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Review Article

Microparticles of Herbal Extracts with Antioxidant Activity

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ABSTRACT

Plants that have antioxidant content have been shown to have efficacy on the body, antioxidants have several drawbacks including being sensitive to environmental factors such as light, heat, pH, and oxygen. Microencapsulation is a method that has several advantages including providing several benefits, namely microparticles formulated to protect the core from the environment, cover up discomfort, maintain volatility or cell survival, separate incompatible substances, protect the body from side effects, and optimize, extend, or target drug effects. The choice of the type of polymer used will determine the characteristics of the microparticles produced, therefore a suitable coating material is needed to produce the microparticles. This review article was made to find out the results of research conducted in the manufacture of microparticles by using polymers which are expected to be useful to provide information on the basis of the selection of polymers and methods of making microparticles produced to maintain the stability of substances that are efficacious as antioxidants. Based on the results of the literature search, microencapsulation is a method used to maintain the stability of antioxidant content that has a therapeutic effect.

Key words: Microparticle, Extract, Antioxidant, Polymer.

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INTRODUCTION

Antioxidants have health benefits such as reduces the occurrence of different disorders like: aging, cancer, anti-inflammatory role related to chronic diseases, like obesity and diabetes, liver disease, cardiovascular disease, cataract, nephrotoxicity, neurodegenerative disorders, antibacterial, anti-allergic, anti-hypertensive, antiviral and skin wound healing effects have been attributed to the role of antioxidants.[1,2]

Due to their antioxidant properties, several health benefits related to their consumption are reported in the literature. The relevant antioxidant activities of bioactive substances may be hampered due to their degradation triggered by light, oxygen, temperature, moisture, solvent, other environmental conditions and existence of unsaturated bonds in the molecular structures. The instability of antioxidant compounds is associated with different processing and storage conditions. These facts have led researchers to investigate new forms of processing that provide minimal degradation. It is therefore envisaged that microencapsulation could preserve the stability of this kind of natural substance, besides allowing their controlled release during the shelf life of the product of interest. Microencapsulation is a promising possibility to stabilize extracts and allow their addition to products in a more stable form.[2-4]

The antioxidant characteristics enable their use in food, cosmetics and pharmaceuticals, either to increase the shelf life of these products, reducing the amount of synthetic antioxidants in their composition, or to promote beneficial effects to the human body. However, as antioxidants compounds are unstable, the application of these bioactive compounds to new products is very restricted.[4]

The application of microencapsulated bioactive compounds as functional applications exhibits significant potential. The ingredients mostly enveloped in a coating material, thereby conferring useful or eliminating useless properties from the original ingredient.[5] The substance that is encapsulated may be called the active agent or core ingredient, while the substances that provide the protection are called the coating or shell materials. The coating material of encapsulates used in food products should be food grade and able to form a barrier protecting the active agent from adverse effects of moisture, heat, light, oxygen, and other reactive components present in the matrix.[6]

Microencapsulation is a process of packaging solids, liquids, or gaseous materials as active material with a continuous film as a coating to form capsules, whereby the functional ingredients are protected from their environment by entrapping them within a protective coating material and forming particles with diameters of a few nanometers to a few millimeters.[6,2] Thus, microencapsulation with an appropriate carrier is an alternative technology for enhancing the storage and enviromental stability of bioactives as well as giving an advance to mask off-flavour.

A number of coating or matrix materials can be selected depending upon desired properties of the final microcapsule including stability and unaltered bioavailability, as well as compatibility with selected microencapsulation techniques and high encapsulation efficiency. Among them, proteins, sugars, starches, gums, lipids, and cellulose derivatives are most popular, as covered elsewhere

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in this book. Ideal coating materials should have a bland, neutral taste and odor, good film-forming properties, low viscosity when present in solutions or suspensions, and desirable gelling and barrier properti. As a coating or encapsulating system is designed to protect the core material from environmental factors that may cause its deterioration and to prevent premature interaction between the core material with other food components, it is of paramount importance when selecting the coating material that it be stable under processing and storage conditions.[6]

The purpose of this review is to provide an evaluation based on the selection of various types of polymers and the method of making microparticle extracts that have antioxidant properties. To achieve this goal, research that explains the results of selecting polymers used in the manufacture of micro particles includes the effect of encapsulation on antioxidant capacity, stability, solubility and content of bioactive compounds.

