ROLE OF NANOTECHNOLOGY IN NEUTRACEUTICALS

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ABSTRACT:

Nanotechnology can enhance the solubility, stability, and bio availability of active ingredients, its application in nutraceutical is expanding quickly. Their small size and high surface-to-volume ratio are what give them their distinctive qualities. However, the possible negative impacts of nanoparticles on human health are also caused by these physico-chemical characteristics. It is necessary to assess the efficacy and safety of novel marketable nutraceutical compositions. The food business is currently being invaded by nanotechnology, which has enormous potential. Applications of nanotechnology in the food sector include: delivering and encapsulating materials at specific locations, boosting flavour, adding antimicrobial nanoparticles to food, extending shelf life, detecting contamination, better food storage, tracking, tracing, and trademark protection. Nutraceutical, which provide health advantages and can replace modern medicine, have gained popularity in recent years. Vegetables and fruits high in nutraceutical are essential to a balanced diet. Food supplements, dietary supplements, processed foods with additional value, and non-food supplements such tablets, soft gels, and capsules are examples of such goods.

KEYWORDS:

Nanotechnology, Nutraceuticals, Nanoparticles, Bioavailability, Food Industry, Encapsulation, Food Safety, Nano-material, Functional food, Health Benefits.

NANOTECHNOLOGY:

The area of nanotechnology that focuses on working with individual atoms and molec ules, particularly when dealing with tolerances and dimensions less than 100 nanom etre. The ability to modify and control a substance at the nanoscale (nm) level is known as nanotechnology (1nm = one billionth of a meter)[1].

Natural nanostructures include things like cell membranes, hormones, DNA, and food components including proteins, lipids, and carbohydrates. According to Helmut Kaise r Consultancy (2009), the number of patent applications and the development of nano products related to food and dairy is expected to increase[2]. Applications of nanotechnology include the addition of various nanoscale materials to food and the use of nano encapsulation methods as means of delivering additional food ingredients. additives in the form of nanoparticles may improve the bioavailab ility or functioning of nutrients an additives, reducing the amounts required in the final food product . To manage the ma terial qualities of foodstuffs, such as in the production of ice cream to promote texture consistency, food businesses are currently generating nanoparticles in emulsions [3].

HISTORY OF NANOTECHNOLOGY:

People were using nanolevel procedures and unintentionally encountering a variety of nanosized things long before the period of nanotechnology. Black hair dyeing was po pular in ancient Egypt and was long thought to be derived from plant materials like he nna. But according to new studies on hair samples taken from ancient Egyptian tombs , the hair was dyed using a paste made of lime, lead oxide, and water.[4] Early use of PbS nanotechnology for an ancient hair dyeing formula. Te ancient Egyptians were able to make the dyeing paste react with sulphur (part of hair keratin) and produce small PbS nanoparticles which provided even and steady dyeing. Probably the most famous example for the ancient use of nanotechnology is the Lycurgus Cup (fourth century CE). This ancient roman cup possesses unusual optical properties; it changes its colour based on the location of the light source. In natural light, the cup is green, but when it is illuminated from within (with a candle), it becomes red. The recent analysis of this cup showed that it contains 50–100 nm Au and Ag nano- particles[5]. Galenite (lead sulfide, PbS) nanoparticles are created during this dyeing process. By reacting the dyeing paste with sulfur (a component of hair keratin), the ancient Eg yptians were able to create tiny PbS nanoparticles that allowed for consistent and equa l coloring. The Lycurgus Cup, which dates back to the fourth century CE, is argua bly the most well known example of the early application of nanotechnology. This ancient Roman cup has unique optical characteristics; dependin g on where the light source is, it changes color. The cup is green in natural light, but t urns red when lit from within (with a candle). According to a recent investigation, this cup includes Au and Ag nanoparticles ranging in size from 50 to 100 nm7[6]. which are responsible for the unusual colouring of the cup through the effects of plasmon excitation of electrons. The ancient use of nanotechnology does not stop here, in fact, there is evidence for the early use of nanotechnology processes in Mesopotamia, Ancient India, and the Maya.[7]

CURRENT APPLICATIONS OF NANOTECHNOLOGY IN FOODS:

Some of the benefits of Nano science have already been seen in the agro food sector, others are still at the research and concept stage. They include the following global applications:

1) Sensory improvements (flavour/colour enhancement, texture modification).

2) Increased absorption and targeted delivery of nutrients and bioactive compounds.

3) Stabilization of active ingredients such as nutraceuticals in

food matrices.

4) Packaging and product innovation to extend shelf-life.

5) Sensors to improve food safety.

6) Antimicrobial to kill pathogenic bacteria in food.[8]

NEUTRACEUTICALS:

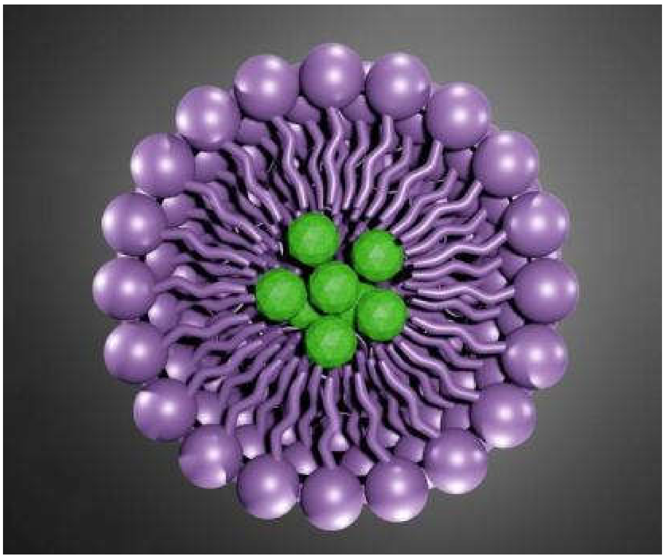
Dr. Stephen DeFelice, the chairperson of the Foundation for Innovation in Medicine, introduced the term "nutraceutical" in 1989 as a combination of the terms nutrition and pharmaceutical. Any substance that may be categorized as a food or a food component that provides health or medical benefits, including illness prevention and treatment, is referred to as a nutraceutical (Brower, 1998; Kalra, 2003; +Biesalski, 2001; Keservani et al., 2010). Any food or food item that may offer health benefits beyond the conventional nutrients it includes is considered a functional food (Keservani et al., 2015d). on the advantages of their end users, or consumers, has given the nutraceutical and functional food industries a unique area of concentration and sparked a notable interest in these products.[9] In recent years, people have attempted to improve their quality of life by changing their diet and using natural and alternative products in place of modern medicine. As a result, the market for nutraceuticals and associated R&D are expanding quickly.[10] Nutraceuticals can be broadly categorized into three groups, such as supplements (nutrients, minerals, etc.), herbals (spices or natural things), and dietary improvement (glucose, probiotics, etc.). Additionally, many use them daily as an alternative to the medications that are now available, improving quality of life and extending the future. They have been shown to have advantages such long half-life, enhanced absorption, fewer adverse effects than medications, and a natural immune-boosting and antioxidant effect.[11]Historically, certain foods used to prevent or treat illness have been classified as drugs by the US Food and Drug Administration (USFDA).*Swarnali Das Paul * and Divya Dewangan Faculty of Pharmaceutical Sciences, Shri Shankaracharya Group of Institutions, SSTC, Bhilai,CG,India.* .Nutraceuticals are bioactive substances that are present in food and have health or medical advantages, such as the ability to prevent and treat illness. They consist of probiotics, vitamins, minerals, antioxidants, polyphenols, and substances obtained from plants. However, the therapeutic effectiveness of many of these compounds is limited due to their low permeability, poor water solubility, and gastrointestinal system degradation.The market for such functional foods and related components is expected to reach approximately $140 billion by 2020, driven by an increase in the demand for innovative food products, fortified healthy foodstuffs, and the simultaneous analysis of healthy food ingredients, which was previously impossible (Intelligence 2016).[12]A good therapeutic alternative for preventing diabetic mellitus and hypertensive problems, or as an adjunct to treatment with conventional drugs, may be nutraceuticals with a well-established impact on pregnancy and an effective safety profile. Potentially successful prospects for innovative nutraceutical include calcium, omega3 polyunsaturated fatty acids, vitamin D, folic acid-resveratrol, alpha-lipophilic acid, zinc, inositol, and probiotics supplement.[13].

According to a recent assessment, the nutraceutical business is growing internationally and is expected to reach $340 billion by 2024. Nutraceuticals are expected to increase at a compound annual growth rate (CAGR) of 7.2% between 2016 and 2024. Numerous variables, including increased demand for nutraceuticals, public knowledge of the advantages of nutrition, and an incremental rate seen in the healthcare graph, are linked to this increase in the growth of the nutraceuticals-based sector.[14]

Formulation of Nanotechnology in Nutraceuticals.

1.Nanoparticles

Nanoparticles Typically, to entrap nutraceuticals in nanoparticles, an aqueous solution of the drug is combined with a co-solvent and a n the presence of hydrophobic polymer in water (i lack of surfactant). The nutraceutical becomes trapped inside the polymeric core when these components mix to form a matrix or carrier, which eventually aggregates and causes condensation (Semyonov et al. 2014). Utilizing materials including proteins, polysaccharides, and synthetic polymers are key components of nanoparticles synthesis (Abd El-Salam and El-Shibiny 2012; Zimet et al. 2011). Alternatives are among the most commonly used natural polymers in the production of polymeric nanoparticles. Because of its exceptional bio compatibility and biodegradability, the US Food and Drug Administration has authorized poly (lactic-co-glycol acid), a readily accessible polymeric substance, for therapeutic use (Yu and Huang 2013). Colloidal particles, which range in size from 100 to 200 nm and have a higher dispersibility, are generally larger than micelles. The drugs are attached to the polymer matrix of these particles by chemical bonding, encapsulation, dispersion, or enclosure smaller size.[15] Furthermore, a taxonomy of NPs according to their size, shape, and chemical makeup is provided. The topic of NP agglomerations and homogeneity is covered, with an emphasis on super paramagnetic NPs and related nano- composites. A nanoparticles can be anything from 1 to 100 nm in size. Compared to bulk metals, metallic nanoparticles exhibit distinct physical and chemical characteristics (such as lower melting temperatures, larger specific surface areas, certain optical qualities, mechanical strengths, and particular magnetization),



characteristics that might prove attractive in various industrial applications. However, how a nanoparticles is viewed and is defined depends very much on the specific application.[16]. NPs come in a variety of sizes, shapes, and configurations. They may be irregular or spherical, cylindrical, conical, tubular, hollow core, spiral, etc[17]

.NPs are typically divided into three types based on their composition: inorganic, carbon-based, and organic

