Recent Trends in Natural Medicines and Nutraceuticals Research

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Abstract

Nature is considered as the classic source of natural medicines that are isolated from myriad flora and fauna that exist on earth. Drugs that are derived from natural products are an emerging domain in drug discovery due to their nontoxicity and enhanced health benefits. Nutraceuticals are bioactive components found in natural products consisting of additional nutritional ingredients, which play a key role in the maintenance of health, including the inhibition and sometimes cure of certain diseases. Nutraceuticals are packed with vitamins and essential minerals, purified in various forms such as herbal products, dietary supplements, and food nutrients. Derived the products like phytochemicals, probiotics, antioxidants, vitamins, and essential minerals are generally isolated from microbial and plant sources. The nanotechnological applications have impacted all research areas, including agriculture, science, and health care. Nanoparticles are promising delivery systems toward a specific target. The diverse nanotechnological tools have introduced several nanodelivery systems, including biogenic nanoparticles, nanospheres, and nanocapsules, which improve the availability of bioactive components. The therapeutic prospects of nano-formulated nutraceuticals are enhanced by nanocarriers. Currently, many nanocarrier systems such as liposomes, micelles, nanoemulsions, and polymeric nanoparticles have come into the picture. The amalgamation of several functional properties of nutraceuticals in one particle can contribute toward the multifunctional nanocarrier development, enhancing the efficacy of many curative and

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diagnostic protocols. The nanotechnological approaches can resolve the issues regarding low bioavailability, poor permeability and solubility, low absorption in the gastrointestinal tract, and lack of long-term stability of natural medicines.

Keywords

Nutraceuticals · Natural medicines · Nanotechnology · Nanocarriers · Drug delivery

11.1 Introduction

Nowadays, nutraceuticals are frequently utilized as therapeutics. A nutraceutical has the physiological advantage which offers guard against chronic diseases. Nutraceuticals are often used to prevent chronic diseases, slow down the aging process, extend lifespan, promote health, and maintain the construction and operation of body systems. At the moment, nutraceuticals have received substantial interest due to their potential therapeutic, nutritional, and safe properties. According to the recent data, these chemicals have shown promising outcomes against a variety of problems. The goal of this review is to give new perspectives on nutraceuticals based on their disease-modifying applications. The impact of herbal nutraceuticals on hard curative conditions associated with oxidative stress, such as Alzheimer's disease, Parkinson's disease, allergies, diabetes, cardiovascular disease, cancer, eye disease, inflammation, and obesity, has been reported. The newly published papers about diverse characteristics of nutraceuticals as a substitute for pharmaceuticals were found in the literature (Nasri et al. 2014).

Nutraceuticals are the combination of biological substances extracted from natural products by non-denaturing procedures to retain their original potentials without any chemical manipulation. These extracts are assessed in animals and humans to establish their biological properties, as is done with drugs. After their characteristics have been recognized, they are promoted to be used up by humans as part of the diet. Nutraceuticals are naturally available as concentrated extracts which, consumed at a dose higher than that exist in the original foods, have an advantageous effect on health, greater than the natural food itself could possess. These products are authentic due to their good bioavailability and natural origin and can usually be consumed in the long term without any side effects in humans or animals.

Nutraceuticals are causing an enthusiastic deliberation because their concept draws the demarcation between medicine and food. The foremost dissimilarity is based on their derivation, this being artificial for drugs and natural for nutraceuticals. Nutraceuticals occupy the void that exists amid drugs and food and strongly entitle their own permissible space, taking into account their features and particularities and empowering the expansion of their full therapeutic potential (Aronson 2017; Santini et al. 2017; Corzo et al. 2020).

Nutraceuticals have recently gained a lot of attention due to their potential nutritional and medicinal effects. They have shown encouraging results in studies on cardiovascular illnesses (Khosravi-Boroujeni et al. 2012), atherosclerosis (Madihi et al. 2013), diabetes (Baradaran et al. 2013), cancer, (Shirzad et al. 2011), and neurological disorders (Akhlaghi et al. 2011). These situations include many changes, such as alterations in redox state (Baradaran et al. 2014). Most nutraceuticals possess antioxidant properties with the capability to counteract this situation (Parsaei et al. 2013). Henceforth, they are considered as strong foundations for promoting health, especially for prevention of diseases such as gastrointestinal disorders (Kiani et al. 2013), diabetes (Mirhoseini et al. 2013), and renal infection (Bahmani et al. 2013; Rafieian-Kopaie 2013).

A concerted attempt has been made to present new perspectives on nutraceuticals based on their ability to treat disease. The usefulness of herbal nutraceuticals on disorders associated with oxidative stress (such as allergy), obesity, cardiovascular disease, cancer, inflammation, diabetes, Alzheimer's disease, and Parkinson's disease, has been highlighted.

