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Nanoencapsulation of essential and vegetable oils to obtain polymeric nanoparticles for dermocosmetics application

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ABSTRACT
Essential and vegetable oils are rich in bioactives, which can act on the skin through their therapeutic properties. However, they are often sensitive to oxidation and degradation, making it necessary to use resources for their protection. The nanoencapsulation of these oils allows bioactives to have their properties protected and optimized through the sustained release of actives, reduced toxicity, and even greater penetration capacity and better distribution in the skin layers, enhancing their effects. Polymeric nanoparticles, particularly, have shown important results for delivery of bioactives to the skin, and can be produced from natural or synthetic polymers, which present biocompatibility and biodegradability. The main methods for obtaining these nanostructured materials are nanoprecipitation, coacervation and ionic gelation, and these methods are the scope of this literature review.

Keywords: Vegetable oils, Essential oils, Nanoencapsulation, Dermal disorders, Dermocosmetics.

1 INTRODUCTION

The skin can be considered the initial feature of contact with the world, the environment and people. Its health and quality straightly affect the individual's self-esteem. When the skin is not healthy, it negatively impacts people's quality of life, influencing social relationship, emotional and physical health and also in the economic field (DA SILVA; SANTOS, 2021).

Individuals who have dermal disorders of skin as acnes, dermatitis, folliculitis ans hyperchromasia such as melasma can suffer from emotional and psychosocial overload which can trigger a misrepresented perception of yourself or to other's perspective. This negative point of view about yourself also affects the individual ability to face the world and its problems. Therefore, it is necessary a biopsychosocial understanding about the individual's illness as well as the development of effective treatments that generates benefits to patients and their quality of life (DA SILVA; SANTOS, 2021).

The current market trends such as *Clean Beauty* and premiumization, observed by the cosmetic and dermocosmetic sectors has pointed the need to align the vegetalization to the efficacy of the treatment. The industry of raw material, biotechnology and nanotechnology has sought to add efficacy to the cosmetic ingredients with natural alternatives to supply the market's demand (MORIMITSU, 2018; MENDONÇA, 2020).

Synthetic raw materials or petroleum-derived compounds used as cosmetic ingredients, such as dyes, preservatives and silicones, have been identified as potential causes of diseases, interfering in the human hormonal system or triggering allergic reactions on the skin and/or scalp (FERREIRA, 2021), motivating scientists to seek innocuous natural substitutes.

Among natural products with high potential in the development of dermocosmetics, essential oils (EO) and vegetable oils (VO) stand out. These natural products are rich in bioactives duly indicated to benefit the health of the skin, being able to help both in the prevention and in the treatment of dermal disorders of the skin. However, because they are sensitive and unstable, their continued use does not provide all of their benefits. An alternative for a better use of its properties is its nanoencapsulation (DOS SANTOS, 2021).

In this sense, conventionally used for drug delivery, polymeric nanocapsules can be used to protect the bioactives present in EOs and VOs and optimize the performance of the cosmetics, through sustained releasing of actives, decreasing of toxicity, greater penetration capacity and better distribution in the skin layers (GUTERRES, 2019; BEGNES, 2020).

When prepared with the aim of acting as bioactive delivery system, the polymeric nanoparticles can be synthesized by several methods. And they must be made up of biodegradable and biocompatible polymers, so that they are completely eliminated by the body in a short period of time, avoiding the accumulation of it in case of repeated administration. Degradation products of these compounds cannot be toxic or immunogenic (VAUTHIER, BOUCHEMAL, 2009; KUMARI, et al., 2010).

2 SKIN AND DERMOCOSMETICS

Cosmetics are products that aim the cleaning and beautifying, which act on the most superficial layer of the skin and do not modify physiological conditions. Cosmeceuticals are products that correct aesthetic problems or are used as treatment cosmetics, as they have therapeutic properties against diseases. The National Health Surveillance Agency (ANVISA) classifies cosmetics as grade 1 and grade 2. The cosmetics considered part of the grade 1 have a superficial effect without causing physiological changes, whereas the cosmetics considered grade 2 have therapeutic properties and need to be proven (ANVISA; BRASIL , 2015; KELMANN, 2017).

Dermocosmetics are formulations for topical use, they have active principles that deliver therapeutic activity, which act in the deeper layers of the skin compared to conventional cosmetics and enabling different types of treatments for the skin. Because they act directly on the cause of the problem through physiological changes, these products are considered grade 2 cosmetics by ANVISA (ANVISA; BRASIL, 2015; SCHORRO, 2020).