1.Organic NPs: This category includes NPs derived from polymers, proteins, carbohydrates, lipids, and other organic substances[18]. Ferritin, liposome, dendrites, and micelles are a few examples of well-known organic nanoparticles. These organic nanoparticles are more appropriate for the biomedical industry, eco-friendly, non-toxic, biodegradable, and affordable. Both liposome and micelles have hollow cores, commonly referred to as nano capsules, and are susceptible to electromagnetic and thermal radiation. Organic NPs are the perfect option for medication delivery because of these special qualities. When it comes to target medicine delivery, they are incredibly effective.[19].2. Inorganic nanoparticles NPs that are not composed of carbon or organic elements fall into this category. Metal, ceramic, and semiconductor nanoparticles are common examples of this class. Metal nanoparticles (NPs) can be mono metallic, bimetallic, or poly metallic and are entirely composed of metal precursors. Bimetallic nanoparticles can be generated in layers (core–shell) or from alloys.These NPs have special optical and electrical features because of their localized surface plasmon resonance characteristics. Furthermore, several metal nanoparticles have special biological, magnetic, and thermal characteristics. Because of this, they are becoming more and more crucial components for the creation of nano devices that have a wide range of physical, chemical, biological, biomedical, and pharmacological uses (more on these uses are covered in the review's applications section).Nowadays, the production of advanced materials depends on the size-, shape-, and facet-controlled synthesis of metal nanoparticles.[20].Semiconductor materials, which have characteristics of both metals and non-metals, are used to make semiconductor nanoparticles. When compared to bulk semiconductor materials, these NPs exhibit notable changes in their characteristics with bandgap tuning and have distinctively large band-gaps. These NPs are therefore crucial components for electrical, optical, and photo catalytic devices. Inorganic solids known as ceramic nanoparticles (NPs) are composed of metal and metalloid oxides, carbides, phosphates, and carbonates, including calcium and titanium. They can be amorphous, poly crystalline, dense, porous, or hollow, and are often created by heating and then cooling the mixture. Because of their great stability and high load capacity, they are mostly utilized in biomedical application. How ever they are also employed in other fields as phonics, microelectronics, dye degradation and catalysis[21]. Nanoparticles Based on Carbon In the fields of nanoscience, material science, engineering, and technology, carbon-based nanoparticles are highly popular. Carbon nanostructures are made up of several low-dimension carbon allotropes, including geographer, fullerene, and carbon nanotube. Because of their special hybridization qualities and sensitivity to synthesis perturbations, carbon nanostructures allow for fine-grained mechanical property adjustment. Drug delivery, tissue engineering, biosensor, imaging, diagnosis, and cancer treatment are just a few of the biological applications for carbon nanostructures, which have special electrical, mechanical, and structural properties.[22] Carbon nanotube: In 1991, Maximize made the initial discovery of the carbon.Carbon nanotube can be divided into two varieties: single-walled and multi walled. •Geographer: By wrapping into fullerene, stacking into graphite, and rolling into nanotube, geographer serves as a building block for other carbon allotrope. Wide surface area, high mechanical strength, thermal stability, good conductivity, and a sp2 hybridized honeycomb lattice structure with negligible energy band gaps are just a few of graphite's exceptional qualities.Fullerene: Due to its spherical shape, fullerene (C60) is often referred to as buckyballs. The first fullerene was discovered in 1980 by H. Kroto, R. Smalley, and R. Curl, and it was named after BuckministerFuller . Because fullness have excellent carrier capacity, low background current, great chemical stability, and strong bio compatibility, they are also employed to build biosensors. Uses for Nanoparticles In the field of food technology, micro- and nanotechnology are powerful instruments.[23] Developing micro- and nanoparticles with an active ingredient as bioactive compounds, improving flavor, odor, and packaging coating molecules, and creating polymers derived from food (proteins, carbohydrates) such as chitosan, alginate, gelatin, agar, starch, or gluten are all made possible by the electroscope technique, which is booming. Because it is easy to use, inexpensive, requires few solvents, and yields products in a single step, the electroscope technique offers more benefits for developing micro- and nanoparticles than traditional methods like nano precipitation, emulsion-diffusion, double-emulsification, and layer-by-layer.Further study is needed to prepare regulated and/or prolonged release systems of fertilizer or agrochemical—a strategy that might also be used in the agrifood industry. Because of its special qualities, such as their huge specific surface area and ease of separation with magnetic fields, magnetic iron oxide nanoparticles have found application in a variety of sectors. They have been applied to food-related processes such as food analysis, protein purification, and enzyme immobilization. The fundamental ideas and developments of magnetic iron oxide nanoparticles in food analysis, protein purification, and enzyme immobilization are outlined in this paper. They have also been assessed for their invaluable contribution to food engineering[24].

Drug delivery:

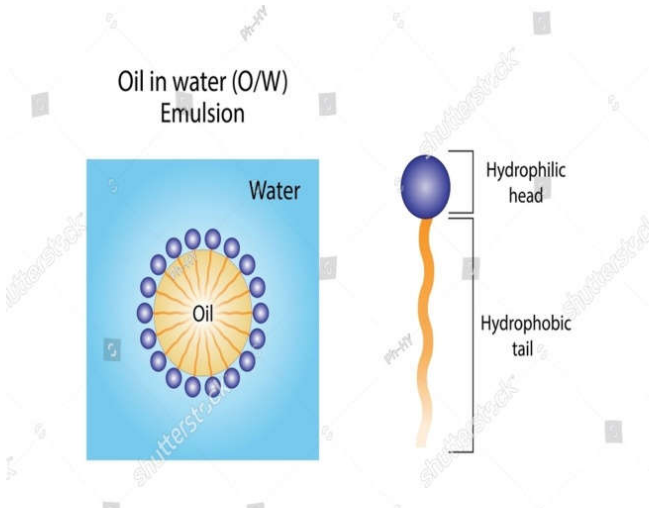
TABLE 1

Route	Main use	Challenges	Benefits of nanoparticles
Oral	Systemic absorption,functional food	Poor solubility,GI degradation	Protects drug,enhances absorption
Topical	Skin health, cosmetics,dermatology	Low permeability, degradation	Enhanced skin penetration,sustained action
Ocular	Eye disease,oxidative stress protection	Short retention,poor absorption	Better corneal delivery and prolonged effect
Rectal	IBU,local gut therapy,	Poor patient	Mucosal adhesion

	systemic delivery	compliance, variability	and bypass of first-pass metabolism

2.Nanoemulsion

The nano emulsion to traditional emulsions, they have improved functional qualities. It is possible to regulate the emulsification structure and composition to effectively encapsulate and transport bioactive lipophilic substances. In the food sector, nano emulsions may be used to provide antimicrobial, coloring and flavoring ingredients, and nutraceuticals. Food quality, shelf life, nutritional value, and functional qualities can all be improved by using nano emulsion formulations of active substances to create biodegradable coating and packaging films. The creation of food-grade nano emulsions utilizing both high-energy and low-energy techniques, as well as their



evaluation.[25].Sage forms, including liquids, creams, sprays, gels, aerosols, and foams, can be created from nano emulsions, and they can be taken through a variety of similarly varied routes, including topical, oral, intravenous, intranasal, pulmonary, and ophthalmic. They have been used as an aqueous foundation for organic deliverable in the cosmetic and pesticide industries. They have a better solubilization capacity than simple micellar dispersion and more kinetic stability than coarse emulsions.[26].The benefit of nano-emulsion:

* Lower the surfactant concentration; 3–10% may be adequate.

* The topical application droplets are sufficiently tiny to disperse uniformly throughout the skin.

*They can effectively transport active chemicals via the skin.

*The large surface area of the emulsion system, the system's general low surface tension, and the O/W droplets' The improved penetration of the active drugs is a result of less inter facial tension.

* The nano emulsion's small size allows it to pass through the rough skin surface, improving the active ingredients' penetration.

* The system's fluidity (at low oil concentrations) and lack of thickness may provide them a favourable skin feel and visual appeal.

* Reduced energy consumption

* Improved patient compliance

* Assists in flavour masking

* Liquid dosage form offers defense against oxidation and hydrolysis as a medication in the oil phase of an o/w emulsion. [27]. Nanoemulsion-Based Systems' Drawbacks

1. The application of high concentrations of co-surfactant and surfactant, which are required to stabilize the nano droplets.

2. Limited ability to dissolve compounds with a high melting point.

3. For pharmaceutical applications, the surfactant needs to be nontoxic.

4. Environmental factors like pH and temperature have an impact on nano emulsion stability. When patients receive nanoemulsion, these parameters alter.[28].

