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MAIN NANOCARRIERS USED IN ESSENTIAL OILS WITH ANTIOXIDANT PURPOSES: A LITERATURE REVIEW[1]

PRINCIPAIS NANOCARREADORES UTILIZADOS EM ÓLEOS ESSENCIAIS COM FINALIDADES ANTIOXIDANTES: UMA REVISÃO DE LITERATURA

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ABSTRACT

Essential oils are oily, volatile, aromatic liquids widely used in the food, dental and cosmetic industries due to their antibacterial, antifungal and antioxidant properties. However, they have some limitations such as low oxidative stability and high volatility, which can be overcome with the use of nanotechnology. Thus, the objective of this study was to investigate which are the main nanocarriers of essential oils for antioxidant purposes. This study is characterized as an integrative literature review. Data collection was performed from March to April 2019, in the Bireme electronic database. The Boolean descriptors and operators used were: Nano* AND Essential Oils AND Antioxidant. Articles in English, Spanish and Portuguese were included in the sample. The search in the databases resulted in the collection of 58 articles, of which 22 met the inclusion criteria. All nanocarriers of essential oils maintained or increased antioxidant activity, reducing tissue damage action due to oxidative stress. Research has shown that the use of nanotechnology is effective when applied as carriers of essential oils for antioxidant actions.

Keywords: free radicals, oxidative stress, nanoemulsions, nanoparticles.

RESUMO

Os óleos essenciais são líquidos oleosos, voláteis, aromáticos, amplamente utilizados nas indústrias alimentícia, odontológica e cosmética, devido a suas propriedades antibacterianas, antifúngicas e antioxidantes. Contudo, apresentam algumas limitações como por exemplo baixa estabilidade oxidativa e alta volatividade, as quais podem ser superadas com o uso da nanotecnologia. Dessa foram o objetivo desse estudo foi investigar quais os principais nanocarreadores de óleos essenciais com finalidades antioxidantes. Este estudo se caracteriza como uma revisão integrativa da literatura. A coleta dos dados foi realizada no período de março a abril de 2019, na base de dados eletrônica Bireme. Os descritores e operadores boleanos utilizados foram: Nano AND Essential Oils AND Antioxidant. Foram incluídos na amostra artigos nos idiomas inglês, espanhol e português. A busca nas bases de dados resultou na coleta de 58 artigos, dos quais 22 preencheram os critérios de inclusão. Sendo que todos os nanocarreadores de óleos essenciais mantiveram ou aumentaram a atividade antioxidante, reduzindo ação danos teciduais devido ao estresse oxidativo. A pesquisa mostrou que o uso da nanotecnologia é eficaz quando aplicado como carreadores de óleos essenciais para ações antioxidantes.*

Palavras-chave*: estresse oxidativo, nanoemulsões, nanopartículas, radicais livres.*

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INTRODUCTION

Essential oils are found in the tissues or on the surface of plants (trichomes), such as flowers, sprouts, seeds, bark, leaves, herbs, woods, fruits and roots, are aromatic volatile oily liquids responsible for vegetable odor, soluble in organic solvents and unstable in the presence of light, oxygen, heat and metals (ZIZOVIC *et al*., 2007). They contain a large number of components and are widely used in the food, dental and cosmetic industries because of their antibacterial, antifungal and antioxidant properties (BAKKALI *et al*., 2008). Since natural antioxidants are considered a rational curative strategy to prevent diseases associated with oxidative stress (SOUZA *et al*., 2017).

Oxidative stress is considered to be a disturbance between the antioxidant/pro-oxidant state in favor of excessive generation or slower removal of free radicals, which can lead to biomolecular damage to proteins, lipids and nucleic acids, with consequent loss of biological functions and/or homeostatic balances and tissue injury (WINTERBOURNE, 2015).