However, dermocosmetic formulation can be satisfactorily effective in the treatment of a disorder of the skin. In addition, knowledge about the anatomy of the skin is required, as well as the understanding of the influence and performance of the actives in this structure (ROCHA, 2019, SCHORRO, 2020).

The skin is a complex organ that acts as a mediating boundary separating the organism from the environment, protecting the body from harmful antigens, chemicals, dehydration, overhydration and ultraviolet radiation. It has resilience, selective permeability, stores antioxidants, controls thermoregulation through fluctuations in cutaneous blood supply. And about perspiration, It can also stimulate epidermal regeneration when it is injured. It is made up of three layers: epidermis, dermis and hypodermis (MOHAMED; HARGEST, 2021).

There are many pathologies or dysfunctions that can affect the skin, and dermocosmetic formulations can help in the treatment of many of these dysfunctions, as they have activies that allow treatment in deeper regions of the skin (SCHORRO, 2020).

Brazil has a strong dermocosmetics market in constant growth, endorsed by the consumers themselves and by the vast range of raw materials that the Brazilian territory presents, which enables the creation of innovative products and a greater variety of products on the market (MENDONÇA, 2020; SILVA, 2021).

In 2020, the Personal Hygiene, perfumery and Cosmetics industry grew by 4.7%, reaching R$ 122.408 billion, according to the International Euromonitor, which classified Brazil as the 4th largest consumer market for cosmetics in the world, second only to the United States, China and Japan (SILVA, 2021).

To ensure that a dermocosmetic formulation effectively fulfills its purpose, it is necessary to consider that the properties of the actives and the vehicles influence the diffusion of substances through the skin and consequently the efficacy and the quality of cosmeceuticals. Therefore, technologies that allow the permeation of actives in different layers of the skin have been studied by scholars. (KIS, 2022; NORLEN, 2022; YOSHIDA, 2022).

The relationship between the active and the influence that it will have on the skin is through permeation and penetration. Penetration comes from the passage of the active through the stratum corneum, while permeation is the passage of the active through the epidermis until reaching the dermis (ALVES, 2015). Factors related to the active affect its permeability in the skin, such as its hydrophilicity, degree of ionization, enzymatic degradation, charge and size of the molecule, water/oil partition coefficient, further the factors related to the formulation, such as the concentration of the active, the presence of promoters to aid in the absorption of the active, oil/water composition, particle size and pH (MATIELLO, et al., 2019).

Among the many actives that can be used in the formulation of dermocosmetics, more recently there has been a strong appeal for the use of natural or bioactive actives contained in EOs and VOs, ensured by BBeauty and Clean Beauty (KERCHER, 2022). There are no data on the movement of consumption of cosmetics with natural products in Brazil. A survey carried out by Nielsen IQ, in 2021, pointed to a growth of 8.1%, equivalent to US$ 406 million for this industry in the United States (NIELSEN IQ, 2021).

Among the natural ingredients available for formulations that meet this market, OEs and VOs are abundant in Brazil and can add various attributes to formulations (FINE, 2016; KOYAMA, 2020).

3 ESSENTIAL OILS AND VEGETABLE OILS

EOs are natural, lipophilic, aromatic and highly volatile. They are extracted from stems, leaves, flowers and evn roots, through distillation or cold pressing techiniques (BASER, BUCHBAUER, 2010).

The constituents of EOs are secondary metabolites of plants, derived from terpenoids or phenylpropanoids, which form complex mixtures of low molar mass compounds (CRAVEIRO, QUEIROZ 1993).

The use of EOs has been directed towards biological properties, including antioxidant, photoprotective, bactericidal, virucidal, fungicidal, antiparasitic, insecticide and other medicinal properties, such as analgesics, sedatives, anti-inflammatories, spasmolytics and local anesthetics. EOs must be used in a diluted form, as they can cause photosensitization and dermatitis (MOSS, 2003; KOYAMA, 2020).

Despite all their magnificent properties, EOs are sensitive compounds and can easily decompose if not processed, handled or stored correctly and exposed to heat, moisture, light or oxygen (SCHWEIGGERT, 2007). When oxidized, terpenoids have shown skin sensitization ability, leading to allergic contact dermatitis and hypersensitivity (DIVKOVIC, 2005).

Regarding OVs, these are mainly composed of triacylglycerides, which are triesters of glycerol with 3 molecules of fatty acids, extracted from seeds and fruits (FINE, 2016).

