JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Bioavailability of Nutraceuticals: Challenges and Opportunities

Mr. Aditya Kirmirwar ,Dr. S. Mhaske , Dr. P. Fitwe , Mr. Ganesh Mehta ,
Mr. Prathamesh Masne
Student
Satyajeet college of pharmacy

1.INTRODUCTION

1.1. NUTRACEUTICALS

Nutraceuticals are oral dietary components naturally found in foods and believed to have a medical or health benefit. Dr. Stephen Defelice, who combined the words ‘‘nutrition’’ and ‘‘pharmaceutical,’’ coined the term in 1989.[1]

Foods that are naturally high in nutrients, like spirulina, garlic, and soy, or particular parts of foods, such omega-3 oil from salmon, might be considered nutraceuticals. They go by other names, such as dietary supplements, nutritional supplements, and medical foods. The products that fall under this category include separated nutrients, nutritional supplements, genetically modified "designer" foods, herbal goods, and processed foods like cereals and soups. Their purported safety as well as possible nutritional and medicinal benefits have piqued curiosity.[3]

One of the most crucial research topics is the function of dietary active chemicals in human nutrition, with broad ramifications for industry, regulators, consumers, and healthcare professionals (Bagchi D, 2006). Foods and nutrients are essential to the body's regular operation. They assist in preserving an individual's health and lowering their risk of contracting certain illnesses. As a result of the widespread acknowledgment of this fact, the relationship between"nutrition" and "health" was established, and the term "nutraceuticals" developeloped.

Nutraceuticals are a vast class of compounds found in both natural and processed foods that are said to have positive effects on human health and wellness. Examples of these compounds include vitamins, carotenoids, flavonoids, curcuminoids, polyunsaturated fatty acids, proteins, peptides, dietary fibers, oligosaccharides, and minerals.

Nevertheless, the potential benefits of many of these compounds are not fully realized due to their relatively low and/or variable oral bioavailability.

The low bioavailability of nutraceuticals can be caused by a variety of physicochemical and/or physiological processes, such as restricted liberation from the food matrix, low solubility in gastrointestinal fluids, and formation of insoluble complexes with other components in the gastrointestinal tract (GIT). [2]

The largest organ in the human body, the skin ages naturally as a result of both internal and external influences. While external factors like tobacco smoke, ultraviolet (UV) radiation, poor nutrition, and hormone imbalances can hasten the aging process of cells, internal variables are part of the natural aging process within cells.Numerous internal and external elements, including the biologic evolution of cells, ultraviolet (UV) radiation, tobacco use, nutritional inadequacies, and hormonal imbalances that cause skin cell disintegration, all have an ongoing impact on skin aging. Free radicals and inflammation cause skin cell deterioration, which impairs healing mechanisms and breaks down collagen and elastic fibers. Ageing skin is characterized by telangiectasias, wrinkles, roughness, loss of elasticity, and diminished pigmentation.[1]

Health Applications: Nutraceuticals have been associated with various health effects, such as:

- **Antioxidant Activity**: Some nutraceuticals act as antioxidants, protecting our cells from oxidative damage.
- **Anti-Inflammatory Properties**: Certain compounds help reduce inflammation in the body.
- **Anti-Cancer Potential**: Researchers have explored nutraceuticals for their potential in cancer prevention and treatment.
- **Cholesterol Regulation**: Some nutraceuticals may help manage lipid levels.
- **Overall Well-Being**: Nutraceuticals contribute to general health and longevity.[3]

1.1.2. CLASSIFICATION OF NUTRACEUTICALS

Nutraceuticals are categorized on the basis of foods available in the market:

1) Traditional nutraceuticals

2) Non-traditional nutraceuticals

1) **Traditional nutraceuticals** are simply natural with no changes to the food. Food contains several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in salmon or saponins in soy

2) **Non-traditional nutraceuticals** are artificial foods prepared with the help of biotechnology. Food samples contain bioactive components which are engineered to produce products for human- wellness.[4]

1.2. BIOAVAILABILITY OF NUTRACEUTICALS

The amount of a medicinally active ingredient that enters the systemic circulation and is accessible at the site of action is known as its bioavailability. It is among a drug's or phytochemical's most important pharmacokinetic characteristics. Plant polyphenols, which include curcumin, resveratrol, epigallocatechin gallate, and so on, and carotenoids, which include lycopene, β-carotene, lutein, and zeaxanthin, have drawn significant interest from the scientific community, consumers, and food manufacturers due to their potential applications in lowering blood pressure, decreasing cancer risk factors, regulating the digestive tract, bolstering immune systems, regulating growth, controlling blood sugar levels, lowering cholesterol, and acting as antioxidant agents.[2]

Many bioactive ingredients' bioavailability is influenced by the type of food matrix they are ingested with. Nutraceuticals that are coingested may have different bioavailabilities depending on the food matrix's structure and composition. Because food matrix qualities affect oral bioavailability, food formulations can be tailored to enhance

the biological activity of nutraceuticals. For instance, nutraceuticals that are included in or coinested with functional foods or excipient foods can be developed to enhance their oral bioavailability.[2]

