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Functional Foods and Nutraceuticals: Biochemical and Safety Insights

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Abstract

In recent years, food and pharmaceuticals have emerged as major players in the field of preventive healthcare. Interestingly, this modern concept of the role of food is echoed by the wisdom of ancient thinkers. ". . . differences of diseases depend on nutriments" was emphasised by Hippocrates over 2000 years ago when the correlation between food and diseases was little to none. His revolutionary insight laid the foundation for future research on establishing food as a prevention against diseases. This realisation has prompted the introduction of new concepts of 'Functional Foods' and 'Nutraceuticals' to determine our approach towards wellness through dietary modifications. With the increase in global interest and emphasis on FFs and nutraceuticals, understanding their biochemistry and mechanisms is crucial for their effective application. This article attempts to explore and examine the bioactive compounds in FFs and nutraceuticals and their benefits in disease prevention and as therapeutics. Moreover, holistic understanding, regulatory limits and safe administration of these nutritive products is essential for the suitability as well as best utilization.

Keywords: Bioactive Compounds; Diet; Food; Health; Nutraceutical; Regulatory; Supplements

Abbreviations

CVD: Cardiovascular Diseases; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; IBS: Irritable Bowel Syndrome; RCT: Reverse Cholesterol Transport; FDA: Food and Drug Association; EFSA: European Food Safety Authority; FSSAI: Food Safety and Standards Authority; SIBO: Small Intestinal Bacterial Overgrowth; CAGR: Compound Annual Growth Rate; MESC: Ministry of Education, Science and Culture; FOSHU: Foods for Specified Health Uses.

Functional Foods (FFs) and Nutraceuticals

Introduction

Functional foods are items that provide benefits beyond essential nutrition [1]. They can be foods with naturally occurring bioactive (e.g. turmeric), foods fortified with bioactive (e.g. probiotic dairy) or modified items with additional nutritive values (e.g. golden rice). They are non-specific biological therapies with extraordinary health benefits with role of stimulant sometime to increase immunity levels.

In 1984, the concept of 'functional foods' was formally introduced by a research team led by Professor Soichi Arai at the University of Tokyo under the "Systemic Analysis and Development of Functional Foods" project, which was funded by the Ministry of Education, Science and Culture (MESC) of Japan. In 1991, Japan's Ministry of Health and Welfare announced "Foods for Specified Health Uses (FOSHU)," the world's first policy to legally permit the commercialisation of functional foods. Its first product, hypoallergenic rice, was

approved in 1993 and made headlines in Nature News: "Japan explores the boundary between food and medicine" [2].

Functional foods contain bioactive compounds that aid in metabolism and other molecular processes. They are introduced as part of a regular diet and may contain compounds like polyphenols, fatty acids, carotenoids, and vitamins. They interact with various metabolic pathways to enhance homeostasis and regulate functioning, thus preventing diseases.

Nutraceuticals, conversely, are concentrated forms of bioactive substances extracted from food. In 1989, Dr Stephan L. DeFelice (M.D) coined the term 'Nutraceutical' by combining 'nutrition' and 'pharmaceutical'. As the term suggests, these food derivatives are consumed as supplements to provide therapeutic effect. They are available in various formulations, such as tablets, capsules, powders, and syrups. According to the modern concepts, the personalised nature of nutrition is vital in view of tailored dietary recommendations, dependent on diverse responses to functional elements approaches are well aligned with hygienic and health goals. These functional foods must be prepared, marketed and used in compliance to regulatory guidelines.

Importance in Modern Health

A part from the usual medical concerns caused by genetic defects and age-linked complications, chronic diseases caused by poor lifestyle are in prevalence. Diseases like cardiovascular diseases (CVD) and obesity, which were formerly prevalent in people of middle to older ages, are now widely observed in younger kids. Similarly, diseases caused by dietary negligence and poor diet are causing chronic disorders, among other factors like stress and pollution. As a result, medical experts have inclined towards utilising the benefits of FFs and nutraceuticals, which lies in their capacity to prevent and manage various chronic diseases. For instance, bioactive compounds like polyphenols have been linked to improving CVD by lowering blood pressure Figure 1.