Current research on microencapsulation of extracts

The encapsulation technique is considered a promising protection method which involves packaging smaller core materials in the wall matrix. Encapsulation technology is defined as a technique in which a substance in a solid, liquid, or gas state (encapsulation agent or active core) is packed with encapsulation material (wall or shell material). Encapsulation agents can be engineered to release active ingredients gradually through specific triggers (such as fractures due to heat, solvation, diffusion, and pressure), and can be engineered to be opened in specific areas of the body. Capsules are vesicles or small particles that can range from sub-microns to several millimeters. The size of the dispersed particles or powder formed can be classified as macro (> 5000 μm), micro (1.0-5000 μm) or nano (<1.0 μm). Many morphologies can be produced for encapsulation, but three main morphologies are more commonly used: mononuclear capsules, which have one core enveloped by a wall material, a polynuclear core, which has two or more nuclei covered by a wall material; and aggregates, which have many nuclei embedded in the matrix.[3]

Several parameters are used to verify the quality of encapsulation, and their characteristics depend on the encapsulation process used. Encapsulation efficiency is one of the most important quality parameters of the encapsulation technique because it determines the ability of the wall material to hold the core material inside the microcapsules. This parameter allows us to determine whether the encapsulation method and the wall material used are capable of coating the core material efficiently. Particle size is another quality parameter that must be observed and its reduction. The encapsulation method can improve the properties of delivery, solubility, and bioavailability because it produces a higher surface area per unit volume, increasing its biological activity. Small size, on a micro and nano scale, can provide long gastrointestinal retention times caused by increased bioadhesive properties in the mucus that covers the intestinal epithelium. Particles made with biopolymers can also use ζ-Potential as a quality parameter. This parameter determines the surface properties by measuring the difference in effective electric potential generated by the surface charge density of the biopolymer used and depends on the pH of the medium. The ζ-Potential measurement can be used to verify the stability of aggregation and to control the retention and release of bioactive molecules among other functions.[3]

In many reviews, microencapsulation has been used for protection, modification, and controlled delivery of many food ingredients, including acidulants, flavors, sweeteners, colorants, enzymes and microorganisms, antioxidants, leavening agents, and nutritional ingredients such as vitamins and minerals.[6] Research on microencapsulation of extract which had been reported in many publications was summarized in Table 1.

Polymers for microencapsulation

Although various encapsulating agents can be used, both individually and in combination, some characteristics should be observed, such as their ability to form films, biodegradability, resistance to gastrointestinal tract, viscosity, solids content, hygroscopicity, and cost. An effective combination of appropriate coating materials and encapsulation techniques is the key for developing a microencapsulated system as it plays an important role in the physical and chemical properties of the resulting microparticles, such as particle size, porosity, density, flowability, integrity, reactivity/stability, and release properties. For each active ingredient the appropriate choices of process and wall materials depend greatly on the end use of the microencapsulated particles.[6]

Among various encapsulating agents, such as gum Arabic, lactose, maltodextrins, and xanthan gum, maltodextrins with degrees of dextrose equivalence (DE) between 10 and 20 are frequently used in the spray-drying process. These substances have several advantages, including the ability to contain the acidulants, such as adipic acid, ascorbic acid, citric acid, fumaric acid, and malic acid, protect the sensitive substances, reduce the hygroscopicity of the products, reduction of stickiness of the fruit extracts, and provide a high degree of flow and fast dissolution of the microparticles in water.[16]

Chitosan has been chosen as the microencapsulating agent because of its wide applicability as a biodegradable, biocompatible and non-toxic polymer. The fact that it is also a natural and low- cost polymer increase the interest in its use in encapsulation of a natural active substance. Chitosan microparticles are able to prolong the residence time of drugs applied topically thus improving the drug bioavailability.[7]

Gum Arabic (GA) is considered an encapsulating agent par excellence has reasonable emulsifying properties with acceptable protecting effects, but its viscosity at high concentrations limits its industrial applications and it is used mainly due to its high water solubility characteristics, low viscosity, and emulsifying properties.[18] On the other hand, its high price has motivated the search for total or partial substitution of this encapsulant. Maltodextrin (MD) a hydrolysed starch, offers advantages as a microencapsulation material is the most commonly used material for this purpose, especially for encapsulating extracts and low-cost material with a neutral aroma and flavor, high water solubility and low viscosity at high solids content, being able to pro-vide effective protection against oxidation ; however, it has low emulsifying capacity and protective effects.[18] Because a single wall material does not meet the requirement of high powder recovery with satisfactory quality characteristics, combining wall materials may be beneficial.

For this reason, it is necessary to subject them to processes like spray-drying to extend their shelf-life but without affecting their useful properties. To this end, carrier materials like maltodextrins, inulin and gums need to be added to the solutions to prevent stickiness and the loss of volatile compounds. Maltodextrin, derived from starch hydrolysis and made up of β-D-glucose chains, is one of the most commonly-used and studied carriers due to its high solubilization capacity, mild flavor, low cost and ability to reduce stickiness and improve product stability. Maltodextrin's properties are defined by the degree of starch degradation, indicated by the dextrose equivalent value (DE) which measures the content of reducing-end groups. Different DE values result in distinct properties due to modifications of this substance's physicochemical parameters. One way to evaluate these changes consists in determining the glass transition temperature (Tg), which decreases at higher DE values. A high maltodextrin Tg, for example, provides a stable glassy matrix at room temperature.[38]

Biopolymer microparticles can be used to encapsulate lipophilic bioactive agents, which can be manipulated to protect bioactive agents from degradation in products during storage or within the

Table 1: Various manufacturing results of various microparticle extracts polymer.