However, essential oils have some limitations because they are highly insoluble in water due to their lipophilic nature and have low oxidative stability because they are volatile compounds (MARTINS *et al*., 2009). Encapsulation nanotechnology can be applied to protect essential oils from degradation by direct contact of external factors such as light, oxygen, chemicals, heat and pressure, as well as increasing bioavailability in biological fluids (DUCLAIROIR *et al*., 2003). The nanocarriers are able to transport the drug to a specific destination to perform its therapeutic activity with maximum safety. They must be capable of encapsulating the drug, bringing the drug to the target, releasing the drug and dissolving in the biological media to be eliminated by the body (ETHERIDGE *et al*., 2013).

In addition, such systems are capable of improving the pharmacological and therapeutic properties of conventional drugs and reducing their side effects. The high drug load, the physical and chemical stability, and the low systemic toxicity offered by these nanocarriers represent the main factors to be considered for effective drug delivery (PARVEEN; MISRA; SAHOO, 2012).

Due to the importance of essential oils in antioxidant action, the aim of this study was to investigate in the current literature the main nanocarriers used to carry and protect antioxidant essential oils, considering the lipophilic characteristics and low stability that can be overcome by the use of nanotechnology.

MATERIAL AND METHODS

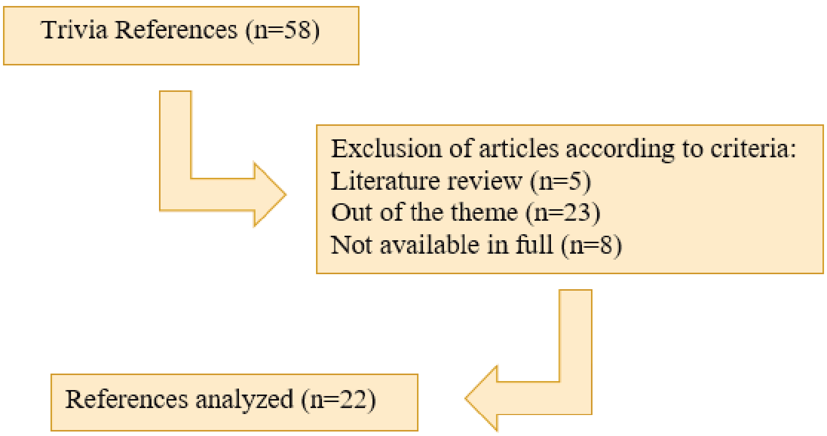
This study is characterized as exploratory, of the type integrative review of the literature. The search for the studies occurred in the months of March and April of 2019, in the electronic database Bireme (Virtual Health Library). The descriptors and Boolean operators used were: Nano* AND Essential Oils AND Antioxidant.

The inclusion criteria used to select the articles were: complete articles and available online in full, published in Portuguese, English and Spanish, using nanocarriers for essential oils for human antioxidant application. Studies of bibliographic review were excluded from the sample.

After the search in the database, the titles and abstracts were evaluated and the studies that included the inclusion criteria were selected for reading in full. The following characteristics of the publications were recorded: year of publication, name of the author (s), type of nanocarrier and essential oil used.

The search in the databases resulted in the collection of 58 articles, of which 22 adequately met the criteria and were selected for inclusion in the study. Figure 1 shows the flowchart with the selection strategy of the included articles. The publications that composed the sample of the present study were published between the years of 2009 and 2019.

Figure 1 - Flowchart with the article selection strategy.



RESULTS AND DISCUSSIONS

This study showed that nanocarriers used for essential oils with antioxidant purposes were chitosan nanoparticles, silver nanoparticles, starch nanoparticles, biocompatible gold nanoparticles, alginate nanocapsules with chitosan, nanoemulsions, lipid nanoparticles, nanofibers, nanosponges and colloidal lipoidal carrier, being that nanoparticles of chitosan, nanoemulsions and lipid nanoparticles were the most used (Table 1).

Table 1 - Publications that composed the study sample.