Uses Using nano emulsions to deliver drugs Several drug delivery techniques, such as topical, ocular, intravenous, intramuscular, intranasal, and oral delivery, use nano emulsions. They use their adjustable charge and rheology to produce aqueous solutions and their lipophilic nature to dissolve medications that are insoluble in water. Nano emulsions are employed as ultrasound imaging agents and provide benefits for hydrophobic medications.DRUG DELIVERY 1.Oral Administration : By loading drugs—especially protein drugs—into lipids, lipids can be employed as nano emulsions to improve the absorption process overall and increase drug absorption in the GIT.

2.Topical administration : It is difficult to improve drug penetration for topical application because of their poor dispersibility and skin-irritating properties. Soybean lecithin, tween, and polymer are examples of nano emulsions that combine a concentration gradient and improved penetration.

3. Intravenous administration : Parenteral nano emulsions transform into stealth delivery systems for medications with limited therapeutic indices and reduced bioavailability. By adding a hydrophilic moiety to nano emulsions, permeability and retention are improved for tumor targeting.

4. Targeted medication administration : A common trans dermal medicine delivery method is nano emulsion technology. Because of their small size, wide surface area, ease of transportation, and surface drainage, nano materials can connect more substances and collect at the skin's surface.[29] 5. Cosmetics using nano emulsion : For optimal dispersion of active substances in skin layers and controlled cosmetic delivery, newer materials (NEs) are becoming more and more crucial. They facilitate skin penetration and are appropriate for carrying lipophilic substances, which raises the concentration of active ingredients. Additionally, NEs contain bioactive properties that improve the function of the skin barrier and decrease trans-epidermal water loss. Because they don't cream,sediment, floculated, coalescence,they are suitable in cosmetics. Kemira Nano Gel is a novel nano-based gel created by TRI-K Industries and Kemira to increase the efficacy of skincare products. By converting an oil-in-

water concentration into sub micron emulsions, the novel NE Carrier technology reduces trans epidermal water loss and promotes skin development. This technique gives skin a pleasant sensation and is very helpful in moisturizing, anti-aging, and sun care products.[30]

6. The use of nano emulsion in cell culture Cell cultures are employed in the production of biological substances and in vitro tests. Cells have had trouble absorbing chemicals that dissolve in oil. A novel technique for supplying oil-soluble materials to mammalian cell cultures is the use of new encapsulated compounds (NEs). Because of their excellent bioavailability, these transparent, phospholipid-stabilized NEs enhance cell growth and vitality and enable toxicity testing of oil-soluble medications in cell cultures.

7. Nano emulsion as a preparation for antimicrobial For optimal dispersion of active substances in skin layers and regulated cosmetic delivery, NEs are becoming more and more crucial. They have a small droplet size, promote skin penetration, and raise the concentration of the active component.

In addition, NE's exhibit bioactive properties that prevent creaming, sedimentation, flocculation, and coalescence, as well as lowering trans-epidermal water loss . Kemira Nano Gel is a novel nano-based gel created by TRI-K Industries and Kemira to increase the efficacy of skincare products. By converting an oil-in-water concentrate into sub micron emulsions, the novel NE Carrier technology reduces water loss and promotes the growth of new skin. Creams for moisturizing, anti-aging, and sun care benefit greatly from this technique.

8. Using nano emulsion to enhance oral administration of poorly soluble medications. Nano emulsion is often used to increase the solubility of medications that are not very soluble. Due to their poor water solubility, BCS class II and IV medications have difficulties when administered in traditional dose forms. A solution for increased solubility and therapeutic efficacy is provided by nano emulsions.[31].9. The Use of Nano emulsions in Cancer Treatment In cancer treatment, nano emulsions can be employed as a vehicle to increase the rate of drug release following intra tumor and intramuscular injections (W/O systems). Additionally, because it is a non-irritating method and increases the transport of anti-cancer medications via lymphatic permeation via the skin, it improves trans dermal drug delivery.

10. Non-emulsion medication administration in the lungs. Because of its non-invasive administration through inhalation aerosols, ability to bypass first-pass metabolism, direct delivery to the site of action for the treatment of respiratory diseases, and large surface area for both local and systemic drug action, the lung is the most crucial target for drug delivery.

The potential for relatively uniform drug dose distribution among the alveoli, improved drug solubility from its own aqueous solubility, sustained drug release that thereby lowers dosing frequency, increases patient compliance, lowers the incidence of side effects, and the possibility of drug internalization by cells are just a few of the many benefits that colloidal carriers—also known as nano carrier systems—offer in pulmonary drug delivery.

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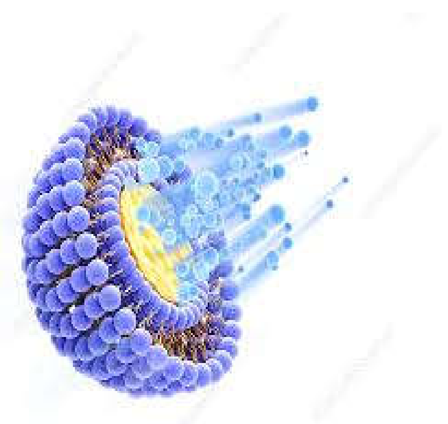
11. Intranasal medication delivery using nano emulsions A dependable method of administering medications, in addition to Parenteral and oral routes, is the intranasal drug delivery system. The nasal mucosa has become a therapeutically viable route for administering systemic medications and also seems to be a good technique to get around the barriers that prevent pharmaceuticals from entering the target location directly. Additionally, this method is well-tolerated, non-invasive, and painless. Because of its relatively permeable epithelium, large availability of immune active sites, and decreased enzymatic activity, the nasal cavity is one of the most effective sites. Targeting pharmaceuticals to the brain presents a number of challenges, particularly for hydrophilic and high molecular weight medications. This is due to the endothelium's impermeable nature, which separates the blood and brain from the systemic circulation. The nasal mucosa's olfactory region serves as a direct conduit between the nose and the brain, and disorders like meningitis, Parkinson's disease, Alzheimer's disease, migraine, depression, and schizophrenia can be treated using drug-loaded nano-emulsions. There have been reports of risperidone nano-emulsions being prepared for nasal administration to the brain. The nasal route is thought to be more successful than the intravenous method for this emulsion. The development of vaccines is another therapeutic purpose for intranasal drug delivery systems. Mucosal antigen is administered to induce Immunity the first intranasal vaccine is currently available for purchase. The use of nano-based carriers is one of the most promising delivery methods because it can protect biomolecules, encourage nanocarrier interaction with mucosae, and guide antigen to lymphoid tissues. Therefore, the use of nano-emulsions in intranasal drug delivery systems is expected to have a major impact on the ability to target medications to the brain in the treatment of central nervous system illnesses. For longer-acting rizatriptan benzoate, Bhanushalietal created gel and intranasal nano-emulsion formulations. To create thermos triggered mucoadhesive nano-emulsion a variety of mucoadhesive agents were tested.[32].

