NUTRACEUTICALS AS A NANOMEDICINES: IN THE MODERN WORLD OF MEDICINES

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ABSTRACT

This review article mainly provides an insight of application of nanotechnology in the field of nutraceuticals for the delivery of different food products which are rich in different vitamins, micronutrients, and other medical properties etc. Nanotechnology helps in solving the several critical challenges in delivery, absorption, safety, solubility, and stability of nutraceuticals. It also enhances the pharmacological properties and protect the nutraceuticals from the chemical and physical degradation. This article is giving the overview of nutraceuticals as a nanomedicine in the modern world of medicines and the medicinal properties of different nutraceuticals.

KEY WORDS: Nanomedicines, Nutraceuticals, Bioavailability, Phytosomes, Liposomes, Nano-emulsions, Micronutrients, Vitamins.

INTRODUCTION

Nutraceuticals are the materials that supply nutrition to our body when they are taken as a food supplements. They have ability to prevent diseases and helps in improving over all human health. The term and the idea of nutraceuticals was given by Dr. Stephen L. Defelice, who is also a chairperson and the founder of the 'foundation of Innovative Medicines' in NEW YORK city in the year 1989[1]. Nutraceuticals are genetically engineered food elements which improve the health of body by fighting against different serious diseases. In so many daily life experiences and research papers that has be shown that the Nutraceuticals have proven to provide so many health benefits such as immunity booster, act as antioxidants. They are safer than drugs with less toxic and side effects also having long half-life which result in improved bioavailability as compared to the chemical drugs [2, 3].

Some Important Constituents of Nutraceuticals [1, 2, 3]

1) **Dietary supplements:** Coenzyme and Carnitine.
2) **Micronutrients:** Vitamins and Minerals.
3) **Functional foods:** Probiotics and Prebiotics.
4) **Polyphenols:** Anthocyanins, Flavones, Stilbenes, Isoflavones.
5) **Terpenoids:** Carotenoids.

Nanotechnology is the production of nanoparticle-based drugs with the use of materials, equipment, and systems in nanoscale (intermediate range between atoms and the molecular scale) which acts as therapeutic agents [4]. These all are very essential for our body as antioxidants supplementary is used in form of nutraceuticals to control cell and tissue damage. Although the body contains its own natural antioxidants, but antioxidants can also use as nutraceuticals as per need of body. Also, carotenoids which we can get from fresh vegetables like tomatoes, green vegetables, carrots etc. which can prevent our body from cancer like diseases also help improve several cardiovascular diseases [3]. Probiotics also important type of nutraceuticals which help in reducing the growth of harmful bacteria in you GIT as they are living microorganism found in dairy products like sour milk and yoghurts etc. (lactobacilli). Carnitine is also important for bone health and to treat hypercholesterolaemia due to its effective action on blood lipids which are synthesized in liver and kidney from dietary amino acids are lysine and methionine [2]. So, we can say that nutraceuticals are widely helping in improving the quality of life by changing people diet by using natural products. But the real challenge come when the some of the important foods show poor bioavailability which are essential for our healthy body as they have short half-life and get removed from body without supplying its main active medicinal benefits [1]. This review mainly focus on how the nanotechnology can help as a nanomedicine in field of nutraceuticals so that we can use different food products as the immunity booster or in providing beneficial health benefits.

WHAT ARE NANOMEDICINES?