They have in their composition vitamins, minerals and substances enshrined in the cosmetic industry such as squalene. They have antioxidant, bactericidal, antiviral, antifungal, antiseptic and anti-inflammatory activity. They are widely used in the cosmetic industry due to their moisturizing capacity (FINE, 2016; ROSÁRIO, 2021). Because they are rich in unsaturated fatty acids, they are photosensitive and degrade with heat (MALACARNE, 2014; VIEIRA, 2018).

Both essential oils (EO) and vegetable oils (VO) are natural products rich in bioactives, which have several pharmacological properties that can benefit skin health and, therefore, are highly indicated

to compose dermocosmetic formulations. Nevertheless, they are mostly sensitive and unstable products, susceptible to oxidation and degradation, and because of it it requires the use of protective systems. Its indiscriminate use or its use in high concentrations can lead to the appearance of allergic reactions. A potential alternative to preserve, enhance and reduce the concentration of its use while we can still enjoy the benefits of these products is through the development of polymeric nanoparticles (DOS SANTOS, 2021; LOBATO, 2021; SALLUSTIO, 2022).

The insertion of vegetable and essential oils in polymeric nanoparticles promotes the preservation of the quality of the bioactives, increasing the solubility, stability, bioavailability, absorption and permeability of the biocompounds, also enabling a greater passage in the treatment. Conventional dermocosmetics have limitations in the effectiveness of several treatments due to the stratified structure of the skin, which makes it difficult for the penetration and permeation of the actives, which end up being retained in the stratum corneum, and do not reach the deeper layers of the skin (DELSHADI, 2020; LOBATO, 2021).

Thus, to achiev the expected result, the actives contained in the formulation need to reach their target and effectively accomplish the topical action without being absorbed by the body, thus avoiding an unwanted systemic effect. Therefore, the bioactive must be absorbed by the epidermis, reaching the basal stratum and eventually the dermis (KIS, 2022; NORLEN, 2022; YOSHIDA, 2022).

An effective alternative, considered an advanced method to promote the releasing and action of bioactives in the appropriate place for treatment, is the development of nanocosmetics.

The first developed nanocosmetic was launched in Paris in 1993. In Brazil, the first national product was commercialized in 2005. However, Brazil still lacks specific legislation that regulates both the dermocosmetics and nanocosmetics sectors, classifying these products as cosmetics of grade 2 (FORNASIER; BORTOLI, 2018; MENDONÇA 2019; SHAH, 2021).

The evolution of nanotechnology has enabled the development of carriers capable of overcoming dermal barriers, delivering bioactives to their site of action more effectively than other forms of presentation. For this purpose, nanoparticles that allow the interaction of hydro and liposoluble elements are used. (TEIXEIRA, 2010).

4 POLYMERIC NANOPARTICLES

The International Organization for Standardization – Technical Committee (ISO-TC, 2005) states that something occurs at the nanoscale when there is control of matter and processes that typically, but not exclusively, occur below 100 nm in one or more dimensions and present properties unique observed at the nanoscale.

The definition of the National Nanotechnology Initiative of the US (NNI, 2004) establishes that nanotechnology must be between 1 and 100 nm as a reference dimension. The lower limits define the size of the atoms used in the construction of the devices, and the upper limit is defined by the ability to manipulate matter down to 100 nm and to observe the resulting phenomena. This definition delimits what is or is at the nanoscale or microscale and indicates that nanotechnology is given by the ability to design, build or manipulate devices, materials or functions at the nanometric scale.

According to the International Union Of Pure And Applied Chemistry (IUPAC, 2007), in some cases due to specific behaviors (transparency or turbidity, ultrafiltration, stable dispersion, etc.) the limit of 100 nm is extended. It is occasionally accepted to use the prefix "nano" for dimensions smaller than 1000 nm. Polymeric nanoparticles are conventionally considered to be presentations in dimensions smaller than 500 nm prepared using different methods (LI, SZOKA, 2007; GHODKE et al., 2016; HAYLES, et al., 2017).

The term nanoparticle includes nanocapsules and nanospheres, which differ according to their composition and structural organization (SCHAFFAZICK and GUTERRES, 2003).

