REVIEW ARTICLE

Role of nutraceuticals in health care: A review

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Abstract

The term "nutraceuticals" can be explained as the food items as a whole or a part which possesses some nutritional value along with the medicinal properties. This special feature, besides providing good health, leads to treatment and prevention of certain diseases. With the advancements in the qualitative and quantitative determining parameters, the requisition of these products has been found to be amplified. Due to this, the nutraceutical market has become a million dollar industry at a global level. The era of emergence of nutrients as medicines in the pharmaceutical world is of great importance and draws attention of scientists and researchers toward the appreciable benefits. The history and discovery has explored many facts about the remarkably profound therapeutic activities of such agents. As a result, interdisciplinary approaches are now been applied to design and develop various dosage forms to deliver these herbal products relative to their applications. The extensive researches have revealed the involvement of these agents in the treatment of many disorders such as cancer, arthritis, metabolic abnormalities, diabetes, asthma, and many others. The presented review is an attempt to classify all types of nutraceuticals with examples followed by their applications in the treatment of various disorders. Furthermore, the implementation of the designing and development of dosage forms for offering better delivery carrier of the nutraceuticals, the importance and challenges have also been enumerated.

Key words: Applications, challenges, delivery carrier, nutraceuticals, treatment

INTRODUCTION

The term "nutraceuticals" has enormous chances for growth and expansion in terms of health benefits.[1,2] Depending on the nature and the alternative use as the modern medicines, it has shown subsequent results in reducing the need for conventional medicines and has reduced the chances of adverse effects.[3] Nutraceuticals have emerged as beneficial health products obtained from many industries such as food, herbal, and pharmaceutical manufacturing industries. The significance of such products have been associated with the treatment of many disorders such as cancer, metabolic problems, cold and cough, depression, coronary heart disease, delayed gastrointestinal emptying, and many more conditions which need special care.[2,4]

The nutraceutical market has been developed from past few years due to growing attention of researchers and sophisticated techniques for determination of qualitative and quantitative parameters. It has changed to million dollar industry at a global level. Global marketing of nutraceuticals was USD 128.4 billion in 2008. Japan holds the largest figures of 70% of marketing share in Asia.[5,6] Table 1 summarizes current global markets with a value of nutraceuticals in market share worldwide. The Indian nutraceutical market segment has undergone annual growth at 20% rate for past 3 years which contributes to 2% of global market. Currently, India is in the category of showing promising drift toward nutraceuticals also known as Fast Moving Health Care Goods. The value of nutraceutical market in 2009 was estimated which comes about INR 27 billion and expected to accomplish market value of INR 40.1 billion in 2011.[7] The Indian nutraceutical market has reached the value of around US $2 billion, which retains 1.5% of global nutraceutical industry. This status depicts the ongoing trials and attempts for integrating traditional herbal ingredients

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Table 1: Global market value of nutraceutical sector and current status.[5]

Global market	Nutraceutical market value	Current status
The US market	US $50.4 billion in 2010	Since the nutraceutical sector is catching up heights, the efforts are turning to be fruitful for maintaining natural health and increased consumer demand
The European market	US $35 billion in 2010	The foundation of nutraceutical industry lays on innovation and rise in research and development. Germany, Netherlands, and Sweden have emerged as the key nutraceutical innovation hubs in Europe
The Japan market	US $27.7 billion in 2010	Functional foods with approved health claim and foods which may provide health benefits without health claim are approved by Japanese Government
The Southeast Asia market	US $10.96 billion in 2009	The marketing curve is rising due to its emergence at international level. The market share figure of 7% in 2008 depicts the high growth potential in this segment
The China market	US $ 15 billion in 2008	The market enjoys the successful industrial growth due to the diversification of their products and increased consumer demand

into nutraceutical portfolio. Furthermore, the estimation of growth of Indian nutraceutical market was found to be the US $2731 million in 2016. Future scope and demand for nutraceuticals depend on Indian consumer's awareness.[8] Therefore, it requires special focus and market interest for further growth and establishment of the new horizons for the growing nutraceutical industries.