Year	Author	Nanocarrier	Essential oil
2009	Chen *et al.*	Nanoparticle of Chitosan	Eugenol and Carvacrol
2014	Vilas; Philip; Mathew	Silver nanoparticles	*Myristica fragrans*
2015	Esmaeili e Asgari	Nanoparticle of Chitosan	Carum copticum
	Natrajan *et al.*	Alginate and Chitosan Nanocapsules	Turmeric and lemongrass
2016	Periasamy; Athinarayanan; Alshatwi	Nanoemulsion	*Nigella sativa L.*
	Singh *et al.*	Solid lipid nanoparticle	Sesame seed

2017	Celebioglu; Yildiz; Uyar	Nanofibers of inclusion complex of cyclodextrins	Thymol
	Hwang *et al.*	Nanoemulsion	Whey Protein Concentrate
	Kamel; Abbas; Fayez	Lipoid colloidal carrier	Rosmarinus officinalis, Zingiber officinale e Vitis vinífera
	Qiu *et al.*	Nanoparticle starch	Mentone
	Souza *et al.*	Nanostructured Lipid Carriers	Tea Tree Oil (Melaleuca alternifolia)
2018	Balasubramani *et al.*	Nanoemulsion	*Ocimum basilicum L*
	Borges *et al.*	Nanoemulsion	*Rosmarinus officinalis L.*
	Carbone *et al.*	Lipid nanoparticles	*Rosmarinus officinalis L., Lavandula x intermedia "Sumian", Origanum vulgare subsp. hirtum* e *Thymus capitatus*
	Gündel *et al.*	Nanoemulsion	*Cymbopogon flexuosus*
	Kumar *et al.*	Nanosponges	*Psoralea corylifolia*
	Lopes *et al.*	Nanocapsule	Eugenol
	Meghani *et al.*	Nanoemulsion	Cinnamon
	Pivetta *et al.*	Lipid nanoparticles	Thymol
2019	Benedec *et al.*	Biocompatible gold nanoparticles	Origanum vulgare
	Kavaz; Idris; Onyebuchi	Nanoparticle of Chitosan	Cyperus articulatus
	Shetta; Kegere; Mamdouh	Nanoparticle of Chitosan	Peppermint and green tea

Source: Prepared by the authors from the results obtained in the Bireme database.

Periasamy; Athinarayanan; Alshatwi (2016) used an essential oil nanoemulsion of *N. sativa* (NSEO-NE). The size of the NSEO-NE droplet was approximately 20-50 nm in diameter. The anti-cancer properties of the NE preparation were studied using a modified methylthiazolyl diphenyl tetra-zolium bromide assay as well as analyzes of nuclear cellular and morphological absorption. NSEO-NE significantly reduced the viability of Michigan Cancer Foundation-7 (MCF-7) breast cancer cells. The nucleo-cytoplasmic morphological features of NSEO-NE treated cells included the formation of cell membrane bubbles, cytoplasmic vacuolization, chromatin marginalization and nucleation fragmentation. The results clearly indicate that NSEO-NE induces apoptosis in MCF-7 cells.

Hwang *et al.* (2017) aimed to produce multiple nanoemulsion (MNE) of whey protein concentrate (WPC) and to study how the level of protein concentration and type of antioxidant affected the physicochemical properties and oxidative stability of the oil of fish in MNE. Spherical forms of emulsions ranging in size from 190 to 210 nm were observed indicating the successful production of MNE. In comparison to free fish oil, fish oil in MNE exhibited lower values of the peroxide value (PV), p-anisidine and fish oil oxidation formation, indicating that the oxidative stability of fish oil in MNE was increased. The combined use of Vitamin C and E in the MNE resulted in a reduction in PV and the value of p-anisidine, and in the development of the oxidation manufacturer.