Polymer	Compound	Content	Method	Results	Reference
Chitosan	Plinia cauliflora (jabuticaba) fruit peel extract	Polyphenols	Spray drying	– After 60 days (97 ± 9% and 83± 4%, respectively) and at a stress temperature for 30 days (74± 19%) it was verified that the microparticles were better than the extract in maintaining the total polyphenols at the three temperatures studied ($p<0.05$). – The results showed the development of stable chitosan microparticles encapsulating jabuticaba peel extract successfully produced by spray drying. – These microparticles were capable of protecting the total polyphenols contained in the extract, promoting the stability of these compounds during storage, which enhables their application in food or cosmetic products.	4
Chitosan	Aloe vera	a-tocopherol	Spray drying	– The particles were spherical, with a rough surface, micrometric (D[4,3] = 9.59 mm), unimodal and polydisperse (SPAN of 1.12). The final a-tocopherol acetate concentration in the powder was 91% of the expected amount. – The microparticles were capable ofmaintaining the concentration of a-tocopherol acetate for a longer time than a commercially available pulverized form of a-tocopherol acetate.	7
Chitosan	Rutin	Rutin	Formulated by a rotor-stator homogenize at the homogenization speed 10,000 rpm.	– The characterization of the prepared films showed that chitosan-coated microparticles are well dispersed in the gelatin film. The addition of microparticles into the gelatin film decreased the elongation-at-break and water vapor permeability of the biopolymer. – The light barrier properties of edible films show that UV light is absorbed with the addition of microparticles to the biopolymer matrix. – The FTIR absorption spectra for biocomposite films indicated good protection of antioxidant rutin, which remains unaffected in the presence of the higher permeability. – These characterizations show that the incorporation of chitosan-coated microparticles charged with antioxidant rutin into gelatin films is an ideal option for the development of active packaging for extending shelf life.	8
Alginat, Chitosan	Pomegranate Peel Extract	Ellagitannins (polyphenols)	Spray-drying	– Production yields were about 40% for alginate microparticles and 41% for chitosan. Mean diameters were 2.45 µm and 2.80 µm, and encapsulation efficiencies were 81.9% and 74.7% for alginate and chitosan microparticles, respectively. The spray-drying process preserved the antifungal activity against Candida albicans. – In this study, these agents did not differ in yield, size, efficiency of encapsulation, or antifungal activity. The amount of the extract in the microparticles was quantified by HPLC, and the process of encapsulation preserved the antifungal activity of the extract against C. albicans, which is responsible for mycosis in the buccal region.	9
in Alginate–Chitosan copolymer microbeads.	Extracts of six different medicinal herbs, nettle (Urtica dioica L.), hawthorn (Crategus laevigata), raspberry leaf (Rubus idaeus L.), olive leaf (Olea europea L.), yarrow (Achillea millefolium L.) and (Glechoma hederacea L.)	Polyphenolic	Electrostatic extrusion.	– Raspberry leaf encapsulating microbeads exhibited the highest total phenol content and antioxidant capacity, followed by hawthorn, while olive leaf microbeads contained the lowest total phenol content. – High encapsulation efficiency was obtained for all extract encapsulating microbeads (80–89%). Nettle extract-containing microparticles were character- ized with the largest particle size and irregular shape, due to a high content of microelements (copper, strontium, and zinc), which affected the geling process of alginate.	5

