance

Entering the Italian market requires strict adherence to D.Lgs. 169/2004 (transposing EU Directive 2002/46/EC). While pharmaceutical pre-authorization is not required, companies must complete a mandatory electronic notification via the Ministry of Health's NSIS portal:

- **Operator Registration (OSA):** Companies must register their business (SCIA) and ensure their manufacturing facility holds standard health registrations (CE 852/2004).
- **Botanicals (Plant Extracts):** regulated by the strict Ministerial Decree of August 10, 2018 (Belfrit list[108]). Plants must have a recognized history of consumption prior to 1997 to avoid complex Novel Food authorization. Formulators must maintain a technical safety dossier proving the absence of contaminants and can only use physiologically approved claims.
- **Probiotics:** Italy utilizes pioneering guidelines. Products must guarantee a minimum of 1 billion live cells per strain per daily dose until expiration. Strains must be genetically identified, registered, and possess EFSA QPS status. The only permitted physiological claim is "Favorisce l'equilibrio della flora intestinale."
- **Labeling restrictions:** labels must explicitly state "Integratore alimentare," list ingredients by descending weight, highlight daily limits and Reference Nutritional Values (VNR), and include mandatory warnings regarding children and dosage limits.

9.4. The Tuscany Landscape

Tuscany has established itself as a global hub of excellence for the nutraceutical industry, effectively bridging the gap between rigorous university-led scientific research and advanced industrial production. The region is heavily supported by local government initiatives that fund the study of native functional ingredients.

9.4.1. Academic and Scientific Core

University of Pisa

The Nutrafood Interdepartmental Research Centre (Nutraceuticals and Food for Health)[109] at the University of Pisa brings together over 150 researchers and professors across a wide array of departments, including Clinical and Experimental Medicine, Pharmacy, Biology, Veterinary Sciences, and Agriculture. The centre's primary objective is to create powerful synergies between basic and applied research, utilizing highly interdisciplinary expertise to study the health benefits of foods and their active compounds.

Equipped with specialized laboratories and advanced research infrastructure, Nutrafood covers the entire research and development lifecycle. This comprehensive approach starts with primary production, studying

[103] Alfasigma Italia
[104] Consumer Healthcare - Gruppo Menarini
[105] https://www.esi.it/
[106] Unifarco
[107] Laborest - Nutraceutici con evidenze scientifiche
[108] Food supplements, the BelFrIt list of allowed botanicals - FARE
[109] Nutrafood – Università di Pisa – Centro Interdipartimentale di Ricerca Nutraceutica e Alimentazione per la Salute

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the factors that influence nutraceutical levels in food, and moves through laboratory identification, extraction, and experimental cellular testing, all the way to verifying clinical efficacy. To achieve this, the centre leverages cutting-edge capabilities in metabolomics, genomics, transcriptomics, biochemistry, pharmacology, and microbiology, ensuring thorough assessments of food biosafety, quality, and overall health value.
Beyond foundational research, the centre provides critical, direct support to the commercial industry. It conducts rigorous clinical and bioactivity testing to scientifically verify the safety and efficacy of new molecules, while also performing advanced sensory analysis to optimize the taste profiles and stability of functional foods. A major focus is placed on waste valorisation and upcycling, where the centre develops innovative extraction methods to recover high-value molecules from Tuscan agricultural by-products, such as grape pomace and olive pressing remnants. Additionally, Nutrafood actively partners with industry players to offer specialized training programs, such as the MasterFood, designed to educate and prepare the next generation of sector professionals.

