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Microencapsulation of phenolic compounds: Technologies and novel polymers

Microencapsulación de compuestos fenólicos: Tecnologías y polímeros novel

E. Macías-Cortés[1], J.A. Gallegos-Infante[1], N.E. Rocha-Guzmán[1], M.R. Moreno-Jiménez[1], L. Medina-Torres[2], R. F. González-Laredo[1]*

[1]*TecNM/Instituto Tecnológico de Durango, Felipe Pescador 1830 Ote., 34080 Durango, Dgo., México.*
[2]*Universidad Nacional Autónoma de México, Facultad de Química, 04510 Ciudad de México, México.*

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Abstract

Recently, the interest and use of bioactive phenolic compounds have increased in the food and pharmaceutical fields. This has been due to the health benefits of polyphenols reported by many researchers based on their antioxidant activity and biological properties that enable them as potential ingredients for nutraceutical formulations. Therefore, microencapsulation represents the needed chemical and thermal stability that otherwise may weaken the active core and their effects because of environmental conditions such as heat and humidity. In this context, microencapsulation is the technological option to preserve nutraceutical molecules and provide the desired product integrity and stability. Furthermore, it may permit better managing of physical and sensorial properties, such as masking the distinctive astringency that most phenolic compounds display. In this review recommended encapsulation techniques such as spray drying, extrusion, molecular inclusion in cyclodextrins, electrospray and liposomes are discussed, also the different wall materials, including polysaccharides, proteins, whey protein, different mucilages, inulin, zein and FucoPol that have been used to microencapsulate phenolic compounds are described.

Keywords: antioxidants, nutraceuticals, polyphenols, microencapsulation, wall material.

Resumen

Recientemente, el interés y uso de compuestos fenólicos bioactivos han aumentado en la industria alimentaria y farmacéutica. Esto debido a los beneficios a la salud de los polifenoles reportados por muchos investigadores en función de su actividad antioxidante y propiedades biológicas que los habilitan como ingredientes potenciales para formulaciones nutracéuticas. Por tanto, la microencapsulación representa la estabilidad química y térmica necesaria para evitar la degradación del núcleo activo y menguar sus efectos por condiciones ambientales como calor y humedad. En este contexto, la microencapsulación es la opción tecnológica para preservar principios activos y proporcionar la integridad y estabilidad deseadas del producto. Además, puede permitir un mejor manejo de sus propiedades físicas y sensoriales, como enmascarar la astringencia distintiva que muestran la mayoría de los compuestos fenólicos. En este artículo de revisión, se discuten las técnicas de encapsulación recomendadas, como microencapsulación por secado por aspersión, extrusión, inclusión molecular en ciclodextrinas, electro aspersión y liposomas; también se describen los diferentes materiales pared, incluyendo polisacáridos, proteínas, proteína del suero, mucílagos, inulina, zeína y FucoPol que se han utilizado para microencapsular compuestos fenólicos.

Palabras clave: antioxidantes, nutracéuticos, polifenoles, microencapsulación, material pared.

1 Introduction

In living organisms, metabolism is the set of biochemical reactions that take place into the cells in order to synthesize complex compounds from simpler ones or degrade complex substances and obtain simpler ones (Kornberg, 2019). In this way, plants have a secondary metabolism in addition to the primary metabolism that enables them to produce and amass compounds of diverse chemical nature. The products of this metabolism, called secondary metabolites, are involved in plants protection against biotic and abiotic stresses. These metabolites are differentially distributed among plant taxonomic groups, displaying important biological properties, performing sustainable ecological functions; they are characterized by their different uses and potential applications as medicines, insecticides, herbicides, perfumes or dyes (Pagare *et al*., 2015).

* *Corresponding author. E-mail*: rubenfgl@itdurango.edu.mx
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An important group produced by the secondary metabolism of plants is phenolic compounds. There are more than 7000 known structures of them between flavonoids, tannins, phenylpropanoids, lignans and coumarins (Wink, 2010). Molecules such as polyphenols are planar organic compounds based in one or more six-carbon aromatic rings, to which one or more hydroxyl groups (-OH) are bonded. The term phenol now is used for any of a group of related acidic compounds that are hydroxyl derivatives of aromatic hydrocarbons. There is a huge number of compounds of biological, medical and commercial importance that are included in this definition (Quideau *et al*., 2011; Belščak-Cvitanović *et al*., 2018).

Polyphenols may play an important biological role in different applications such as in nutraceutical products. Therefore, in order to keep their efficacy, it is important to preserve their stability, bioactivity and bioavailability, besides taking care on their unpleasant taste and astringency, which are factors that could limit polyphenols applications. Consequently, to maintain phenolic compounds safe from external (e.g., environment) and internal (e.g., gastrointestinal) degradation, microencapsulation could be a good option to protect and manage those molecules (Fang and Bhandari, 2010). There are reports that describe different techniques to microencapsulate phenolic compounds like Fang and Bhandari (2010), while Bartkowiak *et al*. (2017a) and others present the use of novel polymers such as Aloe vera mucilage (Medina-Torres *et al*., 2018), psyllium husk mucilage (Álvares-Monge-Neto *et al*., 2017) or microencapsulation with inulin (Pauck *et al*., 2017). However, despite all this information, there are few specific reports that focus on the microencapsulation of polyphenols using novel materials, being this an opportunity to show the current state-of-the-art in this important field. In this way, the aim of this review is to summarize currently available knowledge of the most common microencapsulation techniques, including newer ones like electrospray or liposomes by supercritical fluids, in addition to revise the novel polymers used for microencapsulation in recent years.

2 Phenolic compounds

From a chemical point of view, in the group of phenolic compounds there are natural components belonging to several subgroups (Belščak-Cvitanović *et al*., 2018).

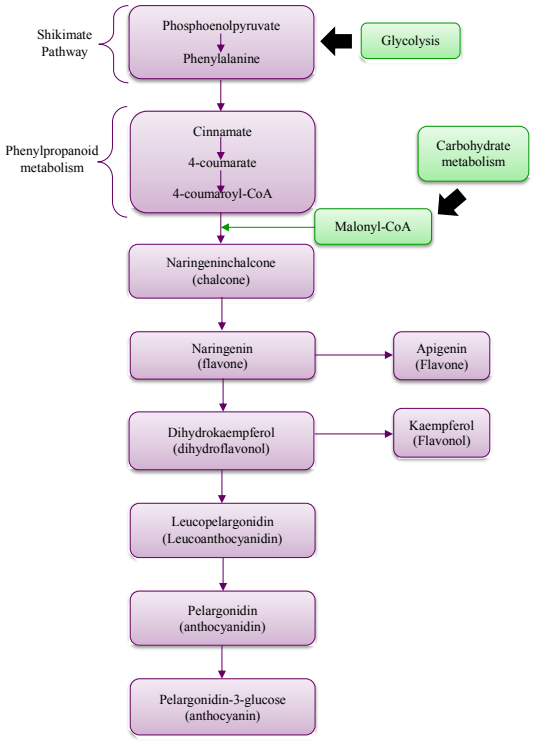

Fig. 1. Biosynthetic pathway leading to the different flavonoids classes.

The term *polyphenol* should be used to describe plant secondary metabolites derived entirely from the shikimate derived phenylpropanoid or the polyketide pathways (Figure 1), containing more than one phenolic ring and lacking any nitrogen-based functional group in their basic structural expression (Quideau *et al*., 2011). In aqueous solution, the H^+ ions from the OH^- groups can dissociate from the phenol molecule, turning it weakly acidic (Stewart and Stewart, 2008).

Polyphenols are aromatic hydroxylated compounds found in food and plant sources like vegetables, fruits or leaves, probably as a result of antioxidant or defense mechanisms; therefore, those phenolic compounds are essential to plant life, for example as a barrier against microbial attacks or making their leaves inedible to herbivorous predators (Apak *et al*., 2007). Robards and Antolovich (1997) have described in detail the main metabolic pathways of polyphenols production as shown in Figure 1.

Phenolic compounds are classified in simple and complex phenols (Figure 2). Depending on their structure, they can be divided into subgroups, according to the number of carbons that

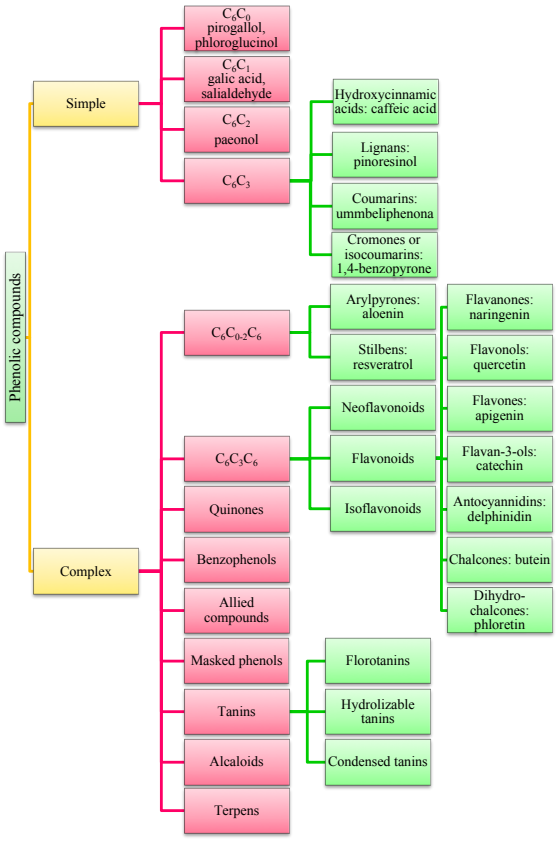

Fig. 2. Phenolic compounds classification.