1.2.1. ORAL BIOAVAILABILITY OF NEUTRACEUTICALS

The percentage of a nutraceutical that is actually absorbed and enters the systemic (blood) circulation in an active form is known as the oral bioavailability of the supplement. It is only with these nutraceuticals that they can be delivered to the organs and tissues where they can work their healing magic. There are several obstacles that hinder ingested nutraceuticals from entering the bloodstream in an active state, including first-pass metabolism, poor solubility in GI fluids, delayed absorption from the GIT, and chemical instability after digestion.[5]

1.2.2. BIOLOGICAL FATE OF NEUTRACEUTICALS AFTER ORAL ADMINISTRATION

Oral administration of bioactive agents is a favored route for chronic disease prevention or treatment since it requires low level of application skills, cutbacks the likeliness of disease transmission, reduces medical cost and allows flexible intake schedule. However, upon oral administration, the physicochemical environment of GI tract may partially influence the solubility, stability, bioavailability and efficacy of nutraceuticals depending on their specific chemical structures. First-pass metabolism by intestinal cells and the liver considerably lowers the concentration of bioactives that enter the systemic circulation after absorption by the gut wall. In order to increase a compound's oral bioavailability, delivery systems with functional properties that can improve solubility, enhance cellular uptake and transport, alter compound release kinetics, and bypass rapid metabolic activities have become increasingly popular in numerous studies. A synopsis of the basic physiological and physicochemical processes involved in oral drug administration, digestion, absorption, and metabolism is given in this section. [6]

2.FACTORS AFFECTING BIOAVAILABILITY OF NUTRACEUTICAL

External Factors	Environmental factors and food availability
Food Processing related factors	Thermal treatment, homogenization, cooking and methods of culinary preparation, storage
Food related factors	Food Matrix, Presence of positive or negative factors for absorption
Interaction with other compounds	Bonds with proteins or polyphenols with similar mechanism of absorption
Polyphenols related factors	Chemical structure, amount introduced and concentration in diet
Host-related Factors	Intestinal factors and systemic factors

2.1. ENDOGENOUS FACTORS

2.1.1. INTERACTION OF NUTRACEUTICALS WITH GASTROINTESTINAL TRACT

The oral cavity (mouth), stomach, small intestine, and large intestine (colon) are the various parts of the gastrointestinal tract. Their physiological processes, digestive environments, and points of position are different. To understand the mechanisms impacting the bioavailability of nutraceuticals, the important characteristics of each sector within the GIT are covered in this section.[7]

MOUTH:-

The "entry gate" for food entering the GIT is the mouth. Here, food items are diced up using mechanical operations and combined with saliva to create boluses. The saliva is a complex fluid with a pH of 5.0 to 8.0 that is released by the salivary glands. Saliva is composed of 99.9% water and 0.5% other substances that play a significant role in the masticatory process and ensure food lubrication. These substances include electrolytes (Na^+, Cl^-, K^+, and HCO_3^-) that ensure food dispersion and dilution, proteins (staterins, proline-rich proteins, histatins, and lysozomes), and salivary peroxisomedase. Depending on the kind of food, the length of time food stays in the mouth varies, ranging from a few seconds for liquids to several minutes for semisolid and solid foods.[7]

STOMACH:-

The bolus that forms in the mouth is initially ingested by the esophagus, after which it travels into the stomach cavity and combines with the stomach secretions to produce the gastric chyme. The stomach's capacity is 1.5 liters when it is fully loaded, and it secretes 2.5 liters of gastric juice every day due to the action of specialized cells like parietal cells, which release hydrochloric acid (HCl); chief cells, which release pepsinogen, which is converted into pepsin by the action of HCl; G-cells, which release gastrin, which aids in the reconstruction of the stomach mucous membrane; and goblet cells, which release mucin. With a pH of between 0.9 and 1.5, gastric juice has a high acidity level. It also contains many substances such as water (99%), HCl (0.4% to 0.5%), pepsin, lipase, glycoprotein, and mucus, as well as calcium, sodium, and potassium salts. The pH may fluctuate between 1.5 and 4.0 over the three to four hours that stomach digestion may take. Food matrices and nanoparticles are altered by the physicochemical processes that occur in the stomach, such as the digestion of proteins and fats, the mechanical stresses brought on by gastric movement, and so on. The rate of gastric emptying is a significant factor in the bioavailability of bioactive compounds, such as pharmaceuticals and nutraceuticals. This rate is impacted by various factors such as the meal's type and volume, food matrices' composition and physicochemical properties, consumers' emotional states, and the body itself.[7]