Nanocapsules are a reservoir system and have a high loading capacity. They are composed of a core, surrounded by a polymeric membrane, where the bioactive can be found dissolved in the core and/or adsorbed to the polymeric wall. In general, while the core protects the bioactive agent, the polymeric shell controls its release. When the polymeric membrane is continuous, the release occurs by diffusion of the active in the polymer. When the membrane is porous, the release of actives occurs by diffusion through pores in the polymeric matrix (SEVERINO, 2016; SANTOS, 2019).

Nanospheres are a matrix system and have a low load capacity. They are formed by a dense polymeric matrix, where bioactives can be found trapped or adsorbed (SEVERINO, 2016; SANTOS, 2019). As the active is dispersed in the polymer, its release occurs through erosion, diffusion and swelling processes.

A new nanostructured system known as lipid core nanocapsule (LCN) was proposed by Jager et al. (2009), where the oil core is composed of medium chain triglycerides (MCT) and a surfactant (sorbitan monostearate, commercially known as SPAN 60) of low hydrophilic lipophilic balance (HLB), and the shell is composed of polycaprolactone (PCL) polymer. They present different core dispersion properties when compared to conventional nanocapsules, where control of the active release is achieved by varying the polymer and lipid concentration. TCM can be replaced by EO or VO for the encapsulation and preservation of these materials.

Encapsulating agents determine the characteristics of the final product, their properties influence the size and structure of the nanocapsule, regulate stability during production, storage and

consumption in relation to the external environment, and regulate skin permeation and release of core material when needed (BAKRY et al., 2016).

The size of the nanostructures is a determining factor for the interaction with cell membranes and for the penetration of bioactives through biological barriers, however, for cosmetic or dermocosmetic use, it is expected that the formulations perform topical action and do not reach the bloodstream leading to a systemic action (PASZKO et al., 2011; SILVA, SILVA, 2018).

The permeability and controlled release of nanocapsules in the skin layers are linked to the pH presented by the formulations. Throughout the human body, the skin has different pH, mostly with an acidic pH, so nanostructures tend to have better permeability when they have a slightly acidic pH (LEONARDI et al., 2002; ALMEIDA et al. 2009; FRANK et al. 2017; DA SILVA et al. 2020).

The permeability of bioactives in the skin is also influenced by the partition coefficient between the vehicle and the stratum corneum, being precise to the cutaneous permeation by the diffusion of the active substances in the epidermis (GUTERRES, 2007).

Encapsulation must promote core isolation until the release can occur at a controlled time and place, ensuring the effectiveness of the system, reducing the necessary amount of additives and expanding the applications of the compounds of interest. The main factors that affect release rates are related to the interactions between shell and core material, as well as core volatility, core to wall material ratio, particle size, and shell material viscosity (CASANOVA, 2016).

Nanoencapsulation of hydrophobic bioactives promotes improvements in the performance of labile and volatile substances, and provides a sustained release of charged actives, prolonging their emitted effects. It can be carried out through various delivery systems (GUTERRES, 2019; BEGNES, 2020).

The use of polymers for nanoencapsulation of active ingredients in cosmetics allows masking the physicochemical properties of encapsulated bioactives and improving their interaction with cell membranes, facilitating their penetration into the skin (GUTERRES, 2019; BEGNES, 2020).

Polymers must have specific characteristics and properties such as the ability to form semipermeable microporous structures (matrices or membranes), swelling (expansion) when in contact with water, ability to complex with actives and bioadhesion to formate nanocapsules (KOZLOWSKA, 2019; SOUTO, 2020).

4.1 PREPARATION METHODS OF POLYMERIC NANOPARTICLES

Polymeric nanoparticles (PNs) can be synthesized from natural and synthetic polymers. Among synthetic polymers, biodegradability and biocompatibility are key factors to ensure quality and efficiency in the delivery and release of bioactives (KOZLOWSKA, 2019; SOUTO, 2020).

In cosmetic formulations, biodegradable aliphatic polyesters such as poly (lactic acid) (PLA), poly(lactic-co-glycolic acid) (PLGA), and polycaprolactone (PCL) are widely used as well as biocompatible polyacrylates and derivatives of cellulose (JAISWAL, 2015; NASTITI, 2017; KOZLOWSKA, 2019; SOUTO, 2020).

Aliphatic polyesters are widely used for coating implantable drugs because they are susceptible to degradation in a biological environment. Among these polymers, PLGA is the one with the shortest degradation time (VILLANOVA, et al., 2010).

The mechanisms used to release the nanocapsule core can be combined increasing the system performance. Diffusion occurs when the nanocapsule shell is intact and the release rate is governed by the chemical properties of the core and shell material and some physical properties of the shell (CASANOVA, 2016).

