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Design of soft lipid nanocarriers based on bioactive vegetable oils with multiple health benefits

Ioana Lacatusu [a], Gabriela Niculae [a], Nicoleta Badea [a], Raluca Stan [a], Ovidiu Popa [b], Ovidiu Oprea [a], Aurelia Meghea [a,*]

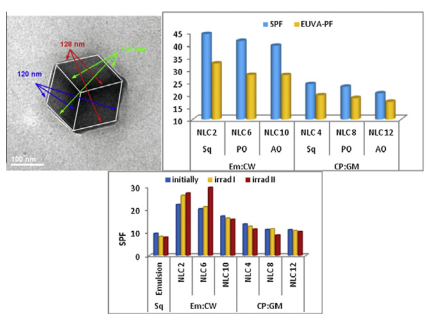
[a] Faculty of Applied Chemistry and Materials Science, University POLITEHNICA of Bucharest, Polizu Street No 1, 011061 Bucharest, Romania
[b] Faculty of Biotechnology, University of Agronomic Sciences and Veterinary Medicine, Bucharest, Marasti Street No 59, 011464 Bucharest, Romania

HIGHLIGHTS

- Soft and functional nanocarriers based on Pumpkin and Amaranth oils are achieved.
- *In vitro* antioxidant activity was superior for nanocarriers based on Amaranth oil.
- Co-loaded vegetable nanocarriers have greatly improved the photoprotective effect.
- Avobenzone and Octocrylen were co-released from nanocarriers in a prolonged manner.
- The co-loaded nanocarriers have been formulated into advanced cosmetic prototype.

GRAPHICAL ABSTRACT

a. The cubic shape of vegetable – lipid nanocarriers; b. The photoprotective properties of vegetable nanocarriers co-loaded with 3% AVO and 7.5% OCT; c. Effect of UV irradiation of cosmetic prototypes based on vegetable co-loaded nanocarriers (3.75% OCT and 1.5% AVO)



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ABSTRACT

The general objective is to design and synthesize soft and functional nanocarriers based on vegetable oils (Pumpkin and Amaranth oils) able to co-encapsulate and co-deliver two UV-A and UV-B filters (Avobenzone, Octocrylen) and to explore their efficiency in developing advanced bio-cosmetic prototypes. The exploitation of vegetable oils with safe utilization and biological efficiency in obtaining soft nanocarriers represent an innovative approach that provides a significant advance in the nanotechnology field. The obtained vegetable nanocarriers having mean diameters of 100 and 160 nm were tested *in vitro* for their antioxidant, photoprotective and drug release properties. The *in vitro* ability to capture free radicals was superior when the nanoparticles were prepared in Amaranth oil/solid lipids system. Study of UV absorbing effect revealed that co-loaded vegetable nanoparticles have greatly improved the photoprotective properties, the obtained SPF being of 40–45 and FP-UVA of 27–34. These values are associated with a high protective effect, e.g. more than 99% against UV-B and 92% against UV-A radiation. *In vitro* co-release experiments demonstrated that both Avobenzone and Octocrylen filters were released in a prolonged manner. The ultimate objective was to formulate the newly co-loaded nanoparticles into advanced cosmetic prototype and compare it with conventional cream. The soft vegetable-nanocarriers produced significantly higher UV-protection than the conventional cream. The use of appropriate renewable vegetable sources for obtaining soft bio-active nanostructures with broad health benefices has the potential to satisfy both the industrial and consumer needs, thanks to their safety and sustainability.

* Corresponding author.
E-mail addresses: nicoleta.badea@gmail.com (N. Badea), a.meghea@gmail.com (A. Meghea).

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1. Introduction

In recent years it has become more evident that the development of new drugs alone is not sufficient to ensure progress in human health. The use of natural remedies is highly approached in human health, in particular cosmetics with an ongoing search for developing efficiently health products with broad biological relevance.

The investigations based on sun protection studies have gained continuous concern and have captivated a great interest among specialists, being widely accepted that skin exposure to UV radiation induces a wide range of adverse effects, such as sunburn, photoaging, photoimmunosuppression and photocarcinogenesis [1–3]. Indeed, dangerous phototoxic and photoallergic reactions accompanies an increased use of cosmetic products containing high amounts of synthetic UV-filters. Benefits derived from a wide use of sunscreens in cosmetic products are unfortunately accompanied by several adverse reactions of UV filters (e.g. contact dermatitis, allergic, irritant, and phototoxic and photoallergenic reactions) [4,5]. In recent years the side effects such as photoallergic and phototoxic type of molecular UV absorbers (organic nature) are frequently reported in literature [6,7]. Since a photoprotective cosmetic formulation is applied on large skin surfaces, they may cause the penetration and bioaccumulation of significant quantities of UV chemical absorbers [8]. These percutaneous absorption processes may cause various adverse health effects, such as endocrine disruption activity, decrease in SOD activity and even mutagenic and carcinogenic effects [8,9]. Moreover, the organic UV-filters contaminate the environment in high concentrations [10], fact that has lead to some studies which underline the need to re-assess the potential benefits of extensive use of organic UV-filters from both ecological and medical viewpoint [11,12].