SMALL INTESTINE:-

The duodenum, jejunum, and ileum are the three sectors that make up the small intestine, which is the longest part of the human gastrointestinal tract (6 to 8 m). The "pylorus sphincter," a valve that opens and shuts permanently,

allows the gastric juice to go from the stomach into the duodenum where it is combined with the intestinal fluid. Pancreatic juice, intestinal juice, and bile are the three digestive juice types combined to make the intestinal fluid. The pancreas secretes 1,500 mL of pancreatic juice per day, which is composed of water, inorganic salts (sodium, potassium, and calcium bicarbonate), and pancreatic enzymes (trypsinogen, chymotrypsinogen, procarboxypeptidase, nucleotidases, elastase, collagenase, lipase, lecithinase, cholesterol esterase, and amylase). The pH of pancreatic juice is alkaline (8.0-8.3). Contains proteolytic enzymes (dipeptidase, aminopeptidase, nucleotidases, nucleosidase, and arginase), enzymes that break down carbohydrates (amylase, sucrase, maltase, lactase, etc.), and enzymes that break down lipids (lipase). The specialized cells in the small intestine secrete 1,500 mL of intestinal juice per day. Its pH is in the range of 6.3 to 9.0. The liver secretes or excretes bile, which is then held in the gall bladder (700 mL each day). With a pH range of 7.0 to 7.7, bile is an alkaline fluid with a complex composition. It comprises various inorganic salts, such as carbonates, bicarbonate, sodium taurocholate, and sodium glycocholate, as well as bile pigments like bilirubin, cholesterol, lecithin, and trace amounts of fatty acids and soaps. The most thorough breakdown of food takes place in the small intestine because of the distinct activities of the enzymes lactase, proteases, lipases, amylase, and maltase. The small intestine guarantees the maximum absorption of nutraceuticals and nutraceutical-loaded nanoparticles because of its enormous size (260–300 m2)*.[7]

LARGE INTESTINE:-

The large intestine or colon is the final GIT segment collecting and eliminating all that remains undigested in the stomach and small intestine. For instance, diet fibers (cellulose, pectins, resistant starch, etc.) in the ingested foods are not digested in the stomach or intestine, but they are fermented in the colon under the action of over 400 species of the bacteria. In order to cure the diseases such as colon cancer, irritable bowel syndrome, and destruction of certain parasites (amebiasis), local treatment is necessary at colon level. That is why a targeting strategy for the bioactive substances in the colon is their encapsulation in the gastro-resistant materials that do not degrade in acidic pH or under the action of gastric and intestinal enzymes, such as anionic polymers (pectins, guar gum, alginic acid, carrageenans, etc.) andmethacrylic acid copolymers. These polymers are water soluble within the pH range of 6.5 to 7.5 allowing the release of bioactive substances within the colon.[7]

2.1.2. INTERACTION WITH OTHER DIETARY COMPONENTS

Research on the relationship between food and nutraceuticals is a complicated and developing field. They can both affect and be influenced by different food components. Here are a few crucial exchanges to think about:

BIOAVAILABILITY:-

• Fats in Diet: Dietary lipids are necessary for the best absorption of several nutraceuticals, particularly fat-soluble

vitamins (including vitamins A, D, E, and K) and phytochemicals (like carotenoids).[13,16]

• Fiber: High-fiber diets can bind some nutraceuticals, decreasing their absorption. For instance, fiber may reduce some minerals' and antioxidants' bioavailability.[9]

SYNERGISTICS EFFECTS:-

• Complementary Nutrients: Nutraceuticals' benefits might be amplified when paired with particular meals. For example, when combined with vitamin C, iron absorption from plant sources might be enhanced.[17,18]

• Polyphenols and flavonoids: These substances, which may be found in tea, red wine, and fruits and vegetables, may enhance the health advantages of other antioxidants by collaborating with them. [19]

ANTAGONISTIC MOVEMENT:-

• Competing Nutrients: Some minerals, including magnesium and calcium, may compete with nutraceuticals for absorption, which might lessen their efficacy.[20]

• Medication: Certain nutraceuticals may have a detrimental interaction with certain drugs, changing how well they are absorbed or work. For instance, grapefruit juice may prevent some medications from being metabolized.[19]

DIRTARY PATTERNS:-

• Mediterranean Diet: Because of its high antioxidant content and advantageous lipid profile, this diet, which is heavy in fruits, vegetables, whole grains, and healthy fats, might augment the effects of nutraceuticals. [19]

• Western Diet: This diet, which is heavy in processed foods and poor in nutrients, may cause nutraceuticals to interact less well, reducing the potential health advantages.[20]

GUT MICROBIOTA:-

Modulating the gut microbiome using nutraceuticals can impact the metabolism and absorption of nutrients. Through the promotion of a healthy gut environment, probiotics and prebiotics can augment the advantages of nutraceuticals.[21]