Chitosan, maltodextrin	Rooibos extract	Aspalathin, a dihydrochalcone antioxidant	Spray drying	– Three formulations (50, 100 and 150 g chitosan/kg powder) were compared to the pure spray- dried extract and maltodextrin containing powders (250 and 500 g maltodextrin/kg powder) in terms of physicochemical properties (particle size and morphology, moisture sorption isotherms, compatibility, bulk density and compressibility) and aspalathin stability during accelerated storage. – All the formulations produced amorphous, hygroscopic powders with deliquescence at relative humidity (RH) > 65%. The moisture content of the powders was lower than their monolayer moisture content calculated using the Brunauer-Emmet-Teller (BET) and Guggenheim- Anderson-de Boer (GAB) models. Isothermal microcalorimetry showed no interaction between extract and carbohydrate polymers. Aspalathin degradation in the powders, subjected to accelerated stability testing (40 °C/75% RH for 96 h), followed fractional conversion kinetics. – The presence of chitosan in the powders decreased the stability of aspalathin during storage compared to the pure extract and maltodextrin-containing powders.	[10]
Sodium Alginat	Quercetin	Quercetin	Ionic gelation	– Aggregates of polymer and precipitated quercetin are found homogeneously distributed within the particle matrix, that may be helpful to increase the drug load. In addition, the details of the particle surface (cracks, holes and other imperfections) appear to govern the non-homogeneous swollen and erosion. – These findings provide complementary evidence on alginate microparticle structure to be considered when the design of this kind of carriers is intended.	[11]
Sodium caseinate and Alginate	β-karoten	Carotenoid	Emulsions	– The β-carotene-loaded microparticles had a particle size (1.87 ± 0.03 μm) larger than that of caseinate emulsions (0.48 ± 0.01 μm) ($P < .05$). – Microparticles were stable to aggregation over a wide pH range (3–7) and at high salt levels (0–1000mM NaCl), and protected β-carotene from degradation during storage. – An in vitro digestion experiment showed that the β-carotene in microparticles had a higher bioaccessibility and chemical stability (67.57 ± 2.72% and 80.03 ± 1.95%, respectively) than in emulsions (30.03 ± 1.87% and 70.87 ± 1.52%, respectively) ($P < .05$)	[12]
Inulin, Sodium Alginate	Maqui (Aristotelia chilensis [Mol.] Stuntz)	Anthocyanins	Spray-drying	– The encapsulation technology using either Inulin or Sodium Alginat can be used as a protection strategy for Maqui Juice (MJ) anthocyanins by producing stable anthocyanin-rich microparticles. – Moreover, both Encapsulating Agent improves the Bioaccessibility by 10% comparing to MJ. The use of MJ as a raw material offers an additional protection effect for anthocyanins while following a more sustainable process.	[13]
Alginate and β-cyclodextrin	Blood Orange Juice	Anthocyanins, Bioflavonoids, and other Polyphenols	Spray drying	– The spray-dried applied conditions were able to obtain a concentrate dried extract without the loss of Antioxidant Activity and with Total Polyphenol Content and Total Monomeric Anthocyanin values of 35–40% higher than that of the starting material. They were also effective in producing microparticles with 80–100% of encapsulation efficiency. – The 2% sodium alginate was capable of improving the extract shelf life, while the beta-cyclodextrin (1 : 1 molar ratio with dried extract) prolonged the extract antioxidant efficiency by 6 hours.	[14]
Alginate aerogel microparticles	Passion fruit bagasse extract	Polyphenols, including piceatannol.	Emulsion-Gelation method	– Alginate aerogels derived from 1wt% solution led to a higher Gallic Acid loading and, therefore, this formulationwas used to impregnate Passion Fruit Baggase Extract (PFBE). The loading of PFBE, total phenolic, and piceatannol contents based on grams of raw aerogel were 0.62 g, 10.77 mg, and 741.85 μg, respectively, which means a loading efficiency of total phenolics and piceatannol of 47.1% and 34.7%. – DSC analysis and X-ray diffraction showed that particles behave as amorphous materials and ORAC assay revealed that impregnated aerogel microparticles presented antioxidant capacity.	[15]
Maltodextrin	Maoberry Fruit Extract	Anthocyanin	Spray drying	– The AE (Antidesma puncticulatum Miq.) microparticles were successfully prepared in maltodextrin by the spray-drying method. The optimal processing conditions providing high microparticle yield and encapsulation efficiency of anthocyanins, with a low moisture content, could be achieved using the CCD. – All tested variables significantly influenced the production yield, moisture, and encapsulation efficiency of anthocyanin content of the resultant microparticles.	[16]