Scuola Superiore Sant'Anna (SSSA)

Institute of Crop Science[110] develops scientific activities covering several aspects of the plant-based food production and supply chain. Global attention to this sector greatly increased in recent decades in relation to multiple factors, such as the need to produce and provide healthy, safe, and high-quality food for a growing world population, while reducing the environmental impacts. The Institute tackles major environmental and food security issues that impact on societal sustainability, according to United Nations Sustainable Development Goals. Interdisciplinary research and education activities are run by a group of researchers in the field of crop physiology and molecular genetics, agronomy and horticulture, microbes, soil and water sciences, and crop storage and processing.
Another interdisciplinary institute is the Interdisciplinary Health Science Cente Institute of Life Sciences[111], where researchers in fields related to medical sciences, bioengineering, computer science, management, social sciences, and law work together to promote global health and to effectively address the challenges facing healthcare systems. In particular, at the institute there a research groups with extensive experience in nutraceutics, collaborating with various regional and extra-regional companies on the development of functional foods and nutraceuticals, with particula reference to the protection of the heart and brain.

University of Florence

Interdepartmental Research Center for Food Valorization (CeRA)[112] brings together various departments from the University of Florence across the agricultural, pharmaceutical, and medical fields to study topics related to food quality, as well as its nutritional and functional aspects. It features specialized laboratories dedicated to agro-environmental analysis, sensory analysis, nutrient evaluation, and the analysis of molecules with nutritional and functional significance. Additionally, its facilities support research in nutrition pathophysiology, molecular biology for characterizing mutations and polymorphisms, economics, and marketing. Among its primary lines of research are the study of phenolic substances derived from complex plant matrices, pigments, and phytohormones, alongside the upcycling and valorisation of waste matrices within the agri-food sector.
The centre's primary objectives involve promoting, coordinating, and developing interdisciplinary research in the field of nutrition while continually improving laboratory techniques and methodologies. It aims to formulate coordinated research programs at both national and European levels, actively strengthening ties between domestic and international research centres. Beyond foundational research, the centre is deeply dedicated to scientific dissemination, organizing academic courses and master's programs, and managing post-graduate training. It also prioritizes technology transfer by interacting with producer and consumer organizations, offering targeted services to both groups, and working to obtain official recognition and certification for innovative products and processes.

[110] Institute of Crop Science | Scuola Superiore Sant'Anna
[111] https://www.santannapisa.it/en/health-science
[112] CeRA - Centro Interdipartimentale di Ricerca per la Valorizzazione degli Alimenti - UniFI

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University of Siena[113]

Several research groups are currently active at the University of Siena. The Department of Biotechnology, Chemistry and Pharmacy focuses specifically on studying the composition of numerous natural products to characterize their antioxidant and nutraceutical content, alongside conducting the corresponding *in vitro* testing. Additionally, the Department of Life Sciences is dedicated to the genetic traceability as well as the chemical and nutraceutical characterization of agri-food resources. This department also investigates the presence and recovery of nutraceuticals from food processing waste (upcycling) and studies the broader nutraceutical effects of natural antioxidants.

National Institute of Research (CNR)[114]

The Institute of agricultural biology and biotechnology (IBBA) mission is to advance the understanding of the molecular mechanisms regulating biological systems of agricultural interest (plant, animal, and microbial) at various levels of organization (cellular and organismal), serving as a foundation for programs aimed at optimizing and diversifying their use while enhancing overall agricultural production quality.

9.4.2. Tuscan Industrial Ecosystem & CDMOs

The region hosts cutting-edge companies that operate globally, offering both branded innovations and highly specialized Contract Development and Manufacturing Organization (CDMO) services:

- Aboca (Arezzo) is an Italian and international leader in health and wellness supplements and medical devices, distinguished by its commitment to 100% natural and biodegradable formulations derived from medicinal herbs. Operating under the philosophy of "innovating by tradition," Aboca reinterprets pathophysiological mechanisms by treating the body as an interconnected whole, rather than merely addressing isolated symptoms. Utilizing advanced research tools, such as Substance Object Maps (SOM) to analyze complex product compositions for safety and efficacy, the company develops natural matrices that support the body's internal homeostasis and effectively treat specific pathologies. Deeply rooted in the Tuscan hills with its advanced Factory 4.0 operations, Aboca operates a fully vertically integrated supply chain. It controls every step of the process, from the certified organic farming of raw materials to the rigorous pharmacological and clinical verification of its end products. This dedication to both human and planetary health is formalized through its legal status as an Italian Benefit Corporation (*Società Benefit*) and its certification as a top-scoring B Corp, reflecting a business model centered on the Common Good and biodiversity. Beyond manufacturing, the company actively promotes the link between nature, science, and society through its cultural outreach arms, the Aboca Museum and Aboca Edizioni publishing house. As of 2025, the company reported a robust turnover of €310 million and employs 1,800 people, including 400 working abroad. It maintains a strong global footprint with dedicated branches across six countries (Spain, France, Poland, the USA, Germany, and Belgium) proving that sustainable, nature-based innovation can successfully scale on the international stage.
- PharmaNutra (Pisa) was founded in 2003, and it is a rapidly expanding pharmaceutical and nutraceutical group specializing in clinical nutrition, dietary supplements, and medical devices aimed at restoring osteoarticular capacity. In 2025, the company reported a turnover of €132 million, operating with 100 direct employees and a specialized sales force of more than 160 professionals. PharmaNutra distinguishes itself through a strong focus on scientific innovation and direct control over its production chain. Rather than simply marketing existing formulas, the company focuses on proprietary research, achieving global recognition for two core innovations:

[113] Chimica per le Scienze Agroalimentari |
[114] Institute of agricultural biology and biotechnology (IBBA) | Consiglio Nazionale delle Ricerche

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- Sucrosomial® Technology, a highly bioavailable and stomach-friendly delivery system that forms the basis of its flagship SiderAL® iron supplements.
- Cetylated Fatty Acids (CFAs), a patented formulation utilized in brands like Cetilar® and Lipocet® to improve joint function, mobility, and provide musculoskeletal relief.

Backed by over 150 clinical studies and 21 global patents, PharmaNutra continues to scale its international footprint, driving strategic growth and brand visibility through its dedicated subsidiaries in key markets like the United States and Spain.

- BioDue [Healthea Group] (Barberino Tavernelle – FI) was founded in 1986 in the productive heart of Italy, BioDue is a premier Contract Development and Manufacturing Organization (CDMO) that serves as a cornerstone of the wider Healthea Group. In 2024, BioDue reported a dedicated turnover of €62 million with a workforce of 240 employees. Today, operating under the Healthea Group umbrella, which unites multiple companies, operates seven production facilities across Europe, and generates an overarching group turnover of €100 million, BioDue leverages extensive industrial scale and flexibility to serve the global healthcare market. The company specializes in the full-service development, manufacturing, and marketing of dietary supplements, foods for special medical purposes (FSMPs), medical devices spanning over 10 therapeutic areas, and cosmetics. Rather than operating purely as a manufacturer, BioDue acts as a strategic partner, offering highly customized, end-to-end solutions that guide clients from initial concept and formula development directly through to ready-to-market finished packaging. Supported by advanced R&D and stringent international certifications (including GMP, FDA, and various ISO standards), BioDue's versatile manufacturing hubs house over 60 production lines. This robust infrastructure allows the company to process everything from traditional formulas to highly complex, high-tech formats like unstable raw materials and probiotics. A standout innovation in their portfolio is the advanced "Caps-in-Caps" technology, a biphasic delivery system that enables the controlled, dual-release of active ingredients, optimizes bioavailability in targeted gastrointestinal sites, and ensures the stability of otherwise incompatible components within a single oral dosage.