Balasubramani *et al.* (2018) evaluated the antibacterial, antioxidant and larvicidal activity of *Culex quinquefasciatus*, essential oil of nanoecapsulated *Ocimum basilicum L*. and observed that nanoemulsion showed significantly more antibacterial activity against enteric bacterial pathogens *Enterococcus faecalis* (MTCC-2729), *Staphylococcus aureus* (MTCC-441), *Salmonella paratyphi*

(MTCC-735), *Klebsiella pneumoniae* (MTCC-432) and antioxidant capacity. These proposed results for nanoemulsion based on plant essential oil is thermodynamically stable and the formulated nanoemulsion can be used for various biomedical applications, food industry and drug delivery.

The study developed by Borges *et al.* (2018) evaluated the anti-inflammatory potency of nanoemulsions containing essential oil of *Rosmarinus officinalis L. in vitro* and *in vivo*. The authors performed tests with diphenyl picrylhydrazyl (DPPH) and *2,2'-azino-bis* (*3-ethylbenzothiazoline-6-sulfonic acid*) (ABTS), cellular antioxidant activity (CCA), nitric oxide production, cell viability and activity anti-inflammatory in zebrafish. By analytical gas chromatography coupled to mass spectrometry (GC-MS), they found that the major compounds are 1,8-cineole and camphor. The nanoparticles were obtained by a low energy method and presented an average size smaller than 200 nm. The encapsulation efficiency by spectrometry and gas chromatographic analysis was 67.61 and 75.38%, respectively. In the CCA assay, all the samples presented percent inhibition values similar to the quercetin standard, indicating antioxidant activity. The study also showed that the nanoparticles did not present toxicity to the macrophages, in addition to demonstrating antioxidant activity and potentiating the effect of the essential oil on the proliferation of viable fibroblasts. Nanoemulsions also showed the ability to potentiate the anti-inflammatory action of essential oils, exerting immunomodulatory activity by inhibiting the production of the pro-inflammatory mediator, nitric oxide.

The work published by Gündel *et al.* (2018) aimed to develop nanoemulsions containing essential oil of *C. flexuosus* through a method that does not use organic solvent and with temperature control to avoid the volatilization of the oil, characterize and evaluate stability and the antimicrobial activities and antibiofilm of these nanoemulsions. The nanoemulsions presented adequate physicochemical characteristics (mean size < 200 nm, polydispersity index < 0.3, negative zeta potential and acid pH) and nanoencapsulation of *C. flexuosus* oil increased the efficacy of its therapeutic effect against microorganisms (*Pseudomonas aeruginosa* and *Staphylococcus aureus*) evaluated in this study in relation to free oil.

Meghani *et al.* (2018) formulated two nanoemulsions (NE): NE cinnamon oil and NE cinnamon oil encapsulated in vitamin D. The hydrodynamic size of the cinnamon oil NE and the vitamin D encapsulated cinnamon oil was observed on average as 40.52 and 48.96 nm, respectively. The effect on a human lung alveolar carcinoma cell line (A549) along with the possible mechanism underlying its cytotoxic and genotoxic potential was explored. And they observed a significant cytotoxic effect ($p < 0.05$) and dependent on the concentration of both NEs in A549 cells. The Comet and CBMN assay showed that both NEs induce DNA damage and increase the frequency of micronuclei in a concentration-dependent manner. In addition, the occurrence of DNA damage was correlated with cell cycle arrest in the G0 / G1 phase. The authors concluded that the observed antibacterial effect of NEs made them suitable for use in preserving food against microbial deterioration. In addition, cinnamon oil can be used as a carrier in the food industry to provide lipophilic nutraceuticals like vitamin D in nano form.

Nanoemulsions are being widely used to nanoencapsulate essential oils from various plant sources for antioxidant purposes, thus obtaining anti-microbial activities (BALASUBRAMANI *et al.*, 2018); (GUNDEL *et al.*, 2018); (MEGHANI *et al.*, 2018), anti-inflammatory (BORGES *et al.*, 2018), besides having positive effects on cancer (PERIASAMY; ATHINARAYANAN; ALSHATWI, 2016) and in the reduction in fish oil oxidation (HWANG *et al.* ., 2017). Chitosan nanoparticles have also been used to nanocarrier essential oils for antibacterial purposes, as shown by studies by Chen *et al.* (2009); Kavaz; Idris; Onyebuchi (2019) and Shetta; Kegere; Mamdouh (2019).