Maltodextrin	Hydroalcoholic extracts of two mushrooms species, Suillus luteus (L.: Fries) (Sl) and Coprinopsis atramentaria (Bull.)	Resulting in species such as glu- tathione (GSH), a-tocopherol (vitamin E), ascorbic acid (vitamin C) and lipoic acid	Spray-drying	– The spray-drying of the extracts using an extract/maltodextrin ratio of 1/20 and an inlet temperature of 170 °C resulted in good encapsulation yield (around 50%) and effi- ciency (43.5–62.6%.). – The microencapsulated extracts with maltodextrin did not lose antioxidant activity, and the combination Suillus luteus (L.: Fries) (Sl) and Coprinopsis atramentaria (Bull.) (Ca) (1:1) was shown to be the best as it revealed synergistic effects. The microspheres with Sl:Ca (1:1) and with the free extract (in the same proportion) were incorporated into cottage cheese. – The results showed that, in com parison with the free form, the encapsulated extracts became more effective since the antioxidant activity was preserved over time.	17
Gum Arabic, Maltodextrin	Acerola (Malpighia emarginata DC.)	Antioxidant compounds, such as ascorbic acid (AA), carotenoids (CA) and phenolic.	Spray and freeze-drying	– Phenolic compounds showed significan and positive correlations with all antioxidant assays. The microencapsulation efficiency was greater than 50% for phenolic compounds and total flavonoids; in addition, high antioxidant activities were also observed. – In general, spray and freeze-dried powders have better physicochemical characteristics. The spray-dried treatment presented the best profile due to the retention of higher concentrations of bioactive compounds (except ascorbic acid), and antioxidant activity by FRAP and ORAC assays, supported by low moisture content, aw, hygroscopicity, particle size and higher solubility.	18
Gum Arabic and Maltodextrins	Jussara (Euterpe edulis Martius) extract	Anthocyanins	Spray drying	–Microparticles showed high anthocyanin retention, above 88%. Anthocyanin profiles were similar to the microparticles and jussara extract and two anthocyanins identified were cyanidin 3-rutinoside and cyanidin 3-glucoside. –The maltodextrin 30 DE provided the formation of powders of higher moisture content, more hygroscopic and with a lower glass transition temperature. The blend ofmaltodextrin 10 DE and gum Arabic (50:50 and 75:25) can be selected as a good alternative as carrier agents for jussara extract.	19
Maltodextrin, Gum Arabic	Rhodomyrtus tomentosa (Ait.) Hassk.	Flavonoids	Spray Drying	–The optimized condition for microencapsulation was of maltodextrin to gum Arabic ratio 1 : 1.3, total solid content 27.4%, glycerol monostearate content 0.25%, and core to coatingmaterial ratio 3 : 7, resulting inEE 91.75%. –Prepared at the optimized condition, the flavonoids extract microcapsules (FEMs)were irregularly spherical particles with lowmoisture content (3.27%), high solubility (92.35%), and high bulk density (0.346 g/cm3). –DPPH radical scavenging activity ofFEMs was not decreased after spray drying ($P > 0.05$) and higher than those in citric acid and rutin at the same concentration.	20
Maltodextrin and Gum Arabic	Extract of Baccharis dracunculifolia	Phenolic compounds: caffeic acid, p-coumaric acid, and catechin.	Spray-drying	–Microparticles containing (1→6)-β-d-glucan (lasiodiplodan) and B. dracunculifolia extract associated with maltodextrin and gum arabic was studied as a matrix material. Microparticles of 0.4 μm mean size and high phenolics content (3157.9 μg GAE/g) were obtained under the optimized conditions. The microparticle size ranged from 0.23 to 1.21 μm. –Thermal analysis indicated that the microparticles demonstrated high thermal stability.	21
Maltodextrin and Gum Arabic	Guarana (Paullinia cupana Kunth, Sapindaceae) Extract	Polyphenols	Spray-drying	–The spray-drying technique and the processing conditions selected gave satisfactory encapsulation efficiency (80–110%) and product yield (55–60%). The mean diameter of microparticles was around 4.5 μm. –The DPPH radical scavenging capacity demonstrated that microparticles can protect the semipurified extract of guarana from the effect of high temperatures during the process maintained the antioxidant capacity. –In vitro dissolution tests demonstrate that all formulations complete dissolution within 60 min. Microencapsula- tion improved the technological characteristics of the powders and preserved the antioxidant properties.	22
Maltodextrin (MD), colloidal silicon dioxide (A), arabic gum (E) and β-cyclodextrin (β -CD)	Psidium guajava L.	Alkaloids, tannins, flavonoids and phenolic compounds.	Spray drying	– The results of the present study showed that the spray dried guava leaves extracts present potential antioxidant and antimicrobial activities. Psidium guajava leaves extract showed antibacterial activity against S. aureus and also showed antifungal activity against C. glabrata. – The spray dried guava leaves extracts exhibited stronger antimicrobial activity against S. aureus and C. glabrata, evidenc- ing their potential as a natural antimicrobial agent for medicinal, cosmeceutical and food purposes	23