2.2. EXOGENOUS_FACTORS

2.2.1. PHYSIOCHEMICAL PROPERTIES OF NUTRACEUTICALS

- The bioavailability of nutraceuticals, which are food-derived products with health benefits, is influenced by several physiochemical properties. Here are the key factors:
- Solubility: The extent to which a nutraceutical dissolves in bodily fluids affects its absorption. Generally, higher solubility leads to better bioavailability.[22]
- Stability: Nutraceuticals must be stable in their formulation to retain their efficacy. Factors like pH, temperature, and light exposure can affect stability.[5]
- Molecular Weight: Smaller molecules tend to be absorbed more easily in the gastrointestinal tract. Larger molecules may require specific transport mechanisms.[5]
- Lipophilicity: The affinity of a compound for lipids can enhance absorption, particularly for fat-soluble nutraceuticals, which may require dietary fats for optimal uptake.[23]
- Formulation and Delivery System: The form in which a nutraceutical is delivered (e.g., capsule, tablet, liquid) can influence its release and absorption. Encapsulation techniques can protect sensitive compounds and enhance bioavailability.[24,25]
- Particle Size: Smaller particle sizes increase surface area, enhancing dissolution and absorption rates.[17]
- pKa and Ionization: The degree of ionization at physiological pH can impact solubility and permeability across cell membranes.[5]
- Presence of Other Compounds: Interactions with other nutrients, dietary components, or drugs can enhance or inhibit absorption. For example, some vitamins and minerals may compete for absorption.[20]
- Gastrointestinal Motility: The speed at which food moves through the digestive tract can affect nutrient absorption. Nutraceuticals may be absorbed more effectively when gastrointestinal motility is optimal.[7]
- Microbiome Interaction: The gut microbiota can influence the bioavailability of certain nutraceuticals by metabolizing them into more bioactive forms.[21]

Understanding these properties helps in the formulation and development of nutraceuticals to maximize their health benefits through improved bioavailability.

2.2.2. FOOD MATRIX AND PROCESSING METHODS

Nutraceuticals are the bioactive chemicals in food that offer health advantages. The food matrix and processing techniques can have a substantial impact on the bioavailability of these compounds. Let's examine these two variables in more detail:

- FOOD MATRIX

Food Matrix Structure: Proteins, fibers, carbs, and lipids can all affect how well nutraceuticals dissolve and are absorbed. For example, diets high in fat improve the absorption of fat-soluble vitamins, such as A, D, E, and K.[8,14,15]

Physical State: How nutrients are released during digestion might vary depending on the food's form (solid, liquid, or powder). For example, liquid or emulsified forms may improve a particular compound's absorption.[9]

Relationships with Other Substances: Certain nutrients can promote or prevent the absorption of other substances. For instance, through their synergistic actions, certain phytochemicals (like flavonoids) can increase the bioavailability of other nutrients.[10]

Food Structure: Digestion may be impacted by the microstructure of food, or the arrangement of its cells and tissues. For example, compared to processed diets, unprocessed foods may release bioactive chemicals more slowly.[11]

- PROCESSING METHOD

➢ Cooking: Techniques such as boiling, roasting, or steaming might change how bioavailable nutrients are. For example, boiling tomatoes releases more lycopene, but overcooking might destroy some vitamins.[12]

➢ Fermentation: By dissolving complicated substances and generating bioactive metabolites, this process can increase bioavailability. Dairy products with fermentation, for instance, can enhance the body's ability to absorb calcium and other minerals.[13]

➢ Extraction and Concentration: The concentration of bioactive chemicals may be raised by techniques like juicing or extracting them, which may improve their bioavailability. However, the removal of fibers may also impair the overall health advantages.[10]

➢ Microencapsulation: This method can enhance the stability and absorption of delicate substances in the gastrointestinal tract while shielding them from deterioration.[8]

➢ pH Variations: The solubility and stability of several nutraceuticals can be affected by changes in the acidity or alkalinity of food. For example, the pH of the digestive tract influences the absorption of curcumin from turmeric.[11]

3. CHALLENGES IN BIOAVAILABILITY

The degree and speed at which the active components of nutraceuticals are absorbed and made accessible at the site of action is referred to as bioavailability. Although nutraceuticals have been shown to have potential health advantages, their bioavailability is hampered by a number of issues. Comprehending these obstacles is essential for refining formulations and augmenting the effectiveness of treatments.

3.1. Poor Solubility:- The limited solubility of many nutraceuticals in gastrointestinal fluids, especially phytochemicals and some vitamins, restricts their absorption. For instance, the bioactive ingredient in turmeric,

curcumin, has a poor water solubility and a restricted bioavailability. It's crucial to find ways to increase solubility, including employing liposomal formulations or solid lipid nanoparticles.[22]

3.2. Degradation and Instability:- Environmental elements including heat, light, and oxygen can degrade and diminish the effectiveness of nutraceuticals. For example, heat and light can cause vitamins A, C, and E to break down, which reduces their bioavailability. Formulations like microencapsulation that shield these substances can lessen the impact of this problem.[26]

3.3. Burning Fat and the First-Pass Effect:- Certain nutraceuticals require a lengthy metabolic process after absorption in order to enter the systemic circulation. Their bioavailability may be considerably decreased by this first-pass action. For instance, the liver quickly metabolizes the flavonoid quercetin, reducing its potential for bioactivity. It is imperative to develop delivery strategies that improve systemic circulation or elude first-pass metabolism.[27]

3.4. Relationships with Food Ingredients:-Nutraceuticals' bioavailability may be impacted by food matrices. For example, dietary lipids can improve lipophilic chemical absorption whereas certain fibers can prevent the absorption of other compounds. Dietary fat intake has a considerable impact on carotenoid absorption. Understanding these connections is vital for making successful dietary recommendations.[28]

3.5. Individual Response Variability:- The degree of bioavailability can differ greatly amongst people because of things like age, gender, genetics, and general health. For example, genetic variations in drug-metabolizing enzymes can change how some nutraceuticals are metabolized, which can have a variety of therapeutic effects. Strategies for personalized nutrition may be able to address these differences.[29]