Figure 1: Fruits-A Natural Source of Nutraceuticals.

Biochemistry of Bioactive Compounds

Bioactive substances provide benefits through complex physiological interactions between compounds and various physiological processes, such as enhancing enzymatic activity, antioxidation, and strengthening the immune system. The following are some of the many perks of incorporating nutraceuticals and FFs into a daily regime.

Antioxidant Properties: ROS are free radicals produced naturally during cellular metabolism. Production of ROS can increase through UV exposure, smoking and pollution. Its accumulation over time leads to damage of cells and tissue. Excess ROS can cause damage by oxidating bases of nucleic acids and cause mutation. Lipid peroxidation, the effect of lipid oxidation, is said to be one of the causes of neurodegenerative diseases like Alzheimer's and Parkinson's disease. Furthermore, ROS accumulation also results in damage to cardiovascular functioning and triggers cancer cell production by promoting metastasis.

Many compounds from FFs and nutraceuticals possess antioxidant properties. They combat oxidative stress by neutralising reactive oxygen species by donating an electron to the free radicals and converting them into more stable, i.e., less reactive molecules. Certain enzymes (e.g. glutathione) reduce ROS by breaking it down to hydrogen peroxide. Antioxidants protect lipids from oxidation [3].

Anti-inflammatory Benefits: Inflammation is an immune response towards invading particles like pathogens, damaged cells or other irritations. It aims to protect by removing the causal stimulus and initiate healing.

Various cytokines, enzymes and pro-inflammatory molecules (e.g. histamines and prostaglandins) contribute to inflammation by promoting vasodilation and increasing permeability in blood vessels. This allows immune cells and plasma proteins to arrive at the site of infection and initiate inflammation, phagocytosis and tissue recovery.

However, chronic inflammation leads to various diseases. ROS are produced as an immune response during inflammation, excess of which can cause tissue damage. Excessive inflammation also contributes by:

- Progression of CVD by causing plaque formation
- Promoting neurodegenerative diseases (like Parkinson's disease) by causing neuroinflammation
- Increasing insulin resistance and contributing to Type 2 diabetes and obesity

Bioactive compounds like curcumin act as an anti-inflammatory agent by downregulating the production of pro-inflammatory cytokines, thus helping to control

inflammation. Prostaglandins are produced by the action of enzymes called cyclooxygenases (COX-1 and COX-2). Nonsteroidal anti-inflammatory drugs (NSAIDs), like aspirin, reduce inflammation by targeting COX-2 [4]. Certain antioxidants, like sulforaphanes (found in cruciferous plants), are also known to control inflammation.

Modulation of Gut Microbiota: Gut microbiota is known to aid metabolism and comprises various microorganisms, primarily bacteria, fungi, and viruses. These organisms help break down complex elements (e.g., dietary fibres) that are not digested by enzymes. Moreover, these organisms contribute to the synthesis of various vital vitamins (e.g. B12). Some of these organisms are known to synthesise neurotransmitters like dopamine and serotonin, linking metabolism to cognitive health.

A healthy gut biome is essential for the proper functioning of metabolism. The imbalance of these organisms in the gastrointestinal tract leads to a condition called 'dysbiosis'. It is commonly caused by consuming highly processed foods, antibiotic usage and infection. It can lead to irritable bowel syndrome (IBS), obesity and type 2 diabetes. It can also lead to the weakening of the intestinal barrier and lead to a phenomenon known as 'leaky gut', where the permeability of the intestine increases, allowing toxins and pathogens to cross the barrier and enter blood flow [5].

Various bioactive can help enhance gut health. Prebiotics and probiotics are some of the most prominent and effective compounds beneficial for gut microbiota. Prebiotics contain non-digestible fibres, which selectively stimulate the activity of gut bacteria and increase their population. Probiotics contain live microorganisms which restore the biome balance when consumed in adequate amounts.

Cardiovascular Health: Cardiovascular disease (CVD) refers to a group of disorders that impact the heart and blood vessels. It is one of the leading causes of. Although various factors, like genetics and environmental factors, influence CVD, it is primarily experiencing a rise due to poor lifestyle.