- Buona (Sesto Fiorentino – FI) with over 20 years of industry experience, operating corporately as Buona S.p.A. Società Benefit / Steve Jones is an all-Italian company dedicated exclusively to pediatric health and maternal well-being. In 2024, the company achieved a turnover of €43 million, supported by a specialized workforce of 69 employees. Buona designs, develops, and markets a comprehensive portfolio tailored specifically to the needs of children from their very first days of life. The company's product lines encompass advanced infant formulas (such as the BBmilk range), targeted dietary supplements, and pediatric medical devices. Their formulations address a wide spectrum of childhood health categories, including immune system support, gastrointestinal balance (probiotics), respiratory wellness, sleep regulation, and dermatological protection. Operating at the intersection of rigorous scientific research and a deep-rooted commitment to family care, Buona places a strong emphasis on pediatric compliance. The company utilizes carefully selected raw materials, subjects every production batch to strict microbiological testing, and heavily focuses on optimizing the taste and format of its products to ensure they are both safe and well-received by children. Reflecting its guiding principles of "love, science, and the common good," the company formally operates as an Italian Benefit Corporation (Società Benefit). This legal status institutionalizes Buona's commitment to creating a positive social impact, ensuring that environmental sustainability, ethical production, and the overall well-being of future generations are firmly embedded into its core business model.

- LaBiotre (Tavarnelle Val di Pesa) was founded in 2011 and is an Italian company specializing in the advanced technological extraction of medicinal herbs. Combining deep industry expertise with a rigorous focus on quality, the company maintains full control over its botanical supply chain to supply premium raw materials for innovative softgels, capsules, and tablets. Recently integrating as a Benefit Corporation (Società Benefit) and securing strategic investment from the Labomar Group, LaBiotre generated a dedicated turnover of approximately €5.6 million in 2024. LaBiotre distinguishes itself

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through highly specialized, low-temperature extraction processes designed to preserve the delicate organoleptic and functional properties of the natural phyto-complexes. The company exclusively utilizes food-grade solvents (such as water, ethanol, and vegetable oils) to produce a wide range of botanical solutions, including multi-extracts, liposomal phytobilayers with enhanced bioavailability, and anaerobically fermented botanical substrates. A hallmark of LaBiotre's technological capability is its proprietary drying and granulation method, which yields Free Flowing Labiotre Granules (FFLG). This unique granular format ensures a highly uniform particle size and superior flowability, minimizing raw material loss and optimizing machine performance during the industrial manufacturing of dietary supplements. By closely linking raw botanical properties with targeted delivery technologies, LaBiotre provides highly standardized active molecules tailored to specific formulation needs across the health and wellness sector.

- Carepharm (Ciggiano - Arezzo), is a dynamic Italian company with over a decade of experience dedicated to the development of state-of-the-art natural dietary supplements. Operating at the intersection of nature and science, the company champions "avant-garde nutraceuticals," successfully applying rigorous pharmaceutical techniques to the highest-quality raw materials of natural origin to ensure optimal therapeutic performance. With a strong commitment to 100% Made in Italy excellence, Carepharm offers a highly effective portfolio that addresses a wide variety of therapeutic needs. Its product lines are specifically formulated to support sleep and mood (highlighted by the popular Ansioten range, including the innovative Ansioten Biotic which targets the gut-brain axis), intestinal and digestive health, cardiovascular wellness, and cognitive function. Backed by ISO 9001:2015 certification for stringent quality control and safety, every Carepharm supplement is formulated under strict protocols and regularly notified to the Italian Ministry of Health. Today, while maintaining its operational and production heart firmly anchored in Tuscany, the company is actively expanding its footprint through strategic B2B partnerships and a dedicated Export Department, aiming to bring its advanced natural health solutions to the broader international market.

- Hope Srl (Lucca), operating as Hope Nutraceuticals, is a dynamic Italian company with over 15 years of experience in the pharmaceutical and dietary supplement sectors. The company focuses on the rigorous research, development, and commercialization of innovative raw materials and high-quality nutraceutical formulations. Hope Srl distinguishes itself through an uncompromising approach to ingredient selection, investing heavily in sourcing certified, premium raw materials. Their research and development efforts are dedicated to creating advanced formulations that activate optimal synergy between specific active principles, ensuring maximum safety, bioavailability, and clinical efficacy for the end consumer. The company's expanding product portfolio addresses a wide spectrum of therapeutic and wellness needs. They offer targeted solutions developed specifically for neurological, psychological, osteoarticular, vascular, and aesthetic health, featuring specialized product lines such as Ripanerv, Colinbrain, and Harzati. Proudly rooted in the Tuscan territory, Hope Srl combines continuous scientific innovation, strict laboratory quality control, and an efficient distribution network to deliver concrete, science-backed health and wellness solutions across Italy.