PNs synthesis methods can be based on the polymerization of monomers (in situ polymerization), where polymers are formed simultaneously with nanoparticles; or methods that work with the dispersion and precipitation of preformed polymers, which are more commonly used. The polymer and the obtaining techniques influence the structure, the physical-chemical properties of the PNs, the inclusion efficiency and the active release kinetics (CASANOVA, 2016; GUTERRES, 2019).

Nanoencapsulation methods can be classified as top-down or bottom-up. The top-down method, also called comminution, generally uses mechanical energy or another form of energy to decrease the size of particles. Among the processes of the top-down method are emulsification by ultrasound and emulsification by evaporation of the solvent. In the bottom-up method, the nanostructure is built from the process of self-association of molecules, where they are induced by characteristics of the environment where they are found, such as the solvent, ionic strength, pH, concentration and temperature. Among the synthesis processes of the bottom-up method are nanoprecipitation, coacervation, ionic gelation and complex inclusion (SANGUANSRI, AUGUSTIN, 2006).

PNs can be produced from preformed polymers with solvent emulsification-evaporation, solvent displacement, salting-out or solvent emulsification-diffusion techniques (CASANOVA, 2016; GUTERRES, 2019).

Regarding the nanoencapsulation methods, chemical and mechanical methods are found in the literature (CARVALHO et al., 2016). Among the chemical methods are nanoprecipitation (interfacial deposition of preformed polymer), coacervation, cocrystallization, molecular inclusion and interfacial polymerization, and among the mechanical methods are spray drying, spray cooling, extrusion and fluidized bed.

Among the methods reported in the literature, the method of nanoprecipitation, coacervation and ionic gelation stand out (CARVALHO et al., 2016) and for this reason, these will be the topics addressed in this review.

4.1.1 Nanoprecipitation technique

Nanoprecipitation is also known as interfacial deposition or solvent displacement technique and takes place at the interface of an oil/water (O/W) emulsion through precipitation or interfacial deposition of a preformed polymer (LAMMARI, 2020).

Among the available techniques, nanoprecipitation is the most widespread, presenting a greater number of studies in the literature and it is widely used industrially due to its simplicity of execution, the use of few reagents, greater ease of controlling the size of the particles, low contamination of the resulting suspension and higher yield of the formulations (PEREIRA, 2018).

In this technique, an organic solvent which is miscible in water composes the internal phase of the PNs, where the bioactive is dissolved or dispersed. Surfactants are used as stabilizing agents in this phase to prevent particle coalescence. The external phase is aqueous and contains an O/W surfactant. The external phase is dispersed in the internal phase, promoting the emulsification of the system, under magnetic stirring. The organic phase can be added to the aqueous phase all at once, drop by drop, in small portions or by controlled addition rate (MORA-HUERTAS et al., 2012; ALI; LAMPRECHT, 2013; LAMMARI, 2020).

When the organic solvent mixes with water, due to the decrease in surface tension between the phases which increases the surface area, the polymer insoluble in the aqueous phase precipitates giving rise to nanoparticles. In this process, the formation of PNs goes through three stages: nucleation, growth and aggregation (ALI; LAMPRECHT, 2013; LAMMARI, 2020).

Nanoprecipitation was used by Yingngam et al. (2019) for the preparation of menthol nanocapsules, extracted from peppermint essential oil (*Mentha x piperita*), surrounded by poly(ε-caprolactone). Nanocapsules of 122 to 354 nm, high trapping efficiency (98.18 ± 1.05%), polydispersion between 0.148–0.284, and zeta potential ranged from -22.47 to -30.86 mV were obtained. The results obtained by scanning electron microscopy indicated spherical morphology. The menthol trapping efficiency in the nanocapsules depended on the mass proportions of menthol and polycaprolactone, whereas no difference was observed for the stabilizer. The high entrapment efficiency of menthol was related to its hydrophobicity, which facilitated dispersion in the oily core of nanocapsules. Kinetic stability lasted for at least 90 days where particle size remained constant due to delayed aggregation. Furthermore, the thermogram of the charged nanocapsules shifted to higher temperatures, indicating that nanoencapsulation improved the thermostability of menthol and

fluorescence intensity profiles showed that the nanocapsules facilitated the rapid penetration of the charged substance into the viable epidermal layer by the hair follicle and transepidermal pathways. The nanocapsules showed a cytotoxicity limit in accordance with ISO 10993–5:2009 (Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity), indicating that they are less toxic than H_2O_2 and can be used for the delivery of menthol to the skin.