3.6. Limitations of the Delivery System:-

Even though several administration methods seek to increase bioavailability, problems with formulation and implementation still exist. For example, the production of liposomal and nanoparticle formulations can be expensive and difficult, which may prevent them from being used widely. Furthermore, the stability of these systems throughout storage and in the gastrointestinal tract might be an issue.[23]

4. STRATEGIES TO IMPROVE BIOAVAILABILITY

4.1. Nanoparticles and Nanoemulsions:-

Hydrophobic nutraceuticals may now be more effectively delivered through the use of nanoemulsions and nanoparticles, which improve their solubility and absorption. Nanoemulsions: Oil-in-water emulsions stabilized by surfactants are known as nanoemulsions. They boost the solubility of lipophilic substances and increase their surface area for absorption. Research has indicated that as compared to traditional formulations, curcumin-loaded nanoemulsions have a noticeably better bioavailability.[31]

Nanoparticles: Nutraceuticals can be added to nanoparticles to improve absorption by increasing permeability and cellular uptake. For instance, investigations on animals have demonstrated enhanced bioavailability of resveratrol-loaded nanoparticles.[30]

4.2. Lipid based Delivery System:-

Hydrophobic nutraceuticals can become more soluble when formulated in lipid-based ways, such as self-emulsifying drug delivery systems (SEDDS).

SEDDS: When these formulations come into contact with gastrointestinal fluids, they spontaneously produce an emulsion that improves the absorption of substances such as omega-3 fatty acids. They enhance the passage of bioactive substances past the intestinal barrier, enhancing their systemic availability.[32]

4.3. Solid Disperson:-

By dispersing a nutraceutical in a polymer matrix, solid dispersion methods increase the nutraceutical's rate of dissolution and, thus, its bioavailability.
Polymer Matrices: Poorly soluble chemicals can become more soluble by using polymers such as polyethylene glycol (PEG) or polyvinylpyrrolidone (PVP). Research has revealed that solid dispersions of curcumin with PVP considerably increase its bioavailability.[33]

4.4. Microencapsulation:-

Microencapsulation improves the release profile of delicate nutraceuticals while preventing deterioration. Techniques: A number of approaches, including as coacervation and spray drying, can be used. Probiotics, for example, have been demonstrated to be more stable and bioavailable throughout gastrointestinal transit when they are microencapsulated.[34]

4.5. Use of Absorption Enhancer:-

Some chemicals have the capacity to modify membrane permeability, which improves the absorption of nutraceuticals.
Bioenhancers: Compounds such as piperine (found in black pepper) and quercetin can greatly boost the bioavailability of curcumin and other nutraceuticals by blocking metabolic enzymes and improving intestinal absorption.[35]

4.6. Formulation with Other Nutrients

Nutraceuticals can improve absorption when combined with other nutrients in a synergistic way. Synergistic Effects: For instance, it has been demonstrated that co-administering calcium and vitamin D increases

the bioavailability of both substances. Through cooperative processes in the gastrointestinal system, such combinations can improve absorption.[36]

To optimize the health advantages of nutraceuticals, it is imperative to improve their bioavailability. Promising approaches to address the problems caused by low solubility and stability include the use of absorption enhancers, solid dispersions, lipid-based systems, nanoemulsions, microencapsulation, and synergistic formulations. Nutraceuticals' effective delivery and therapeutic potential will be enhanced by ongoing research and innovation in these fields.

5. OPPORTUNITIES IN NUTRACEUTICALS

Over the past few decades, the nutraceuticals industry—which includes food-based products with additional health benefits—has experienced substantial expansion. This industry encompasses nutritional supplements, functional foods, and herbal items, appealing to customers increasingly focused on health and wellbeing. The present research delves into the nutraceuticals market's opportunities, emphasizing significant trends, obstacles, and potential chances going forward.

5.1. Market Development and Patterns

Grand View Research (2023) projects that the worldwide nutraceuticals market will develop at a compound annual growth rate (CAGR) of around 8.2%, reaching USD 722 billion by 2027. [37,38,39] This rise is being driven by several trends:

- Increased Health Awareness: With a greater emphasis on preventative healthcare, customers are more motivated to seek items that boost their well-being.
- Aging Population: The need for nutraceuticals that support healthy aging is rising as a result of the expanding older population's increased susceptibility to chronic illnesses.
- Nutritional Personalization: Customers are increasingly looking for supplements that are specifically designed to meet their unique health requirements and genetic profiles.
- E-commerce Expansion: As a result of the rise in online shopping, nutraceuticals are now more widely available, giving businesses access to a larger market.
- Sustainable Production and Sourcing processes: Businesses are adopting sustainable production and sourcing processes in response to customer preferences for environmentally friendly and sustainably derived products.

5.2. KEY OPPORTUNITIES

- Functional Foods: Significant prospects exist for innovations in functional foods, which offer health advantages beyond basic nutrition. Probiotics, omega-3 fatty acids, and plant-based proteins are among the most in-demand ingredients.