Nanotechnology increases the bioaccessibility and bioavailability of different nutraceuticals for a broad range of clinical applications. Nutraceuticals and bioactive compounds exhibit different hydrophobic and hydrophilic properties. Hydrophilic chemicals are water-soluble and easily absorbed across the lumen of the digestive tract before entering the systemic circulation. Due to their poor solubility nature, long side chains, reactivity, low permeability, and other factors, hydrophobic bioactive compounds have low bioaccessibility and bioavailability. Polyphenols, tocopherols, carotenoids, phytosterols, fatty acids, and fat-soluble vitamins are only a few examples of hydrophobic complexes. This article explores the importance of nanometric delivery systems that assist in increasing the bioavailability and bioaccessibility of hydrophobic bioactive substances. Micelles, reverse micelles, molecular complexes, liposomes, emulsion droplets, solid lipid particles, microemulsions, filled hydrogel particles, biopolymer nanoparticles, and polyelectrolyte complexes are some of the most common delivery methods.

Liposomes are proficient in loading hydrophilic, amphiphilic, and lipophilic compounds and components either in the aqueous core or embedded in the phospholipid bilayer, on the liposome-continuous phase interface (McClements 2019). Microemulsions and micelles are similar in composition, except that microemulsions include both surfactant and carrier lipid, whereas micelles include only surfactant. The micelles get swelled after the addition of carrier lipid. In this situation, swollen micelles and microemulsions are interchangeable.

Nanoemulsions are spherical droplets with a diameter of 100 nanometers that feature a surfactant or protein shell and a lipophilic center. They're good in transporting lipophilic compounds that have been distributed in water (Davidov-Pardo and McClements 2014).

In the upper gastrointestinal system, hydrogels protect oil droplets and control their bioaccessibility, enabling the bioactive compounds to be released in the colon (McClements 2019). In molecular inclusion, a "host" molecule entraps a "guest" bioactive molecule with non-covalent interactions (Joye and McClements 2013). One of the renowned host molecules is 2-hydroxypropyl-β-cyclodextrin (HP-β-CD). The enhanced solubility of the complex, alteration of membrane properties, higher stability of the bioactive molecules, and close proximity of the complex to the intestinal walls act as bioavailability boosters.

11.2 Method

11.2.1 Nanoencapsulation and Nanodelivery of Nutraceuticals

The term "nutraceutical" was first used and created by Dr. Stephen DeFelice in 1989, which is derived from "nutrition" and "pharmaceutical" (Kalra 2003). The World Health Organization defined incorporated probiotics in food products as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" (Petchsomrit et al. 2017). The use of probiotics inhibits the growth of potentially harmful bacteria and the immunity mechanisms are reinforced. The beneficial properties are improving lactose tolerance, modulating immunity, lowering cholesterol, controlling intestinal infection or prevention and improving iron deficiency (Prasertmanakit et al. 2009). Considering their professed health benefits, probiotics have been combined with a wide range of dairy products, including cheese, yogurt, and frozen dairy desserts. The loss of probiotics during food processing is one of the most significant technological obstacles as the production of stable and viable probiotic cultures is regarded as an immense challenge for the industry (Rodrigues et al. 2012). Apart from the process of food production and storage method, the survival of probiotic microorganisms is strongly influenced by the barriers of human gastrointestinal tract (stomach acid, pancreatic juice, and bile) (Schell and Beermann 2014). Microencapsulation techniques with different matrices are convenient to improve the viability and avert undesirable losses of probiotics and the targeted delivery in the gastrointestinal tract (Anal and Singh 2007).

11.2.2 The Challenge of Incorporating Nutraceuticals into Food

Nutraceuticals are composed of several categories with effective doses of nutraceutical ingredients, to meet the specific health or medical benefits of consumers (Fig. 11.1). But nutraceuticals hold some limitations in their effective incorporation into supplements (Augustin and Sanguansri 2015). The shelf life and properties of the food may be affected by undesirable interactions among nutraceuticals and certain components of the food matrix. Chemically unstable nutraceuticals may be subjected to degradation during storage or digestion. Innumerable delivery mechanisms are designed to transport nutraceuticals to protect them from degradation during processing or by digestive enzymes. This method also improves the stability, covers any kind of undesirable odors and taste, and improves the bioavailability and solubility of nutraceuticals (He and Hwang 2016).