- Falorni Nutra (Falorni Pharma Group – Sesto Fiorentino – FI) is a premier CDMO based in Sesto Fiorentino, Tuscany. The company is dedicated entirely to the highly specialized, third-party production and packaging of dietary supplements and probiotics. At the core of its operations is a state-of-the-art, 5,000-square-meter facility specifically designed and built to meet the rigorous demands of advanced nutraceutical manufacturing. Recognizing the delicate nature of live microorganisms and highly hydro-labile ingredients, Falorni Nutra has equipped this facility with a dedicated, custom-engineered HVAC system. Beyond core manufacturing, the broader Falorni Group leverages its deep pharmaceutical heritage to offer comprehensive, end-to-end services. This includes advanced secondary packaging, serialization, and logistics support, positioning Falorni Nutra as a highly reliable, full-service partner for pharmaceutical and food supplement brands worldwide looking to scale their probiotic and specialized nutritional portfolios safely and efficiently.operates a 5,000-

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square-meter facility dedicated entirely to highly specialized third-party production of supplements and probiotics.

- Laboratori Aliveda (Crespina Lorenzana – PI), is an Italian centre of excellence founded in 2013 and specializing in the development and manufacturing of innovative phytotherapeutic supplements. The company leverages a strictly scientific approach, blending traditional botanical knowledge with modern science to create targeted solutions across key therapeutic areas, including neurology, gastroenterology, and otolaryngology. A core strength of Aliveda is its ability to manage a complete, in-house vertical supply chain. Operating from a 3,000-square-meter manufacturing facility, the company controls every phase of the product lifecycle, from the meticulous sourcing of natural raw materials and the development of advanced formulations to full-scale production and commercialization. This structural autonomy allows Aliveda to operate as a highly adaptable CDMO and strategic B2B partner, offering flexible R&D, bespoke formulations, and production services tailored to meet international regulatory requirements for global commercial partners. Furthermore, Aliveda's commitment to scientific rigor is supported by active collaborations with the Department of Experimental Medicine at the University of Pisa. Through this partnership, the company conducts advanced in vitro testing on natural active ingredients, ensuring that their phytotherapeutic solutions offer clinical validity and consistent efficacy alongside conventional medicine

10. Nutraceuticals Key Market Trends

Prioritization of mental and immune health by consumers around the world is driving the sales of nutraceuticals that support stress relief, sleep, mood, and cognitive function. Companies are focusing on incorporation of vitamin C, zinc, probiotics, ashwagandha, L-theanine, and magnesium in their offerings. Formulations targeting burnout, anxiety, and sleep disorders are especially relevant amid rising workplace stress and digital fatigue. This nutraceuticals market trend is becoming central to product innovation and marketing.

Growing emphasis on veganism, ethical concerns, and environmental awareness are expected to bolster the sales of plant-based nutraceuticals. Nutraceuticals made from algae-based omega-3s, pea protein, or botanical extracts are highly preferred over animal-derived products. Brands are reformulating supplements and functional foods to exclude allergens, GMOs, and animal components while retaining efficacy and bioavailability. As plant-based lifestyles go mainstream, this nutraceuticals industry trend creates more new opportunities.

The demand for functional beverages is slated to rise at a robust pace over the coming years. Increasing incorporation of functional ingredients in beverages and abandonment of soft drinks is expected to help create new opportunities via this segment in the future.