- Herbal Supplements: Conventional medicine is beginning to recognize the benefits of traditional herbal treatments. Products like adaptogens, which combine traditional knowledge with contemporary research, are very intriguing.
- Targeted Supplements: There is a potential to produce supplements addressing specific health needs, such as immune support, gastrointestinal health, and mental wellbeing, appealing to specialized audiences.
- Technological Integration: With individualized health solutions, biotechnology and AI advancements may speed up product development, increase efficacy, and boost customer involvement.
- Regulatory Support: Governments in a number of places are starting to show greater support for the nutraceuticals sector by establishing more transparent regulatory frameworks that can encourage innovation and market entry.

6. CASE STUDIES AND EXAMPLES

Nutraceuticals—dietary supplements, functional foods, and herbal products—are becoming more and more well-known due to their possible health advantages. However, bioavailability—the degree and speed at which active substances are absorbed and used by the body—often limits their efficacy. This paper looks at several case studies and illustrations that show how bioavailable nutraceuticals are, talking about what influences absorption and possible ways to improve it.

6.1. Turmeric's Curcumin

Case Study: Using Piperine to Increase Bioavailability

Overview: Although curcumin, a bioactive component of turmeric, has limited bioavailability, it is well-known for its anti-inflammatory and antioxidant qualities.

Results: According to a research, co-administration of piperine inhibits the metabolic glucuronidation of curcumin, hence increasing its bioavailability (Shoba et al., 1998).
Methods of Formulation: The use of lipid-based and nano-emulsion formulations to improve curcumin absorption has been studied recently.[40]

6.2. Omega-3 Fatty Acids

Case Study: Bioavailability of Fish Oil vs. Algal Oil

Overview: The absorption of omega-3 fatty acids, especially EPA and DHA, can vary depending on the source and formulation.

Results: Research has shown that the bioavailability of omega-3s can differ between individuals with different digestive health conditions and can be affected by the absorption rates of algal oil and fish oil. Emulsified Formulations: Studies have demonstrated improved bioavailability when compared to regular fish oil capsules.[41]

6.3. Resveratrol

Case Study: Walle et al. (2004) assessed the metabolism and absorption of resveratrol and found that large oral dosages were associated with low plasma concentrations. This study brought to light the difficulties in obtaining adequate bioavailability because of substantial first-pass metabolism.

Results: Low plasma levels, indicating poor bioavailability, were observed despite substantial consumption.[42]

6.4. Quercetin

Case Study: Boots et al. (2008) investigated quercetin's bioavailability in various forms. Studies have shown that quercetin glycosides are more absorbable than their aglycone form, indicating that the presence of a sugar moiety improves solubility and bioavailability.

Results: Glycoside forms exhibited enhanced bioavailability, underscoring the significance of dietary context for absorption.[43]

6.5. Coenzyme Q10

Case Study: A study by Baggio et al. (2018) evaluated several formulations of CoQ10. When compared to conventional oil-based formulations, they discovered that a novel solubilized administration method greatly increased plasma bioavailability.
Results: Higher plasma levels in the solubilized form suggested improved absorption.[44]

6.6. Probiotics

Case Study: The advantages of probiotics for gut health are well-known. Examples include Lactobacillus and Bifidobacterium strains. Their capacity to pass through the digestive system and be bioavailable are essential for their effectiveness.

Result: A 2016 study by Ouwehand et al. showed that probiotic survival rates were greatly increased by encapsulating methods such the use of alginate beads, which improved patient outcomes in clinical settings.[45]

7. FUTURE DIRECTIONS

7.1. Enhanced Delivery System

Advances in medication delivery methods, such liposomal formulations and nanotechnology, are improving the bioavailability of nutraceuticals. These techniques increase absorption rates and more precisely target particular regions.[46]

7.2. Personalized Nutrition

As the field of nutrigenomics grows, there is increasing interest in tailoring nutraceutical intake based on individual genetic profiles. Understanding how genetics influence nutrient absorption and metabolism can lead to personalized recommendations that optimize bioavailability.[47]

7.3. Synergistics Formulations

The synergistic benefits of mixing several nutraceuticals are the topic of research. Certain substances can improve one another's effectiveness and absorption, improving overall health results.[47]

7.4. The Role of Gut Microbiome

A key factor in the bioavailability of nutraceuticals is the gut microbiota. Future studies may explore further the ways in which distinct bacterial strains impact the metabolism of different substances, which might result in probiotic-nutraceutical combos with improved efficacy.[48]

7.5. Regulatory Development

Regulations will change as the industry for nutraceuticals expands. Tighter regulations on bioavailability testing and claims might enhance the caliber of products and boost customer confidence.[46]

7.6. Advance Analytical Technique

The pharmacokinetics of nutraceuticals will be better understood through the application of cutting-edge analytical techniques like mass spectrometry and high-performance liquid chromatography, which will result in improved formulations and dosage recommendations.[46]

Nutraceutical bioavailability appears to have a bright future ahead of it, as scientific and technological developments open the door to more customized and potent solutions. Through an emphasis on delivery mechanisms, personalized reactions, and the relationship with the microbiota, the sector can improve the therapeutic potential of nutraceuticals.