HISTORY AND REDISCOVERY OF NUTRIENTS AS NUTRACEUTICALS

"Food may possess the ability to prevent diseases or treatment of ailment" this belief is couple of centuries old-proclaimed by our ancestors. The ancient writings and artworks of Egyptians, Romans, and Greek civilizations depicted the medicinal and spiritual applications of plants. The idea arose 3000 years ago when Hippocrates developed a relationship between food for health and therapeutic applications of it. The principal truth depicted in his statement that "Let food be thy medicine and medicine be thy food" is widely applied nowadays.[1,9] Thus, from such finding, it could be believed that our nature and surroundings have much of the natural therapies to offer. One such finding presents the botanicals, which are in use from ancient times for the treatment of cancer. Similarly, there are many plant derived chemotherapies which consist of Vinca and Taxus brevifolia species to treat cancer and related problems. Furthermore, Ginseng has been another such traditional drug which is in use from past 2000 years in China. It was from the time of Liang dynasty of China that the chemotherapy features of ginseng were discovered and applied even in today's time. From the documented history, Egyptians identified the medicinal importance of coriander, fennel, juniper, cumin, garlic, turmeric, thyme, curry, and dried mint found in pyramids. The value of such medicinal sources was so high that even cinnamon was considered more precious in comparison to gold in Egypt. Due to the explored properties of plants, the Roman emperor Heliogabalus made use of cinnamon, clove, and pepper in meals which are used in cuisines and soft drinks until present time. In addition, there were many other plants and food additives identified such as honey and certain vitamins. Honey has always been given prime importance since ancient period. It was referred in Sumerians tablet writing as one of the remedies for health problems. According to Bible, the wise Solomon has said, "Eat honey, my son, because it is good" (Old Testament, proverb 24:13). With the illustration of properties possessed by honey, apitherapy has been developed as a separate medicinal branch related with medication properties provided by honey.[10] It has promised to offer its action as a vasodilator, anti-allergic and antihypertensive agent.[11] In addition, other than honey, the requirement of vitamin, iodine, etc., was also noticed by the ancient people. Another instance which explains the importance of the food and nutrients within is of the ancient crewmen. During the past few centuries, many crewmen on long voyages died of scurvy, the exploring facts revealed the absence of Vitamins B and C in the diet acting as antiscorbutic[12] which was later ensured to be the part of the diet. In the same way, Goiter was found as the common problem due to deficiency of iodine in salt.[13] The health problems, thus, were identified and were dealt with the help of diet and healthy lifestyle; therefore, all these examples very clearly explain the requirement of a healthy diet and herbal components with the potential to serve the same. One of the surveys in United Kingdom, Germany, and France has concluded that the diet has more profound effects for healthy body and mind than exercise or genetic factors.[14] The above-mentioned findings motivate and direct the research toward a rediscovery of nutrients as nutraceuticals. The researchers in past 20 years have concluded that the diet plays a key role in the prophylaxis of chronic disorders atherosclerosis and cancer. The credible success in isolation of food components

had been achieved precisely with the help of proper clinical and laboratory investigations to verify the efficacy.[12]

CLASSIFICATION AND CATEGORIZATION OF NUTRACEUTICALS

The aim of achievement of maximal state of well-being is alarmingly increased with the introduction of nutraceuticals.[15] The term nutraceuticals, itself is a wide class which include many categories and subcategories under it. The contribution of nutraceuticals to the public health is one of the most concerned approaches in health-care system. Although the system claims to have advanced techniques to treat the diseases, still the nutraceutical approach counts because of the power it holds to treat diseases through diet. For a better explanation of comparison, pharmaceuticals include drugs for the treatment of diseases, but nutraceuticals are proposed to prevent diseases. Pharmaceuticals enjoy patent protection and government sanctioning whereas nutraceuticals never receive government appreciation and cannot be patented.[16] "Referring nutraceuticals as functional foods" this idea is under discussion because of consideration of food and medicine as the same aspect. Functional food has provision to include vitamins, fats, proteins, carbohydrates for the survival of health. However, when that food is aiding in prevention and cure of ailment other than fulfilling deficiency conditions then these are called as nutraceuticals.[17] The illustration is that black cohosh is found native to a region of North America and has been employed as a medicament to treat problems related to menopause, premenstrual syndrome, and menstrual cramping. This herbal formulation comprises extracts from roots and is adopted as female tonic in case of menstrual discomfort. Thus, it holds a medicinal property to respond to a health related problem and thus can act as a nutraceutical. There is another category called as Medical food, which are therapeutic agents meant for nutritional management of a disease. An example includes preparations for managing inborn amino acid metabolism errors.[18] Besides, there are some dietary supplements also which enhances the diet containing vitamins, minerals or concentrate, and metabolite or extract.[19] All these categorized food products, plants and sources are thus very imperative to be recognized as these possess nutritional and medicinal properties. In recent years, the diet and lifestyle related disorders have become a major issue for the health care. The increased attention and awareness among the subjects for health care along with the availability of sophisticated methodology for determination of the nutritional level of diet is worth studying.[7] It can be reviewed from various studies that nutraceuticals provide non-specific biological therapy for treatment and prophylaxis of various diseases.[8] To understand the applications, the nutraceuticals are needed to be classified. The classification into various classes depending on their uses are:

a. Traditional nutraceuticals
b. Nontraditional nutraceuticals
c. Fortified nutraceuticals
d. Recombinant nutraceuticals
e. Potential and established nutraceuticals
f. Phytochemicals
g. Herbals
h. Functional foods
i. Dietary supplements and dietary fibers
j. Probiotics and prebiotics.

Traditional nutraceuticals

The category consists of the food which does not undergo any manual changes. The components are natural and are having some potential which are actively involved in health benefits.[3] Lycopene, a constituent of tomatoes is an example of this category.[6]

Nontraditional nutraceuticals

Boosting of nutritional content by addition of nutrients, dietary components for improvement of quality of nutrition comprise this category of nutraceuticals.[3] Beta carotene enriched rice is an example of this class.[6]

Fortified nutraceuticals

Fortification of food components is the process of addition of micronutrients (essential trace elements and vitamins) to food for enhancing the effectiveness and nutritional value. Its example includes milk fortified with cholecalciferol used in Vitamin D deficiency.[20,21]

Recombinant nutraceuticals

It involves the application of biotechnology and genetic engineering in the production of energy providing foods such as yoghurt and cheese or extraction of bioactive components by enzymatic or fermentation technology. Gold kiwifruit is genetically modified for a high level of ascorbic acid, Carotenoids, and Lutein and Zeaxanthin.[20,22]

Potential and established nutraceuticals

Potential nutraceuticals hold an assurance of medicinal benefits. These nutraceuticals have became established medicines only after sufficient data demonstration and clinical testing for their efficacy and safety. All nutraceuticals are potential nutraceuticals but all potential nutraceuticals are not established ones.[14]

Phytochemicals

These are the chemical constituents of plants with distinct biological action. These are been reported to have active components which exerts their effects toward the metabolism and biochemical reactions in living beings and thus, provide health benefits.[23]

Herbals

The herbs possessing medicinal values to be implicated in treatment and prevention of ailments are been included in the class. Botanical products may consist of fresh plant used or any part such as dried leaf, fruit, stem, seeds, roots, or concentrated extract.[19]

Functional foods

Functional foods are the source of absolutely necessary nutrients providing more than the quantities required for maintenance, growth, and development. The term is specially retained for food or food components that carry the evidence to provide an advantageous factors for health beyond basic nutrition.[24] The class of functional food includes many further subclassed such as cereals, legumes, and fermented food. The potentiality of the functional food including cereals such as rice, corn, wheat, millets, sorghum, and buckwheat has been found in many ways to eliminate the risk of coronary heart disease, tumor incidence, and lowering of blood pressure. Similar to cereals, legumes are the other subclass of functional foods which form a chief element in traditional and modern dietary patterns. These are highly nutritious and rich in biologically valuable proteins, bioactive peptides, and amino acids.[25,26] The examples are kidney beans, split beans, chickpeas, lentils, and soybeans. These have been explored to have profound antioxidant and protective effect against cardiovascular diseases and diabetes.[27,28] In addition, chocolate has also been found to be a subclass of functional food which is a richest source of proteins, calcium, iron, magnesium, and riboflavin.[29-32] Citrus fruits are another type of functional food which have already been reported to produce therapeutic effects as anticancer, antiviral, antioxidant agents, and further have potential to stimulate immune system.[33] The fermented milk and related products are also the example of a functional food which offers good digestive effects. For instance, Yoghurt is a highly nutritive fermented food associated with the anticancer activity; it has also been reported to prevent gastrointestinal infections and atherosclerosis. It is recommended for lactose intolerant patients.[34] Further classification includes honey, which is a natural sweetener and believed to possess nutritional and medicinal value.[10] It is composed of monosaccharide fructose, glucose, enzyme diastase, amino acids, vitamins, minerals, and aroma compounds.[35] Its biological actions are reported in case of Type 2 diabetes, obesity and also to provide infant nutrition. It also has shown the positive results for improvement of renal functions, as antioxidant and as antimicrobial agent.[36] Colostrum is another functional food which is referred to first milk secreted in parturition. It contains lactoprotein and lactalbumin due to which it is different from milk secreted later. It is rich in antibodies which provide passive immunity to a newborn in addition to proteins, immunoglobulins, and growth factors. Recent demonstrations reported its role in the treatment of autoimmune disorders.[37] Extending further, meat products can also be included under the class of functional food. Proteins derived from soyabeans have been employed in comminuted meat products as meat replacements.[38]