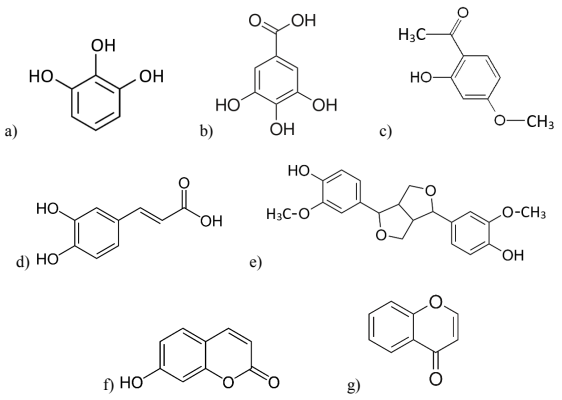

Fig. 3. Common structures of polyphenols: a) pyrogallol, b) gallic acid, c) paeonol, d) caffeic acid, e) (+)-pinoresinol, f) umbelliferone, and g) 1,4-benzopyrone.

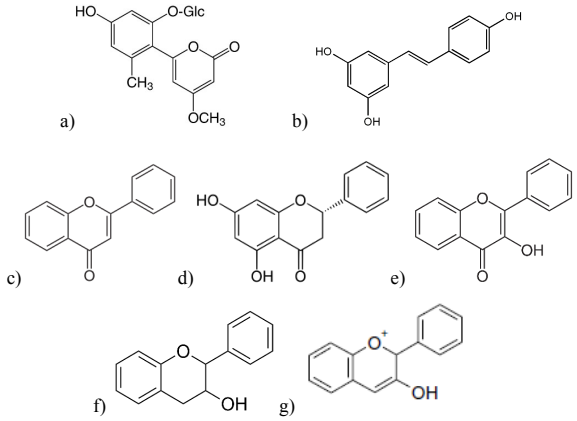

Fig. 4. Basic structural skeleton of a) aloenin, b) resveratrol, c) flavone, d) flavanone, e) flavonol, f) flavanol, and g) anthocyanidin.

conform their general skeleton that may include side-chains (C_n) bonded to phenolic aromatic rings (C_6). Simple phenols can have a C_6-C_0 structure, in this classification are pyrogallol and phloroglucinol (Figure 3a), where no carbon chains are present. Under the classification of C_6-C_1, gallic acid (Figure 3b) and protocatechuic acid are found. Phenolic compounds with C_6-C_2 structure are less distributed in nature than C_6-C_1 or C_6-C_3 compounds, those compounds are called acetophenones, in which paeonol (Figure 3c) can be a good example. The C_6-C_3 compounds are phenylpropenes or phenylpropanes, representing four major types of compounds: hydroxycinnamic acids (Figure 3d, caffeic acid), lignans (Figure 3e, (+)-pinoresinol), hydroxycoumarins (Figure 3f, umbelliferone) and chromones or isocoumarins (Figure 3g, 1,4-benzopyrone) (Robards and Antolovich, 1997).

Complex phenols are a group of polyphenols containing different structures that implies the linking of more phenolic rings and simple phenols. In the classification based on a C_6-C_0-2-C_6 skeleton are the aryl-pyrones (C_6-C_0-C_6) that are characterized by two rings bridged with a carbon like aloenin (Figure 4a). In the case of C_6-C_2-C_6 or stilbenes there is an unsaturated two carbons chain between rings, like in resveratrol (Figure 4b).

Compounds with a C_6-C_3-C_6 skeleton are flavonoids, the most common structure found among complex polyphenols. In a basic way, the structure contains two aromatic rings, A and B, which are typically linked by a three-carbon connection, forming the heterocyclic ring C (Manach *et al.*, 2004). Differences in substitution patterns and presence of insaturation in ring C result in the main flavonoid classes: flavones (Figure 4c), flavanones (Figure 4d), flavonols (Figure 4e), flavanols

(Figure 4f), isoflavones, flavanonols, chalcones and anthocyanidins (Figure 4g), of which flavones and flavonols are the most commonly occurring and structurally diverse (Balasundram *et al*., 2006).

Tannins is another important group among complex phenolics, which includes hydrolysable tannins, condensed tannins and phlobatannins. The first group may be subdivided in gallotannins and ellagitannins that are esters of gallic and ellagic acid with glucose. The second group is also known as proanthocyanidins that are polymers of polyhydroxyflavan-3-ol monomers (i.e., catechins). The third group is also identified with phlobaphenes, a reddish, alcohol-soluble and water-insoluble, very complex phenolic substance (Khanbabaee and van-Ree, 2001).

2.1 *Chemical properties of phenolic compounds*

Plant polyphenols show a variety of bio-physicochemical properties that makes them unique and remarkable natural products. These compounds have been related with diverse biological roles, including antibiotic, antifeeding and antinutritional actions. In these cases, polyphenols allow plants to resist against microbial pathogens and herbivores attacks. They also provide protection against solar radiation (i.e., DNA damaging by UV-B light), in addition to be a factor in plant reproduction, nutrition, and growth (Quideau *et al*., 2011).

Such properties might be explained from the elementary structural arrangement of all polyphenols (Figure 5). In this structure, the phenyl ring holding a hydroxyl group constitutes an amphiphilic molecule that combines the hydrophobic character of the phenolic aromatic nucleus with the hydrophilic character of its polar hydroxyl substituent, which can act either as a hydrogen donor or as an acceptor. This distinctive structure justifies the ability of polyphenols to delocalize electrons, which support the molecule capacity to exchange electrons or hydrogen atoms. Additionally, if there are more than one hydroxyl group, the metal chelation might also be possible. Therefore, the capacity of phenolic molecules to absorb UV light provides protection against DNA damage by solar radiation (Belščak-Cvitanović *et al*., 2018; Quideau *et al*., 2011). This has encouraged the research on antioxidant polyphenols to prove their potential role in the prevention of degenerative diseases, such as cancer, cardiovascular, inflammatory and neurodegenerative illnesses (Gábor, 2013).

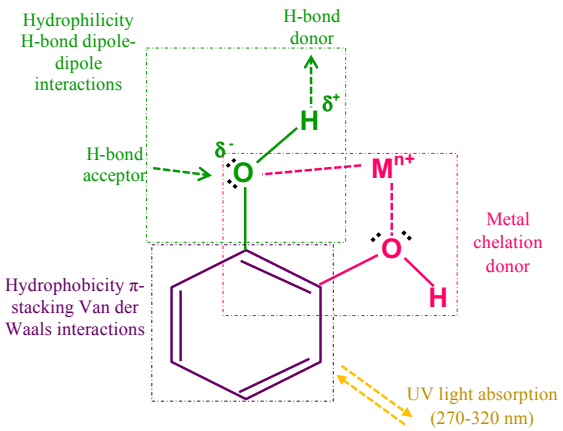

Fig. 5. Basic mechanisms of radical-scavenging based on antioxidant action.

2.2 *Why to protect phenolic compounds?*

Microencapsulation has been considered as an amazing method for improving delivery systems, providing prolonged or controlled release of food ingredients and increasing bioavailability, stability, and targeting of bioactive compounds (Pasukamonset *et al*., 2016). Particularly, plant polyphenols found in nature are sensible to light, heat and oxygen (Trucillo *et al*., 2018). Therefore, microcapsules can preserve phenolic compounds and other isolated substances and release them when needed. Entrapment of these compounds is imperative for many important reasons, the first one is to protect the active compounds from degradation by reducing their reactivity to the external environment, for example to UV light, heat, moisture, air oxidation or chemical action (i.e., acid or alkaline reactivity) (Jeyakumari, 2016). Encapsulation helps to reduce or retard the evaporation or mass transfer rate of a volatile active ingredient to the external medium, changing the physical characteristics of the core material. This process also changes the physical properties of bioactive compounds, making them easier to handle, converting them from a gas or liquid state into a solid phase, achieving controlled and targeted release of the active ingredients, improving shelf life of capsules by preventing degradation reactions, and masking taste or odors of a valuable core (Mishra, 2016a).