Chen *et al.* (2009) prepared nanoparticles with antioxidant and antibacterial properties through grafting of eugenol and carvacrol in chitosan nanoparticles, where antioxidant activities were analyzed with *2,2-diphenyl-1-picrylhydrazyl* (DPPH). The antibacterial assays were performed with a representative gram-negative bacterium, *Escherichia coli*, and a gram-positive bacterium, *Staphylococcus aureus*. Grafted eugenol and carvacrol conferred antioxidant activity on chitosan nanoparticles, and the chitosan nanoparticles produced by the essential oil components achieved equivalent or better antibacterial activity than unmodified chitosan nanoparticles. Cytotoxicity assays using 3T3 mouse fibroblasts showed that cytotoxicity was significantly lower than that of pure essential oils.

Chitosan nanoparticles were also used in the work of Esmaeili and Asgari (2015), the authors encapsulated Carum copticum (CEO) essential oil in chitosan nanoparticles by ionizing emulsion gel with pantasodium tripolyphosphate and sodium hexametaphosphate, separately as crosslinkers. The nanoparticles were analyzed by Fourier transform infrared spectroscopy, ultraviolet-visible spectroscopy, differential scanning calorimetry, scanning electron microscopy and dynamic scattering of light. The nanoparticles exhibited an average size of 30-80 nm with a spherical shape and regular distribution. *In vitro* release profiles exhibited an initial burst release followed by sustained release of the CEO at different pH conditions. The amount of CEO release of the chitosan nanoparticles was higher at acidic pH for basic or neutral pH, respectively. The biological properties of the CEO, before and after the encapsulation process, were evaluated by the *2,2-diphenyl-1-picrylhydrazyl* (DPPH) radical and disc-agar diffusion method, respectively. The results indicated that the encapsulation of the CEO in chitosan nanoparticles can be protected from quality.

Natrajan *et al.* (2015) in their study developed an alginate (AL) and chitosan (CS) nanocarrier for the encapsulation of essential oils. The results of the characterization studies showed that 0.3 mg/mL AL and 0.6 mg/mL CS produced particles of minimum size (<300 nm) with good stability. It was also observed that the oil-loaded nanocapsules were hemocompatible, suggesting their use for future biomedical and pharmaceutical applications. In addition, the antiproliferative activity of nanocapsules loaded with turmeric oil and lemon balm oil showed significant antiproliferative properties as well as free oil.

Kavaz; Idris; Onyebuchi (2019) synthesized chitosan nanoparticles (CSNPs) containing essential oil of *Cyperus articulatus* (CPEOs) in their study. The nanoparticles were characterized by scanning electron microscopy, Fourier transform infrared spectroscopy and UV-Vis spectroscopy. CPEOs showed more *in vitro* radical elimination bioactivity than CSNPs and CPEO-CSNPs at initial storage times. CPEO-CSNPs showed the highest antioxidant activity over an extended period of time. The antimicrobial activity of two strains of bacteria, *Staphylococcus aureus* and *Escherichia coli* showed that all the chitosan nanoparticles loaded with CPEO inhibited bacterial growth at lower concentrations. The *in vitro* trypan blue exclusion assay showed that CPEO-CSNPs are more cytotoxic against breast cancer cells after 48h. The bioactivity and physico-chemical properties of CPEO-CSNPs have shown promising applications in the food and pharmaceutical industries.