As a result, the performance of a sunscreen formulation relies not only on the physical–chemical properties of the filters encapsulated, but also on the carrier used to deliver them. In the soft matter field, lipid nanoparticles composed from lipids and surfactants well tolerated by the human body [13,14] have demonstrated their applications as delivery vehicle for many active compounds in pharmaceutics and cosmetics [15–18]. The ability of both kinds of lipid nanoparticles (of SLNs and NLCs type) to enhance the photoprotection by synergistically combining of the organic UV absorbers and different lipid mixtures has been shown in previous research of authors [19,20]. Nevertheless, the association of lipid nanocarriers with plant medicine still remains less explored in the bio-nanotechnology field.

The use of appropriate renewable vegetable sources for obtaining new bio-active lipid nanocarriers with broad health benefices and improved delivery properties, has the potential to satisfy both the industrial and consumer needs, thanks to their safety and sustainability. Based on our results, different lipid nanocarriers prepared with a natural oil from vegetal area – Grape seed oil, have manifested effective antibacterial and antioxidant properties [21] and were able to provide a better sustained release of active compound than lipid nanocarriers prepared with individual oil or conventional nanoemulsions [22]. Moreover, owing to the complex mixture of vegetable oil, the obtained lipid nanocarriers contain many imperfections in the final solid lipid core which may lead to appropriate host spaces for more than one lipophilic compound.

Therefore, the work developed in this study pursues a dual objective: (1) to design soft and functional lipid nanoparticles based on a high content of vegetable oils and to apply them as simultaneous co-encapsulation and co-delivery systems for two types UV-A and UV-B-filters; (2) to explore the vegetable nanocarriers efficiency in developing advanced cosmetic prototypes that possess broad spectrum effectiveness and minimal side effects. The multiple co-encapsulation of bio-active compounds into efficiently soft lipid nanocarriers and testing their applicability represents a significant progress in the bio-nanotechnology field and area of pharmaco-cosmetic products. In this study, the anti UV-A/UV-B effect and anti-oxidant properties will be supplied by a combination of high content of bio-active vegetable oils (*Pumpkin oil* and *Amaranth oil*) with minimum amounts of synthetic UV-A and UV-B absorbers (*Avobenzone* and *Octocrylene*) localized inside the same lipid nanocarrier. The selected natural bio-active oils enriched in Squalene, linoleic acid, oleic acids and so on, are known to have multiple health benefices e.g. anti-oxidant properties, anti-acne action, anti-inflammatory etc. [23–27]. Moreover, the complex co-encapsulation process has the main advantage of cumulating the main specific properties of bio-active compounds originated from vegetable sources with UV-blocking effect of synthetic UV-filters that may result in synergistic and complementary biological effects.

2. Experimental

2.1. Materials

The surfactants, Sodium Colate, Synperonic PE/F68 (block copolymer of polyethylene and polypropylene glycol) and L-α-Phosphatidylcholine were obtained from Merck (Germany) and Sigma Aldrich Chemie GmbH (Germany). The solid lipids used were: glycerol monostearate (GM) obtained from Cognis GmbH (Germany), cetyl palmitate (CP) obtained from Acros Organics (USA), Carnauba wax (CW) and Emulgade SE/PF (Em) was provided by Elmiplant S.A. (Romania). The UV – filters, Avobenzone – AVO and Octocrylene – OCT were purchesd from Merck and Sigma Aldrich, respectively. The cream base (which contains stearats, glycerine, fatty alcohols, emulsifier, emollients and an antioxidant – butylhydroxyanisole) was provided by Elmiplant S.A. The vegetable oils enriched in squalene have been obtained by cold pressed method from *Amaranthus* and *Cucurbita seeds* spp. and have been further processed by supercritical and Soxhlet extractions. The content in squalene, fatty acids, tocopherols and microelements of vegetable oils have been determined by HPLC/DAD, HPLC/MS, GC–MS, ICP–MS. The bio-active composition of Amaranth oil was: 6.43% squalene, 24.54% linoleic acid, 17.29% oleic acid, 9.32% palmitic acid, 1.58% stearic acid, 0.39% linolenic acid, 0.0675% α, γ, δ-tocopherols. The Pumpkin oil composition was: 19.44% squalene, 43.65% linoleic acid, 20.45% oleic acid, 6.46% palmitic acid, 3.05% stearic acid, 0.55% linolenic acid, 0.0806% α, γ, δ-tocopherols. Tris[Hydroxymethyl] aminomethane, 5-Amino-2,3-dihydro-1,4-phthalazinedione (Luminol) were purchased from Sigma Aldrich Chemie GmbH and hydrogen peroxide was obtained from Merck (Germany).

2.2. Synthesis of vegetable lipid nanocarriers co-loaded with OCT and AVO

Nanostructured lipid carriers (NLCs) were prepared by a combination of high shear and high pressure homogenization techniques. In brief, an aqueous phase which consisted of double-distilled water and 3% surfactant mixture (Sodium Colate:Tween 20:Poloxamer = 40:9:1, w/w) and various lipid phases (mixture of solid lipids, including GM/CP, and Em/CW, and vegetable oil – AO or PO) were separately prepared. A concentration of 1% active compounds with an appropriate ratio between UV-B and UV-A actives were added in the lipid phase to form a clear molten solution. The ratio between OCT and AVO has been chosen to be of 7:3 in order to increase the rate of the UV-B protection and therefore the SPF value.