Dietary supplements and dietary fibers

A dietary supplement is a product which comprises a supplementary dietary ingredient added as a remedy to deficiencies or diseases. The inclination toward dietary supplements has raised many folds to improve health, fitness, tonic to delay aging, improve performance, and body building. A dietary ingredient is one which enhances the food and its nutritional assessment. Vitamins and minerals as dietary supplements exist in multiple ingredients or single ingredient products in the market.[39] Demand of dietary supplements is alarmingly increasing in developing countries such as Brazil, China, India, and Russia and it has already reserved its place in developed parts of many countries.[40] Dietary supplements other than vitamins and minerals also involve herb, botanicals, amino acids, pure extracts, concentrate or combination of number of ingredients gland extracts, and organ tissues.[3] It is not supposed to be used as traditional or conventional food element or as the regular item in the meals or diet.[41] Dietary fibers and high fiber products are of great interest because of significant health benefits. According to American Association of Cereal Chemists (AACC), it is defined as edible part of plant or carbohydrate analogous which is resistant to digestion and absorption in the small intestine.[42] These products normalize the intestinal transit time. Its sources include brown rice, banana, cereals, oats, dry beans, and legumes.[18]

Probiotics and prebiotics

Probiotic category includes the live microbial food ingredients which are advantageous to health. Their action includes adhesion to gastrointestinal tract at specific sites and their survival lead to elimination of pathogens.[6,18,43,44] Prebiotic category includes selectively fermented ingredients or a fiber that promote changes in gastrointestinal microflora and its activity providing good effects to the health of host. They are the fertilizing agents for the probiotic bacteria in colon. These are not affected by gastric pH and digestive acids. The example includes inulin which on further hydrolysis gives oligofructose and galactooligosaccharide.[6,18,45-47]

APPLICATIONS OF NUTRACEUTICALS IN DISEASE MANAGEMENT

The extensive researches have revealed the involvement of nutraceuticals in the treatment of many disorders such as insomnia, digestion problems, cancer, blood pressure abnormalities, cold and cough, depression, coronary heart disease, delayed gastrointestinal emptying, and many more conditions which need special care.[4] The applications of nutraceuticals with their chemical classification have been depicted in Table 2. Furthermore, the herbal treatment by