Maltodextrin (MD), gum Arabic (GA), and whey proteins (WP)	Mulberry	Polyphenols	Spray drying	– The Whey Proteins based samples had the highest powder yield and smallest particles using scanning electron microscopy. Maltodextrin led to higher solubility, hygroscopicity, color stability, and anti-α-glucosidase activity. – The combined wall-materials, especially, Whey Proteins with Gum Aarabic or Maltodextrin, increased the polyphenols stability and their antioxidant capacity during storage better than their individual counterparts.	24
Maltodextrin/ apple- pectin	Extracts from Fadogia ancylantha, Melissa officinalis and Tussilago farfara	Polyphenol (flavonoids and cynnamicacid derivatives)	Spray-drying	– A maltodextrin/pectin (M/P) matrix was studied for its ability to carry sensitive polyphenol-rich extracts via spray-drying. – The use of a 10:1 M/P weight ratio (11% w/v) led to encapsulate 3% w/v polyphenol-rich extracts forming stable powders made up of well-formed and micronized particles suitable for storage and handling.	25
κ-carrageenan and maltodextrin	Morinda citrifolia L. extract	Phenolic and flavonoid	Spray-drying	– The results showed that the percentage of 2,2-diphenyl picrylhydrazyl (DPPH) scavenging activity of the spray-dried powder was the highest for the 1:2 ratio (volume ratio of M. citrifolia L. extract to additive solution) at 90 ◦ C, with maltodextrin at a concentration of 33 mg/ml. – The results also showed that the microcapsules had a regular spherical shape. The spray-dried M. citrifolia fruit extract showed high antioxidant activity (28.36% DPPH activity), thus suggesting that it might be useful as a food additive and/or ingredient under the above optimum operating conditions.	26
Gum arabic and xanthan gums	extract of Eschweilera nana Miers leaves	Flavonoids, such as rutin and hyperoside	Spray-drying	– Results showed that, using the spray-drying technique, it was possible to obtain microparticulate systems containing E. nana extract with high encapsulation efficiency of rutin and hyperoside, which may be associated to a possible interaction between the polymers and the extract. – All microparticle formulations were amorphous, hollow, and spherical with smooth surfaces. Thermal analysis revealed that the microencapsulation process conferred thermal protection to the extract. The release profile of rutin was carried out and showed that from the microparticles it was slower than the extract.	27
Lauric acid (LA) and oleic acid (OA) at different ratios (70/30 and 80/20 g:g) as carriers (SLM).	Unripe banana starch films	Ascorbic acid	Spray chilling	– The film produced with microparticles containing a lauric acid/ oleic acid ratio of 80/20 (g:g) as carrier and a carrier/core ratio of 75/25 (g:g) presented the lowest water vapor permeability and retained the highest antioxidant activity (84%) during film processing.	28
PVP and colloidal silicon dioxide	Curcuma longa L.	Curcumin	Spray drying	– The microparticles were spherical in shape, and an increase in outlet temperature from 40 to 80 °C resulted in a significant increase in the yield of microparticles from 16 to 53%. – The total curcuminoid content (17.15 to 19.57 mg/g), curcumin content (3.24 to 4.25 mg/g) and antioxidant activity (530.1 to 860.3 μg/mL) were also affected by the spray drying process. – The solubility of curcuminoid from C. longa remarkably improved 100-fold in the microparticles.	29
Inulin	Olive leaves extract	Polyphenols	Spray-drying	– Olive leaves extract (OLE) was microencapsulated with inulin (OLE-IN) by spray-drying using a central composite design. Oleuropein encapsulation efficiency and recovery values were over 87% in the OLE-IN microparticles obtained under optimal conditions.	30
(HE/rapeseed oil/pectin) and a cross-linked solution ($CaCl_2$)	Hibiscus sabdariffa L. extract	Polifenol, Anthocyanins	Ionic gelation	– Microencapsulation of hibiscus anthocyanin resulted in improved enteric protection of bioactive compound, mainly in microparticles generated by dripping-extrusion. Application in jelly candy has shown to be technically feasible, with retention of up to 73% of bioactive compounds and mean sensorial acceptance of 70% tasters.	31
Gelucire 50/13 (Stearoyl polyoxyl-32 glycerides)	Wild garlic (A. ursinum) extract	Allicin	Spray-congealing process	– The microparticles exhibited spherical shape, mean diameter in the range 100–200 μm, high encapsulation efficiency and good stability during three months of storage, with no signs of chemical or physical modifications. – Encapsulation of wild garlic extract in Gelucire 50/13 microparticles by spray congealing proved to be a successful strategy to improve solubility and dissolution rate of the extract maintaining the antimicrobial activity and providing advantageous technological properties.	32