Nanomedicines are novel drug delivery system which comes under nanotechnology. The word “nano” means “dwarf”. Nanomedicines are tiny material size range between 1 to 100nm. They can be produced through various methods:

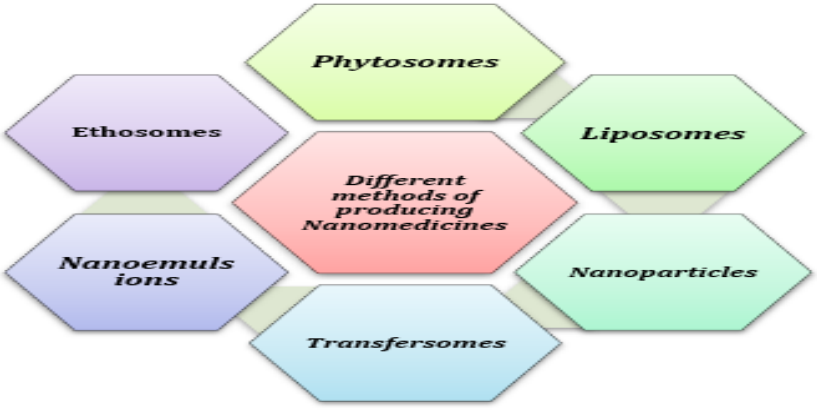

Fig: 2: Different types of nanomedicines carriers.

Phytosomes

Phytosomes also known by Phyto-Phospholipid complex. In first phytosomes are invented for cosmetic formulations but now days they are widely use in field of drug delivery system of herbal or nutraceuticals products. They are used as the medium for hydrophilic nutrients as well as lipophilic nutrients. They are given orally and get penetrate through lipoidal bio-membrane easily because of presence of phospholipid bilayer at its outer covering. And finally reach to systemic circulation. The complex of Phyto-Phospholipid is result of the formation of chemical bonds between phospholipids and hydrophilic nutrient [5,6]. Phytosomes, also known as phyto-phospholipid complexes prepared by complexing the naturally active phyto-constituent with phospholipids is a vesicular drug delivery system that enhance the absorption and bioavailability of poorly water-soluble drugs which gives intended pharmacological effect [7].

Liposomes

The liposome is the lipid bilayer structure of phospholipid and cholesterol where cholesterol is responsible for liposomal drug-delivery system and phospholipids are meant for the slow degradation of active pharmaceutical ingredients [8]. Liposomes are also known as microscopic, sealed lipid bilayer structure and nanometric lipid bilayer vesicles which contain hydrophilic drug molecules inside it. But its advantage is it also contain some molecules of lipophilic drug molecules encapsulated in between the lipid bilayer. Liposomes are biodegradable, chemically inert and their outer lipid bilayer is like the biological membranes of the cells which help them to increase its bioavailability in body by enhancing drug penetration [9].

Nanoemulsions

Nanoemulsion is one of the promising ways to extend food product shelf life which include water, oil, surfactants, and other additives such as bioactive compounds, preservatives, flavors, and colors [10]. Normally the Ordinary Different emulsions have its size range between 0.1-100 micron. But nanoemulsions have size ranging between 10-100nm. Nanoemulsion also known as microemulsion. There are mainly four types of emulsions i.e., o/w, w/o, w/o/w, o/w/o. For water soluble drugs w/o emulsion type is made in which the water is in dispersed phase and oil will be in continuous phase [5,9,11]. And the less water soluble i.e., lipophilic drugs are made into o/w emulsion where water is in continuous phase and oil in dispersed phase, so that when the macrophages eat the small emulsifier coated oil drug it gets released or concentrated in the targeted tissue.

Ethosome

Ethosomes is a type of unique drug delivery system in which ethanol is present in high amounts. In ethosome vesicles, ethanol, and skin lipids interact synergistically improve the distribution of active ingredients into the deep layers of the skin by increasing fluidity and lowering lipid multilayer density [12]. These types of drug carrier basically used for the transdermal drug delivery systems. They help the drug to enter deeper inside the skin and reach the systemic circulation. They are made up of mainly phosphatidylserine, phosphatidylcholine, phosphatidic acid these are phospholipids, and they also contain ethanol and distilled water. The higher the concentration of the ethanol more easily drug get entre inside the stratum corneum of skin. Both the water soluble and lipid soluble drugs can be delivery through this system Basically, used in the delivery of anti-inflammatory drugs [11].