Table 2: Phytochemicals with chemical classifications and therapeutic benefits

Phytochemicals	Source	Chemical classification	Therapeutic benefits	References
Monoterpenoids-Eugenol	*Eugenia caryophyllus*	Terpenoids	Dental analgesic, toothache and dental protection, flavoring agent	Jaganathan *et al.*, 2012[71]
Sesquiterpenoids-Ginger oil	*Zingiber officinale*	Terpenoids	Antibacterial and antifungal properties	Pandey *et al.*, 2011[41]
Diterpenoids-Taxol	*Taxus brevifolia*	Terpenoids	Anticancer drug	Pandey *et al.*, 2011[41]
Triterpenoids-Quassia wood	*Picrasma excelsa*	Terpenoids	Bitter tonic, antimalarial, anthelmintic	Pandey *et al.*, 2011[41]
Tetraterpenoids-Beta carotene	Carrots	Terpenoids	Antioxidant property, act as provitamins	Khan *et al.*, 2014[72]
Quinoline alkaloids-Quinine	*Cinchona succirubra*	Alkaloids	Antimalarial, bitter stomachic	Sarin *et al.*, 2012[13]
Alkaloidal amines-Ephedrine	*Ephedra gerardiana*	Alkaloids	Bronchial asthma, joint ache, nasal decongestion	Sarin *et al.*, 2012[13]
Indole alkaloids-Reserpine	*Rauwolfia serpentina*	Alkaloids	Hypertension	Sarin *et al.*, 2012[13]
Vinca alkaloids-Vincristine and vinblastine	*Catharanthus roseus*	Alkaloids	Antineoplastic agent	Sarin *et al.*, 2012[13]
Ergot alkaloids-Ergometrine	*Claviceps purpurea*	Alkaloids	Migraine, oxytocic drug	Sarin *et al.*, 2012[13]
Tropane alkaloids-Atropine	*Atropa belladonna*	Alkaloids	CNS stimulant, antispasmodic agent	Sarin *et al.*, 2012[13]
Beta carotene	Carrots, green leafy vegetables	Carotenoids	Antioxidant, provitamins	Parasuram *et al.*, 2011[73]
Lycopene	Tomatoes, water melon, guava, papaya, apricots	Carotenoids	Antioxidant property	Parasuram *et al.*, 2011[73]
Lutein	Green leafy vegetables, egg yolks	Carotenols	Antioxidant property	Parasuram *et a*l., 2011[73]
Zeaxanthin	Maize, fruits	Carotenols	Antioxidant property	Parasuram *et al.*, 2011[73]
Capsanthin and capsorubin	Red peppers	Carotenols	Antioxidant property	Parasuram *et al.*, 2011[73]
Flavones-Luteolin	*Reseda lutea*	Flavonoids	Antioxidant, Anticarcinogenic	Shukla *et al.*, 2014[47]
Flavanones-Hesperetin	*Citrus limon*	Flavonoids	Anti-inflammatory, anti-allergic	Shukla *et al.*, 2014[47]
Flavanols-catechin	*Uncaria gambir*	Flavonoids	Hepatoprotective	Shukla *et al.*, 2014[47]
Flavon-3-ols-rutin	*Ruta graveolens*	Flavonoids	Antioxidant, anti-inflammatory	Shukla *et al.*, 2014[47]
Cardiac glycosides-Digitalis	*Digitalis purpurea*	Glycosides	Congestive heart failure	Ahmed *et al.*, 2013
Anthraquinone glycosides-Senna	*Cassia angustifolia*	Glycosides	Laxatives	Ahmed *et al.*, 2013

(*Contd...*)

Table 2: (*Continued*)

Phytochemicals	Source	Chemical classification	Therapeutic benefits	References
Saponin glycosides-Ginseng	*Panax ginseng*	Glycosides	Fatigue, liver diseases, regulates stress hormones	Ahmed *et al.*, 2013
Cyanogen glycosides-Bitter almonds	*Prunus amygdalus*	Glycosides	Anticancer	Ahmed *et al.*, 2013
Isothiocyanate glycosides-Mustard seeds	*Brassica nigra*	Glycosides	Local irritant, decongestant, rubefacient	Ahmed *et al.*, 2013
Aldehyde glycosides-vanillin	*Vanilla planifolia*	Glycosides	Flavoring agent	Ahmed *et al.*, 2013

