Enhancing Bioavailability and Biological Efficacy of Bioactive Nutrients with Nano Micelles

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Abstract

In addition to their fundamental nutritional value, nutraceuticals have a variety of biological advantages. However, because of poor absorption and low bioavailability, their biological efficacies are frequently constrained. Nanomaterials have garnered great attention as prospective delivery systems of nutrients and phytonutrients for many uses. Nano micelles are Nano-sized colloidal structures with a hydrophobic center and hydrophilic exterior. They have demonstrated excellent insights in the fields of food and nutraceutical science due to their distinct properties. We focused on the most recent developments in the design of various nano-micelles for effective nutrition delivery and increased bioavailability. Nanomicelles have been used to increase the efficacy of bioactive ingredients in nutraceutical and health foods. It was important to draw attention to the safety issues with foods using nanotechnology.

Keywords: Bioactive nutrients • Nanomaterials • Nanomicelles • Delivery systems • Bioavailability

Introduction

Due to their health advantages that go beyond their nutritional function, nutraceuticals have recently attracted a lot of interest. The bulk of nutraceuticals that have a good impact on health is made up of bioactive substances that come from both plant and animal sources. Food-derived bioactive chemicals have been shown to have a favorable impact on the main bodily systems and lower the risk of chronic diseases. For instance, secondary metabolites in plants include the polyphenols found in fruits and vegetables. Although they are not necessary nutrients, they might improve human health. Long-chain polyunsaturated fatty acids and carotenoids are two examples of lipophilic bioactive substances that may also be helpful to health. Numerous studies have revealed that bioactive substances produced from food have a range of biological effects, including anti-inflammatory, cancer-fighting, anti-cancer, anti-atherosclerotic, and antibacterial ones. These substances, whether they are present as isolated molecules or extracts, become intriguing components of functional meals, which have numerous uses in the food industry. Bioactive chemicals must undergo a number of processes before exerting their health-promoting effects, including food processing, release from the food matrix, transit through the gastrointestinal tract, and subsequently metabolism. The key elements influencing the biofunctional characteristics of bioactive substances are known as bioaccessibility and bioavailability. As a result, evaluation of these chemicals' bioaccessibility and bioavailability has emerged as a viable study field. The definitions of the related terms vary. The percentage of a molecule that has been liberated from the food matrix and is potentially absorbable in the small intestine is known as bioaccessibility. The amount and rate at which bioactive substances are ingested and digested by humans to produce nutritional effects are known as bioavailability. The nature of bioactive chemicals, including their stability, solubility, and content, the structure of the food matrix, and enterocyte metabolism are some of the variables that affect it. The majority of plant bioactive substances degrade quickly, and light, temperature, oxygen, and storage all have an impact on how stable they are. The low water solubility of hydrophobic substances may have an adverse effect on intestinal epithelial cells' permeability, diffusion, and dissolution. Co-ingested macronutrients and micronutrients found in the food matrix have the potential to alter the bioavailability of bioactive molecules in the gastrointestinal system. As a result of their interactions with bioactive substances, these nutrients may promote or prevent their solubilization and release during digestion.

For bioactive substances to reach a sufficient blood concentration and exercise their beneficial health effects, high bioavailability is necessary. To improve their bioaccessibility and bioavailability, a number of techniques can be applied. They consist of modifying molecules technologically and chemically, formulating dosages, combining dietary ingredients for synergy, and using micro-/nanoparticle delivery methods. The nutritional content of food products has recently been proposed to be improved by a wide variety of engineered nanomaterials. The incorporation of bioactive chemicals into the nanoparticles can stop deterioration and metabolic changes. The improvement of bioavailability, regulated release, efficient transport to particular sites of action, masking effect on undesirable senses, avoidance of interactions with other antagonistic components, etc. are some of their additional advantages. Numerous various nanomaterials, such as nanocapsules, nanofibers, or nanotubes as delivery vehicles for bioactive substances, have been created for use in food-related applications. Nano micelles, which are colloidal dispersions that are nanoscale in size and feature a hydrophobic core and a hydrophilic shell, have shown promise as a means of delivering nutrients. This article offers an overview of the distinctive qualities of Nano micelles that give them a variety of uses. The most recent developments in the design of various Nano micelles for enhanced bioavailability of various nutrients and efficient delivery of those nutrients are critically addressed. Additionally, the contribution of Nano micelles to the enhancement of bioactive component efficacy has been made. Additionally, the safety issues with foods that have undergone Nano processing are also emphasized.