In the study published by Shetta; Kegere; Mamdouh (2019), peppermint oil (PO) and green tea oil (GTO) were encapsulated in chitosan nanoparticles (CS NPs). NP had a mean size range of 20 to 60 nm. Nanoencapsulation maintained the stability of total phenolic content in both OEs, improved antioxidant activity by ~2 and 2.4-fold for PO and GTO, respectively. The antibacterial activity of CS / GTO NPs was more potent than CS / PO NPs and especially against *Staphylococcus aureus* with ~ 9.4 fold improvement compared to pure GTO, and ~ 4.7 fold against *Escherichia coli*.

In the study by Singh *et al.* (2016) sesamol, a phenolic component of sesame seed oil, nanoencapsulated in solid lipid nanoparticles (SLN-S) was used. The SLN-S prepared by the microemulsion method had a nearly spherical shape with a mean particle size of 120.30 nm and its oral administration at 8 mg/kg body weight showed significantly better hepatoprotection than free sesamol and a hepatoprotective antioxidant activity well-established in CCl4-induced subchronic liver injury in rats. Evaluations were made in terms of histological changes in hepatic tissue, hepatic injury markers (serum alanine aminotransferase, serum aspartate aminotransferase and serum lactate dehydrogenase); oxidative stress markers (lipid peroxidation, superoxide dismutase and reduced glutathione) and a marker of pro-inflammatory response (tumor necrosis factor-alpha).

Souza *et al.* (2017) evaluated whether treatment with bacterial essential oil nanoparticles of *Melaleuca alternifolia* (TTO) prevents or reduces hepatic damage in silverfish experimentally infected with *Pseudomonas aeruginosa*. Liver samples from fish infected with *P. aeruginosa* showed increased levels of thiobarbituric acid reactive substances (TBARS), protein carbonylation and advanced protein oxidation products (AOPP), while catalase (CAT) activity was reduced in comparison with uninfected animals. Prophylactic treatment with nanoencapsulated TTO prevented these changes. Due to these results, the authors concluded that infection caused by *P. aeruginosa* causes liver damage by inhibiting the antioxidant defense system, contributing to the pathophysiology of the disease. Thus, treatment with nanoencapsulated TTO may be an important approach for preventing infection damage in fish.

Carbone *et al.* (2018) under study developed nanostructured lipid transporters (NLC) as a system for the liberation of Mediterranean essential oils (*Rosmarinus officinalis L., Lavandula x intermedia "Sumian", Origanum vulgare subsp. Hirtum and Thymus capitatus*) selected on the basis of their antioxidant and anti-inflammatory properties. The NLC composite from Softisan (as solid lipid) was produced by the phase inversion temperature and high pressure homogenization using two different emulsifier systems. Regarding the polydispersion index, the best formulations were with *Rosmarinus, Lavandula* and *Origanum* as essential oils (PDI between 0.126 and 0.141, size < 200 nm). The *in vitro* biological viability and anti-inflammatory activities were evaluated in Raw 264.7 cells (macrophages cell line), while the in vitro antioxidant activity was verified by the DPPH test. *Lavandula* and *Rosmarinus* NLC were found to be the most biocompatible formulations to a concentration of 0.1% (v/v), while they were able to induce dose dependent antiinflammatory activity in the order *Lavandula> Rosmarinus ≥ Origanum*.

The study by Pivetta *et al.* (2018) aimed to encapsulate thymol in nanostructured lipid carriers (NLCs) composed of natural lipids and to evaluate their anti-inflammatory and antipsoriatic activity *in vivo*. The carrier containing thymol was produced by the ultrasonography method and presented 107.7 nm in size, zeta potential of -11.6 mV and encapsulation efficiency of 89.1%. Thymol-NLCs were incorporated into a gel, which was tested *in vivo* on two different mouse models with inflammation of the skin, showing anti-inflammatory activity. This formulation was also tested in mice with imiquimod-induced psoriasis and showed better healing. Thus, the authors concluded that thymol-NLCs are an interesting formulation for the treatment of inflammatory skin diseases.