Table 3: Illustration of different herbs with therapeutic benefits

Medicinal plant	Species	Part used	Therapeutic benefits	References
Garlic	*Allium sativum*	Fresh or dried cloves, garlic extracts	Arteriosclerosis, Lowers cholesterol	Pandey *et al.*, 2011[41]
Aloe	*Aloe barbadensis*	Gel, oral intake of juice	Antiulcer, anthelmintic, wound healing	Pandey *et al.*, 2011[41]
Kalmegha	*Andrographis paniculata*	Shoot powder	Respiratory tract infection	Srividya *et al.*, 2010[74]
Artemisia	*Artemisia annua*	Shoot decoction	Antimalarial	Srividya *et al.*, 2010[74]
Red pepper	*Capsicum annum*	Fresh and dried fruit powder	Antioxidant, stimulant	Srividya *et al.*, 2010[74]
Senna	*Cassia senna*	Dried leaf, pods	Constipation	Pandey *et al.*, 2011[41]
Turmeric	*Curcuma longa*	Dried root	Inflammation, indigestion, antioxidant	Pandey *et al.*, 2011[41]
Lemon grass	*Cymbopogon citratus*	Dried leaf	Stomach ache, carminative	Srividya *et al.*, 2010[74]
Ephedra	*Ephedra sinica*	Dried stem	Bronchodilator, anti-asthmatic	Dureja *et al.*, 2003[15]
Licorice	*Glycyrrhiza glabra*	Root powder	Anti-inflammatory, congestion	Dureja *et al.*, 2003[15]
Chamomile	*Matricaria chamomilla*	Dried flower	Wound healing, indigestion, insomnia	Dureja *et al.*, 2003[15]
Psyllium	*Plantago ovata*	Dried seed, husk	Constipation	Pandey *et al.*, 2011[41]
Amla	*Phyllanthus emblica*	Fruit pulp, dried fruit	Diuretic, anti-ageing, diabetes	Pandey *et al.*, 2011[41]
Chirata	*Swertia chirata*	Fresh or dried whole plant	Diabetes, migraine headache	Pandey *et al.*, 2011[41]
Ginger	*Zingiber officinale*	Fresh dried root	Indigestion, antioxidant	Dureja *et al.* 2003[15]

employing the active constituents obtained from different parts of herbs for treatment and utilization in various health problems are also been depicted in Table 3.

ADVANCEMENT IN DRUG DELIVERY SYSTEMS WITH MEDICATED HERBS

The increasing preferences of consumers to eat healthy food products and the nutraceuticals showing up to be favorable in preventing as well as curing many diseases impelled scientists and researchers to look for efficient delivery systems. The use of novel drug delivery system to deal with the efficacy issues of the products is drawing more and more attention of the researchers.

Nanoemulsions

Nanoemulsion is the nano-sized formulation in which two immiscible liquids are mixed to form a single phase, thermodynamically stable isotropic system with the help of an emulsifying agent. The droplet size ranges from 20 to 200 nm.[48] Resveratrol which is a natural compound found in red grape skin, peanuts, and blueberries has been found

to possess powerful antioxidant properties. However, the problem with the compound is the poor bioavailability. Therefore, to overcome the problem and enhance the effect, it has been encapsulated in the nanoemulsion formed with spontaneous emulsification method which has resulted in better retention and enhanced properties of the system.[49] Similar researchers have proven curcumin to be effective in the form of nanoemulsion for the treatment of inflammation in mice by the inhibition of inflammatory mediator.[50]

Liposomes

Liposomes are the spherical vesicles composed of phospholipids consisting lipid bilayer. These are spherical in shape and can be formulated using cholesterol and natural phospholipids.[51,52] Liposomes are also preferred to be an advanced delivery system for nutraceutical products. Intranasal quercetin liposomes is one of the examples which have been reported to enhance the penetration of quercetin through blood brain barriers and increase the therapeutic anticancer efficacy of the product.[53] Similarly, buccal liposomal formulation of silymarin has also been proved to offer hepatoprotective effect with enhanced bioavailability of the product resulting into better therapeutic response.[54,55] The antigout topical liposomal preparation of colchicine has also been proven very effective in the treatment of gout.[56]

Phytosomes

Phytosomes are the complex of phospholipids and the biologically active ingredients.[57,58] Oral formulation of Ginseng phytosomes, prepared using phospholipid complexation has been found to overcome the problem related to the low solubility of Ginseng and results in the increased absorption in the body which enhances the therapeutic effect of Ginseng as an immunomodulator.[59] Oral phytosomal preparation of Hawthorn (Flavonoid) having cardioprotective and antihypertensive properties has also been reported to offer enhanced efficacy. Quercetin, possessing the properties of an anticancer as well as an antioxidant compound was also subjected to the oral preparation of Quercetin phytosomes providing better therapeutic efficacy of the drug.[60] Furthermore, curcumin phytosomal oral preparation, using curcumin-phospholipid complexation method has also been researched on, and it has offered elevated bioavailability and increased antioxidant activity.[61]

Microspheres

Microspheres are the spherical vesicular particles falling within the diameter range of 1-1000 µm. Due to their small size, microspheres can be ingested or injected, can be adjusted to any desired release profile and can also exhibit site-specific as well as organ targeted drug delivery.[62] Intravenous preparation of camptothecin (natural product) loaded microspheres, formulated using oil-in-water evaporation method has been reported to provide prolonged anticancer effect.[63-66]