Maltodextrin/ Modified Maize Starch combination	Echium amoenum petal	Anthocyanins	Spray-drying	– The results of this study showed that the combination of maltodextrin (MD)/modified maize starch (MMS) can trap the anthocyanins extracted from IBE with high encapsulation efficiency. Among all treatments tested, the combination of MD/MMS (1:1) led to the better protection of anthocyanin compounds. – The FTIR spectra confirmed the formation of microcapsules, while DSC studies indicated that the thermal stability of IBE could significantly be increased. The morphology of all treatments demonstrated spherical wrinkled and non-fractured surfaces in microstructures. – A formulation containing MD/MMS (1:1) had the best stability of anthocyanins over 60 days storage and also showed a slight reduction of antioxidant activity over the same period.	33
β-cyclodextrin and chitosan	White wines	Glutathione	Spray-drying	– SEM showed spherical microparticles, with wrinkled surfaces for β-CD/GSH and smooth surfaces for chitosan/GSH. A wide distribution of particle size was observed. In general, β-CD/GSHshowed an average diameter smaller than the chitosan/GSH microparticles. – FT-IR showed a possible interaction between GSH and both polymers. DSC and DRX showed that encapsulation process produced a marked decrease in GSH crystallinity. – The encapsulation efficiency was 25.0% for chitosan/GSH and 62.4% for β-CD/GSH microparticles. The GSH release profiles from microparticles showed that β-CD can control the release behaviors of GSH better than chitosan in a model wine.	34
B-glucan and β-cyclodextrin	Saffron	Anthocyanins	Spray-drying	– The findings of this study showed that β-glucan has potential to encapsulate saffron bioactives and improves its stability during passage through simulated GI tract conditions. – Encapsulation increased the availability of anthocyanins in intestinal section, which can lead to their maximium abosrbtion during oral digestion. The presence of anthocyanins in β-glucan matrix was clearly depicted through SEM and FT-IR spectroscopy.	35
Pea Protein	Propolis extract	Phenolic	Spray-drying	– The best propolis extract (PE) concentration was 5% (w/v) and pea protein (CPP) was 2% (w/v), presenting the highest encapsulation efficiency and yield, although all the microparticles presented lower antioxidant activity than PE. – ATR-FTIR and X-ray diffraction techniques suggest that encapsulation occurred because they demonstrated that there was an interaction between PE and CPP, and the microparticles showed amorphous state, respectively. – The PE showed antimicrobial activity against Gram-positive and Gram-negative bacteria. Microparticles in which 2.5% and 5% of PE and 2% of CPP were used showed bacteriostatic and even bactericidal effect against Staphylococcus aureus and Listeria monocytogenes.	36
Alginat-calsium caseinate, Chitosan-pectin coated alginat	Green tea extract	Flavan-3-ol antioxidants and caffeine	Ionic gelation	– Employing alginate in combination with soy or hemp proteins provided large and hard particles, while reinforcement with whey proteins and bovine serum albumin provided the most spherical and softer particles (lower hardness and elasticity), with average diameters around 700-800 μm. The combination of alginate and calcium caseinate or whey proteins enabled to retain the highest content of polyphenols and caffeine in the formulated particles (up to 80%). – Chitosan or pectin coating did not improve the physical and morphological properties or the encapsulation efficiency, but conferred better (prolongued) release profile of polyphenols from the particles. The release studies in water and simulated gastric and intestinal fluids revealed burst release of polyphenols (over 50% in first 5-10 minutes) followed by sustained release up to 120 minutes.	37

gastrointestinal tract (GIT) after ingestion, and can also be designed to control the site or rate of the bioactive release within the. Caseinate/alginate microparticles were previously prepared by our group to encapsulate protein nanoparticles so as to protect them and control their release.[12]

Pectin and alginate have been widely used in food applications because of their biocompatibility, biodegradability, non-toxicity, and low cost. Pectin is a natural anionic, linear water-soluble polysaccharide whose main component is galacturonic acid, whereas alginate consists of two monomeric structures (β-D-mannuronic acid (M) and α-L-guluronic acid (G)). Alginate-pectin mixtures have synergistic properties that allow them to form different microstructure of each biopolymer. Some researchers have studied the combination of sodium alginate and pectin citrate when preparing microparticles containing drugs, reporting that this mixture can form strong complexes through chain associations, as well as hydrogels when multivalent cations are added to form particles with high encapsulation efficiency, release kinetics are modified and improved mechanical and chemical stability.[38]

Spray-drying is a well-established and widely used technique for transforming liquid foods or suspensions into a powder in a one-step process. The method is easy to operate, requiring only a few steps to obtain a dry product; the process is easily scaled up and does not require the use of organic solvents, i.e., its use provides a good cost-benefit. Both for food processing and for cosmetic proposes, the technique has been extensively used for the protection and controlled release of bioactive compounds, mainly antioxidants.[26,4] The microencapsulation technique of spray-drying is an effective way to protect drug or food ingredients against deterioration and volatile losses. Since the instability of antioxidant has a direct impact on both colour property and bioavailability, performing microencapsulation by applying the spray drying technology and combining this technique with natural biopolymers may be an efficient way for protecting the important substances that are sensitive to adverse environmental conditions. The protective mechanism consists of the formation of a membrane wall that encloses droplets or particles of the encapsulated material. The choice of a particular method depends on the type of microparticles desired. The properties of the wall structures, size and shape are important considerations. However, in the food and drug industry, spray-drying is still the most popular method of forming microparticles because it is very easy to industrialise and allows for continuous production. Spray-drying is one of the techniques for microparticle production and it offers advantages because it involves low technical costs, is simple (performed in just one stage), versatile (it can be used for the production of microparticles, using different polymers) and, apart from easy control of its parameters, it is capable of producing microparticles of a uniform size. The spray drying process is composed of three steps: atomisation, dehydration, and microparticle collection. This method can include many antioxidant inside the encapsulated material and is easy to scale for industrial production.[26,16,7]

Characterization of microparticles containing extract with antioxidant activity

1. Morphology

Examination of the shape and surface morphology of the microcapsules Scanning Electron Microscopy (SEM) to determine the surface characteristics and the presence of pores on the surface of the microcapsules.[9]