Transferosomes

This type of system is first emerged in early 1990s, in ordinary transferosomes it has been seen that they do not penetrate through the stratum corneum they remain confined to outer layer of stratum corneum only. So, the novel form of transferosomes made by lipid vesicles which are more flexible lipid carrier are used now days to improve its penetration rate result in the drug get reach to deeper in skin and reach systematic circulation easily [9,11].

Nanoparticles

Nano particles also called solid lipid nanoparticles. The drug or active metabolites are entrapped, dissolved, or attached inside the matrix of the polymer like gelatin, albumin, ethyl cellulose, casein, polyanhydrides etc. nanoparticles have its size ranges between < 200 nm [3,9]. They are use in site specific targeting drug delivery system. Nanoparticles can be prepared by two types nanospheres (drug is entrapped inside the matrix of the polymer) and another type is nano capsules (in this type of drug is trapped in the core of the vesicle). Nanoparticles are help in increasing the pharmacodynamic activities of drug in the body.

MERITS OF NANOMEDICINES IN DELIVERY OF NUTRACEUTICALS [3,11,13]

1. They improve the active bioavailability in systematic circulation of different active substances and different food supplements.
2. Increase the solubility of product having low solubility profile.
3. Provide protection from the environmental factors like UV rays, moisture and dirt or contaminations.
4. They improve the overall pharmacological and toxicity profile of unstable ingredients.
5. They help in achieving the target drug delivery.
6. we can control the releasing rate of chosen ingredients and get sustain drug delivery system of drug.
7. We can achieve long shelf life of product.
8. They also help in the encapsulation of taste and the odour.

WHY WE NEED NANOTECHNOLOGY FOR DELIVERY OF FOOD SUPPLEMENTS?

The evidence from so many research papers shown that the balance diet play an important role in determination of different diseases. By taking Different nutraceuticals in our diet help our body in maintaining good body organ health, help in the growth of our body also improve the metabolism process. The foods like egg, milk, glucosamine, probiotics, vegetables, different spices, vitamins, fats, proteins (15 - 20%), carbohydrates (30 -40%), oils, minerals and so on all these are required by our body as per daily need to safe body from different diseases life malnutrition, skin infection, GIT problems, obesity, liver, and different organs disorders.

As shown in fig:3 we get all the essentials components for balance diet or for healthy body from our daily life normal foods also. Deficiencies of different nutrients due to improper diet can cause the degradation or lack of nutrients in our tissue organs which further result in improper physical, physiological and biological functions and in last we get the symptoms of different diseases and deficiency in body [2,5] so, it seen in different cases that taking all sufficient amount of nutrients from daily food diet is not possible then the nutraceuticals are way to solve this problem by taking nutraceuticals in case of oneself feel the appearance of clinical symptoms of any disease by knowing that they are not taking good diet. Nutraceuticals are the food supplements that are rich in different nutrients, minerals, vitamins etc. are given with the property of medications by using different technology of pharmaceuticals which help in improving quality of life and health of an individual. Nutraceuticals are given in different forms like powder, tablets, capsules, in drink form, soups and tinctures. According to different research the researchers found that Nutraceuticals are to be proved to provide different health benefits naturally by acting as immunity booster, antioxidants, improve gut flora, prevent different deficiency states. Due there these properties their demands are widely increases in the world. Different dietary foods and functional foods whose demands are widely increase in recent time are omega-3 fatty acids, probiotics, calcium, magnesium, herbal extracts, product rich in protein like nuts, grains etc., different vitamins, polylactic acid, curcumin, lycopene etc. [14].