Singh *et al.* (2016); Souza *et al.* (2017); Carbone *et al.* (2018); Pivetta *et al.* (2018) opted for the use of solid lipid nanoparticles to nanoencapsulate *Sesame seed* oils; Tea tree oil; *Rosmarinus officinalis L., Lavandula x intermediate "Sumian", Origanum vulgare subsp. hirtum and Thymus capitatus*; Thymol, respectively. Singh *et al.* (2016) and Souza *et al.* (2017) verified the hepatoprotective activity of these nanoparticles with essential oil, whereas Carbone *et al.* (2018) and Pivetta *et al.* (2018) investigated whether the anti-inflammatory action of oils remained with encapsulation. Studies already bring also metallic nanoparticles, such as silver (VILAS; PHILIP; MATHEW, 2014) and gold (BENEDEC *et al.*, 2019), associated with essential oils.

The authors Vilas; Philip; Mathew (2014), evaluated the use of the essential oil of Myristica fragrans enriched in terpenes and phenylpropenes in the reduction and stabilization was evaluated. The study points to the pertinence of the use of essential oil of *M. fragrans* for the synthesis of silver (Ag) crystalline nanoparticles (NPs) - of size 12-26 nm, spherical. The study demonstrates the strong chemo-catalytic potential and antibacterial activity of Ag NPs, besides presenting a strong capacity of donation, reduction and elimination of free radicals. In this way, the authors believe in the strong potential of nano-Ag synthesized to be used in so-called green chemistry.

In the work developed by Benedec *et al.* (2019), the authors proposed a new method of green synthesis mediated by *O. vulgare* extract (OVE) of biocompatible gold nanoparticles (AuNPs) that have antioxidant, antimicrobial and improved plasmonic properties. The spherical biocompatible NPs had an average size of 40 nm and excellent aqueous stability. In addition to presenting very good antioxidant activity and interesting inhibitory effects against *Staphylococcus aureus* and *Candida* *albicans*. Cytotoxicity assays have shown that AuNPs are better tolerated by normal human dermal fibroblast cells, whereas melanoma cancer cells are more sensitive.

In addition to the most commonly used nanocarriers, such as nanoemulsions, chitosan nanoparticles and solid lipid nanoparticles, there are studies that bring nanofiber encapsulated essential oils for use in food (CELEBIOGLU; YILDIZ; UYAR, 2017), lipid colloidal carrier for photoprotection (KAMEL; ABBAS; FAYEZ, 2017), starch nanoparticles with antimicrobial activity (QIU *et al.*, 2017), nanosponses, improving the photostability and antibacterial activity of essential oils (KUMAR *et al.*, 2018), and nanocapsules with antimicrobial and anti-inflammatory effects (LOPES *et al.*, 2018).

The study published by Celebioglu; Yildiz; Uyar (2017) provided an encapsulation for thymol through cyclodextrin inclusion complex nanofibers (CD-IC NF) by electrospinning technique. Although pure thymol is highly volatile, thymol volatility was effectively suppressed by the inclusion complex, where about 88-100% of the oil was preserved. The increase of aqueous solubility to hydrophobic thymol was demonstrated by phase solubility diagram. Loading of thymol in thymol / CD-IC NF conferred the ability to eliminate DPPH radicals to these nanofibrous webs. Thus, thymol / CD-IC NF showed antioxidant activity together with greater solubility in water and high thymol thermal stability. In summary, encapsulation of essential oil compounds such as thymol in electromagnetic CD-IC nanofibers may promote their potential application in foods and oral products by associating the large surface area of nanofiber webs along with inclusion complexation of CD that provides water solubility improved and antioxidant property, and high temperature stability for thymol.