11. Looking to the future of nutraceuticals

Nutraceuticals offer potential preventive care and in some cases treatment for diseases at a low cost. Nutraceuticals can offer faster development times and occasionally they can be administered as native compounds in herbal form or as core food ingredients. Their health impacts can be conveniently determined because epidemiological studies can establish their safety profiles, cutting down the time and cost of clinical trials. Disease prevention strategies are expensive and highly regulated. Nutraceuticals could help improve disease prevention, while cutting down cost, time, unpleasant medication, and clinical procedures.

11.1. Clinical recommendations

Nutraceuticals may be applicable for several different indications due to their multi-targeted actions. This necessitates elucidation of the various underlying mechanisms, pharmacokinetics, and pharmacodynamics of the active compounds. Preclinical research with active compounds would provide clarity for quality, efficacy, and mechanisms of action. Clinical evaluation of these natural compounds can provide further evidence of

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efficacy and safety of nutraceuticals. Clinical assessment will also provide a paradigm shift in nutraceutical classification as drugs rather than as supplements. Furthermore, drug discovery, development, preclinical and clinical testing receives significant funding internationally, whereas funding for research on nutraceuticals and supplements, which are consumed by over 170 million Americans, receives little investment. Further investment in clinical research for nutraceuticals will increase their status among scientists and increase consumer trust, thus also potentially increasing market value.

11.2. Future research recommendations

Considering the current regulatory frameworks surrounding nutraceuticals and growing public interest in this market, there is a need to identify and systematically summarize existing literature on the benefits and safety of nutraceuticals. Future studies need to identify opportunities and gaps in medicinal properties of nutraceuticals, key target markets, and propose steps to improve health using nutraceutical products. Epidemiological/observational studies can shed light on the effectiveness of these products as well as develop a safety profile for further clinical assessments. In this regard, meta-analysis of available clinical trials and/or pilot studies can be a useful tool to compare the effectiveness of two or more nutraceutical formulations. Collectively, these studies can provide the foundation for providing clinical recommendations and robust guidelines for effective nutraceutical marketing.

12. Conclusions

Nutraceuticals have emerged as a crucial segment in the global healthcare and wellness industry, driven by increasing consumer interest in natural health solutions, personalized nutrition, and preventive medicine. However, despite their growing market potential, the sector faces significant regulatory and scientific challenges. A major hurdle remains the lack of uniform definitions, classification systems, and standardized regulatory frameworks across different regions.

While developed markets like the USA, Europe, and Japan have established regulatory pathways, inconsistencies in safety assessment, labelling requirements, and approval processes hold back the harmonization of global trade.

Countries such as India and China, with strong traditional medicine systems, are incorporating nutraceuticals into mainstream healthcare, yet regulatory compliance remains complex due to varying levels of scientific substantiation and oversight. The efficacy and safety of many nutraceuticals remain under debate due to limited large-scale clinical trials and mechanistic studies. Although traditional medicinal systems like Ayurveda, Unani, and Siddha have long utilized plant-based nutraceuticals, their integration into evidence-based medicine requires further research. Addressing these gaps necessitates a multidisciplinary approach involving pharmacognosy, biotechnology, nanotechnology, and artificial intelligence to enhance bioavailability, stability, and targeted delivery of nutraceuticals.

The rapid advancements in nanotechnology-driven formulations, precision nutraceuticals, and artificial intelligence-based predictive modelling present opportunities to improve product development and therapeutic efficacy. However, ensuring consumer safety through rigorous quality control, post-market surveillance, and toxicological evaluations is paramount.

Future research must focus on standardizing analytical techniques, establishing robust clinical validation protocols, and harmonizing global regulatory policies to facilitate smoother market entry and consumer trust. Sustainability and ethical sourcing of nutraceutical ingredients also require urgent attention, given the increasing demand for plant-based bio-actives. Strengthening collaborations between industry, academia, and regulatory authorities will be key to overcoming current barriers and unlocking the full potential of nutraceuticals in modern healthcare. As the global interest in functional foods and plant-derived bioactive compounds continues to rise, bridging the gap between traditional knowledge and scientific validation will shape the future trajectory of the nutraceutical industry.

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