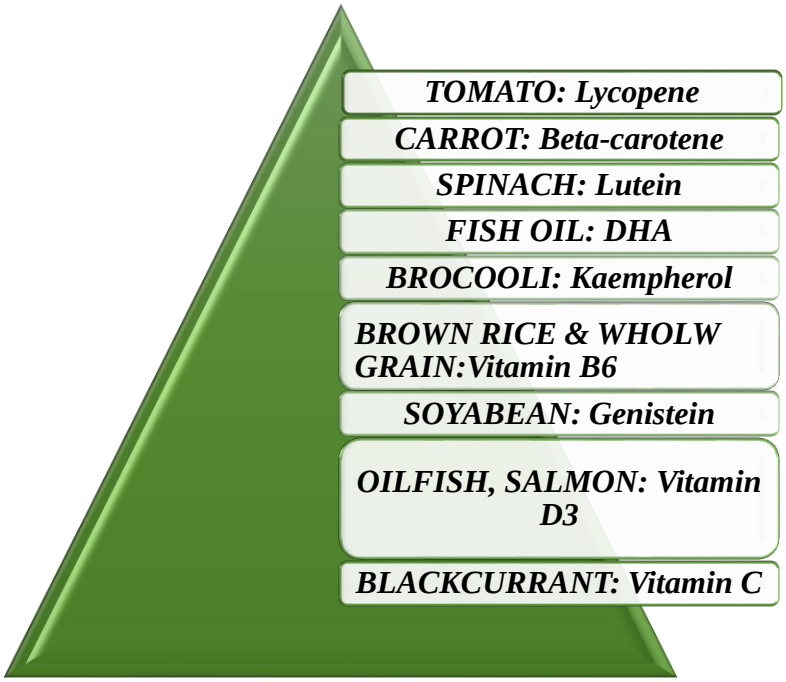

Fig3: List of food derived bioactive compounds need to formulate as Nutraceuticals: As they are rich in biologically active compounds whose deficiency may result in different diseases and imbalance in healthy lifestyle [6].

Despite of having so many health benefit properties of the nutraceuticals in different research papers we came to know that problem arises there when the concept of administration, metabolism, and in stability properties profile comes for example: essential fatty acids like omega-3 are one of the important nutrients which help in maintaining a healthy body as they are the important part of the cell wall of different cells in our body also provide energy to do work by keeping heart, lungs, immune system working properly. This fatty acid we basically get from the fish, seafood, nuts, walnuts, plant oils, soybean oil, flaxseed oil etc. [3,5,9]. Omega-3 class there are long chain of long-chain polyunsaturated fatty acids which help in fighting against heart disease and act as cardioprotective also act as anti-inflammatory and vasodilatory effect, but problem arises here that when they are administered, they are highly in risk of to be oxidation of the polyunsaturated fatty acid which further result in undesirable flavours and odours in product. Here the nanotechnology helps as alternative to protect omega fatty acids against oxidations reaction by enhancing the stability also the solubility of product which help in maintaining the colour, flavour, odour as well as the nutritional properties of the product. In case if they are taken in large quantity there may be a risk of heart diseases. So, with the help of nanostructure of it we can also achieve the control release of the omega-3 fatty acid and reduce the chance of toxicity and serious disease like cancer [15].

NANOTECHNOLOGY IN NUTRACEUTICALS

Improve bioavailability: -

Bioavailability known as the rate and extent of any therapeutic active compound that the systematic circulation and show its effect at the site of their action. Nutraceuticals like curcumin, gallate {plant polyphenols} and lycopene, lutein, beta carotene and zeaxanthin also many more carotenoids are used to lower the B.P, reduce cancer risk, regulate growth and blood glucose level in our body but they are poorly soluble compounds (hydrophobic in nature) the compounds which poorly soluble in oil and water can cause problem in the route for their administration, transport also in the bioavailability orally[15]. So, by encapsulation of them in different nanomaterials help in increasing their bioavailability for example: encapsulation of triglycerides in liposomal nanoparticles they get converted into the free fatty acids and monoglycerides which are combined with the different bioactive materials which help it to cross the cell membrane and then transported to the systematic circulations. Also, by decreasing in the size of nutraceuticals it helps in achieving the bio accessibility of the nutraceuticals [5].