In the food industry, microencapsulation process can be used for many reasons because is a useful tool to improve delivery of bioactive molecules like antioxidants, minerals, vitamins, phytosterols, lutein, fatty acids, lycopene, to mention few of them, and

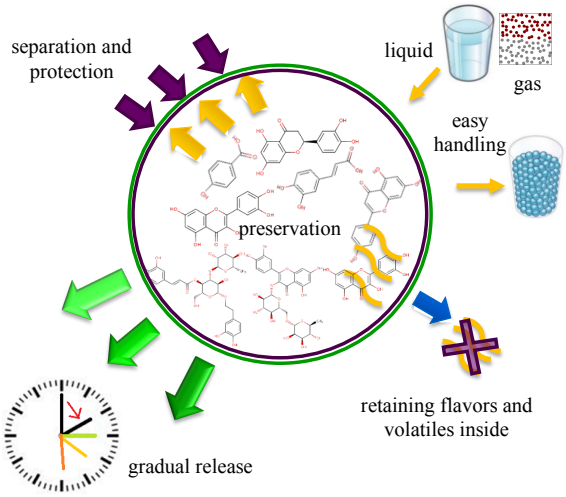

Fig. 6. Microencapsulated products properties.

also living cells like probiotics into foods (Nedovic *et al*., 2011). In the mentioned list polyphenols can be already included as candidates to be successfully encapsulated.

Encapsulation can mix incompatible compounds by separating components within a mixture that would otherwise react with each other and finally, but not less important, enhancing the visual aspect and marketing concept of the final encapsulated product (Jeyakumari, 2016; Mishra, 2016a) (Figure 6). In the case of some types of microcapsules, like liposomes, it is possible that phenolic compounds get better bioaccess to cells due to their lipidic bilayer morphology (Bonechi *et al*., 2018).

3 Encapsulation techniques

Encapsulation is a process of retaining an active agent within a protective material (Nedovic *et al*., 2011), which are in nanometer or micrometer to millimeter range. It is a technique used for obtaining a barrier that retards chemical reactions with the external environment, promoting an increase in the shelf life and gradual release of the encapsulated compounds, stabilizing them in a solid matrix (Labuschange, 2018). In almost all cases, microencapsulation refers to a technology that builds a functional barrier between bioactive molecules (core) and wall materials in order to evade chemical and physical changes and to maintain all the biological, functionality, and physicochemical properties of the bioactive material (Barky *et al*., 2016).

All microencapsulation techniques are formed by three principal processes on a time scale: the first step consists in forming a shell wall around the core material; in the second process, it implies keeping the core materials intact inside to avoid any release of content; and in the last step, it is expected that the core material be released later at the right time and at the precise rate (Mishra, 2016b). The election of the best encapsulation technique will be linked to the final particles required in function of some important factors like their size, physical properties of wall materials, core material, controlled release and costs (Martín-Villena *et al*., 2009).

Historically, the first microencapsulation application was in the 1930´s in Dayton, Ohio, by Barrett K. Green, a chemist who developed ink gelatin microcapsules to produce the first carbon-free carbon paper. This paper was made with gelatin ink microcapsules on a front page, while a second sheet of paper was coated with acidic clay. When making a trace on the first page, the pressure broke the microcapsules, impregnating the second page with the dye (Fanger, 1974). This patent was just the beginning of the multiple applications of microencapsulation.

3.1 Spray drying

Spray drying has its origin in the United States, with the first patented design registered in 1872. It was thought at the dairy industries for continuous production of milk powder. Since then, the process has been adapted to many design modifications, to the point of having stood out as an industry-friendly drying technique (Anandharamakrishnan and Ishwarya, 2015). Spray drying is one of the most used and practical microencapsulation techniques around the world, because it provides rapid evaporation of water and maintains relatively low temperatures in the particles (Rigon and Zapata-Norena, 2016).

This technique is defined as the transformation of feed from a fluid state into a dried particulate form by spraying the feed into a hot drying medium. The basic process of spray drying requires feeding a prepared solution or dispersion of bioactive compounds into a spray dryer and then atomizing with a nozzle or spinning wheel inside a chamber provided with hot air. Then, the droplets and hot air get in contact, evaporating the solvent. The process ends when the dried particles obtained are separated by a cyclone from the humid air and collected in powder form (Figure 7) (Fang and Bhandari, 2012). In the microencapsulation principle, any substance such as

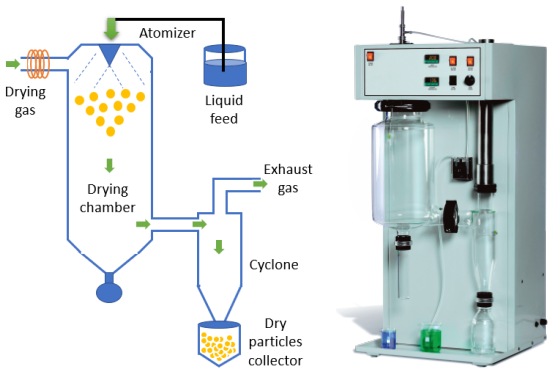

Fig. 7. Spray dryer scheme and commercial instrument.

modified starch, maltodextrin, gum or other substances are used as the wall materials. In this spray drying process, the bioactive material is homogenized with the wall material, and then this dispersion is fed into a spray dryer and atomized. At very short times, water is evaporated from the drop by the hot air, forming a shell made of wall material around the core, developing a microcapsule (Fang and Bhandari, 2010).

Stable spray drying can enclose the bioactive molecules in a matrix layer, while the solution containing both the core compounds and the encapsulate are transformed from liquid form to a dry and stable solid. There are some differences in the characteristics when drying of the wall and the core components, which are encapsulated during the spray drying. The wall material dries at a much faster rate than the solvent, allowing the wall material to crust or coat around the drop containing the core, and creating dry microencapsulated particles at the end of the spray drying process (Anandharamakrishnan and Ishwarya, 2015). The main parameters to be monitored in this process are inlet and outlet temperatures, flow rate, and properties of the material to be encapsulated (Esquivel-González *et al*., 2015).

Spray drying is the most used encapsulation technique due to its lower cost compared with other methods. In pharmaceutical, food and agrochemical industries this technology seems to be the most practical method to transform fluid constituents into a solid presentation in order of simplifying storage and extending shelf life (Trujillo-Cárdenas *et al*., 2018).

In representative examples, cinnamon (*Cinnamomum zeylanicum*) infusions were microencapsulated using maltodextrin. Researchers obtained microcapsules of 6-30 μm with an encapsulation efficiency up to 85%, and microencapsulation yields from 27.5 to 49.6, being the best conditions for the optimal product an inlet temperature of 160 and 180°C at 10 mL/min of feed rate. The initial concentration of cinnamon infusion was about 29.3 mg of GAE/g of cinnamon and an EC_{50} for DPPH$^{\bullet}$ inhibition of 0.3 mg of cinnamon/mL. Microparticles with a deflated-balloon like shape were obtained, containing a total phenolic content from 16.4 to 20.2 mg of GAE/g of cinnamon, preserving from 55.9 to 68.8% the original total phenolic content, while DPPH$^{\bullet}$ inhibition increased respect to the infusion, with EC_{50} of 3.36-5.96 mg of cinnamon/mL (Santiago-Adame *et al*., 2015).

There are many polyphenol sources, one of them and the most used is the grape. Boonchu and Utama-Ang (2015) made an optimization of extraction and microencapsulation of bioactive compounds from red grape (*Vitis vinifera* L.) pomace. They performed the extract microencapsulation using different amounts of maltodextrin (7-28% w/v) and carboxymethylcellulose (CMC) (0-1.4% w/v). The results showed that the microencapsulation using 10.21% of maltodextrin and 0.21% of CMC were the better proportions to maximize the polyphenol compounds, minimizing bitterness and astringency, their initial experimental values were 106.8 of total phenolic compounds, 16.1 mg/g of catechin, 2.5 mg/g of epicatechin and 0.0033 mg/g of resveratrol. After encapsulation, they changed to 13.5 of total phenolic content, 0.6 mg/g of catechin, 0.1 mg/g of epicatechin and 0.00066 mg/g of resveratrol. With these data, the percentage of retention was about 12.6% of total phenolic compounds.

Finally, Wang *et al*. (2016) made microcapsules of tea polyphenols using hydroxypropyl methylcellulose phthalate as coating material. Those microcapsules had a smooth surface with a particle size distribution of 10-200 μm with retention up to 80% and phenols encapsulation efficiency about 71%. Those microcapsules preserved the antioxidant activity measured by DPPH$^{\bullet}$ assay above 85% (120 min) while the free tea polyphenols showed 80% at 120 min. It is important to say that the tea phenolics stability in storage against high temperature, extreme acid and alkaline environments was improved by microencapsulation; even the antioxidant activity of tea polyphenols could be preserved by microencapsulation. In conclusion, it could be affirmed that spray-drying as a microencapsulation technology still bids high for its production rates at low operating costs, producing microcapsules that are stable and easily to add in food matrices or nutraceutical products (Chávarri *et al*., 2012).