3.Nano liposomes

Phospholipid, a lipid bi-layer with an aqueous core, make up liposome, which are nanoscale spherical vesicles. To maintain their size within nano-metric scales, such as small liposome (20–100 nm) and large liposome (>100 nm), nanoliposomes have a superior surface area and an acceptable stability profile . Lipids and phospholipids make up the majority of these carriers.[33]. Are powerful nano carriers because of



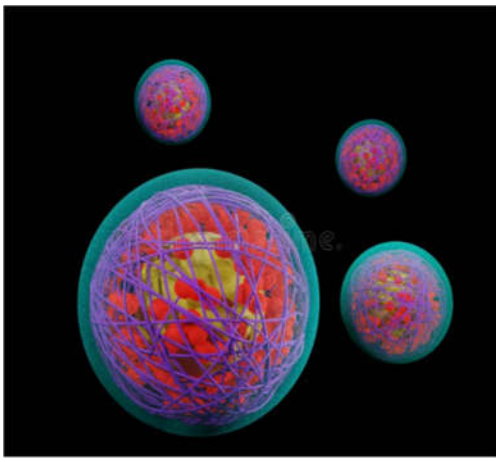
their amphiphilic nature, which allows them to simultaneously encapsulate and massively release hydrophobic and hydrophilic molecules for mutual benefit.

Fig 3

Because of their high sensitivity to the skin's surface, distinguishing phospholipids and their bi-layer structure can promote the entry of nutraceuticals and bioactive substances into specific regions..[34]Doxorubicin, amphotericin B, nystatin, and vincristine are a few examples of medications that come in liposomal carriers.Since digestible lipids increase the amount of mixed micelles that can dissolve and also carry hydrophobic molecules throughout the body, their use in nano-delivery systems improves the pace at which nutrients are absorbed.[35] Liposomes have garnered a lot of attention as effective delivery systems for medications, minerals, and other bioactive substances. They are also perfect models for biological membranes. This page aims to give a general overview of the definition of liposome and nanoliposomes, together with information on their characteristics and methods of synthesis. Additionally, it describes the many uses of nanoliposomes in nano-therapy, including as gene therapy, targeted cancer, and diagnostics. Lastly, liposome and nano liposome structure and function are contrasted with those of other lipid nano carriers.[36]. The first nano vesicular drug delivery vehicles, liposome have shown tremendous promise over the last three decades and have been effectively implemented in real-time clinical settings. Liposomes are appealing nano carriers in the drug delivery field because of their capacity to encapsulate both hydrophilic and hydrophobic medicines, as well as their bio compatibility and biodegradability. In addition, significant technological progress has been achieved in the development of second-generation liposome, which are referred to as ligand-targeted liposome, triggered release liposome, cationic liposome, and stealth liposome. As a result, liposome are now widely used in[37]The study of liposome technology has advanced from traditional vesicles to "second-generation liposome," which produce long-circulating liposome by adjusting the vesicle's size, charge, and lipid composition. Glycolipids and silica acid are two examples of the substances that have been used to create liposome with altered surfaces. This paper mini review focuses on the strengths, limitations, and regulatory requirements regarding liposomal drug formulations based on FDA and EMEA documents. It summarizes solely nano-lipids and their applications in medicine, including scalable techniques in treating terrible diseases like cancer, AIDS, paralysis,[38].Although liposome have numerous potential uses in the creation of functional meals, their usage in food systems has been restricted by the high cost of phospholipids and the difficulty in locating a large-scale, continuous production method that works for the food industry. Furthermore, after liposome and the encapsulated substance enter the intestinal environment, more data is required to assess their bioavailability and effectiveness.[39]Phospholipid and cholesterol make up the bio molecular delivery system known as a nano liposome. It resembles the cell membrane in both structure and characteristics. By encasing hydrophilic nutrients in the central hydrophilic cavity and hydrophobic nutrients in the lipid bi-layer, nanoliposomes can increase nutritional stability and lessen the harm that gastrointestinal enzymes and acids to nutrients. Liposome unique lipid composition allowed them to readily merge with intestinal Mucosal cells and absorb and exchange lipids, facilitating the body's absorption of the nutrients they contained (He et al., 2018). Nano liposome encapsulation greatly increased the stability of EGCG in simulated intestinal fluid. The remaining EGCG in 1.5 hours was 31.2% and 47.7%, respectively. While the EGCG residues were 3.4% and 3.5%, respectively, in EGCG solution. The degradation of ECG's antioxidant activity in vitro may be successfully postponed by nano liposome encapsulation (Zou et al., 2014). As carriers, phosphorylation and cholesterol were used to create EGCG nanoliposomes. The findings demonstrated the high gastrointestinal stability of EGCG nanoliposomes. Caco-2 cells exhibited dose-dependent absorption of EGCG nanoliposomes at varying doses (Xiaobo et al., 2014).[40].The utilization of nanoliposomes as delivery systems for bioactive compounds to target certain organs, like the liver and brain, is an intriguing area of research in nutraceuticals. The most convenient way to introduce a drug into the body is orally. Food can also be used as a vehicle for substances that have been shown to have positive effects on the body. However, in order to accomplish a certain effect, one must overcome digestion, which might decrease the amount of molecules absorbed into the bloodstream.[41]..Nanoparticles A rigid polymeric membrane that keeps the medication inside the reservoir or chamber is called a nano-capsule. The polymeric wall of a nano-capsule is composed of macro molecules, phospholipids, non-ionic surfactant, and an oil core. Because their cores and shells are well defined, nano-capsules can be identified from the nano-particles. Nano-capsules are also known as hollow polymer nanostructures when they are composed of polymers. There are numerous sizes of nano-capsules, which vary in size from 10 nm to 1000 nm. Their protective coating, which is typically phosphoric, readily oxidized, and delays the release of active chemicals, is what makes them so well-liked. Among the many potential medical applications for nano-capsules are drug delivery, food enhancement, nutraceuticals, and self-healing materials. The advantages of encapsulating techniques include precision targeting, controlled release, and protection of these compounds in harsh environments.[42] ..POLYMER DEFINITION: "Polymers are long-chain organic molecules that are assembled from numerous smaller molecules known as monomers." They also have a number of uses in pharmaceutical preparations, including drug formulation and the manufacturing of bottles, syringes, vials, and catheters. POLYMER CLASSIFICATION: According to the place of origin: a) Natural polymers, such as albumin, keratin, collagen, proteins, and carbohydrates, such as starch b) Synthetic polymers, such as poly amides, polyester, and polyacrylamide. In accordance with bio-stability: a) Biodegradable Polymers: such as proteins, carbohydrates, polyester, etc. b) Non-biodegradable polymers, such as acrylic polymer, HPMC, and ethyl cellulose. Natural Polymers: These are substances that come from natural sources, such as plants and animals. Natural polymers that are utilized in the creation of pharmaceutical goods include proteins, enzymes, muscle fibers, polymers, polysaccharides, and sticky tradesman. Chitosan, arrangement, acacia, gelatin, agar, shellac, and guar gum are some of the well-known natural Polymers. The specific uses of plant-derived polymers in pharmaceutical formulations include the production of viscous liquid formulations, implants, films, beads, micro particles, nanoparticles, inhaler and injectable systems, and solid monolithic matrix systems.[43].A synthetic polymer Industrially created chemical compounds called synthetic polymers are made up of many molecules joined by a covalent connection. There are several different types of synthetic polymers with different main and side chains. Polythene and polystyrene are the most widely used synthetic polymers. The synthetic polymers that are most frequently utilized are: 1) PLA (polyacrylamide). 2) Polyanhydrides 3) PGA, or polyglycolides 4) Orthoesters made of polymers 5) Co-glycolides of poly lactates (PLGA) 6) Glutamic acid polymer Polycyanoacrylates (7) 8) Polymeric acid 9) Lactoprotein polymer 10) Methacrylic acid polymer 11) N-vinylpyrrolidone polymer; 12) Ethylene glycol polymer 13) Methacrylate polymer; 14) Acrylamide polymer 15) Vinyl alcohol, or poly.[44]..Structure: A nano vesicular system developed in a core-shell configuration makes up the nano-capsule structure. A polymeric membrane or coating makes up the shell of a typical nano-capsule. Nano-capsules, which are made up of a liquid core or polymer matrix encircled by a polymeric membrane, resemble vesicular systems in that the medicine is contained within their cavity. The active ingredients are contained within the cavity as a liquid or solid molecular dispersion.[45].Biodegradable polyester is the kind of polymer that is utilized. Typical polymers utilized in the creation of nano-capsules include poly-lactoprotein (PCL), poly(lactic) (PLA), and poly(lactide-co-glicolide) (PLGA). Certain drug-delivering nano-capsules contain naturally occurring polymers such albumin, sodium alginate, chitosan, and gelatin. In addition to polysaccharides and saccharide, liposome are another type of nano-capsule shell. An oil surfactant that has been specially chosen to work in tandem with the chosen medication within the polymeric membrane makes up the core of a nano-capsule .[46].