The majority of CVDs are caused by high cholesterol, LDL, and hypertension. These lead to plaque formation, narrowing the walls and reducing blood flow. When the artery carrying blood to the brain is blocked, it leads to brain stroke. Hypertension, or high blood pressure, damages arteries and reduces blood circulation. Obesity also increases the risks of CVDs by increasing blood pressure. Deposition of fat occurs around the heart and blood vessels, which can obstruct blood flow, leading to brain stroke and heart attack. Similarly, insulin resistance developed in an obese individual and diabetic patient leads to high blood sugar and increased fat deposits around arteries. This deems them at high risk of CVDs.

Neuroprotection and Cognition: Neurodegenerative diseases like Parkinson's disease and Alzheimer's are proven to have a correlation with oxidative stress, mitochondrial damage and neuroinflammation. These factors affect neurons and deteriorate them over time, leading to cognitive and motor dysfunctions, and memory loss. Bioactive compounds, which help reduce the above factors, have shown potential in preventing neurodegeneration. Compounds like omega-3 and curcumin have been reported to be beneficial for cognitive health as they provide protection against ROS damage and inflammation [6].

Cancer Prevention: When a normal cell undergoes genetic mutation and grows uncontrollably, it gives rise to cancer cells. Some of these cells succeed in evading mechanisms of the immune system and lead to the formation of tumours. This mutation is triggered by various factors like inflammation, oxidation and genetic modifications. Defects in tumour suppressor gene (e.g. TP53), which functions in apoptosis of cancer cells, prevent it from producing necessary proteins, leading to uncontrolled growth of cells. Oncogenes responsible for cell growth turn into cancer-causing cells through genetic faults.

Antioxidants help prevent tumour formation by neutralising ROS, which causes DNA damage and genetic instability, leading to mutations. Anti-inflammatory compounds prevent cytokine formation in neurons involved in cancer progression [7]. Sulforaphane (present in broccoli) can induce apoptosis and is considered for therapy against tumours [8].

Ageing: Ageing is a natural phenomenon influenced by multiple factors, such as genetics, lifestyle, and environment. It is characterised by a decrease in physiological functions and susceptibility to diseases caused by the accumulation of cellular damage. Collagen protein is responsible for structural integrity and is present in skin, tendon, cartilage, and bone. This protein is degraded over time as a result of senescence.

Proper diet and lifestyle can regulate ageing by decreasing cellular damage. Bioactive compounds that aid in oxidative stress and inflammation help reduce cellular injury and slow senescence. Telomere metabolism is also closely related to oxidation status. As a result, antioxidants and anti-inflammatory agents can slow down the shortening of telomeres, which is a hallmark of ageing. Polyphenol compounds like flavonoids inhibit collagen degradation by reducing inflammation. Collagen production can be induced by consuming compounds which stimulate fibroblast (cells that contribute to collagen production). Geroprotectors like metformin (medication for Type 2 Diabetes) are studied in geroscience as a possible drug for longevity [9].

Bioactive compounds present in FFs and nutraceuticals are derived from various sources from plants and animals. In the following section, we will discuss the participation of various biological actives that contribute to health.

Polyphenols: Polyphenols are plant-derived compounds which are secondary metabolites of all vascular plants. It is characterised by one or more hydroxyl rings over a benzene ring, which gives it the ability to scavenge ROS. Apart from having exceptional antioxidation properties, polyphenols are anti-inflammatory, anti-allergenic and cardioprotective. It can increase cellular glucose metabolism by inducing the expression of GLUT1, and can be used as a therapeutic agent in diabetes treatment. Being equipped with multiple functions makes polyphenols a great therapeutic and functional compound.

- Flavonoids
- flavanols (e.g. catechin, theaflavin)
- flavonols (e.g. quercetin, kaempferol)
- flavones (e.g. luteolin, apigenin)
- isoflavones (e.g. daidzein, genistein)
- flavanones (e.g. eriodictyol, hesperetin)
- anthocyanidins (e.g. cyanidin, delphinidin)

Natural sources: Fruits (berries, apples, citrus fruits), vegetables (onion, broccoli, spinach, legumes), nuts (walnut, peanut, almonds), beverages (tea, wine) and cocoa.

Phenolic Acids: These are compounds derived from cinnamic acid and benzoic acid.

