Liposome Technology: Enhancing Functional Foods and Nutraceuticals for Health and Vitality

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In 1965, British researcher Bangham made the groundbreaking discovery of liposomes by dispersing phospholipids in water and examining them under an electron microscope. Later, in 1968, Sessa officially coined the term "liposomes" to refer to these structures. Since 1971, liposomes have been recognized as a prominent microencapsulation technique for delivering drugs to treat various diseases. This method involves encapsulating materials in capsules, allowing for controlled release at specific locations and rates. Over time, liposomes have evolved significantly from being utilized primarily as pharmaceutical, therapeutic,and personal-care delivery systems to gaining prominence as promising candidates for functional food ingredients research. Liposomes are closed vesicles that self-assemble, featuring a phospholipid bilayer structure that sets them apart from the surrounding water environment. These particles vary in size, ranging from 10 nm to several micrometers, encompassing a wide range of dimensions.

When phospholipids are dispersed in an aqueous medium, they exhibit "the hydrophobic effect," causing the hydrophobic tail to interact with the polar environment and shield the surrounding aqueous medium. Additionally, van der Waals interactions and hydrogen bonding between phospholipids and water molecules play a role in organizing the phospholipids into closed bilayered vesicles. This way liposomes provide a distinctive capability to transport both hydrophobic and hydrophilic molecules simultaneously (Liu *et al.*, 2020)

Liposomes have been employed to encapsulate different bioactive compounds (BACs) in the form of nanoliposomes or micro liposomes enabling their application as functional food ingredients. By employing liposome technology, it becomes possible to improve the solubility and bioavailability of a wide range of nutrients. Additionally, this technology enables controlled release at specific locations, making it a valuable method for encapsulating various bioactive compounds (BACs) in functional foods and nutraceuticals

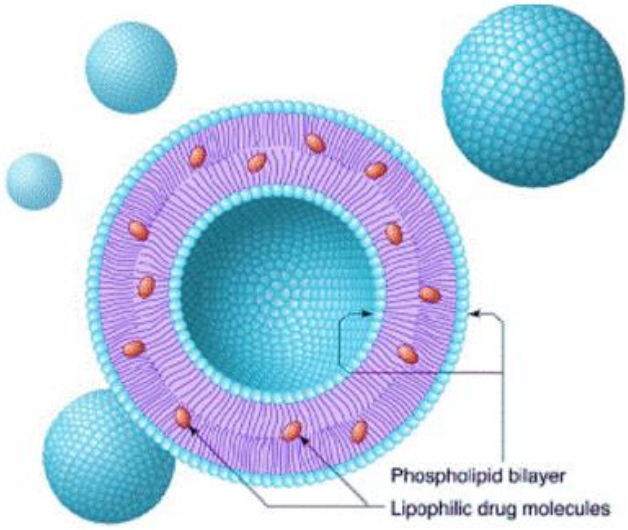

Figure 1: Structure of liposomes

Classification

Liposomes can be categorized into three groups based on their surface charge: neutral liposomes, negative liposomes, and positive liposomes. Additionally, considering the number

and structure of lipid bilayers, liposomes fall into three types: unilamellar vesicles (ULV), multilamellar vesicles (MLV), and multivesicular vesicles (MVV).

TYPE OF LIPOSOMES	ABBREVIATION	DIAMETER	SCHEMATIC REPRESENTATION
Small unilamellar vesicles	SUV	20-200nm	
Large unilamellar vesicles	LUV	Above 200 nm	
Giant unilamellar vesicles	GUV	Higher than 1 µm	
Multilamellar vesicles	MLV	0.5-5 µm	
Multivesicular vesicles	MVV	Higher than 1 µm	

Table 1: Classification of liposomes based on number and structure

Liposome Preparation

The preparation process of liposomes for functional food applications typically involves four essential stages: (Ajeeshkumar *et al.*, 2021)

(1) drying lipids dissolved in an organic solvent,

(2) exposing the lipid to an aqueous medium,

(3) purifying the resulting liposome,

(4) analyzing the final product.

1. **Drying of lipids dissolved in organic solvent**

The primary constituents forming the wall of liposomes are phosphatidylcholine (PC), phosphatidylethanolamine(PE), phosphatidylserine(PS), and phosphatidylglycerol (PG). Phospholipids are dissolved in a solvent or a mixture of solvents to achieve a uniform distribution of lipids in the solution. For lipophilic bioactive compounds (BACs), an appropriate solvent may be added to the mixture and then dried.On the other hand, for hydrophilic BACs, they can be added to the dried lipids during the hydration process with the aqueous phase.

2. **Exposure of the lipid to aqueous media**

Hydrophilic bioactive compounds (BACs) are introduced into the aqueous phase to be encapsulated by binding with the hydrophilic components of the phospholipids through a hydration process of the lipid phase (LP). On the other hand, hydrophobic BACs can be entrapped within the phospholipid bilayer.

3. **Refining the synthesized liposome**

Frequently used purification techniques include, centrifugation, ultrafiltration, column chromatography, dialysis and the ion-exchange chromatography method. The successful encapsulation of the desired compound is accomplished by eliminating unwanted substances such as unencapsulated BACs and solvent residues.

4. **Final product analysis**

The liposome characterization are mainly done through zeta potential, polydispersive index (PDI), size distribution, encapsulation efficiency (EE) and visual appearance (Panahi *et al.*, 2017).Encapsulation Efficiency (EE) refers to the percentage of BAC that is trapped inside the liposomes, relative to the total initial amount of BAC used in the process. The zeta potential results reveal the effective surface charge of the liposomes, which significantly influences their aggregation and stability. PDI (Polydispersity Index) quantifies the width or variability of size distributions. This parameter allows us to assess any changes in the size of liposomes after loading with BACs by measuring the uniformity of the size distribution.