8. CONCLUSION

Bioavailability, or how well these substances are absorbed and used by the body, is a major problem for nutraceuticals, which are food-based supplements that provide health advantages beyond basic nutrition. Their bioavailability may be hindered by elements including the food matrix, processing techniques, and the intrinsic chemical makeup of the bioactive chemicals. For example, some substances could be poorly soluble or break down during digestion, which would restrict their absorption.
Novel delivery methods have been created to improve nutraceuticals' bioavailability in order to overcome these obstacles. Techniques based on nanotechnology, including nanoencapsulation, have demonstrated promise in increasing the stability and solubility of bioactive substances, which in turn improves absorption. One type of nanocarrier that may encapsulate both hydrophilic and lipophilic molecules, preventing their breakdown and promoting improved absorption in the gastrointestinal system, is a liposome, which is a spherical vesicle with a phospholipid bilayer. Furthermore, the creation of amorphous systems has been investigated as a means of enhancing the delivery of nutraceuticals that are poorly soluble. By changing bioactive chemicals into an amorphous state, which is more soluble than their crystalline counterparts, these systems can increase the rate of dissolution and bioavailability.
Notwithstanding these developments, there are still a number of obstacles in the creation and use of nutraceuticals. It is crucial to guarantee the quality and purity of raw materials since contamination with pesticides, heavy metals, or other dangerous compounds can be hazardous to one's health. Natural variances in plant sources and processing techniques make it difficult to maintain uniformity in the content of nutraceutical goods. Additionally, there may be interactions between pharmaceutical medications and nutraceuticals that might change their respective efficacies.

In conclusion, increasing the bioavailability of nutraceuticals is still a major topic of work, despite the fact that they have a great deal of promise to improve health and prevent disease. Potential remedies are provided by developments in delivery techniques, such as amorphous formulations and nanotechnology. To fully reap the benefits of nutraceuticals, however, issues with safety, standardization, and quality control must be resolved.

9. REFERENCE

1. Nutraceuticals: A Review by Skylar A. Souyoul . Katharine P. Saussy . Mary P. Lupo. Dermatol Ther (Heidelb) (2018) 8:5–16. https://doi.org/10.1007/s13555-018-0221-x

2. The Nutraceutical: Bioavailability Classification Scheme: Classifying Nutraceuticals According to Factors Limiting their Oral Bioavailability by David Julian McClements, Fang Li and Hang Xiao.
https://doi:10.1146/annurev-food-032814-014043

3. A review on nutraceuticals: Classification and its role in various disease. https://www.researchgate.net/publication/322821916

4. Classification, Regulatory acts and Applications of Nutraceuticals for Health by Jagtar Singh and Shweta Sinha. www.ijpbs.com

5. Improving oral bioavailability of nutraceuticals by engineered nanoparticle-based delivery systems by Mingfei Yao, David Julian McClements and Hang Xiao. www.sciencedirect.com

6. Common delivery systems for enhancing in vivo bioavailability and biological efficacy of Nutraceuticals by Yuwen Ting, Yike Jiang, Chi-Tang Ho and Qingrong Huang. www.sciencedirect.com

7. Bioavailability of nutraceuticals: Role of the food matrix, processing conditions, the gastrointestinal tract, and nanodelivery systems by Cristian Dima, Elham Assadpour, Stefan Dima and Seid Mahdi Jafari. https://DOI:10.1111/1541-4337.12547

8. Rojas, J., et al. (2021). "Microencapsulation Techniques for Nutraceuticals." *Food Science and Human Wellness*, 10, 380-388.

9. McClements, D. J., & Decker, E. A. (2014). "Designing Food Structure to Improve Nutrient Bioavailability." *Critical Reviews in Food Science and Nutrition*, 54, 235-249.

10. Pérez-Jiménez, J., et al. (2010). "The role of phytochemicals in the health benefits of fruits and vegetables." *Nutrition Bulletin*, 35, 292-302.

11. Decker, E. A., et al. (2014). "Emulsions in Food: The Importance of the Food Matrix." *Annual Review of Food Science and Technology*, 359-385.

12. Bohn, T., et al. (2012). "Cooking methods affect the bioavailability of carotenoids from vegetables." *Food Chemistry*, 130, 298-305.

13. Buchweitz, M., et al. (2017). "Fermented Dairy Products and Calcium Bioavailability." *Critical Reviews in Food Science and Nutrition*, 57, 1038-1049.

14. Borel, P., et al. (2013). "Bioavailability of Vitamin E." *Nutrition Reviews*, 71, 454-472.

15. McClements, D. J., & Decker, E. A. (2014). "Designing Food Structure to Improve Nutrient Bioavailability." *Critical Reviews in Food Science and Nutrition*, 54, 235-249.

16. Borel, P., et al. (2013). "Bioavailability of Vitamin E." *Nutrition Reviews*, 71, 454-472.

17. Boileau, T. W. M., et al. (2002). "Absorption of Carotenoids from Foods and Supplements: A Review." *Journal of Nutrition*, 132, 399-402.

18. Hercberg, S., et al. (2001). "Iron Bioavailability in Diets Rich in Legumes." *American Journal of Clinical Nutrition*, 73, 959-966.

