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Proceeding Paper

Strategies to Encapsulate Natural Extracts in Lipid-Based Nanocarriers †

Aurora Silva [1,2], Clara Grosso [1], Maria Carpena [2], Pauline Donn [2], Sepidar Seyyedi-Mansour [2], Paula Barciela [2], Ana Perez-Vasquez [2], Lucia Cassani [2], Miguel A. Prieto [2,*] and Maria Fátima Barroso [1,*]

[1] REQUIMTE/LAQV, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr António Bernardino de Almeida 431, 4249-015 Porto, Portugal; mass@isep.ipp.pt (A.S.); claragrosso@graq.isep.ipp.pt (C.G.)

[2] Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Faculty of Science, University of Vigo, E32004 Ourense, Spain; mcarpena@uvigo.es (M.C.); donn.pauline@uvigo.es (P.D.); sepidar.seyyedi@uvigo.es (S.S.-M.); pau_barci@hotmail.es (P.B.); anaperezvazquez00@gmail.com (A.P.-V.); luciavictoria.cassani@uvigo.es (L.C.)

* Correspondence: mprieto@uvigo.es (M.A.P.); mfb@isep.ipp.pt (M.F.B.)

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Abstract: Numerous photosynthetic organisms possess bioactive properties, with algae standing out for their distinctive characteristics that attract interest from diverse industries. For instance, the pharmaceutical industry has great interest in features like the neuroprotective, anti-glycemic and cytotoxic properties found in some algae species. Nonetheless, it is imperative to design efficient systems capable of releasing the bioactive compounds present in these extracts. In this regard, nanoparticles have attracted considerable attention across various fields, particularly in drug delivery applications. Lipid-based nanoparticles have emerged as a promising solution, offering numerous advantages. These nanoparticles exhibit high biocompatibility and biodegradability, making them suitable for use in biological systems. Additionally, they possess the ability to encapsulate both hydrophilic and hydrophobic drugs, thereby expanding their versatility. One remarkable attribute of lipid-based nanoparticles is their ability to cross the blood–brain barrier, a crucial physical barrier responsible for regulating the entry of chemicals into the brain and maintaining central nervous system homeostasis. Overcoming this barrier presents a significant challenge in the treatment of central nervous system disorders. Therefore, the objective of this study is to provide an overview of the latest advancements in the nanoencapsulation of natural extracts using lipid-based vesicular delivery systems.

Keywords: algae; nanocarriers; phytosomes; bioactive substances

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1. Introduction

Numerous photosynthetic organisms possess bioactive properties, and among them, algae have gained significant attention due to their distinctive characteristics that capture the interest of representatives of diverse industries. The pharmaceutical industry recognizes the potential of algal species that exhibit neuroprotective, anti-glycemic, and cytotoxic qualities [1–4], among other properties, for the development of new products. However, to effectively utilize these bioactive species and their compounds, efficient systems for their release must be developed. Nanoparticles, especially lipid-based nanoparticles, have emerged as promising solutions for various applications, including drug delivery [5,6].

Lipid-based nanoparticles offer several advantages that make them attractive for use in biological systems. Firstly, they exhibit high biocompatibility, ensuring minimal immunogenicity [7] and allowing more bioactive molecules to be available in the body after ingestion. Biomolecules can reach their target organs at an effective concentration when they are nanoencapsulated, which increases their circulation half-lives and improves their bioactive stability [5], using, for instance, the modification of the nanoparticle surface via techniques such as PEGylation, this being a covalent surface modification with polyethylene glycol, an inert substance that is not easily digested [8,9]. The blood–brain barrier-crossing capacity of lipid-based nanoparticles is one of their most noteworthy features, especially because the treatment of central nervous system disorders presents a substantial challenge in overcoming this barrier [10]. In addition, the use of lipid-based vesicular delivery systems allows one to overcome challenges associated with the direct application of algae extracts, such as stability issues and undesirable organoleptic characteristics.

The current importance of this subject, together with the known characteristics of the algae extracts, led us to conduct an overview of the latest advancements in the nanoencapsulation of natural extracts using lipid-based vesicular delivery systems.

2. Discussion

Algal polysaccharides present versatile chemical characteristics and significant bioactive potentialities, which have been extensively described. Thus, they are excellent biomaterials for nanocarrier design. The applications of these algae compounds as drug delivery systems have been reported in a recent review [11]. However, reports of lipid-based delivery systems used to encapsulate the bioactive compounds of algae are relatively scarce. A few of the latest studies are presented in Table 1.