- hydroxybenzoic acid (e.g. gallic acid, salicylic acid)
- hydroxycinnamic acid (e.g. caffeic acid, coumaric acid)

Natural Sources: fruits (blackberries, grapes, pomegranates), vegetables (spinach, broccoli, radish), nuts (walnuts, hazelnuts, almonds), beverages (coffee, tea), and beans (black and white).

Stilbenes: Used in the manufacturing of dye. The most popular functional compound of this subclass is resveratrol (found in grapes, berries, cocoa, and peanuts), which is produced by plants as a secondary metabolite in response to injury or pathogen attack. This bioactive is widely proven for its multifactorial properties, including antioxidation, cardiovascular benefits, anti-inflammatory properties and anti-ageing effects [10].

Lignans have phytoestrogen properties, which lower breast cancer and menopausal symptoms in females. Predominantly found in flax seeds, lignans decrease the risk of CVD and osteoporosis [11].

Fatty Acids (Primary sources are fish and nuts)

- MUFAs (monounsaturated fatty acids): Increases level of HDL [12].
- PUFAs (polyunsaturated fatty acids): Predominantly found in flax seeds One of the few compounds that crosses the blood-brain barrier and induces cognition by reducing neuroinflammation [13]. These contribute as structural FAs for the integrity of cells and neural functions. Despite its functions, mammals lack a system to synthesise PUFAs.
- **Linoleic acid (omega-6):** Essential component of ceramide. Moderate intake can reduce LDL-C. Arachidonic acid (omega-6 FA) is a precursor for many lipid metabolites
- **Linolenic acid (omega-3):** Omega-3 FA, primarily EPA and DHA, participates in various functions, including transportation of compounds to and fro BBB., Supplementation during pregnancy leads to improved cognition in children.

HDL is predominantly known as 'good cholesterol' as function to reverse cholesterol transport (RCT) [14].

Carotenoids: Pigment found in red, yellow and orange fruits with antioxidative properties.

- Carotene
- α-carotene: Precursor of vitamin A, which produces collagen (structural protein). It also reduces ROS and supports eye and skin health. It can be found in carrots, pumpkins and sweet potatoes.
- β-carotene: Precursor to vitamin A and ROS scavenger. Found in green leafy vegetables, carrots and sweet potatoes.
- Lycopene: Found predominantly in tomatoes, it is a potent antioxidant and modulates gene expression to promote DNA and apoptosis.

Xanthophyll: Yellow pigment which possesses antioxidative properties and support eye health by acting as natural blue-light filters. These are sourced from algae and seafoods.

- Primary xanthophyll (lutein, zeaxanthin, β-cryptoxanthin)
- Secondary xanthophyll (astaxanthin and canthaxanthin)

Fiber: It is a complex carbohydrate which is non-digestible. It helps regulate blood sugar. Prebiotics are fibres which additionally stimulate gut microbiota.

- **Soluble Fibres (e.g. oats):** Water soluble and regulate hunger.
- **Insoluble Fibres (e.g. legumes):** Insoluble in water and help food move through the system

Vitamins

- **Vitamin A** derives retinoic acid, which shows anti-ageing properties by stimulating collagen production.

Also vital in optical health as it indirectly produces retinal, a critical component for vision. Examples: Fish, eggs, carrot.

Vitamin B Complex

- **Thiamine (B1):** It metabolises carbohydrates. Examples: Whole grains.
- **Riboflavin (B2):** Precursor for coenzymes involved in energy production and metabolism. Examples: Eggs
- **Niacin (B3):** Part of coenzyme NAD (essential in multiple cellular processes). Example: Chicken
- **Pantothenic acid (B5):** Involved in synthesis of coenzyme A. Example: Avocado
- **Pyridoxine (B6):** Involved in glycogenolysis and gluconeogenesis. Example: Poultry.
- **Biotin (B7):** Catalyse carboxylases involved in metabolism of amino acids, FAs and glucose. Examples: Eggs
- **Folic acid/ Folate (B9):** Crucial in RBC production and nucleic acid synthesis as a cofactor. Examples: Broccoli
- **Cyanocobalamin (B12):** Essential in neural functions and forms RBCs alongside B9. Examples: lean meat
- Vitamin D
- **Ergocalciferol (D2):** Synthesised by plants. Promotes bone health by regulating calcium and phosphate metabolism. Example: Mushrooms
- **Cholecalciferol (D3):** Synthesised by animals. Promotes calcium absorption. Example: Exposure to UVB rays is enough for self-production.
- **Vitamin E:** Potent antioxidant and protects lipids from oxidation, supporting health and immunity [15]. Example: Sunflower seeds.
- **Vitamin K:** Coenzyme in blood clotting. Example: green leafy vegetables.