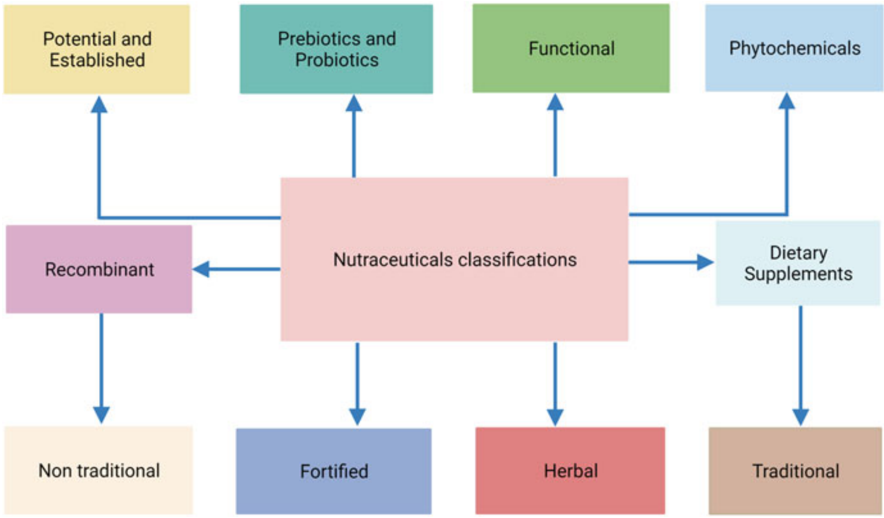

Fig. 11.1 Schematic classification of nutraceuticals

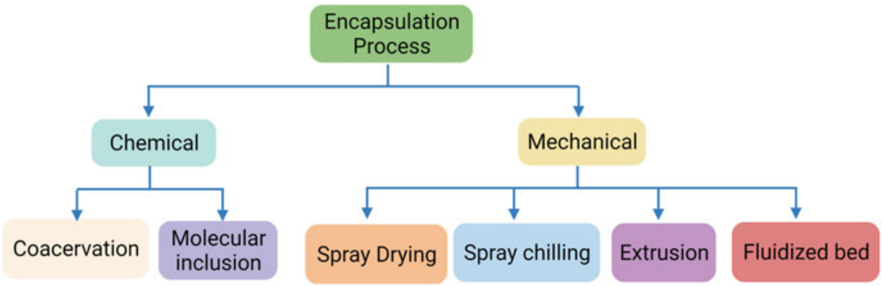

Fig. 11.2 Encapsulation process categories (Carvalho et al. 2016)

11.2.3 Nanoencapsulation and Delivery

The establishment of a delivery system encompasses several steps, from the selection of source materials to the development and commercialization of a final product. Microencapsulation can be divided into two main categories: mechanical processes and chemical processes (Fig. 11.2).

The chemical processes comprise the methods such as cocrystallization, molecular inclusion, coacervation, and interfacial polymerization. The mechanical processes include methods such as spray-chilling/spray-cooling, spray-drying, extrusion, and fluidized bed (Carvalho et al. 2016). The produced microparticles are subjected to further characterization and analysis in terms of physical structure, shape, and controlled release (Estevinho et al. 2016). Especially the controlled release mechanism needs the intervention of a mathematical model to properly design a controlled release system, which ensures the release of a bioactive compound at desired site, at desired time, and at the desired rate. The aforementioned mechanism depends on the nature and quantity of the encapsulating agent, the encapsulation technique, and the environment where the release takes place. The most applicable release mechanisms comprised of dilatation (with gel formation and swelling), osmosis, diffusion, and biodegradation.

11.2.4 Gastroretentive Delivery Systems

Delivery systems falling into this category are created to have a lengthier period of retention in stomach, which improves absorption through the upper gastrointestinal tract. Numerous methods such as mucoadhesion, expansion, floatation, shape modification, and sedimentation have been employed to expand the gastric residence time of nutraceuticals (Murphy et al. 2009). According to Petchsomrit et al. (2017), gastric retention period of curcumin was improved by encapsulation in alginate sponges produced by freeze-drying method. An 8 h retention of encapsulated curcumin in gastric fluid and remaining buoyancy over another 8 h were an amalgamation of alginate:HPMC (4:2) sponges rendered sustained liberation of curcumin up to 71%. Gastroretentive delivery systems were found to be helpful in the treatment of peptic ulcers and gastrointestinal cancer and expanding the availability of inadequately soluble bioactive compounds.

11.2.5 Intestinal Targeted Delivery

Certain compounds are greatly variable and get degraded in gastric fluids. A suitable approach to upsurge their bioavailability and delivery into intestinal conditions can be achieved through using stable biopolymers for efficacious delivery into intestinal system. According to Penalva et al. (2015), folic acid encapsulated in zein nanoparticles is efficiently protected from gastric environment and discharged only at intestinal conditions. Mucoadhesive characteristic of zein's outer surface interacts with mucus layer and epithelium surface for a long time increasing concentration of folic acid in blood for almost 24 hours. The negative charge of protein matrix and folic acid under an alkaline environment permits targeted release in intestine.