Applications of Liposomes

Liposomes offer advantages in various applications, including food, functional food, and BACs delivery systems.

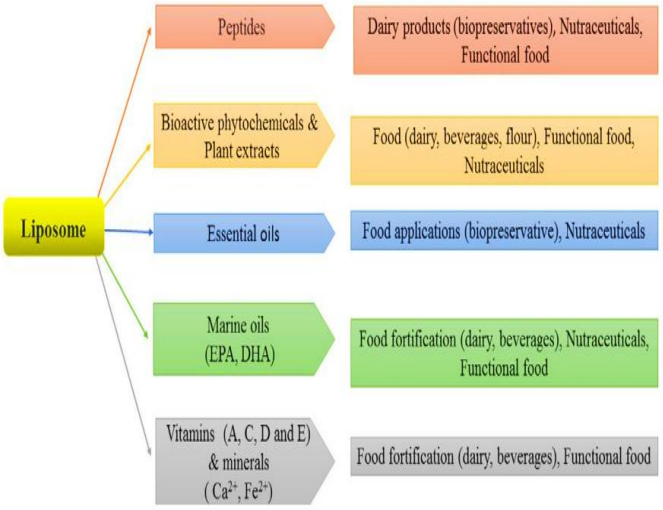

Figure 2: Application of liposomes in food industry

1. **Encapsulation of antimicrobial peptides**

Antimicrobial polypeptides, like nisin and lysozyme, exhibit inhibitory effects against gram-positive pathogens such as *Listeria monocytogenes*, *Staphylococcus aureus*, and Bacillus spp. These peptides are effective in controlling undesirable bacteria in food products like cheeses and contribute to prolonging their shelf life.Nevertheless, there are several limitations associated with the direct addition of nisin or other antimicrobials to food products. For instance, when nisin is added directly to milk, a notable reduction in its antimicrobial activity has been observed due to its adherence to milk fat globules.

Thus, the encapsulation of nisin and other antimicrobials within systems like liposomes presents a promising solution to address these limitations and create antimicrobial formulations more suitable for food applications, particularly in cheeses. The co-localization of liposomes and microorganisms during cheese ripening suggests that liposomes could potentially be utilized to deliver antimicrobial agents precisely to the areas where microorganisms are present in food products. This targeted approach may enhance the effectiveness of antimicrobial treatment in foodstuffs. The use of nanoliposomes containing nisin, formulated with distearoylphosphatidylcholine (DSPC) and distearoylphosphatidylglycerol (DSPG), demonstrated effective inhibition of the growth of *L. monocytogenes* strains in UHT-processed milk samples for 48 hours at 25°C. Remarkably, this antimicrobial effect was observed regardless of the milk's fat content. Liposomes were found to enhance the antilisterial activity of pediocin AcH in various food matrices, including beef tallow and muscle slurries(Emami*et al.*,2016)

2. **Encapsulation of polyphenols**

The potential health benefits of polyphenols and their usage as additives in functional foods have been constrained by factors like limited stability, conditional solubility, and poor bioavailability. Additionally, they are known to impart unpleasant tastes, such as astringency, when incorporated into food products.

(Takahashi*et al.*,2009) findings indicated that encapsulated curcumin, a natural polyphenolic compound derived from turmeric, exhibited a swifter absorption rate and improved absorption compared to its free form or a blend of curcumin and lecithin. Furthermore, the plasma's antioxidant activity after consuming orally administered curcumin enclosed in liposomes was notably greater than the antioxidant activity observed in the other two treatment groups.

3. **Encapsulation of essential oils**

Essential oils are intricate and volatile compounds produced by aromatic plants as secondary metabolites, known for their potent

fragrance. These oils exhibit a diverse range of biological traits, including antioxidant, antifungal and bactericidal effects.Nonetheless, it is widely recognized that the majority of essential oils are inherently unstable from a biological perspective, making them susceptible to factors such as oxygen, light, and temperature.The utilization of liposomes has been suggested as a strategy to enhance the solubility and bioavailability of essential oils, offering protection and the ability to regulate their release.

4. **Encapsulation of vitamins**

Numerous vitamins exhibit instability within food systems, making them prone to degradation. The pace and degree of degradation are influenced by factors such as the chemical makeup of the vitamins, attributes of the food matrix, processing circumstances, and conditions during distribution and storage.Using liposomal encapsulation seems to offer a viable approach to safeguard both water-soluble and lipid-soluble vitamins from degradation.

Liposomes containing encapsulated Vitamin E and C, formed using SPC (soy phosphatidylcholine), were introduced into orange juice with the aim of creating a fortified beverage that enhances its nutritional content. (Marsanasco*et al*., 2011).

5. **Encapsulation of marine oils**

The beneficial impacts of marine oils on health are directly associated with the existence of oils that encompass long-chain ω-3 polyunsaturated fatty acids (PUFAs), namely EPA and DHA.The primary drawbacks of marine oils stem from their heightened vulnerability to oxidation, a consequence of their elevated levels of polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs).In the latest developments, a nanoliposome powder containing shrimp oil has been created to facilitate and expand its utilization in the realm of food and beverages. The formulation of nanoliposomes with shrimp oil was devised and subsequently converted into powder form using freeze-drying and spray-drying techniques.(Gulzar &Benjakul, 2020)

Conclusion

The utilization of liposome technology has emerged as a practical and effective method for the creation and utilization of bioactive compounds (BACs) in the context of functional foods and nutraceutical applications. Liposomes provide a successful strategy for safeguarding and managing the release of delicate substances, prolonging the shelf life of food products, preserving the integrity of functional components post-consumption, and enhancing the absorption of bioactive molecules.

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