Fig. 8. Buchi ® equipment for microencapsulation by extrusion and handmade microcapsule extrusion.

3.2 Extrusion

This technique is the mildest one among all technologies for microencapsulation because it does not use high temperatures; therefore, bioactive compounds are not thermally degraded (Chew and Nyam, 2016). It consists in letting pass the bioactive compounds mixed with the wall polymer throughout a nozzle or extrusion needle in order to form a falling drop into a calcium solution, allowing an ionic gelation to occur and enclosing the core compounds. Extrusion is a technology that can be easily adapted; it can be possible to obtain microcapsules with sophisticated equipment like Buchi® Encapsulator, or using a simple syringe with or without extrusion needle in a calcium bath (Figure 8). In this technique, the parameters to be controlled are alginate and calcium concentrations and their ratio. If an over concentrated calcium solution is used, the microcapsule will be small but hard due to a major sodium exchange by calcium, occurring a harder ionic gelation with alginate. In contrast, if a low concentrated calcium solution is used, the resultant microcapsule will have a fragile wall due to the weak ionic gelation between calcium and alginate. Furthermore, the needle gauges or nozzle diameter is another important parameter that could determine the particle size. To confirm this, Pasukamonset *et al*. (2016) reported no formation of microcapsules of *Clitoria ternatea* extract at concentration of sodium alginate and $CaCl_2$ below 1.0 and 1.5% (w/v), respectively.

There are many research articles reporting the use of extrusion technology with good encapsulation results. Some authors (Sun-Waterhouse *et al*., 2011) have reported microencapsulated olive oil added with 300 ppm of caffeic acid and 1.5% w/w sodium alginate shells, proving good storage stability of microcapsules. Encapsulated oil was stored at 20 or 37°C for 30 days and then subjected to stability and quality evaluation. Results showed an initial phenolic content of 0.02 - 0.03 mg/g of catechin equivalents for free and microencapsulated oil without caffeic acid and 0.1 - 0.12 mg/g of catechin equivalents for microencapsulated oil with caffeic acid. Products at these concentrations remained stable along the storage time. The microencapsulation efficiency was about 60.6%, while the addition of caffeic acid increased the stability and total phenolic content of the final oil product, showing slower oxidation changes in the encapsulated oil samples.

In the case of yerba mate (*Ilex paraguariensis*), it has a high concentration of polyphenols, and its extract was encapsulated in 2% (w/w) sodium alginate and 2% (w/v) sodium alginate 0.5% (w/v) chitosan little beads to be used as an additive in food products. The beads of 1900 μm of size were evaluated in a gastrointestinal model system to know if there existed any interaction between wall materials and polyphenols. The results showed that in both encapsulation systems, the highest polyphenol content was released in simulated gastric fluid (93.8% for the alginate-polyphenol and 66.6% for the alginate - chitosan - polyphenol systems), while in simulated intestinal fluids, it was more discrete (10.0 and 19.6%, respectively). Nevertheless, the release of polyphenols in the simulated gastric fluid by the system alginate - chitosan- polyphenols is over 60%, is lower than the system alginate - chitosan, therefore authors. This outcome is attributed to the protection provided from the chitosan barrier and its strong interaction with the yerba mate extracts (Anbinder *et al*., 2011).

Chitosan has been used in many experimental microencapsulations by extrusion. An example is the microencapsulation of polyphenols from residual grape pomace of wine production with 1% (w/v) alginate and 3% (w/v) chitosan dissolved in a pH adjusted calcium solution. Authors have reported (Moschona and Liakopoulou-Kyriakides, 2018) microcapsules of 1004-1070 μm with 55 to 79% of encapsulation efficiency. These microcapsules had initial phenolic contents of 13 to 22 mg/g, presenting molecules such as quercetin, kaempferol, trans-ferulic acid, ellagic acid and derivatives of caffeic acid, and showed antioxidant activity measured by inhibition of $DPPH^{\bullet}$ and $ABTS^{\bullet+}$ of 65-94 and 67-97%, respectively.

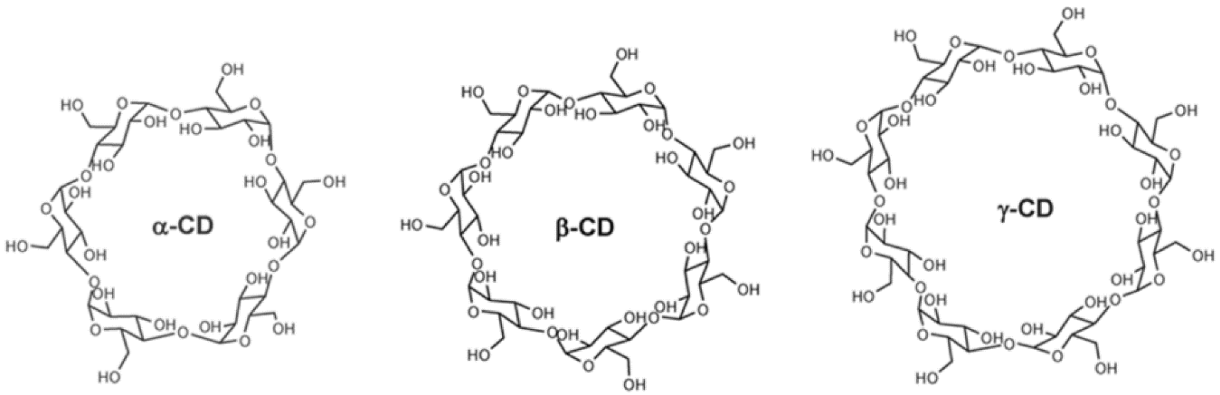

Fig. 9. Molecular structure of the three types of cyclodextrins.

After release test, all samples preserved a good antioxidant activity (49 to 70% of DPPH• inhibition).

3.3 Molecular inclusion: cyclodextrins

Cyclodextrins (CDs) are macrocyclic oligosugars formed by an enzymatic modification of starch with a cavity size varying from 0.5 to 1 nm and they can form non-covalently bonded inclusion compounds with small molecules and polymers via inclusion of these guest molecules in their small cavities (Estrada-Villegas *et al*., 2019). After the starch separation caused by the group of enzymes cyclodextrin-glycosil-transferases, the first and last glucose molecules are joined to form a closed circular chain with α 1-4 linkages. The most commonly CDs are composed of 6, 7 or 8 glycosidic units that are named α-CD, β-CD and γ-CD, respectively (Figure 9). The significance of CDs is that other, usually smaller molecules (called guests), can enter in their cavity forming inclusion complexes with these macrocyclic hosts.

Cyclodextrins can form inclusion complexes with an extensive variety of organic and inorganic compounds, coming partially or entirely into the relatively hydrophobic cavity of the host. Inside of the CD structure the molecular disposition is not hydrophobic, but considerably less hydrophilic than the aqueous medium; thus, it is able to carry on hydrophobic molecules. In contrast, the exterior of the macrocyclic is hydrophilic enough to give to the cyclodextrins their characteristic water solubility (Kalogeropoulos *et al*., 2010).

In this way, the complexation process is made generally in water as solvent. Using this solvent involves some steps. First of all, the complex formation releases the water molecules from inside of the relatively hydrophobic cavity. It also removes the polar hydration shell of the apolar guest molecule. Then, it helps the guest molecule to entry into the empty CD cavity, where it is stabilized mainly by weak, but numerous Van der Waals attractive interactions. Moreover, it also helps to the restoration of the structure of water around the exposed part of the guest molecule. Finally, it makes possible the integration of the guest molecule with the hydration shell of the host CD (Dodziuk, 2006). Therefore, some parameters to be considered are the combination of high moisture and temperatures, which could promote the partial release of the microencapsulated components (Parzanese, 2013).

Encapsulation in cyclodextrins may lead to dissolution rate improvement, enlarged membrane permeability, and enhancement the bioavailability of low-solubility nutraceuticals. CDs may also act as flavor carriers, providing protection against oxidation, decompositions induced by light and heat. Furthermore, cyclodextrins can prolong shelf life of food products and mask or reduce undesired taste and odors (Mourtzinos *et al*., 2007).

In the last years, the use of cyclodextrins has been improved, especially in the encapsulation of pharmaceutical products or nutraceuticals, such as polyphenols. As an example, it was made a polyphenol encapsulation in β-CD of a St John's wort extract (*Hypericum perforatum*, HP) (Kalogeropoulos *et al*., 2010). The methanolic extracts were rich in epicatechin (118.9 mg/g), catechin (8.7 mg/g), quercetin (5.8 mg/g) and malvidine (2.0 mg/g), showing DPPH• inhibition activity of 890.2 mg Trolox/g. For those extracts, the inclusion complex

of HP with β-CD was prepared by mixing the extracts and the CD in a ratio 1:4; all this in aqueous media and consequent freeze-drying. After encapsulation, efficiencies of 27.5, 30.0 and 35.0% were obtained for catechin, epicatechin and quercetin, respectively. The microencapsulation was confirmed by differential scanning calorimetry (DSC) and NMR studies. The results showed that after thermal oxidation, the inclusion complex remained intact even at temperatures where the free HP extract would be oxidized.