11.2.6 Colon-Specific Delivery

Localized treatment of certain bowel diseases such as colon cancer, ulcerative colitis, etc. can be treated with colon-specific systemic transport of proteins and peptides. Delivery systems reliant on pH difference in gastrointestinal tract, pressure difference, and enzyme systems triggered by colonic bacteria are investigated for colon-specific delivery of bioactive substances. For example, colon-specific delivery are achieved by curcumin encapsulated in Eudragit S100, a polymer (pH-sensitive) used as microspheres. A report suggested that only 28.9% of total orally administered curcumin reached the colon after 8 h. More than 80% delivery of curcumin in colon was accomplished when delivered in encapsulated form (Madhavi et al. 2012). This type of colon-specific delivery system can increase the bioavailability of nutraceuticals by overcoming rapid metabolism in the upper gastrointestinal tract.

11.3 Safety Measures, Concerns, and Future Aspects

An important concern of using nanotechnology in the encapsulated delivery system of nutraceuticals is safety. Before a specific delivery system is marketed, proper study for probable risks (allergic and toxic reactions) is mandatory. Nanoparticles act differently in the gastrointestinal tract due to their high surface area and small size (Corona-Hernandez et al. 2013). These properties allow them to pass through physiological barriers (tissue and cell) easily, which may harm biological systems. Additional health risks can be avoided if the tolerable UL (upper intake levels) and RDA (recommended daily allowance) are re-evaluated and re-examined (Cortés-Rojas et al. 2014). Also, a nanoscale delivery system may result in accumulation in human organs or tissues or end up interacting with other compounds. With the continuous advancement of food nanotechnology, verification of the security of all innovative products must be performed. The developers and regulators should be responsible for safety assurance of these novel technologies and products before they are presented to the market. This would be able to raise awareness of public safety concerns regarding the probable influence of nanoscale delivery systems on health. The prodigious potential of nutraceuticals is utilized by establishing encapsulation and delivery of nutraceuticals. The precise mechanism of action and biological effects of some nutraceuticals are still a debatable issue (Watanabe et al. 2013). Further studies are required to develop safe and efficient production. Further future research should be focused on the exploration of the possibility of delivery systems to endorse personalized nutrition and advanced functions of nutraceuticals.

11.4 Conclusion

The biological potential of various components supports the progression of nutraceuticals into new phases aimed at improving patient health. Though this situation is currently under research, it supports the possible management of illnesses such as cancer and diabetes, as well as their negative effects on the skin (photoaging). Algae is one of the most important sources of high-value chemicals, with the potential to prevent oxidation, increase the viability and stability of probiotic bacteria in fermented foods, and improve the texture of meat, fish, and dairy products. However, the other sources remain underexplored. After demonstrating anticancer activity in a single-drug strategy, natural compounds could further enhance the utilization of chemotherapeutic adjuvants or cooperating drugs in combination therapy. Polyphenols are promising molecules for the prevention and treatment of many human pathological conditions (e.g., neurodegenerative diseases).

Avocado, olive oil, fish oil, Docosahexaenoic acid (DHA), phytosterols, psyllium, Eicosapentaenoic acid (EPA), strawberry, flaxseed oil, berberine, nuts (especially pistachio, almonds, and hazelnuts), curcumin, and tea all decreased small dense low-density lipoprotein (sdLDL) levels, low density lipoprotein (LDL) particle size, and LDL particle counts. LDL variations benefit from almost all of the nutraceuticals and particular diet components described above, such as omega-3 fatty acids. The total of silymarin components has the greatest antioxidant capabilities, with concentrations of silymarin flavonoid/flavonolignans, followed by silychristin as one of the strongest antioxidants in the silymarin complex.

Because of the unique properties of nano-sized delivery methods, many nanoparticles have been developed to improve bioavailability for a variety of nutraceuticals and hydrophobic bioactive compounds. As previously stated, understanding the types of interactions that govern colloidal system formation and the conditions in the gastrointestinal tract during digestion can be used to modify a controlled release delivery system that protects and slowly delivers bioactive compounds to a specific absorption site. However, the influence of integrating delivery methods in complex food matrices, as well as the toxicity of such structures, remains unexplored. More study is needed to assess the toxicity and environmental impact of nanoparticle-mediated delivery systems, as well as the effect of the food matrix on the bioavailability of the nanoencapsulated bioactive molecules and the delivery systems' effects on the food matrices. For clinical applications, studies on scaling up the manufacturing process of nanodelivery devices would be critical. Curcumin, coenzyme Q, green tea polyphenols, thymoquinone, quercetin, and other nutraceuticals have been packed as nanoparticles and are effective in "nanochemoprevention" and "nanochemotherapy."

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