4.Nanocapsule

1. It is possible to create polymeric nano-capsules in the desired shapes, sizes, and in manageable amounts. 2. Nano-capsules can be engineered to perform many functions. 3. They can be created as mono disperse particles with precise optical, electrical, magnetic, and biological characteristics. 4. They are adaptable to the intricacy of any application for which they are designed, such as causing the contents to be released in response to the specific bio molecular triggering mechanism in targeted drug delivery systems .[47].The benefits of nano-capsules Increased dosage loading. Reduced medication irritation at the administration site. Increase the drug's bioavailability. Patient compliance is enhanced when the location of localization is controlled and maintained. The system is applicable to a number of administration routes, including as Parenteral, intra-ocular, nasal, and oral.[48]. Negative aspects of nano-capsules Diminished capacity to modify the same dosage. Extremely advanced technology. Recycling does cost a lot of money. It is not possible to abandon therapy.



APPLICATIONS:

A nano-capsule for the delivery of drugs an antibody can be applied to the surface of nano-capsules, which are one thousandth of a millimeter in size, to help guide them from the bloodstream to a generated tumor. An immediate blast that reaches the tumor causes the capsules to rupture and release their medicinal contents. Tiny gold particles that are particular to the laser light and cling to the polymer's surface at a distance of 6 nm, or 6 millionth of a millimeter, enable the capsules to position their drug load capacity at the appropriate moment. b) Using nano-capsules to deliver drugs Drug carriers made of dispersed polymer nano-capsules can provide both effective drug targeting and controlled release at the nanoscale. The type of surfactant and the outer coating's composition mostly dictate the dispersion stability and the principal physiological reaction. The structure and makeup of the capsule walls have a significant impact on their release and degradation characteristics. C) Agriculture and food science Liposomes, which are spherical bi-layer vesicles that form when polar lipids disperse in aqueous solvents, have been extensively researched for their potential to serve as drug delivery vehicles by protecting sensitive or reactive substances before they are released. In addition to buffering against drastic pH, temperature, and ionic strength variations, liposome entrapment has been demonstrated to stable encapsulated, bioactive materials against a variety of environmental and chemical alterations, such as enzymatic and chemical modification. D) Self-healing material nano-capsule- Damage can occur across a wide range of length scales in structural composites, adhesives, polymeric coatings, and microelectronic components. Large-scale damage, like that caused by a projectile or blast, is challenging to repair and, when feasible, calls for the application of bonded composite patches across the effective area 8. Self-healing polymer micro capsules, which contain the healing agent, have been developed as a unique autonomic repair technique for smaller-scale crack damage. These micro capsules must have good adhesion to the host material, sufficient strength, and a long shelf life. E) A novel nuclear nano-capsule cancer weapon Most frequently used to treat cancer, the radioactive chemical astatine, like uranium and radium, emits high velocity alpha particles through the process of radioactive decay, which is around 4,000 times quicker than the beta decay of the emitted electrons. The alpha particle is special for Tagging tumors at the single cellular level because of its huge particle size and low penetrating strength. f) Nano--capsule bandages for infection prevention in the future If the skin is impacted or the healing process is slowed, the traditional dressings must be removed. On the other hand, when the wound becomes infected, nano-capsular dressings automatically release antibiotics. They increase the likelihood that a wound will heal without leaving scars because they don't need to be removed. Additionally, military personnel frequently employ nano-capsular bandages on the battlefield to treat other wound types, such as ulcers. These medications target the treatment before the infection worsens by releasing antibiotics from nano-capsules that are activated by the presence of pathogenic or causative bacterial organisms. The antibiotic capsules that serve as bandages are ruptured by the bacterial toxins.[50].