The liposomal formulation based on nanoparticles the material which is widely used by the experts is phosphatidylcholine nano lipid complex, soya- phosphatidylcholine andrographolide complex which is widely used with those substance having problem of poor absorption of silymarin. In food industry use of nanotechnology is done to modify the absorption of junk foods like ice cream and chocolates by using reduced form of the fats and sugars.

Different nanomedicines forms are used in the formulations of nutraceuticals to improve their absorbance and bioavailability like Nano-capsules in which the different antioxidants which help our body to fight from the free radical damage also different essential oils, vitamins, minerals, coenzyme etc so that their bioavailability in human body.

And Nano-liposomal formulation is used to deliver the enzymes, nutrients and antibiotics containing properties nutrients. It's also used in the supply of genistein, carotenoids, conjugated linoleic acid etc which is an important phytochemical. Also, the encapsulation of vitamin B9 with the zein nanoparticles help in remain confined in the GIT which result in increase in the bioavailability when given orally [3,16,17].

Reduce The Chances of Toxicity and Enhance Stability: -

As Nutraceuticals have so many medicinal and health properties it is important to take them in proper amount and in write manner because so many of the food products may cause toxicity to body if not taken in right manner. For example: vitamin C is important part of the diet because it acts as antioxidant, anticancer, antimicrobial, immunocompetence, antidiabetic, antiradiation as well as antisepsis. Its deficiency may cause kidney disfunction in diabetes. It is a wate-soluble vitamin. So much research shown that taking improper amount of ascorbic acid have negative impact on human health. Vitamin C is highly sensitive in nature as when it exposed to light, alkaline pH, high temperature it loses its function and converted into biologically inactive form. So, encapsulation of ascorbic acid in nanoparticle Chitosan which is cationic polyelectrolyte of N- acetyl glucosamine in nature. Which increases the stability of the ascorbic acid. Chitosan nanoparticles also help in formulation of stable flavours, enzymes, antimicrobial agents etc. because it is lipophilic in nature as chemically it has free amino groups in its structure. It can only be soluble in acidic pH as it under So protonation of amino group [16,18]. Nano structured lipid carriers are used to enhance the stability of the Vitamin A to produce the chemically and physically stable form of bioactive lipid. Also, beta-carotenes are encapsulated within the oil in water type nano emulsion which prevent it from degradation and can be stored for up to 90 days at 4 degrees Celsius in dark. Also, the vitamin D3 has been encapsulated within the protein polysaccharide complex it can be stable for 31 days at 4 degrees Celsius and in boiling milk the stability of vitamin D2 can be improved by encapsulation by caseinate nanocomplexes. Omega-3 fatty acid are encapsulated within solid lipid nanoparticles [9,18].

To Attain the Sustain Release and Target Drug Delivery: -

Nanotechnology in field of nutraceuticals help in achieving tor to overcome the different physiological, biological, and chemical barriers in the delivery of different food products. Novel drug delivery of nutraceuticals can be Achieve by using materials for encapsulation like polysaccharides (starch, gum, pectin); microbial polysaccharides (xanthan gum, dextran); emulsifier like tweens, sugar, snaps, esters, lecithin etc.
which help in the sustain release of bioactive compounds encapsulated in it and to target drug delivery by using appropriate vehicles which intact to the desired site in body[15]. In some research it is seen that the combination of alginate and poly caprolactone is used to prepare the white tea extract which present in core of the polymeric nanoparticles by using the nanoprecipitation techniques. The system of nanoparticles help in protection of polyphenolic extract substances and its release in GIT is controlled also its antioxidant property is maintained for long period of time.