Table 1. Selected studies on the lipid-based encapsulation of bioactive algal extracts/compounds.

Entrapment Technique	Bioactive Compounds	Experimental	Major Outcomes	Ref.
Nanoemulsion	Phytosterol/algal oil (microalgae-derived oil)	Ultrasound emulsification	- Minimize the fishy off-flavor. - Maximize oxidative stability.	[12]
	Coffee oil/algal oil (microalgae-derived oil)	Surfactant: 20% Span 80 80% tween 80	- Protection effect on ultraviolet-A-induced skin damage. - Growth inhibition of melanoma cells.	[13]
	β-carotene/*Dunaliella salina*	Whey protein or soybean lecithin as emulsifiers	- Increased β-carotene and retinol bioavailability in rats.	[14]
	Fucoxanthin/*Sargassum. angustifolium*	Ultrasonic treatment using fucoidan, gum Arabic, and sodium caseinate as natural emulsifiers vs. tween 80	- The best encapsulation efficacy was obtained from the tween 80-stabilized nanoemulsion, followed by sodium caseinate, fucoidan, and gum Arabic nanoemulsions.	[15]
Nanoliposome/phytosome	*Sargassum boveanum*	Optimal conditions with 0.5% lecithin, 30 °C process temperature, and 1313 ppm of the phenolic compounds	- Good stability. - Control of the release of phenolic compounds at different pH values. - The antioxidant activity of the algal extract was maintained.	[16]
	Protein hydrolysates/*Spirulina platensis*	Thin-film hydration method, with lecithin and cholesterol	- Biocompatibility of the peptides. - Accelerated wound healing process. - Increased the population normal human fibroblast cells.	[17]
	Codium tomentosum	Highest % of complexation: time—1 h, temperature—59 °C, and phosphatidylcho line/extract—1:1)	- FTIR and DSC studies confirmed the phyto–phospholipid complex formation - Phytosomes had low particle size and polydispersity - Increased octanol–water partition coefficient	[18]

Some studies have reported that nanoemulsion have several benefits. Recent studies on nanoemulsion as an encapsulation technique highlight not only the increase in the efficiency of antioxidant stability [15] but also the capacity to minimize the unpleasant off-flavors associated with algae extracts and compounds [12]. In another study, a nanoemulsion increased β-carotene and retinol bioavailability in rats [14]. Finally, a nanoemulsion developed with coffee residues and commercially available algal oil was investigated as a protective agent against UVA-induced skin damage and showed efficiency by significantly inhibiting the B16-F10 melanoma cell line's growth (IC_{50} value of 26.5 µg/mL). Additionally, the nanoemulsion was efficient in ameliorating several skin conditions such as erythema and melanin formation in rats [13].

Similarly, researchers have demonstrated the advantages of other lipid-based encapsulation techniques based on the development of nanolyposomes. For example, the nanoliposomes of soybean lecithin loaded with *Spirulina platensis* peptides have been demonstrated to shorten the wound healing period. The results of that study showed that the complex did not exert toxicity on Human Foreskin Fibroblast (HFFF-2) cells in-vivo tests conducted on mice, improving wound healing through increased wound contraction, epithelialization, and increased fibroblast population [17]. In another study, the stability of algae phenolic compounds, extracted from *Sargassum boveanum* entrapped in nanoliposomes, was confirmed [16]. The authors reported optimal experimental conditions of 0.5% lecithin, a 30 °C temperature, and 1.313 ppm for the phenolic compounds, leading to an entrapment rate of 45.5%. The nanoliposome achieved good stability, as well as the capacity to maintain antioxidant activity and to control the liberation of phenolic compounds at different pH values. Finally, a preliminary report on the incorporation of a bioactive extract fraction from *Codium tomentosum* into phytosomes demonstrated that the complex was successfully synthesized, with a low particle size and a high octanol-water partition coefficient [18].

In conclusion, we can state that the use of lipid-based vesicular delivery methods to nanoencapsulate algae extracts has considerable potential for addressing the restrictions associated with the direct application of bioactive substances. Biocompatibility, biodegradability, and the ability to encapsulate both hydrophilic and hydrophobic compounds are all advantages of lipid-based nanoparticles.

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