19. Koh, J. H., et al. (2014). "Bioavailability of phytochemicals in fruits and vegetables." *Food & Function*, 5, 1989-1997.

20. Mann, J. I., et al. (2017). "Dietary fiber: A key factor in nutraceutical absorption." *Nutrition Reviews*, 75, 224-232.

21. Sato, Y., et al. (2020). "Interactions between gut microbiota and dietary compounds: Implications for health." *Journal of Nutritional Biochemistry*, 80, 108392.

22. Zhang, Y., et al. (2020). "Enhancement of curcumin solubility and bioavailability using nanotechnology." *Journal of Nanomedicine & Nanotechnology*.

23. Khan, M. I., et al. (2019). "Enhancing the bioavailability of nutraceuticals using lipid-based delivery systems." *Journal of Nutraceuticals and Dietary Supplements*

24. Ribeiro, A. C., et al. (2020). "Microencapsulation of probiotics: A review." *Trends in Food Science & Technology*, 102, 244-257.

25. Huang, Y., et al. (2021). "Hydrogel-based systems for the delivery of vitamins." *Food Hydrocolloids*, 118.

26. Miller, R. A., et al. (2021). "Stability of vitamins and bioactive compounds in foods: a review." *Food Chemistry*, 343.

27. Meyer, M. R., et al. (2020). "Metabolism of quercetin: mechanisms of bioavailability and interactions." *Molecules*, 25, 1150.

28. Krinsky, N. I., et al. (2003). "Carotenoids and their roles in human health." *Nutrition Reviews*, 61.

29. Fischer, K., et al. (2021). "Genetic variability and nutraceuticals: implications for personalized nutrition." *Journal of Nutrigenetics and Nutrigenomics*, 14, 109-120.

30. Zhang, Y., et al. (2021). "Resveratrol-loaded nanoparticles for enhanced bioavailability: A review." *Molecules*, 26, 3658.

31. Kumar, S., et al. (2020). "Curcumin nanoemulsion: Formulation and in vivo bioavailability study." *International Journal of Pharmaceutics*, 585, 119494.

32. Gao, Y., et al. (2022). "Self-emulsifying drug delivery systems for omega-3 fatty acids: Enhancing bioavailability." *Critical Reviews in Food Science and Nutrition*, 62, 4532-4546.

33. Patel, A., et al. (2023). "Solid dispersion of curcumin with PVP for enhanced bioavailability: A systematic study." *Journal of Drug Delivery Science and Technology*, 78, 103152.

34. Chaudhary, A., et al. (2022). "Microencapsulation techniques for enhancing the bioavailability of probiotics." *Food Reviews International*, 38, 245-261.

35. Bhat, S. G., et al. (2023). "Role of piperine in enhancing the bioavailability of curcumin: A review." *Journal of Nutritional Biochemistry*, 106, 109-116.

36. Chaudhary, A., et al. (2021). "The synergistic effects of vitamin D and calcium on bioavailability." *Nutrients*, 13, 2701

37. Grand View Research. (2023). Nutraceuticals Market Size, Share & Trends Analysis Report By Product, By Application, By Region, And Segment Forecasts, 2023 - 2030.

38. Nutrition Business Journal. (2023). The State of the Nutraceuticals Market.

39. Mintel. (2023). Market Research on Nutraceuticals and Functional Foods.

40. Shoba, G., Joy, D., Joseph, T., Majeed, M., Rajendran, R., & Srinivas, P. S. (1998). "Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers." *Planta Medica*, 64, 353-356.

41. Gonzalez, A. M., et al. (2018). "Comparison of the bioavailability of omega-3 fatty acids from algal and fish oil." *European Journal of Clinical Nutrition*, 72, 98-105.

42. Walle, T., et al. (2004). "Resveratrol is absorbed in humans." *American Journal of Clinical Nutrition*, 79(4), 647-650.

43. Boots, A. W., et al. (2008). "The bioavailability of quercetin: a critical review." *Nutrition and Metabolism*, 5, 3.

44. Baggio, G., et al. (2018). "Comparative bioavailability of different CoQ10 formulations." *International Journal for Vitamin and Nutrition Research*, 88(1-2), 1-9.

45. García-Rodríguez, A., et al. (2023). Personalized nutraceuticals: The future of targeted nutrition. *Journal of Nutritional Biochemistry, 108*, 108103. https://doi.org/10.1016/j.jnutbio.2023.108103

46. Raza, H., & Ali, S. (2023). Nanotechnology for nutraceutical delivery: Advancing therapeutic potentials. *Nanomedicine: Nanotechnology, Biology, and Medicine, 47*, 102555. https://doi.org/10.1016/j.nano.2023.102555

47. Zarrin, M., & Shahid, M. (2022). Regulatory frameworks for nutraceuticals: Global trends and challenges. *Food Control, 142*, 109218. https://doi.org/10.1016/j.foodcont.2022.109218

48. Pimentel, S. S., et al. (2023). Nutraceuticals in mental health: Advancements in cognitive support. *Journal of Clinical Nutrition, 65*(3), 225-236. https://doi.org/10.1016/j.jclinutr.2023.01.008