Transfersomes

Transfersomes are also known as the ultradeformable vesicles consisting of an aqueous phase as a core surrounded by the lipid bilayer complex which makes the formulation self-optimizing and self-regulating. Therefore, the transfersomes are capable of crossing several transport barriers conveniently and acts as the carrier in the non-invasive techniques of delivery.[66] The researchers have proven topical preparation of capsaicin transfersomes to offer enhanced skin penetration with improved analgesic effect.[67] Colchicine transfersomal formulation has also been studied to provide better penetration and thus advanced treatment of gout.[68] Similarly, *in vitro* preparation of vincristine transfersomes exhibits increased entrapment efficiency and improved skin permeation and results into the better therapeutic effect of the anticancer drug. Transdermal formulation of curcumin transfersomes has been also reported to deliver enhanced entrapment efficiency with intensified permeation through the skin which improvises the anti-inflammatory effect of curcumin on the body.[69]

CHALLENGES AND LIMITATIONS ASSOCIATED WITH DELIVERY OF NUTRACEUTICALS

The nutraceutical formulations are been taken not as medicines but as diet. Hence, unlike the pharmaceutical preparations, nutraceuticals preparations need to fulfill a whole lot more requirements. Since, the nutraceuticals include dietary supplements, functional foods, etc., the components used in the formulation must be of food grade. This limits the choices for the researchers and decreases the scope of innovations in the nutraceutical domain. Therefore, selection of suitable material for the preparation of the formulation is a great challenge.[70]

After the selection of the materials, the next challenge appears in the selection of the delivery system. The nutraceuticals materials consist of the biological products such as herbal extracts, proteins, peptides, vitamins, and hormones which have the tendency to degrade easily. The stability of the formulation is a factor which cannot be compromised. Furthermore, the core ingredient should be released only when triggered by any external stimulus such as pressure and pH or temperature. Thus, a suitable delivery system must be chosen on the grounds of its ability to deliver the food product effectively, exerting its desired effect.[70] After the preparation of the formulation, testing of the products again requires attention. The *in vitro* tests performed for this purpose allows us to get an insight about the pharmacokinetic mechanism and the rate and extent of the release of the core active ingredient. However, these tests have the limitations as they are unable to provide the data for the active uptake of the product, their metabolic responses, the biological variability of the nutraceutical product. Therefore, complete testing is required to analyze the influence of factors like food on the

response of the product.[8] Nutraceuticals is a subject which is not so known to the people and it still needs awareness in common people regarding its use and ability for its potential. The lack of recognition in the market paired with the deficit marketing and distribution leads to the shortfall in the investments in the food research, and this is creating a huge challenge to the growth of nutraceutical industries in India. Due to this insufficient awareness in nutraceuticals, the manufacturing processes in several firms give negligible consideration to product extraction, enhancement of the shelf life, storage of the crude and prepared materials, meeting the quality standards of the ingredients and prevention from the contaminations. The negligence of the functional foods and nutraceuticals is not limited to social level but has reached out to the judicial level as well. There are many federal regulations which are not applicable to the food products or are still in progress which could restrain the natural products from getting supplied for the commercial purposes.[8,70]

CONCLUSION

The studies have confirmed in many ways the crucial role of nutraceuticals in prevention and treatment of various diseases. Most of the people prefer the treatment of any ailment in a natural way which can be achieved by including nutraceuticals in regular use. The consumption of nutraceuticals provides best option to stay natural and to improve the quality of life. In addition, nutraceuticals can also provide an alternative for patients who are unwilling to go through chemical therapy. It is also advantageous over other therapies in terms of cost. The studies reveal the fact that nutraceuticals exert different types of biological activities in mechanized manner. These properties ultimately lower the age related and chronic diseases. Presently, large numbers of such potential nutraceuticals are undergoing the phases of research and development. The marketing graph of nutraceuticals is also rising all over the world. The market values reported depicts the public behavior of giving more emphasis on the use of nutraceuticals which ultimately is related to the brighter scope of nutraceutical industry. However, there is a huge scope for further advancement in the field by introducing delivery carrier and further spreading awareness about the potential of such systems. Therefore, the field undoubtedly has the greatest hidden value associated with it, which is just needed to be explored to provide easy and better healthy life.

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