Fortified/Modified FFs	Benefits
Dairy fortified with Probiotics Calcium	Enhancing gut microbiome for better metabolism Increasing bioavailability of calcium, preferably for growth of children
Cereals fortified with micronutrients	Enriched with nutrients, like iron, and enhanced flavour to help achieve daily micronutrient intake for children
Omega-3 eggs	Provide essential proteins and FA in one food item
Plant-based milk	Alternative for lactose-intolerant individuals; Gain nutrition from plant sources through milk
Nutritional drinks	Formulated for targeted consumers like children, elderly and athletes
Snack bars	Commonly formulated with higher protein and fiber content required
Golden rice	GM rice enriched with vitamin A
Gluten-free bread	Alternative for patients with digestive diseases or sensitivity and wheat allergy
Salt fortified with iodine	Target regular administration for preventing goitre
Fortified beverages Alkaline water Vitamin juice	Regulate decrease in pH caused by coffee and tea, which promotes acidosis Promote comprehensive intake of vitamins
Nutraceuticals	
Fish oil	Supplement for omega-3 and omega-6; Source:
Spirulina	Supplement for vitamin C, D, iron and other minerals; Source: BGA
Ashwagandha	Supplement for adaptogen (helps adapt to chronic stress) and vitamin C; Source: Ashwagandha root powder
Ginseng	Supplement for saponins which are anti-inflammatory and brain-stimulating; Source: Ginseng plant
Multivitamin	Supplement formulated with combination of multiple nutrients to fill the nutritional gaps with maximum efficiency

Table 1: Some popular nutraceuticals available in Indian market and their benefits.

Minerals

- Macro minerals: Includes calcium, magnesium, potassium, sodium, phosphorus, sulfur and chloride required for proper metabolism functioning and various processes. Sources are milk, leafy vegetables, banana, meat and sea salt.
- Trace minerals: Includes iron, zinc, copper and manganese. Example: Leafy vegetables, seafood and

whole grains.

- **Glucosinolates** (found in cruciferous vegetables like broccoli and cabbage) are sulphur-containing phytochemicals.
- **Sulforaphane** is a potent bioactive with multifaceted effects, from anti-cancer to neuroprotection. A study on Parkinson's disease concluded that treatment with sulforaphane prevents cell death of neural tissue [8].
- **Probiotic** are live bacteria beneficial for gut microbiome. They support pre-existing microbiota to enhance metabolism. Examples: yogurt.
- **Diarylheptanoid** (Polyphenol)
- **Curcumin:** This bioactive compound found in turmeric display potent therapeutic properties. It scavenges ROS as an antioxidant and exhibit anti-inflammatory effects by inhibiting NF-κB pathway and other proinflammatory processes Table 1. It is therapeutic as anti-cancerous as it induces apoptosis and metabolism of cancer cells. It prevents neurodegenerative diseases by preventing plaque formation of β-amyloid. It is known to help control CVD by reducing C-reactive protein (risk factor for CVD) [16].

Challenges and Consideration

Despite the increase in the trend for FFs and nutraceuticals, various difficulties are faced by industries and consumers. The bioavailability of intended bioactive compounds is crucial for their effectiveness. Certain compounds, like curcumin, have very low bioavailability. It is scarcely soluble in water and displays poor pharmacokinetics. As a result, it fails to exert its potential despite high dosages. Similar problems are displayed by other bioactive compounds, making it a problem for not only consumers but also for manufactures.