Solid lipid nanoparticles carriers have ability to control the release rate of drug loaded inside it and it also have high loading capacity of non-water-soluble drugs [14,15]. Different derivatives of starch are famous because of their great potential to develop hydrogels type matrix in which drugs are encapsulated like Nano-sponges which are the modified form of dextrin, are hyper cross-linked polymers that can be obtained by treating it with cyclodextrins. They used in delivery of the food products in this modern world to reduce their side effects, enhance stability, prolong release. These hydrogel gels when meet the body fluids due to diffusion process the cross-linked polymer start opening and get swell then after some times the encapsulated drug start releasing this process is slow which result in the drug release is controlled for long period of time. Nutraceuticals like curcumin, resveratrol, melatonin, and other bio-actives are delivered through this system.[19]

Nano nutraceuticals To Treat Disorders and Disease: -

Treatment of different diseases by using Nano-nutraceuticals technique is one of its applications. With the help of nutraceuticals today this treatment has saved the lives of so many peoples suffering from different life-threatening diseases like cancer. Nutraceuticals such as garlic, green tea, honey, soya bean etc. can reduce the chances of apoptosis of cancer cells. These foods are used as an anticancer therapy. In some studies, it has found that the epigallocatechin-3-gallate is the widely used as Chemo-preventive in cancer polyphenol which is obtained from the green tea. It inhibits the beta car degradation in corn oil in water emulsions. Also, the cinnamon oil and the encapsulated vitamin D in nanotechnology help in arresting the cell division cycle progression in G1 phase as result in increase in expression of Bax, caspase-9 and decreased in expression of BcL2 proteins along with increase in the apoptotic cell number and decrease in the mitochondrial potential [5,6,20]. To achieve the life-long healthy diet nutraceuticals are most beneficial effect on body like phenols in green tea, red berries, olive oil, red wine etc. has effect on amyloid neurodegenerative diseases.

FOOD	CARRIER SYSTEM	BENIFITS OF NANOTECHNOLOGY	HEALTH BENEFITS
Carotenoid extract (Yogurt)	Nano-emulsions	Improve storage stability, in vitro delay release, enhance viscosity	Help in improving GIT health and immunity
Vitamin D3 (Skim-milk, lassi, plant-based milks)	Nano-lipid carrier, nano-emulsions	Control release in intestinal fluid, protect against degradation	Important for bones& teeth, helps the body to absorption and utilization of calcium
Beta-sitosterol, phytosterols (Butter, puddings)	Nano-lipids carriers, nano-porous based starch aerogels	Enhance stability, antioxidant activity and bio-accessibility	Anti-atherogenic, immune stimulation
Omega-3 fatty acid (Present in salmon and flax seeds)	Solid lipid nanoparticle	Control release can be Achieve, improve solubility	Help in maintaining healthy brain function and control inflammation process, fight against cancer
Alpha-tocopherol	Nanosuspension	Increase bioavailability, improve stability, increase the dissolution rate	Helping with wound healing, promoting healthy skin
Folic acid with commercial resistant starch	Folic acid with commercial resistant starch	Enhance stability and efficacy	Important to maintain healthy genetic materials in cell

TABLE: List of some nutraceuticals delivered using nanotechnology with their benefits to body [2, 6, 9, 21, 22].

Thioflavin T, biodegradable polylactic-co-glycolic acid nanoparticle which is encapsulated with ginsenoside Rg3 this combination has showed the neuroprotective effects also used in the treatment of Alzheimer's diseases. Also, the beta carotene, lycopene, turmerin and curcumin etc. also exert beneficial effect on body by neutralizing the harmful effect of oxidative stress in mitochondrial dysfunction and in other different neural degenerations.

CONCLUSION

Nanotechnology has been used in the field of nutraceuticals due to their advance properties to improve delivery rate by modifying the physical and chemical properties of nutraceuticals which further help in improving the healthy lifestyle and to achieve the balance diet of individual. Also, to prevent and in treatment of different diseases. Nanotechnology gives the platform to different sectors to improve the efficacy and the safety of different products also to reduce the chances of toxicity and having deficiencies of micronutrients by replacing the conventional technologies or by reaching their limits. In short in this review, it is shown that the nanotechnology has a great potential in field of nutraceuticals and herbal drug delivery system, also its utilization in effective disease treatment and prevention.

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