In the study of Kamel; Abbas; Fayez (2017), the projected lipoid colloidal carrier (LCC) was loaded with Diosmin in combination with different essential oils *(Rosmarinus officinalis* (LCC2), *Zingiber officinale* (LCC3) and *Vitis vinifera* (LCC4)), to be used as a photo preparation - topical protection. To investigate the ability of essential oils to potentiate the effects of Diosmin, Diosmin/essential oil-loaded LCCs (LCC2, LCC3 and LCC4) were compared to Diosmin-loaded LCC (LCC1). All LCCs had particle size values ranging from 121.1 - 144.3 nm with uniform distribution and zeta potential values around 30 mV. In addition, they all had high drug encapsulation efficiencies. LCC1 presented the lowest antioxidant and sun block effect *in vitro*. Photoprotective studies *in vivo* showed that all formulated LCCs had a protective effect on the skin when compared to the positive control; however, LCC1 had the lowest anti-erythematous and anti-wrinkle effect. Histological studies proved the efficacy of LCCs designed as anti-photoagents on the skin, with LCC1 showing the lowest anti-inflammatory and anti-wrinkle effect, while LCC2 presented the highest anti-wrinkle effect. These results indicated that the suggested combinations of Diosmin/essential oil improved the antioxidant effects, the solar blockers of Diosmin. After one year of storage, the LCCs presented satisfactory physical stability.

The study by Qiu *et al.* (2017) aimed to evaluate the increase of antioxidant and antimicrobial activities of mentone encapsulated in starch nanoparticles prepared by short chains of glucan.

The nanoparticles exhibited spherical shapes, and particle sizes ranging from 93 to 113 nm. The encapsulation efficiency was 86.6%. Nanoparticles formed at 90ºC showed high crystallization and thermal stability. And the antioxidant and antimicrobial activities of the oil were extended due to the encapsulation in starch nanoparticles.

Kumar *et al.* (2018) presented as a goal of the study encapsulate oil *Psoralea corylifolia* in β-cyclodextrin nanosponges (NS) to overcome the limitations as volatile nature, poor stability, and solubility of babchi oil (BO) wich restrict its pharmaceutical applications. The results obtained from spectral analysis ascertained the formation of inclusion complexes. Additionally, solubilisation efficiency of BO was checked in distilled water and found enhanced by 4.95 times with optimized β-cyclodextrin nanosponges. The cytotoxicity study was carried out by the MTT assay using HaCaT cell lines. A significant improvement in photo-stability of essential oil was also observed by inclusion innanosponges. Lastly, the optimized formulation was tested for antibacterial activity using Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli. Therefore, encapsulation of BO in nanosponges resulted in efficacious carrier system in terms of solubility, photo-stability, and safety of this oil along with handling benefits.

In the study by Lopes *et al.* (2018), the cytotoxic, antioxidant and anti-inflammatory effects of eugenol were evaluated in human neutrophils and keratinocytes. In addition, polymeric nanocapsules were prepared to improve the chemical and irritant characteristics of eugenol. Eugenol presented safety and antioxidant and anti-inflammatory effects on human neutrophils, but presented cytotoxic effects on keratinocytes. However, the nanocapsules were able to reduce their cytotoxicity. An in vivo experiment of 12-O-tetradecanoylphorbol- 13-acetate (TPA) induced irritative contact dermatitis in mice showed that eugenol nanocapsules significantly reduced ear edema in mice when compared to eugenol solution, as well as leukocyte infiltration and IL-6 levels, possibly due to better permeation blockade and irritation.

CONCLUSION

The present study demonstrated that the nanocarriers most used to encapsulate essential oils with antioxidant purposes are nanoemulsions, lipid nanoparticles and chitosan nanoparticles, but also nanocapsules, nanofibers, lipoid colloidal carrier, nanosponges and nanoparticles of silver, starch and biocompatible gold. In the studies, the nanocarriers increased or maintained the antioxidant activity of the oils, thus reducing oxidative stress and consequently the tissue damages. And with an increased antioxidant activity, antimicrobial and anti-inflammatory activities also increased, due to the ability to stabilize free radicals.

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