Solubility and stability of bioactive compounds is one of the major problems biotechnologists face. It is a challenge to dissolve compounds which are prone to sedimentation, are chemically instable or have low storage periods. Similarly, nutraceutical industries experience issues with drug efficacy. The efficiency of a bioactive compound changes with a change in its environment. It may prove to be beneficial when consumed from its source but might fail when consumed as an extract. Scientists proceed through various trials to ensure that the efficacy of the bioactive compound as a nutraceutical upholds the standard they intend to market. Additionally, these industries have to ensure the side-effects and biological implications over individuals of all ages, genders and chronic conditions since it is an over-the-counter projected to be consumed on a regular basis.

Infrastructure

The efficacy and safety of FFs and nutraceuticals depend highly on the quality of their extraction, processing and production. It requires advanced and careful infrastructure to ensure that the products are of superior quality. Nutraceuticals and FFs undergo a comprehensive process of manufacturing, production and quality control before being introduced into the market.

- **Manufacturing and Production:** The sources of bioactive compounds for FFs and nutraceuticals are similar but produced in different manners. The functional compounds are extracted ethically from their natural source of high quality. Scientists ensure that the extracts retain their activity at every subsequent step. Formulations and combinations are developed for FF fortification and nutraceutical production. A medium for bioactive administration is selected for FF, ensuring that the bioactive displays its intended benefit. Consequently, combinations are developed for nutraceutical supplements, aiming for good shelf life and preserved nutritional values. Finalised formulations of FFs and nutraceuticals undergo various safety tests as per guidelines before proceeding to suitable packaging.

- **Quality Control and Assurance:** Nutraceuticals and FFs are subjected to rigorous assessments by the quality control council through food or drug guidelines. The standards of regulations for various countries tend to differ significantly. In USA, the Food and Drug Association (FDA) regulates production of these functional supplements. Since nutraceuticals are not subjected to as rigorous pre-market approval as pharmaceuticals, their efficacy and safety lie solely on manufacturers. Moreover, USFDA is restricted to oppose its report after the product is marketed [17].

In Europe, the European Food Safety Authority (EFSA) evaluate claims on FFs and nutraceuticals. Food Safety and Standards Authority (FSSAI) ensures the quality of nutraceuticals and FFs in India.

Regulation and Safety

Functional foods and Nutraceuticals are promising frontiers in therapy through nutrition. Despite their capacity, a critical issue is lack of standardised regulation, scientific validation, counterfeit products, overconsumption and consumer awareness. Discrepancies between food and drug category result in variety of quality control standards across nations. Comparative to most nations, FSSAI has more stringent regulations [18]. A few key aspects of nutraceutical regulations in India are:

- All business operators dealing with FFs and nutraceuticals must register with FSSAI and acquire licences based on different categories based on the scale of operations.

FSSAI set standards for manufacturing, processing and packaging to ensure safety.

- Functional food and nutraceutical products must adhere to strict labelling guidelines that demand ingredient transparency, nutritional information and recommended dosage.
- Health claims must be substantiated with reliable scientific evidence to avoid misleading advertisements.
- Anti-counterfeit measure is emphasised by FSSAI to protect consumers from fake products.

Despite the regulations, the availability of counterfeit products is jeopardizing consumer safety and damaging reputed brands. Variability in active ingredient concentration, inconsistency in quality and lack of scientific trials compounds the problems as many side-effects go unnoticed.

It is essential to understand that the quality hallmark by the council doesn't guarantee the efficacy of nutraceuticals and FFs. Proper storage, health condition and suggested dosage are necessary to experience gains of functional compounds. Storage of supplements and foods as labelled is necessary to protect them from degradation and maintain potency. Awareness of diseases caused by nutrient deficiency intensifies preference for FFs and nutraceuticals, but discussions over overdosage and its side effects are notably lacking. Consumption of bioactive compounds at labelled dosage is necessary to receive the proposed benefits. Overdosing bioactive compounds may cause varied side effects. While the severity of side effects caused may vary, its biochemistry remains unchanged.

Accumulation of ROS is the leading cause of damage in cells, tissues and organs. Its role in cell signalling is a lesser-known fact by consumers. Low levels of ROS are necessary for normal functioning of biochemical processes. Excessive consumption of antioxidants will lead to loss of ROS-mediated signalling, where it acts as a secondary messenger. ROS is produced by immune cells as an 'oxidative burst' to kill pathogens. Reduction of ROS will adversely lead to increased susceptibility to infections and diseases [19].