In other work, it was reported a microencapsulation of olive leaf extract rich in the bioactive oleuropein (1680 mg/kg of olive leaf) in β-CD mixing the components in aqueous media at a mole ratio of 1:2 and subsequent freeze-drying (Mourtzinos *et al*., 2007). The inclusion complex formation was confirmed by DSC. Besides, DSC showed that the complex of olive leaf extract with β-CD was protected against oxidation, since it continued unbroken at temperatures where the free olive leaf extract was oxidized. Finally, phase solubility studies exposed that encapsulation of olive leaf extracts in β-CD enhanced the aqueous solubility of the polyphenols present by more than 150%.

Finally, it has been described the microencapsulation of caffeic acid phenethyl ester (CAPE) and caffeic acid phenethyl amide (CAPA) by inclusion in hydroxypropyl-β-cyclodextrins (HP-β-CD). Those inclusions were analyzed in order to know their supramolecular interactions with the HP-βCD. As a result, both molecular inclusions were successful, increasing significantly the solubility in the presence of HP-β-CD, concluding that the type of linkage of the carboxylic acid to the side chain (ester or amide) may play a key role on the mode of encapsulation. In fact, as CAPE forms a relatively stable complex with HP-β-CD by accommodating the catechol nucleus inside the CD cavity, the binding could inhibit its interaction with redox-active metal traces (Garrido *et al*., 2018).

3.4 *Electrospray*

Microencapsulation by Electrospray or Electrohydrodynamic Atomization (EHDA) has recently emerged as another microencapsulation option because it can be operated under mild temperatures, being especially adequate for the encapsulation of thermosensitive functional ingredients (Gómez-Mascaraque *et al*., 2017). This technique is based on the microcapsules production from a polymer solution, by applying a high electric field and then obtaining different food product encapsulations (Tapia-Hernandez *et al*., 2015).

John Zeleny was the pioneer in the study of EDHA; however, John William Strutt (aka Baron Rayleigh) studied the stability of jets formed in the electrospraying more than 20 years before Zeleny in 1879. Since then, there were just few improvements achieved to understand the electrospray process until 1952, when Vonnegut and Neubauer investigated the monodispersity of droplets from an electrostatic spray. By 1964, Geoffrey Ingram Taylor made an explanation of the conical shape of the jet (i.e., Taylor cone) and the balance between electrical and surface tension that opposes each other (Ghayempour and Mortazavi, 2013). Following investigations were about the use of electrostatic spraying, finding different applications, where one of them is the microencapsulation (Jafari-Nodoushan *et al*., 2016).

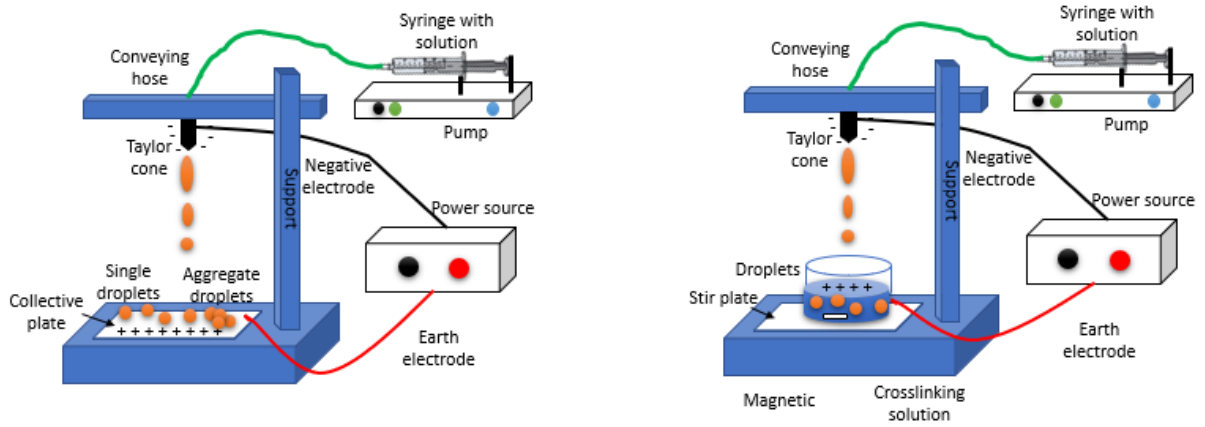

Fig. 10. a) Electrospray in plates, b) Electrospray in solution (Modified from Tapia-Hernandez *et al*., 2015).

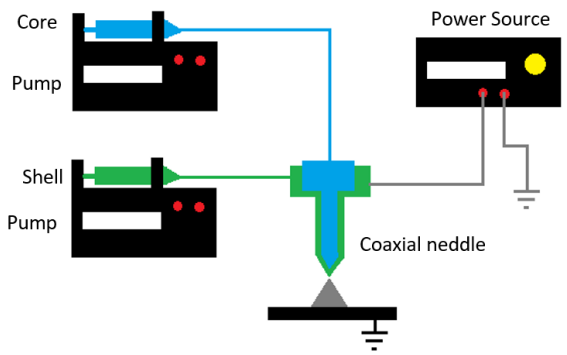

Fig. 11. Coaxial nozzle electrospray set up (Modified from Yuteri *et al*., 2010).

In the microencapsulation by electrospray process, a liquid which is flowing throughout a capillary nozzle is subjected to electrical forces due to a strong electric field generated close to the nozzle, improving a high electric potential. The electric charge carriers move through the liquid and distribute under the liquid surface of the meniscus, the electric forces deform the shape of the normal spherical meniscus to a Taylor cone. When the electric charge accumulated generates sufficient high electric field to produce electrodynamic pressure, overcomes the liquid surface tension and then, a thin liquid jet comes out from the apex. This charged jet is accelerated by an electric field and disrupts into droplets that are trapped due to electrical repulsion of charges in a plate. It is important to mention that in this method no additional mechanical energy is applied, just the electric field (Figure 10) (Jaworek, 2016; Xu *et al*., 2013).

According to Jafari-Nodoushan *et al*. (2016), the most important parameters among the components that integrate the electrospray system are the physical properties of the liquid, (i.e., the electrical conductivity, the surface tension, and the viscosity). Other key factors are the electrical field, the liquid flow rate, the dielectric strength of the surrounding atmosphere, and the system configuration. Any change in parameter values will produce different spraying modes, even if the liquid characteristics or electrical parameters are the same.

In this way, there are three types of electrospray configurations: simple, coaxial and bipolar coagulation. In the simple electrospray or needle-plate configuration, the solution containing the complete formulation (i.e., matrix and bioactive compounds) is fed to a nozzle helped by a pump, selecting the appropriate flow rate level depending on the needed microcapsules sizes (i.e., μL/h for nanocapsules or mL/h for microcapsules). In this configuration, the electrical field required is created by applying a voltage between the needle (nozzle) and the counter electrode using a high voltage power supply. The needed distance between the needle and de counter electrode must be far enough to make possible the drying of the solvent of the final product (Yurteri *et al*., 2010).

The coaxial configuration is a method that produces multilayer micro and nanoparticles using coaxial electrified jets; it means that a small needle is into another bigger one (Figure 11). It has some advantages compared with the conventional electrospray, for example, it can made microcapsules with two or more immiscible fluids (Moghaddam *et al*., 2015). In this configuration, it is possible to have high encapsulation rates (i.e., nearly 100%), to have precise control of the core-shell geometry, and the most important, to provide protection of the core molecules from denaturation and aggregation. An important fact is that this method is an easy scalable process for mass production of microencapsulated bioactive compounds by using an array of electrospray atomizers to increase the production rate (Xu *et al*., 2013; Zhang *et al*., 2012).

Lastly, it is the bipolar coagulation, where two oppositely charged needles are involved. They are directed toward each other for droplets with opposing charges that may attract one another and coagulate (Figure 12). In this configuration, it is possible to obtain different particles such as not mixed, where particles are just added between them by charge attraction; coated particles, where new particles of both substances interact to form a different or new substances; mixed particles that are formed as homogeneous particles from both substances; and finally, nano laden or nano coated, where in the first case small particles are inside bigger ones and in the second case small particles are covering a larger one (Jafari-Nodoushan *et al*., 2016). According to Jaworek (2016), this configuration is not commonly used because of its low encapsulation efficiency.

In general, electrospraying has many advantages over conventional microencapsulation systems. First of all, the droplets size distribution is usually narrow with low standard deviations. Secondly, droplet sizes can be smaller than those available from conventional mechanical atomizers and can be smaller than 1 μm. Finally, the droplets are self-dispersed due to their electrical charge, avoiding agglomeration of microcapsules and coagulation (Jaworek, 2016; Yurteri *et al*., 2010).