TABLE 2

Route	Benefits	Example use
Oral	Enhances bio-availability, protects drug	Curcumin, insulin, peptides
Topical	Localized effect, skin penetration	Anti fungal, corticosteroids
Ocular	Prolonged action in eye	Glaucoma, eye infections
Intravenous	Rapid, targeted delivery	Cancer therapy, brain drugs
Vaginal	Mucosal adhesion, local/systemic delivery	Antivirals, estrogen
Rectal	Good for vomiting patients, local effect	Ant-inflammatory, pediatric use

NANOMEDICINE APPLICATION IN HERBAL PRODUCT:

S. NO	TYPES OF NANO MATREIAL	PLANT SOURCES	BIOACTIVE COMPOUND	FUNCTION	APPLICATION
1.	Emulsion solvent evaporation	*Artemisia annua L.*	artemisinin	Prolong drug release	Anticancer[51]
2.	Microemulsion	Cinnamomum umverum J.Presl	Cinnamon oil	Drug delivery agent	Wound healing,antibacterial activity[52]
3.	Alginate nanoparticles	Ocimum sanctum L.	Methanolic extracts	Bio control agent against bacteria in fabrics	Antibacterial activity[53]
4.	Micro-emulsion technique	Curcuma longa L.	Curcuminoids	Sustained delivery of cur-cumin	Anticancer, antioxidant[54]
5.	Solid lipid nanoparticles	Salvia officinalis L,satureja hortensis L	Phenolic compounds	vehicles	Antioxidant activity[55]
6.	Nano precipitation	Graprs,pea nuts,red	resveratrol	Sustained release	Malignant glaucoma

		wine			therapy[56]
7.	Marinosomes	Curcuma longa L.	Curcumin	Sustained release	Antioxidant and anticancer activity[57]
8.	Nano-carrier transdermal gel a	Curcuma longa L	Curcumin	Drug delivery system	Inflammation [58]
9.	Electrospinning	Centella asiatica	curcuminoids	Sustained delivery of curcumin	Anticancer, Antioxidant[59]
10.	Ethosomes	Sophora flavescens aiton	matrine	Topical application	Improved the percutaneous permeation, anti-inflammatory activity[60]
11.	Elastic liposomes	Camellia sinensis [L]kuntze	[+]-catechin	Drug delivery system	Oral bioavailability[61]
12.	Dialysis method	Camptotheca acuminata decne.	curcumin	Drug delivery system	Inflammation[62]
13.	Liposomes	egg	quercetin	Drug delivery system	Anxiolytic and cognitive - enhancing effects[63]
14.	Liposomes	Cratylia mollis benth	Lectin	-	Antitumor[64]
15.	Liposomal	Artemisia arborescens L	Essential oil	Topical delivery system	Antiherpetic activity[65]

SIGNIFICANCE:

1.FOOD PROCESSING:

Food processing refers to the transformation of raw materials into food products and their various forms, making them market-ready and extending their shelf life. This process includes the removal of toxins, protection against pathogens, preservation, and enhancement of food consistency for improved marketing and distribution. Generally, processed foods have a lower risk of early spoilage compared to fresh foods and are more suitable for long-distance transport from the source to the consumer. The effectiveness of these processes has been enhanced with the use of nanotechnology today. Nano capsule delivery systems play a crucial role in the processing industry by encapsulating simple solutions, colloids, emulsions, bio polymers, and other substances into food products. Nanoscale self-assembled structural lipids function as a liquid medium for transporting healthy substances that are not soluble in water and fats, known as nano drops. Their purpose to prevent the absorption of cholesterol from the digestive tract into the bloodstream[66].

2.PROTECTION OF BARRIERS:

The material used should be impermeable to gases since food goods are kept by keeping them in an inert, low-oxygen atmosphere, which prevents microbial growth and spoiling. Because of their enormous surface area, which promotes the filler-matrix interactions and its performance, nano composites are integrated into the polymer matrix of the substances. Known as polymer nano composites, the nano reinforcements also function as tiny gas barriers by making the material's journey more difficult. Composite materials with complicated metallic ores are called nanoscale. Montenegrin, which is naturally found in volcanic ash, acts as a barrier to stop gases from penetrating. Alternatively, nylons, polyvinyl, PET, PA, epoxy resin, and poly-methane are used to create polymer matrices in food packaging to improve quality. However, poly amide-based nano clay has been extensively developed and marketed under the brand names Durethan, Imperm, and Aegis, and is renowned for its resilience and protection. Since packaging is essential to product commercialization, numerous studies have been conducted on nano composites made of cells and carbon nanotube.[67].