Da Silva et al. (2020) prepared poly(ε-caprolactone) nanocapsules with chitosan loaded with Melaleuca EO (*Melaleuca alternifolia*). The nanocapsules had an average size of 268.0 ± 3.8 nm, polydispersion of 0.204 ± 0.9, indicating a monodisperse system, zeta potential of +31.0 ± 1.8 mV, and pH of 5.06 ± 0, 17, and encapsulation efficiency of 94.9 ± 0.38%. Images obtained by atomic force microscopy (AFM) allowed observing the spherical morphology of the nanocapsules. The nanocapsules demonstrated an improvement of the antimicrobial activity of the EO against *Cutibacterium acnes* and the resultas were promising regarding its use for the treatment of melanoma and also cosmetic.

De Morais et al. (2018) prepared poly(ε-caprolactone) nanocapsules loaded with copaiba vegetable oil (*Copaifera officinalis L.)* and tea tree essential oil (*Melaleuca alternifolia*). The nanoparticles had an average size of 239.23 ± 4 nm and 209.77 ± 72 nm, zeta potential of -31.38 ± 2.21 mV and -31.38 ± 3.23 mV, SPAN (polydispersion) of 1.758 ± 0.13 and 1.94±0.09, and pH of 4.94 ± 0.16 4.78 ± 0.3, for nanocapsules loaded with copaiba oil and tea tree oil, respectively, being considered promising carriers.

Almeida (2008) prepared poly(ε-caprolactone) nanocapsules loaded with grape seed oil and almond oil associated with benzophenone-3. The nanocapsules had an average size of 228 ± 07 and 243 ± 06 nm, polydispersion of 0.19 ± 0.02 and 0.20 ± 0.00, zeta potential of -8.22 ± 1.34 mV and -7.34 ± 0.67 mV and pH of 6.82 ± 0.02 and 6.97 ± 0.24 of grape oil and almond oil, respectively. The presence of chemical sunscreen did not modify the colloidal characteristics and showed encapsulation efficiency greater than 99% when associated with both vegetable oils.

The observed parameters remained adequate after 6 months of storage at room temperature. The photodegradation study showed that the structure of the vesicle did not influence the protection of benzophenone-3 against photodegradation. And its photostability was improved due to entrapment in the system.

Pires (2020) demonstrated that using the same methodology as Jäger (2009), pequi oil (*Caryocar Brasiliense Cambess*) can be used as a viable structuring agent to replace MCT in the preparation of lipid core nanocapsules, as it presented better results in cell viability tests. The lower cytotoxicity of the nanocapsule was attributed to the physical-chemical characteristics and biological activity of pequi oil.

Mattiazzi (2014) prepared nanocapsules and nanospheres of poly(ε-caprolactone) and Eudragit® EPO (cationic polymer composed of methacrylate and neutral esters of methacrylic acid) loaded with pracaxi vegetable oil (*Pentaclethra macroloba*) and with ubiquinone solubilized in this oil. The nanostructures prepared with Eudragit® EPO and loaded with pracaxi vegetable oil proved to be unfeasible because they had limited stability in the dissolution/swelling test, where the polymer dissolved in the oil in 60 days. Poly(ε-caprolactone) proved to be adequate for the encapsulation of pracaxi vegetable oil. The formed nanocapsules had an average diameter of 288±13 nm and 261±55 nm, polydispersion of 0.277±0.01 and 0.225±0.01, zeta potential of -14.83±327mV and -15.37±2.33 mV , pH of 5.9±0.6 and 6.1±0.1 for nanocapsules without ubiquinone and with ubiquinone, respectively. Nanospheres had an average diameter of 204±09 nm and 175±16 nm, polydispersity of 0.202±0.02 and 0.126±0.03, zeta potential of -12.62±2.37 mV and -19.24±5.09 mV and pH of 78±0.2 and 6.8±0.4. The encapsulation efficiency was 100% and 99% for nanocapsules and nanospheres containing ubiquinone, respectively. The photodegradation study demonstrated that the nanostructures promoted an increase in the photostability of the oil and greater stability of the drug. The nanostructured systems demonstrated stability when stored for 90 days at room temperature, with their physicochemical characteristics altered when subjected to heat and humidity. The results indicated that the nanostructures prepared with pracaxi oil can be considered promising carriers to explore the therapeutic potential of ubiquinone.