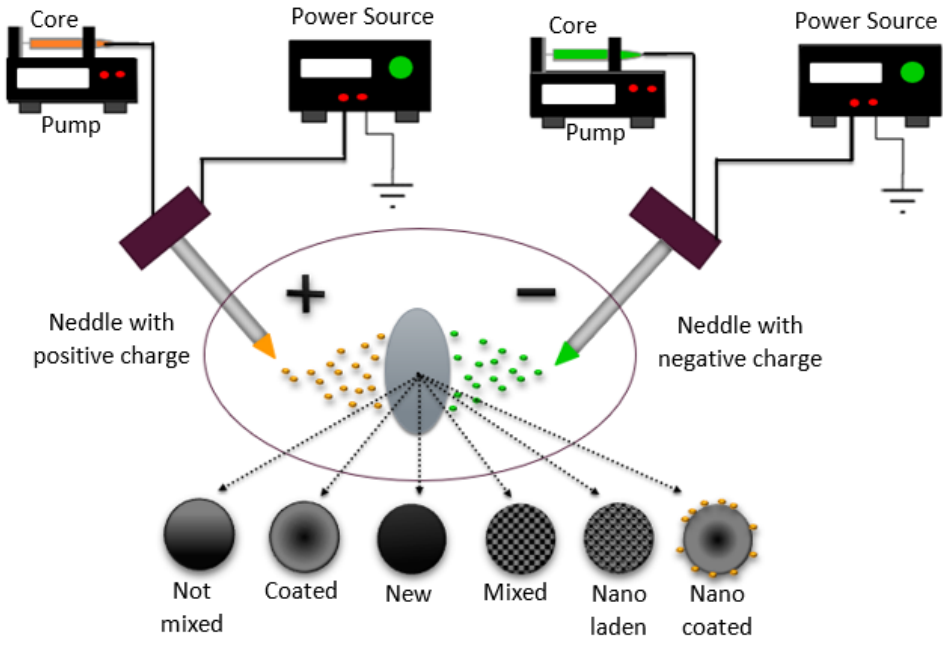

Fig. 12. Bipolar coagulation electrospray set up (Modified from Yuteri *et al*., 2010).

In recent years, some authors have been using this technology because of its benefits. They have tested the potential of the electrospraying technique to obtain food-grade gelatin capsules in the submicron range for sensitive bioactive protection, including the influence of the protein concentration used in the size and morphology of the microcapsules obtained. In this case, gelatin was chosen as wall material due to its use as a food ingredient, its gelation properties and low cost. Gelatin was used to encapsulate the flavonoid epigallocatechin gallate (EGCG) (Gómez-Mascaraque *et al*., 2015). The results showed microcapsules with particle size of 0.1-2 μm and high encapsulation efficiencies (i.e., 96%), retaining the antioxidant activity of the bioactive compound upon encapsulation. Free EGCG in PBS buffer had a radical scavenging activity of 27.2%, while encapsulated EGCG showed 26.8%. In the EGCG release profiles, the free EGCG in PBS buffer lost a 30% of their antioxidant activity and was completely degraded in 100 h, while encapsulated EGCG retained its whole antioxidant activity within this time.

According to Gómez-Mascaraque *et al*. (2017) a green tea extract (GTE) was encapsulated within electro sprayed gelatin and zein microparticles, proving the protective ability of both systems on green tea catechins. The initial extract was composed of flavan-3-ols: epigallocatechin gallate (EGCG, 41.8 g/100g), epicatechin gallate (ECG, 8.9 g/100g), epigallocatechin (EGC, 9.6 g/100g), epicatechin (EC, 6.3 g/100g), gallocatechin gallate (GCG, 2.0 g/100g), gallocatechin gallate (GC, 1.5 g/100g) and catechin (C, 1.0 g/100g). The formed microparticles were about 0.78 μm for gelatin and 0.50 μm for zein and had high encapsulation efficiency (90%). In the recovery test, all molecules encapsulated in gelatin had 75 to 120% of recovery, while the molecules microencapsulated in zein had 88-125% of recovery. Furthermore, those microcapsules are effective in providing protection and stabilizing the catechins during a thermal treatment at 180°C for 12 min. In order to prove the impact of microencapsulation in a real food system, the GTE electro sprayed microcapsules were added to biscuits doughs. They found that the microencapsulation did not protect the green tea extracts. Likewise, the sensorial analysis of the biscuits indicated that addition of the GTE loaded microcapsules did not impact in the acceptability of biscuits, as perceived by consumers. The system may not be the indicated for the type of protection that proteins need to avoid being denaturalized by heat, or to resist high temperatures for a short-periods of time.

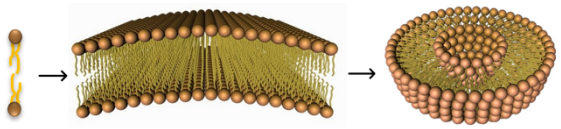

Fig. 13. Bilayer structure of a liposome wall.

3.5 Liposomes

Liposomal microencapsulation has drawn great interest, particularly in the pharmaceutical industry, because this technique can improve the functionality of certain therapeutic compounds, such as solubility enhancement, controlled release, and targeted delivery. This method has been used in the microencapsulation of antioxidants, enzymes, and nutraceuticals, all this in the food industry (Tsai and Rizvi, 2017a). As a result of this method, there is the formation of liposomes, which are spherical vesicles with one or more phospholipid bilayers, separating the inner aqueous environment from the outer aqueous medium (Tsai and Rizvi, 2016). Although natural antioxidants have demonstrated many pharmacological properties, they show poor solubility and inability to cross cell membranes. Therein, the importance of this method resides in the fact that liposomes are biocompatible with phospholipidic vesicles, being able to carry hydrophilic, hydrophobic and amphiphilic molecules (Bonechi *et al*., 2018).

As mentioned before, liposomes are often used as delivery systems of bioactive compounds. During the formation of the liposome, hydrophobic material may be incorporated in the lipid membrane, while hydrophilic molecules present in the aqueous phase may become trapped inside the liposome (Singh *et al*., 2012). Their structure depends on the chemical structure, length and degree of saturation of the hydrocarbon chains present in the solution, pH and the ionic charge of the aqueous phase (Torello *et al*., 2002).

Due to the presence of both lipid and aqueous phases, liposomes can be used in the entrapment, delivery, and release of water soluble, lipid-soluble, and amphiphilic materials, being the underlying mechanism for the formation of liposomes, i.e., hydrophilic - hydrophobic interactions between phospholipids and water molecules (Fang and Bhandari, 2010). The importance of liposomes lies in its similarity with the cell wall membranes, where drugs and bioactive compounds can be encapsulated either into the lipophilic or the hydrophilic compartments, depending on their affinity with water molecules or the lipidic membranes (Trucillo *et al*., 2018). In Figure 13, it is displayed the structure of a liposome wall.

Depending on the lipid composition and method of production, liposomes can aggregate in small unilamellar vesicles (SUV), where there is only one bilayer and the vesicle size is 100 nm or lower. In large unilamellar vesicles (LUV) there is the same number of lamellae, but the size is between 100 nm and 1 μm. In the case of giant unilamellar vesicles (GUV) there are vesicle of sizes above 1 μm. Some authors report unilamellar vesicles (ULV) without any record of sizes (Kajiya *et al*., 2002; Raneva *et al*., 2004; Cuomo *et al*., 2018). Particularly, when there is more than one lamella, these vesicles are considered multilamellar vesicles (MLV), and when there is more than one aqueous nucleus, they are known as multivesicular vesicles (MVV) (Figure 14) (Gaziola-de-la-Torre and de-Pinho, 2015; Tsai and Rizvi, 2017b).

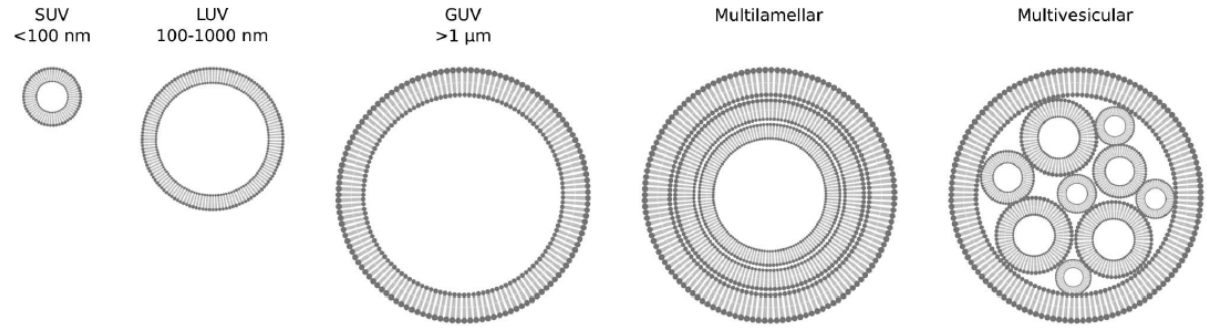

Fig. 14. Types of liposomes (van Swaay and deMello, 2013).