3.Smart Packaging: Sensors are instruments that measure a substance's physical quantity and translate it into signals that can understand. They are employed to control the food items' inside environment, and sensors detect their characteristics on a regular basis. According to a recent survey, oxygen scavengers, moisture absorbents, and barrier packing products currently hold 80% of the market in the smart packaging area. However, to date, the majority of packaging technology offered by nanotechnology has been drawn to meat and pastry products. Temperature, pathogens, oxygen concentration, and other aspects of the food environment are continuously monitored, and indications are employed for appropriate alarms. Using the nano-sensors, they also display the products' shelf life. Examples include gas sensing linked to food product conditions, such as gold nanoparticles-incorporated enzymes foe micro-detection and nano fibrils of nano-based fluoroscopes that detect gases amines to detect the spoiling of meet [fish]. For the detection of volatile organic molecules, titanium oxide and zinc oxide nano composites are among the others. Both security and tagging are accomplished with nano-based. As a result, customer benefits from improved quality identification and produces benefits from quick distribution and food product certification when smart sensors are used.[68].4. Biodegradable The most worrying element influencing environmental features is pollution. Biodegradable plastics were introduced because non-biodegradable plastics alter the composition of soil and cause harmful gasses to build up in the atmosphere, which causes global warming. However, they are weak mechanically and permeable to gases and water. Packaging materials that combine nanotechnology and are composed of natural or manufactured nanoparticles with high mechanical strength and biodegradable, renewable resources outperform these drawbacks. Proteins, carbohydrates, and lipids from plant and animal sources are converted into nanoparticles. Metal oxide nanoparticles and carbon nanotube are also utilized. Furthermore, corn's collagen, rein, and cellulose are converted into nano fibers, which have a high porosity. These nano materials are employed in comfort packaging in addition to nano-based. They also possess other unique qualities, including as sensors, antimicrobial activity, and bio catalysis.[69].Antimicrobial Packaging: One of the defenses is a natural nanoparticles that inhibits bacteria development that causes infections or rotting. There are numerous applications for silver nanoparticles, such as in cookware, refrigerators, electrical appliances, and bio-textiles. In bulk, silver nanoparticles exhibit the necessary activity, and its ions can stop a variety of bacterial biological activities. The antibacterial properties of zinc oxide are enhanced by decreasing particle size, accelerated by visible light, and present in a variety of polymers, including polypropylene. By covering packing materials with titanium dioxide, E.coil contamination can be prevented.Additionally, it is mixed with silver to enhance the disinfecting procedure. A bio polymer made from chitin, chiton has recently been shown to have antibacterial qualities in addition to being an encapsulating material. Products with antimicrobial packaging would be very consumer-friendly and healthful.[70]. 6. Food Packaging: Food packaging must meet specific physical, chemical, or biological requirements as well as provide protection and resistance to tampering. Additionally, it displays the product label, which provides any nutritional data about the meal being ingested. In order to preserve the food and make it marketable, the packaging is crucial. Packaging innovations have produced high-quality packaging, biodegradable packaging, consumer-friendly methods for calculating shelf life, and many other benefits. Packaging nanotechnology is divided into many categories according to the application's goal.[71]. 7. Nutritional Supplements: A report estimates that the entire nano food business will be worth US$5.8 billion in 2012 (US$1303 million for food processing, US$1475 million for food components, US$97 million for food safety, and US$2.93 billion for food packaging). resulting in significant economic profit. Commercial names for supplements include Nutrition-be-nano tech and Nano-nutraceutical. Nano-powders are used to increase nutrient absorption, and nano-cochleas are thought to be an efficient way to transfer nutrients to cells without changing the color or flavor of food items. Nano droplets are dispersed by vitamin sprays to improve nutrient absorption. The primary supplemental component consists of encapsulation techniques, in which iron and zinc nano structured capsules are used to target the human system with necessary probiotics and other items. Because of its size, nanotechnology in food supplements reacts with human cells more effectively than conventional supplements, making them far more effective.[72].

NEUTRACEUTICALS AND DISEASES:

1.NEUTRACEUTICALS AGAINST ALZHEIMER'S DISEASES (AD):

The most common type of dementia is Alzheimer's disease (AD), also known as primary degenerative dementia of the Alzheimer's type (PDDAT), senile dementia of the Alzheimer's type (SDAT), or just Alzheimer's. The following range of nutraceuticals are used to treat Alzheimer's disease

Antioxidants

Since oxidative stress is a major component of most chronic diseases, antioxidants are essential in the treatment of nearly all diseases. Phosphodiesterase and other neurodegenerative disorders are mostly caused by oxidative stress . Phosphodiesterase is an intriguing complex. The primary phospholipid- in the brain is phosphodiesterase, which forms the fundamental structure of the cell membrane. Phospholipid- and membrane phosphodiesterase are crucial for the transmission of metabolic messages between cells. Oral supplements improve neuronal membranes, cell metabolism, and certain neurotransmitters, such as acetylcholine, nor epinephrine, serotonin, and dopamine. Phosphodiesterase also improves cellular metabolism and communication. [73].

: **2.CARDIOVASCULAR DISEASES:**

The prevalence of chronic illnesses like obesity, diabetes, cancer, and cardiovascular disease is rapidly rising. In 2001, chronic illnesses accounted for 46% of the world's disease burden and almost 59% of the 56.5 million recorded deaths worldwide. Heart and blood vessel illnesses together referred to as cardiovascular diseases (CVD) include hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), peripheral vascular disease, heart failure, etc. Only one-third of deaths worldwide were caused by CVD in 1999, but by 2010, it will be the primary cause of death in emerging nations. The majority of CVD may be controlled and prevented. Low consumption of fruits and vegetables has been linked to a higher mortality rate from cardiovascular disease. Numerous studies have shown that eating a diet high in fruits and vegetables can protect against CVD[74].

3.OBESITY:

Almost all age groups and socioeconomic backgrounds are affected by obesity, a composite condition with significant social and psychological ramifications. Between 1980 and 2008, the prevalence of obesity has doubled globally. Over 50% of men and women in the WHO European Region were overweight, and about 20% of men and 23% of women were obese, according to country estimates for 2008. Effective methods for preventing and treating obesity are crucial given the global rise in obesity and its negative health effects. A modest weight loss of 7–10% of the starting weight has been suggested as the goal of weight reduction programs. When energy intake surpasses energy expenditures, an energy imbalance results in obesity. It is necessary to modify one or both energy balance mechanisms in order to cure or prevent obesity. Therefore, strategies for managing weight, such as a functional diet approach, can focus on several facets of the energy balance systems: consumption of food, energy use, and energy storage[.75]4.Parkinson Diseases:

Parkinson's disease is a brain condition that results from nerve damage in certain brain regions. It causes shaking, rigidity in the muscles, and trouble walking. People in their mid-to late-adolescent years are typically affected.

Current status of nutraceuticals in Parkinson's disease:
Vitamin E in food may help prevent Parkinson's disease, according to Canadian specialists.[76].A reduction in clinical symptoms suggests that creatine may change some elements of Parkinson's disease. The effects of glutathione on nerves and its efficacy as an antioxidant have also been studied. The most effective delivery method, long-term dosage, and side effects are still unclear. It is important to keep in mind that there is now inadequate scientific evidence to prescribe dietary supplements for Parkinson's disease, despite exploratory studies suggesting some potential advantages. Patients should be made aware that over-the-counter drugs are expensive, have adverse effects, and interfere with other prescriptions.[77].

CONCLUSION:

Nanotechnology's application in food Because of the remarkable qualities these new materials give their products, the industry and nutraceuticals sector are constantly expanding. Nanotechnology is utilized in nutraceutical goods to increase the solubility, stability, and bioavailability of active components. The majority of nutritional supplements come from plants, but others come from animals. Nutraceuticals are food components with additional health advantages and good nutritional value that can prevent disease. Because of their superior quality, efficacy, safety, and purity, they are widely used by people of all ages to promote health and treat illnesses. Food is any material that has nutritional value; when an organism consumes it, it breaks it down to create energy and maintain life. There is discussion over a negative view of nano foods due to the interaction between nanoparticles and cells. However, the broad potential of nanotechnology in the food industry as a whole and its advantages in offering rich nutritional value, high-quality packaging, and intelligent sensing must be kept in mind, and pertinent research for safer methods of incorporating nanotechnology in the food industry must be put into practice.

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