4.1.2 Coacervation technique

Coacervation is an interaction that occurs through complexation in which a mixture of solutions of substances with opposite charges, which form complexes, precipitate by repulsion of the solvent and form two phases: one “rich in polymers” with precipitated coacervate and another called “poor in polymers” in which the solvent of the solution remains. Coacervation can be simple or complex (MUHOZA, 2022).

In simple coacervation, liquid phase separation occurs by adding an electrolyte to the colloidal solution. Only one polymer participates, and the removal of the solvent surrounding the colloid molecules occurs through the use of another compound that competes with the polymer for water, such as salts or alcohols. As the solvent exits, the polyelectrolyte molecules approach and form clusters (WANG, et al., 2008).

In complex coacervation, mutual neutralization of two oppositely charged colloids in aqueous solution occurs. Through the interaction of different polymers that have opposite charges (generally a protein and a polysaccharide), insoluble complexes are formed, generating phase separation. The deposition of such complexes around a hydrophobic core creates a barrier, thus allowing their

encapsulation. This method is mainly used for encapsulation of hydrophobic substances, it has high encapsulation efficiency, low concentration of wall materials and the possibility of applying controlled release, and no organic solvents are used (MUHOZA, 2022).

Among the advantages of coacervation compared to other methods, the possibility of workin with biopolymers and mild temperature conditions in processing stands out. Among the disadvantages are the speed of agitation and the critical control of concentrations of polymeric materials. That is: coacervation will only occur within a limited range of pH, colloid aconcentration and/or electrolyte concentration (MUHOZA, 2002).

Complex coacervation was used by MEI et al. (2022) to synthesize nano-microcapsules of tea seed oil (extracted from *Camellia oleifera* seeds, TSO), using propolis ethanolic extract (EEP) and phosphatidylcholine (PC) derived from soy to compose the bark. The size of the EEP-PC-TSO nanocapsules ranged from 95.30 nm to 445.23 nm, and the results obtained in Scanning Electron Microscopy (SEM) indicate spherical morphology. With decreasing electrostatic adsorption pH, the main peak of the particle size distribution curves shifted from 130 nm to 425 nm, suggesting that particle size increases with decreasing pH.

The encapsulation efficiency ranged from 67.20 to 93.44%, showing an initial tendency to increase followed by a decrease with decreasing pH. As the homogenization pressure increased from 200 bar to 1000 bar, the average particle size decreased from 412.10 nm to 177.90 nm. The nano-microcapsules had improved antioxidant activity when compared to the mixture of EEP, PC and TSO. The nanoencapsulation synergistically improved the antioxidant activity of the nano-microcapsules, increasing the bioavailability of TSO, by increasing the surface area ratio and the solubility of the hydrophobic core, showing 68% and 54% elimination activity of DPPH and ABTS, respectively.

4.1.3 Ionic gelling technique

Ionic gelation produces nanospheres and nanocapsules through the formation of gelatinous structures, based on the interaction between the opposite charges of a polymer and counter-ions of a cross-linking agent. Two aqueous phases are mixed, requiring only one polymer. In this technique, a solution with cationic polymer is used, the most used being alginate and a solution with sodium tripolyphosphate or calcium chloride, which are polyanions (VALLE, 2021).

Among its advantages, this technique does not require the use of organic solvents, does not require high temperatures or extreme pH. Among its control factors are the polymer concentration, agitation speed and the concentration of stabilizer to obtain the gel, since ionic gelation is based on the electrostatic interaction between the polymer and the crosslinker (CUNHA, 2017).

The technique consists of dripping a cross-linking agent into a polymeric solution containing surfactant, using a syringe or pipette of reduced caliber. The polymer chains electrostatically interact with the oppositely charged medium, forming particles embedded with core material, where the charged medium is used as a crosslinking agent. During ionic gelation, hydrogel granules, also called gelispheres, are produced through the solution's fall (VALLE, 2021).

For the production of charged nanocapsules, the bioactive is added to the polymeric solution containing surfactant which forms an emulsion. The crosslinking agent is added to the emulsion, the cations diffuse into the polymer drops loaded with bioactive, forming a three-dimensional ionic crosslinking network (CUNHA, 2017).