Table 1. Phenolic compounds microencapsulated by liposomes techniques.

Phenolic compounds	Encapsulation material	Method / type of liposomes	References
Green tea catechins (EC, EGC, ECG, EGCG)	Phosphatidyl choline from egg yolk, phosphatidyl serine, dicetylphosphate, stearylamine	MLV from thin film and ULV by MLV sonication	Kajiya *et al*. (2002)
Silibinin	L-α-phosphatidylcholine, cholesterol, dicetylphosphate	Ethanol injection to form SUV	Maheshwari *et al*. (2003)
EC, EGC, ECG, EGCG	Soybean phosphatidylcholine	MLV by thin film and ULV from MLV sonication	Raneva *et al*. (2004)
Curcuma longa extract	Soybean lecithin	Mechanochemical method, type of liposomes no reported	Takahashi *et al*. (2008)
Tea polyphenols (EGCG)	Milk phospholipids (phosphatidylcholine, sphingomyelin, phosphatidylethanolamine, and phosphatidylserine), commercial deoiled soy lecithin (phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol)	Mechanochemical method, type of liposomes no reported	Gülseren *et al*. (2012)
Quercetin	Liposomes made by three different types of phospholipids (unsaturated egg Lipoid E80, 20 unsaturated soy bean Lipoid S100, and saturated soybean Phospholipon 90H), and liposomes made by this material and cyclodextrins	Ethanol injection method, type of liposomes no reported	Azzi *et al*. (2018)
Curcumin	L-α-phosphatidylcholine (egg yolk lecithin) and L-α-phosphatidic acid (egg, chicken) and chitosan	Reversed phase evaporation method to form ULV	Cuomo *et al*. (2018)
Resveratrol	High-methoxy pectin (ED 70% ± 3%), low-methoxy pectin (ED 30% ± 4%), soy lecithin, tween 80 and cholesterol *	thin-layer lipid film /no information of liposomes type	Shao *et al*. (2018)
Acteoside	Soybean, phosphatidylcholine, cholesterol and chitosan (for chitosan coated ones)	Ethanol injection method modified to form small-sized liposomes	Zhou *et al*. (2018)
Galangin	Soybean lecithin, with a phosphatidylcholine content of 70%, cholesterol and Isopropyl myristate	Film dispersion method to form MLV	Zhu *et al*. (2018)
Curcumin	Guar gum, cationic guar gum, egg-yolk phosphatidyl choline and cholesterol	Thin film hydration method / type of liposomes no reported	Pu *et al*. (2019)
Curcumin conjugated in silver nanoparticles	1,2-dimyristoyl-sn-glycero-3-phosphocholine	Lipid film hydration to form MLV	Wehbe *et al*. (2019)

(-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), (-)-epigallocatechin gallate (EGCG), multilamellar vesicles (MLV), unilamellar vesicles (ULV), esterification degree (ED), small unilamellar vesicles (SUV).

* Presence of cholesterol in the liposomal system enhances stability of the formulation (Zhu *et al*., 2018).

The liposomes can carry several common food supplements such as vitamins, minerals, herbal products and antioxidants, playing an important role in improving the pharmacokinetics of the absorption of such nutraceuticals in the body. Furthermore, liposomes have an important advantage over other microcapsules; they can cross membrane barriers of the body, especially if they are structurally designed to perform like biological membranes, in order to deliver the nutraceutical substances (Gupta and Gosh, 2016). In Table 1 is presented a chronological list of examples of microencapsulated phenolic compounds using the liposome method.

There are many processes to make liposomes such as the thin film hydration, the reverse phase evaporation and the ethanol injection method. The use of supercritical conditions is also important, in which the water's droplet is first created and then surrounded by one or more double layers of phospholipids.

In the reverse phase evaporation, Cuomo *et al*. (2018) prepared unilamellar liposomes loaded with curcumin, where a mixture of phosphatidylcholine and phosphatidic acid was made (65/35%); this mix was dispersed in diethyl ether and chloroform containing the curcumin. After this, PBS buffer was added to the organic phase, forming a two-phase system, which was sonicated in order to make an inverted micelles dispersion. Then, the organic solvent was removed, and the inverted micelles system became a liposomes aqueous suspension. In this case, the authors required MLV so they extruded the liposomes solution through polycarbonate membranes. The size of liposomes was around 129 nm, while the final lipid concentration was 16 mg/mL and the concentration of curcumin in liposomes was about 290 μg/mL; therefore, from this data, it was possible to calculate an encapsulation efficiency of 55%.

The ethanol injection is another common method. Zhou *et al*. (2018) prepared liposomes loaded with acteoside by this method, dissolving a mixture of soybean phosphatidylcholine, cholesterol and acteoside in a ratio 10:1:1 in ethanol. After that, the mixture was injected constantly into a phosphate buffer saline solution, removing later the ethanol by rotaevaporation. For chitosan coated liposomes, there were used different concentrations, being the coated with 2% chitosan and the acteoside-liposome the selected for the experimental phase. Authors obtained homogeneous and small-sized liposomes by a pulsed treatment with ultrasonic bath with sizes of 78.5 nm for the acteoside-liposomes and 92.8 nm for the coated chitosan liposomes, and percentage retentions of 81.1 and 88.1%, respectively.

In the case of thin film layer, Pu *et al*. (2019) made curcumin-loaded liposomes uncoated and coated with guar gum using this method. The curcumin, egg-yolk phosphatidylcholine and cholesterol where dissolved in chloroform (ratio 0.5:10:1), then the solvent was evaporated and a thin film formed. Afterwards, the film was dispersed in phosphate buffer and sonicated (i.e., by pulses) by a probe into an ice-cold bath in order to form the liposomes. The concentration of curcumin, phosphatidylcholine and cholesterol was 0.5, 10 and 1 mg/mL respectively, while the guar gum and cationic guar gum coated liposomes were at concentrations from 0.5 to 2.5 mg/mL for each type. Curcumin-loaded uncoated liposomes had a size of 70.1 nm and an encapsulation efficiency of 46.3%. In the case of gum guar coated liposomes, sizes were increasing as long as gum concentration became bigger, starting at 70 nm and finishing at 103 nm, approximately. Same happened with guar gum liposomes taking encapsulation efficiencies of 46 to 63%. It is clear that guar gum is a good option in the coating of liposomes.

The use of supercritical carbon dioxide in the process allows obtaining higher diffusion coefficients of lipids and lower viscosity of the medium bulk. As it can be inferred, the process conditions have influence on the liposome size distribution, permitting a better control (Trucillo *et al*., 2018). Thus, there are some authors using this method to produce this type of microcapsules. Zhao and Temelli (2017) made anthocyanin-loaded liposomes using supercritical carbon dioxide method. They measured the effects of pressure, depressurization rate and temperature on the characteristics of liposomes, obtaining liposomes with mean diameter of 160 nm, encapsulation efficiency of 52.2% and zeta potential of -41.3 mV. As encapsulation material, they used soy lecithin and cholesterol in order to obtain the phospholipid bilayer. In their investigation, they found that elevated pressure and depressurization rates generated smaller particles with higher uniformity, while high temperatures led to reduced sphericity. In this case, the supercritical CO_2 method produced uniform liposomes with more intactness and sphericity than the obtained with the thin film hydration method. In the same way, Trucillo *et al*. (2018) applied supercritical fluids to form liposomes to encapsulate aqueous phenolic compounds extracted from olive pomace. All this was for nutraceutical preparation purposes, using L-α-phosphatidylcholine as a bilayer former and a core of polyphenols.

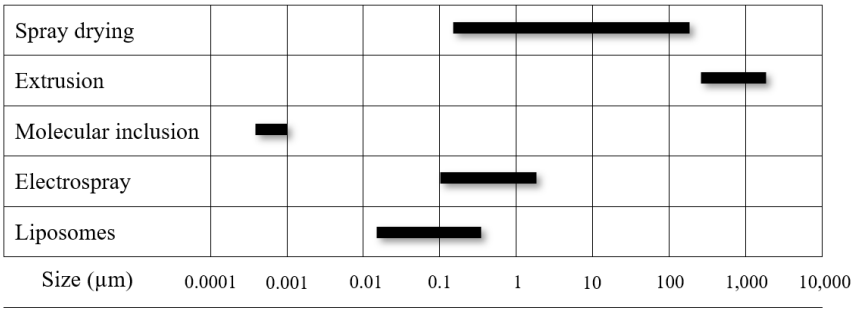

Fig. 15. Particle size of the different microcapsules obtained in the revised techniques.