Types of nano-micelles

Amphiphilic molecules are the most common subunits of Nano micelles, which typically contain both hydrophilic (polar) and hydrophobic (nonpolar) groups. Depending on the solvent, these molecules rotate to create regular or reverse Nano micelles. Regular Nano micelles are created in aqueous media by orienting the hydrophilic portion of the molecules toward the surface and the hydrophobic portion within. The hydrophobic portion of the reverse Nano micelles, on the other hand, is generated in the nonpolar solvent with the hydrophilic portion near the center. The Nano micelles are a promising vehicle for loading many kinds of bioactive chemicals. Since the protective shell of Nano micelles might lessen the direct contact of loading chemicals with the environment and improve their bioavailability, regular Nano micelles could be utilized to load non-soluble compounds and reverse Nano micelles for soluble compounds. Polymeric Micelles (PM), which have restricted size distributions between 10 nm and 100 nm, are a different group. Block copolymer self-assembly is often how Polymeric Micelles (PM's) distinctive core-shell structures, including an "inner core" and an "outer shell," are created. The outside shell is made up of a hydrophilic block of Polyethylene Glycol (PEG), which could shield entrapped compounds from unanticipated interactions and biodegradation in an in-vivo environment, while the inner core is made up of a hydrophobic core for compound entrapment. Polymeric Micelles (PM) have great stability and can deliver bioactive substances to the target site more effectively thanks to their distinctive molecular structures. Additionally, by tailoring the micelle-forming block copolymers, PM can be equipped with smart functions like environment sensitivity and target ability in addition to the ability to include pharmacological or bioactive substances on demand.

Properties of nano-micelles

Micelles' small size, which dictates their fate in vivo, is their main Physico-chemical property. PM typically has a narrow distribution with a diameter range of 10 nm to 100 nm. They can avoid the liver's mononuclear phagocytic system's scavenging and the spleen's inter-endothelial cells' filtration. To achieve consistent, long-lasting circulation in the bloodstream, intravenous injection is recommended. Additionally, PMs are commonly made with the hydrophilic portions of the polymer on the exterior and the hydrophobic portions on the interior core (shell). The primary physicochemical characteristic of micelles is their small size, which determines their course in-vivo. A typical PM distribution has a narrow diameter range of 10 nm-100 nm. They can avoid scavenging by the mononuclear phagocytic system of the liver and filtration by the inter-endothelial cells of the spleen. Intravenous injection is advised to achieve steady, long-lasting blood circulation. Additionally, the polymer's hydrophilic and hydrophobic regions are often placed on opposite sides of the PM's core (shell). The hydrophilic shell provides some protection against metabolism, and the hydrophobic core can accommodate medications with restricted water solubility. The Critical Micelle Concentration (CMC) of Nano micelles typically ranges from 10-6 M to 10-7 M. The formation of self-assemblies and micelles occurs when the CMC is reached; otherwise, amphiphilic molecules exist separately in the aqueous environment. In physiological contexts under non-equilibrium conditions, kinetic stability is far more crucial to medication administration. The kinetic stability kicks in when the monomer concentration is below CMC, which causes the Nano micelles to slowly break down. The drug could be supplied in intact Nano micelles until it reaches the target site due to the slow dissociation. The capacity of Nano micelles to load several hydrophobic medicines is exceptional. Many recently produced medications are water-insoluble and hydrophobic. According to estimates, 70% of newly discovered chemical substances have low water solubility, and many of them are even insoluble in organic media. Low solubility restricts the drug's rate of dissolution and leads to irregular absorption patterns. It turns into a crucial element in limiting the therapeutic effectiveness of several powerful medications. Nano micelle's distinctive structure makes them a suitable delivery system for these insolubility-prone substances. The inner hydrophobic core of the micelles may capture hydrophobic drug molecules, while an outward-extending hydrophilic outer shell layer preserves the water solubility. They might also stop entrapped pharmaceuticals from degrading, which would improve drug accumulation at the target site. Chemotherapeutic drugs have been delivered by Nano micelles as vehicles for the treatment of cancer. To administer small-molecule medications including Camptothecin (CPT), Doxorubicin (DOX), Paclitaxel (PTX), and Docetaxel, dual-functional Nano micelles derivatives from Polyethylene Glycol (PEG) have been developed in the clinic. In order to create dual-functional Nano micelles for cancer treatment, certain other natural compounds, such as vitamin E succinate, epigallocatechin-3-gallate, embelin, and S-trans, trans-farnesyl thiosalicylic acid, have also been conjugated to PEG.

Nano micelles now possess several novel traits thanks to advanced nanotechnologies, like stimulus sensitivity. A micellar system should deliver the medication, maintain its stability during circulation, and release it into the target tissue in response to physiological or environmental cues. "Stimuli-sensitive Nano micelles" are the name given to these Nano micelles. Different triggers, including temperature, pH, enzymatic activities, redox processes, light, ultrasound, and combinations of these, have been utilized to destabilize drug-loaded PM. A recently developed drug Nanocarrier for the treatment of cancer is pH-responsive PMs. Block copolymer micelles with a tertiary amine, pyridine, and L-histidine groups are often pH sensitive. The co-polymers produce micelles when the pH rises above the pKa of the proton-able group, and the pH-sensitive block serves as the uncharged, hydrophobic core of the micelles. The acidic core is protonated and becomes negatively charged when the pH falls below the pKa value. The ionization of the polymers causes the micelles to become less stable because it increases the hydrophilicity and electrostatic repulsion of the molecules. Therefore, in acidic environments such as tumor cells, endosomes, or lysosomes, the therapeutic drugs could be selectively released. Another characteristic of Nano micelles that are heavily researched, particularly in the realm of oncology, is thermo-sensitivity. Drug release in temperature-responsive systems is regulated by changes in the temperature of the microenvironment. In order to release the drug at a higher temperature, such as the local tumor environment temperature (between 40°C and 42°C), the delivery carriers keep the drug load at body temperature (around 37°C). Lower Critical Solution Temperature (LCST) for thermo-responsive polymers is a requirement for them to go through a phase transition. Introduce hydrophobic or hydrophilic co-monomers to achieve the desired LCST range. The polymers with thermos-responsive blocks create water-soluble Nano micelles when the temperature falls below the LCST.