2. Particle size and ζ-potential

Characterization of particle size is important it is known whether the particle size of the microcapsules is in the optimal range. several tools that can be used to measure particle size such as Particle Size Analysis, Atomic Force Microscopy, Coulter Counter and Image Analysis. Measurement of ζ-potential can provide information about the stability of colloidal dispersion systems during storage namely the possibility of aggregate formation on charged particles.[12]

3. Physical properties

The physical characterization of microparticles includes moisture content, density, porosity, flowability, compressibility, swelling and wetting.[4,7,10]

4. Drug load and Encapsulation Efficiency

The success of drug loading can be expressed by actual loading and entrapment efficiency (encapsulation). Determination of the microcapsule drug content was carried out to determine the amount of active substance which can be encapsulated and the efficiency of the method used. The method used depends on the solubility of the coating material and the core material, one of the methods is spectrophotometry

UV-Vis. :

$$\%\ Yield\ of\ the\ process\ (R) = \frac{The\ quantity\ of\ microparticles\ obtained\ at\ the\ end\ of\ the\ process\ (Qf)}{The\ amount\ of\ solids\ added\ for\ the\ preparation\ of\ microparticles\ (Qi)} x100\%$$

$$\%\ Encapsulation\ Efficiency = \frac{Fraction\ of\ active\ substances\ in\ microparticles\ (Qobtained)}{Theorical\ fraction\ of\ active\ substances\ in\ microparticles\ (Qtheorical)} x100\%$$

Microcapsules can contain up to 100 % core material calculated against the weight of the microcapsules. The ideal entrapment efficiency is influenced by various factors such as the type and state of the process.[4]

5. Antioxidant activity

The evaluation of antioxidant activity in vitro microencapsulation was carried out through DPPH evaluation capturing free radicals and ABTS. To prepare the sample, the microparticles are subjected to the same procedure used to determine the efficiency of encapsulation.[5]

6. Drug release

In vitro release tests were carried out to measure the rate and amount dissolving drugs in a medium in the presence of one or more additives contained in the active substance. The release process begins with the dissolution of material on the surface of the particles of the active substance, which forms a clear solution around the particles. Drugs that are dissolved in clear solution are assumed to be stagnant layers which subsequently diffuse from high to low concentrations.[10]

7. Stability

The selected microparticles were submitted to the stability study considering the active substances content during storage at different temperatures. Samples of the selected microparticles were stored under the following conditions: refrigerated temperature (ReT) 2 to 6 °C; room temperature (RoT) 25 °C; and stress temperature (StT) 40 °C.[4]

8. Other Studies

The possible interaction between the polymer and the drug was investigated by using differential scanning calorimetry (DSC) and Fourier-transform infrared spectroscopy (FT-IR). The Thermogravimetric (TG) method and differential scanning calorimetry (DSC) provide valuable data on the polymer thermal compatibility. Measured glass transition temperatures play an important role in the production and release as well. The Spectrometry Method with Fourier-Transform Infrared (FT-IR) Analysis can be performed to follow intramolecular changes during microencapsulation.[11,10]

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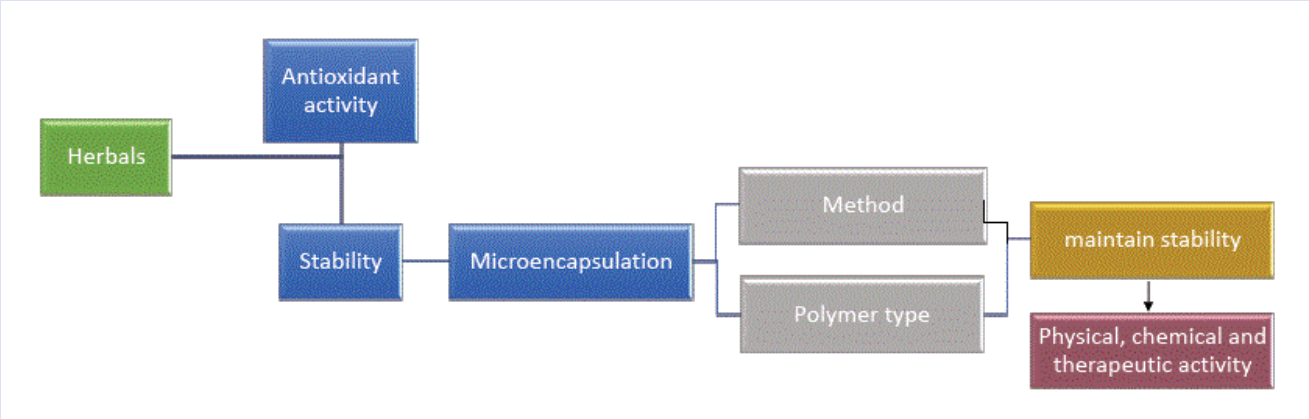
GRAPHICAL ABSTRACT



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