Hypervitaminosis is a condition caused by overdosage of vitamins. In addition to imparting its benefits, different vitamins at higher dosages impart varied effects. Pyridoxine overdosage was reported to cause neuropathy in a case report. When examined, self-administration and not adhering to dosage resulted in neurotoxicity [20].

Hypernatremia is a disorder caused by disturbed homeostasis of water and sodium levels. It can cause brain cell shrinkage on acute levels and may lead to pulmonary edema post 48 hours [21].

Hypercalcemia is an overdosage of calcium. Excess calcium doesn't get absorbed and either calcify at joints, leading to severe conditions like osteoarthritis or accumulates as kidney stones. A suicidal case of mineral toxicity was observed through autopsy. A large quantity of iron tablets was ingested as a suicidal attempt, leading to death after 65 hours. Autopsy showed elevated serum iron levels and deposition of iron on gastric rugae [22].

Prevalent consumption of coffee and tea increases pH and acidity. When pH drops below a level, acidosis occurs. Alkaline water is a product marketed to deal with this increase in acidity. The underlying adverse effect is an increase in pH from the normal range, which will cause 'alkalosis'. It is characterised by shortness of breath, arrhythmia, nausea and numbness, among many other symptoms [23].

Probiotics are generally safe, but similar to other bioactives, its extreme usage will cause bloating and diarrhea. It can also cause infection and trigger immune responses. Small intestinal bacterial overgrowth (SIBO) is a condition caused by excessive growth of gut bacteria. Abdominal pain, nausea, bloating and vomiting are few of the many symptoms of SIBO.

These problems, although prevalent, can be addressed by constructing a multi-faceted system with more clinical trials, improved regulations and increase in public education. Meanwhile, consumers can rely on medical consultants and educate themselves on these products and their benefits.

Current Research and Prospects

The global functional food market is expected to reach $228.79 billion in 2025 from $161.99 billion in 2020, with a compound annual growth rate (CAGR) of 8%. Whereas, the Indian nutraceuticals market size was estimated at USD 26.87 billion in 2023 and is projected to grow at a CAGR of 13.5% from 2024 to 2030. Increasing demand and trend of relying on FFs and nutraceuticals are driving scientists to conduct more comprehensive studies on bioactive compounds. Various studies are underway to discover therapeutic effects of bioactives. Functional compounds are being explored by medical professionals for managing chronic lifestyle diseases like diabetes, obesity, CVD, etc. Advancements for creating technology shaped through machine learning, particularly artificial intelligence, may aid in creating personalised nutrition plans derived from real-time data and wearable technologies. Currently, FFs and nutraceuticals are the mode for delivering bioactives for maintaining daily nutrition intake. In the future, new delivery systems such as nanoencapsulation and 3D-printed supplements are being discussed among bioengineers and biotechnologists. These new propositions will allow dosage to be more precise and

uptake of bioactive to improve the efficacy of administering nutrients.

A new concept for organically manufacturing bioactives called 'pharming' (pharmaceuticals + farming) is being established. Scientists create transgenic animals to make human proteins of medicinal value and then extract them. Livestock have been proven useful in producing required proteins. Production of various other nutrients through transgenic animals is currently being studied gradually while adhering to bioethics.

Despite the aspirations, this field continues to faces challenges such as need for robust and reliable clinical validations. Nevertheless, the synergy between science, technology and sustainable health practices will drive innovation of enhanced functional food and nutraceuticals.

Conclusion

FFs and nutraceuticals are consistent in providing their designated benefits. Their obvious interventions in biochemical processes to decrease cellular damage and enhance metabolism to avoid diseases have not gone unnoticed. This has resulted in driving medical experts to promote and utilise them as therapeutics for chronic disorders. Despite its merits, these bioactive compounds are working adversely due to their consumption without proper awareness. Consumers need to be educated and informed about misconceptions supporting that 'overuse of food and its derivatives is not possible', along with lack of scientific data supporting side-effects of overdosage.

Conflicts of Interest

The authors declare no conflict of interest.

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