As opposed to this, when the temperature exceeds the LCST, the water's hydrogen bonds with the polymer chains break, making the polymers insoluble in water. This instability causes the given pharmaceuticals to release. As temperature-responsive PM, Poly (N-isopropylacrylamide) (PNIPAAm) and Poly (N-alkylacrylamide) compounds have been investigated. In order to enable on-demand medication release, light, including UV, visible, and infrared/NIR light, has also been investigated as an external trigger for PM.Typically, chromophores like azobenzene, pyrene, or nitrobenzyl groups make up the light-responsive PM. The PM's nanostructure can change when it is exposed to light, which can cause the dissolution of Nano micelles and subsequent release of payloads. Hydrolysis, ultrasonography, and redox potential have also been investigated and assessed in several studies for the selective delivery of given substances in addition to the triggers described above. Drugs can be passively accumulated into tumors via Nano micelles. Due to the Enhanced Permeation and Retention (EPR) effect, their tiny size gives them the capacity to extravagate into the interstitium of body compartments with leaky vasculature (tumors and infarcts). However, there are still some issues with quick drug release from micelles and difficulties with drug delivery inside of cells. Antibodies and peptides could be added as ligands on the surface of Nano micelles for active targeting. Based on connections to specific targets and conjugation with locally active signal proteins, they can target specific cells. A specific diseased or malignant cell may take up the active Nano micelles with maximum dissemination and minimal side effects.

Advantages and disadvantages of nano micelles

Nano micelles' size and structural makeup provide them considerable advantages. They have the recognizable core-shell structure of an amphiphilic molecule. Hydrophobic drugs can bind to the hydrophobic core of Nano micelles, increasing their solubility by a factor of many. Additionally, they can lengthen blood circulation, boost drug stability, and shield them from mononuclear phagocyte-mediated removal. Some target moieties, such as a particular surface receptor, a transporter protein, or the phage fusion protein, could be coupled with Nano micelles, giving them the capacity to specifically target certain targets. Higher selectivity and fewer side effects were achieved by integrating or conjugating with specific assembly units, which allowed PM to release the loaded medicines in response to various extracellular and intracellular biological stimuli. Because they are formed of hydrophobic and biodegradable polymeric nanoparticles, nano micelles have the potential to serve as a local drug depot, ensuring a steady supply of therapeutic agents at the intended illness site and enhancing the efficacy of treatment. PM generally has a diameter between 10 nm to 100 nm. The size range is thought to be perfect for intravenous drug delivery without embolism. The stability of micelles in blood dreams is the main issue. The Nano micelles are diluted when administered intravenously, which may cause the balance to shift toward the unimer state and cause them to dissociate. The polymer construction can allow the loaded medications to leak out. As a result, further methods should be created to alter the physical-chemical characteristics of micelles for high stability. Micelle's stability has to be further understood through animal research. It might answer the fundamental queries that fluorescence techniques are unable to resolve.

Conclusion

The use of Nanomaterials in nutrition and the food industry is becoming more and more common as Nanobiotechnology advances. Since all of the properties of Nano micelles are contained within a single cage, they have distinctive architecture. Because of their small size, excellent stability, stimulus sensitivity, and sustained release of hydrophobic chemicals, they offer many benefits. They could make poorly soluble bioactive chemicals more stable and bioavailable while providing effective delivery channels for these treatments to reach the intended tissues. The use of Nano micelles in tailored therapy for various chronic diseases has shown promising results, increasing the effectiveness of the treatment. There are still certain problems, though, that require attention. It is impossible to ignore the possibility that nanoparticles used as food ingredients or delivery systems could result in DNA damage, cellular membrane disruption, and cell death, which would subsequently alter how well systems work as a whole. The effects of Nano foods on human and animal health have not yet been extensively studied in in-vivo settings. Therefore, it would be wise to use caution while introducing Nanomaterial into the food and nutrition systems. To further understand their potential negative impacts on humans and the environment, more research needs to be done. For the actual use of Nano foods, appropriate restrictions are required. Testing should be made mandatory, especially safety inspections. Consumers' worries about Nano foods may be allayed by the openness of these problems and the scientific data around them.

If used properly, Nano micelles could significantly alter the bioavailability and bioefficacy of bioactive substances, which would be good for human health.

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