Nanocapsules loaded with lemongrass oil and nanocapsules loaded with turmeric oil were prepared by Natrajan et al. (2015) using alginate, to compose the bark, and chitosan, through ionic gelation with the aid of an O/W emulsion. An ethanolic solution, containing the essential oil, was added dropwise into an aqueous phase, containing alginate and stabilizer, which underwent sonication. Calcium chloride was used as a crosslinking agent. The emulsion was combined with chitosan and the solvent evaporated to obtain nanocapsules. Nanocapsules with an average size of 256 and 226 nm, zeta potential of 35.7 and 40.6, and encapsulation efficiency of 71.1% and 86.9% were obtained for nanocapsules loaded with turmeric oil and lemongrass oil, respectively. The results obtained in SEM indicated spherical morphology. At pH 7.4 approximately 90% and 42% of encapsulated turmeric and lemongrass oil were released, respectively, over a period of 48 hours. This release profile may be related to the formation of alginic pellicle insoluble in acidic pH, suggesting that the release of oil contained in the nanoparticles is sensitive to pH.

The oregano essential oil (*Origanum vulgare*) has antioxidant and antimicrobial activity from its main constituents: α-terpinene, γ-terpinene, linalool, 4-terpineol and thymol (BLANK, 2016). HOSSEINI, et al. (2013) prepared chitosan nanocapsules loaded with oregano essential oil in a two-step process: O/W emulsification followed by ionic gelation. The surfactant used was Tween 80, used to stabilize the O/W emulsion composed of oregano EO added to the chitosan aqueous solution. Tripolyphosphate was the crosslinking agent. The particles obtained underwent centrifugation, ultrasonication and the suspensions obtained were lyophilized. The nanoparticles showed regular and spherical morphology observed in SEM and AFM, which also indicated that most of the chitosan nanoparticles loaded with oregano EO were distributed at intervals of 40 to 80 nm, and that the particle size increased as a function of loading with essential oil. The mean diameter of the nanocapsules prepared with the chitosan: oregano EO ratio 1:0.1 (w/w) was 309.8 ± 8.3 nm, encapsulation efficiency of 24.72 ± 4.39%. Through the thermogram obtained from TGA analysis, it was possible to observe the displacement of the degradation temperature of the encapsulated oregano EO to higher

temperatures compared to the non-encapsulated EO, reflecting the better thermal stability attributed to the encapsulation. The in vitro release profile of oregano EO from chitosan nanoparticles was described as a biphasic process, with an initial rapid release followed by a slower release. The initial release was attributed to oregano EO molecules adsorbed on and near the surface. The amount of bioactive released initially is high because the dissolution rate of the polymer near the surface is high. For chitosan nanoparticles loaded with oregano EO in a 1:0.1 (w/w) ratio, the burst effect occurred within 3 h and about 82% of encapsulated oregano EO was released from the nanoparticles. The initial release was slower for nanoparticles prepared with higher proportions of EO, as chitosan nanoparticles with smaller particle size would have a higher surface-to-volume ratio, and therefore may result in rapid release of surface-adsorbed oregano EO. The slower release that occurred in the second stage required the swelling and degradation of the compact chitosan nanoparticles, which indicated the suitability of this system for the controlled release of oregano EO.

5 CONCLUSIONS

Polymeric nanoparticles loaded with essential and vegetable oils are a new trend among cosmetics and dermonanocosmetics that have promoted the appreciation of natural products, however they still lack specific regulation.

The development of polymeric nanoparticles containing essential oils and vegetable oils can be affected by several factors. Therefore, the choice of method, polymer, bioactive and stabilizers should not be random. Taking into account the nature and concentration of the components involved in the formulation allows for directing and optimizing processes.

The percentage of inclusion of the actives are apparently influenced by the methods of obtaining them. However, these variations cannot be exclusively attributed to the technique used, considering that other conditions, such as the chemical characteristics of the components, influence this property.

Among the observed processes, nanoprecipitation is the most used due to its ease of execution and large-scale production.

The synthesis of polymeric nanoparticles with smaller sizes and higher yields aims at better skin permeability, optimizing the bioactive delivery process, reaching deeper layers of the skin.

The cosmetic/dermocosmetic market seeks innovations that are met both by the insertion of new molecules in existing delivery technologies and by the development of new systems to incorporate established actives.

The development of such technologies makes opportunities to create new processes, products and high-performance formulations more flexible, which generate better and faster results and

minimize adverse effects. These innovations accompany the emergence and fulfillment of new trends, keeping the cosmetic and cosmeceutical market dynamic and connected to external markets and trends.

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