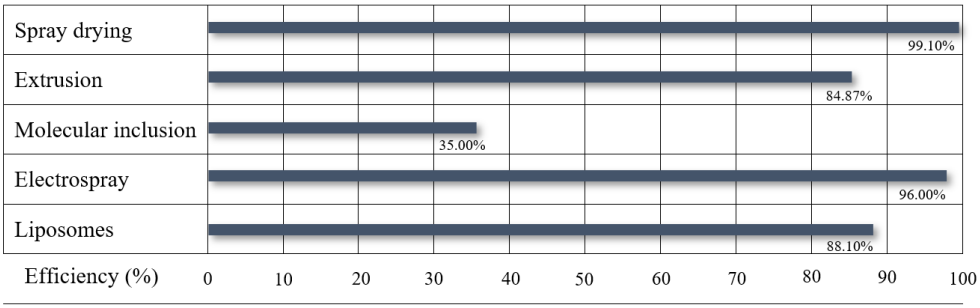

Fig. 16. Maximum microencapsulation efficiency of the different microcapsules obtained in the revised techniques.

The authors made liposomes of different diameters, depending on the pressure applied, i.e., about 265 nm of diameter at 130 bar and smaller than 168 nm at 170 bar. Finally, the researchers obtained encapsulation yields up to 58%.

3.6 Stability of microcapsules

One of the principal reasons to carry on a microencapsulation is to protect the enclosed bioactive compounds from external factors such as oxidation, thermal degradation or gastrointestinal conditions (Fang and Bhandari, 2010). All this has been proved for most of the authors consulted in this review. About protection against oxidation, there are some works corroborating how microencapsulation concedes this action. Moschona and Liakopoulou-Kyriakides (2018) prepared microcapsules with polyphenols from grape pomace as a core substrate and alginate as a wall material; Rocha-Guzmán *et al*. (2010) made a *Quercus resinosa* extract, which was microencapsulated with lactose:caseinate (110:40 g/L); and Lourenço *et al*. (2017) prepared microcapsules of gallic acid and oregano essential oil with fucopol as wall material. In these examples, the encapsulated phenolic compounds were able to preserve their antioxidant activity after microencapsulation by a spray drying process, prooving also the thermal protection of these microencapsulated compounds.

In the case of the protection against gastrointestinal conditions, Zheng *et al*. (2011) demonstrated that microencapsulation provides a good protection of phenolic compounds against this environment, enduring their timely release from microcapsules into the intestine. They prepared bayberry extracts microencapsulated with ethyl cellulose and 1% lecithin as wall material, obtaining releases of 2.56-15.14% of bioactive compounds into a simulated stomach phase, and up to 87.37% in a consequent simulated intestinal phase after 24 h. The latter proved that microencapsulation allows the opportune release on intestine, protecting bioactive compounds from the stomach acidic conditions.

In order to know the shelf life stability, Sun-Waterhouse *et al*. (2011) made microcapsules of olive oil and caffeic acid by extrusion, using 1.5% alginate as wall material. These microcapsules were stored at 20 or 37°C for 30 days and then subjected to stability and quality evaluation. As a result,

researchers observed that the addition of caffeic acid increased the stability and total phenolic content of the final microcapsules, being the oxidation changes mostly slower in the encapsulated oil samples than in the controls. Soto-Castro *et al*. (2019) prepared microencapsulation of betalains with nopal mucilage. Their shelf life study showed microcapsules with no pores or cracks after three months of storage, showing retention of betalains over 90%, which permitted to infer a low oxygen permeability of shells.

In relation to microcapsule sizes, all techniques offer different ranges, going from nanometers to micrometers as introduced in Figure 15. For spray drying, there are particle sizes from 138.1 nm to 200 μm (Rocha-Guzmán *et al*., 2010; Wang *et al*., 2016). The technique with the biggest particle size is extrusion, which affords particles of 450-1900 μm (Chew and Nyam, 2016; Anbinder *et al*., 2011). In contrast, molecular inclusion yields the smallest size, due to the cyclodextrins cavity size (Kalogeropoulos *et al*., 2010). Electrospray is in the middle between molecular inclusion and spray drying, with particle sizes of 0.1-2 μm (Gómez-Mascaraque *et al*., 2015). Finally, there are microencapsulations by liposomes, which present sizes from 20 to 160 nm.

Another important record is the encapsulation efficiency, which is defined as the ratio of mass of encapsulated core material to the mass of the material added for the encapsulation (Jaworek, 2016). Figure 16 shows a comparative summary of the corresponding percentages that can be reached between techniques, being the highest the microencapsulation by spray drying with encapsulation efficiency up to 99.10%, while the lowest one belongs to molecular inclusion by cyclodextrins technique with a 35%.

4 Common microencapsulation wall materials

In any microencapsulation method, the suitable selection of the wall material is a crucial point for the success of the process (Lourenço *et al*., 2017). The ideal encapsulate should have mostly film-forming properties, display emulsifying properties, be biodegradable, become resistant to the gastrointestinal tract, exhibit low viscosity at high solids contents, show low hygroscopicity, and represent low cost (Özkan and Bilek, 2014). Important criteria for selection of an encapsulation material are the functionality that the material wall should provide to the final product, the potential restrictions from properties of the coating material, and the concentration of encapsulates. The most common wall materials used for microencapsulation in the food industry are bio-based ingredients such as the listed in Table 2, which includes examples using carbohydrate polymers, proteins, lipids, etc. (Mishra, 2016a).

4.1 Polymers

Natural polymers are commonly materials with a large molecular weight (MW) that can be taken out from plants, animals, or microorganisms. An example is alginate with a MW up to 4000 Da (Aguayo-Solís *et al*., 2019). Natural polymers are of considerable importance because most of them are biodegradable and known like ingredients “generally recognized as safe" (GRAS), which is an important benefit, particularly in the last years where the actions to reduce synthetic materials and hazardous chemicals have become widespread. In the group of natural polymers can be differentiated two major groups: polysaccharides and proteins (Bartkowiak *et al*., 2017b).

4.1.1 Polysaccharides

Carbohydrates are macromolecules made of carbon and water, although they can also contain nitrogen and phosphorus atoms. They are the most abundant compounds in nature, and they are normally estimated at around 50-80% of the dry weight of vegetables and fruits. Based on molecular structure, carbohydrates are classified as monosaccharides that are the base units of carbohydrates, oligosaccharides made of 2-10 units of monosaccharides connected by glycosidic bonds, and polysaccharides formed by more than 10 units of monosaccharides (Yahia *et al*., 2019).

Polysaccharides are the anhydrides of one or more monosaccharides in which a large number of units are combined. There are two types of polysaccharides: a large chain of only one repeating monosaccharide, also named homopolysaccharides or the heteropolysaccharides that contain more than one type of units. Those macromolecules are the most used wall materials for microcapsules production due to their film-forming and gelation properties. The most reported polysaccharides are alginates, dextrins like maltodextrin, celluloses like ethyl cellulose, and gums like gum arabic and xanthan gum.

Table 2. Examples of wall materials used in the different microencapsulation techniques.

Wall material	Core	References
Freeze drying		
Gum arabic, pullulan, maltodextrin with dextrose	Linoleic acid and methyl palmitate	Minemoto et al., 2000
Maltodextrin	Potassium norbixinate and curcumin	Sousdaleff et al., 2013
Emulsion		
Soy lecithin, modified starch, stearic acid, peanut oil and palm oil	Curcumin, resveratrol	Donsì et al., 2011
Coacervation		
Hydrolyzed collagen, pectin and alginate	Nisin and avocado extract	Calderón-Oliver et al., 2016
Chitosan, xanthan gum and pectin	Palm oil	Rutz et al., 2017
Liposomes		
Performix™ E (soy lecithin with phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol), Cholesterol *	Vitamin C, Vitamin E	Tsai and Rizvi, 2017b
Electrospray		
Gelatin and zein	Green tea extract (flavan-3-ols)	Gómez-Mascaraque et al., 2017
Ethyl cellulose, stearic acid	Vanillin, Ethyl maltol y maltol	Eltayeb et al., 2013
Extrusion		
Alginate and high methoxyl pectin	kenaf oil	Chew and Nyam, 2016
Alginate	Olive oil extra pure and caffeic acid	Sun-Waterhouse et al., 2011
Spray drying		
Inulin and maltodextrin	Prickly pear pulp and extract (betalains, phenols and vitamin C)	Saénz et al., 2009
Opuntia ficus Indica mucilage	Gallic acid	Medina-Torres et al., 2013
Maltodextrin	Cinnamon infusion (phenolic acids, flavonoids)	Santiago-Adame et al., 2015
Gum arabic and polydextrose	Blackberries extract (anthocyanins and polyphenols)	Rigon and Zapata-Norena, 2016

Symbol code: Polar (⁂); Nonpolar (●); Bipolar or amphipathic: (֍); Stability (*) (Zhu *et al*., 2018)

The major advantages of these biopolymers are their good water solubility and low viscosity at high concentrations (Nesterenko *et al*., 2013).

The alginate is a group of natural marine polysaccharides extracted mainly from seaweeds and constituted by two linear copolymers of 1-4 glycosidically linked α-L-guluronic acid (G) and its C-5 epimer β-D-mannuronic acid (M) (de-Vos *et al*., 2010). They are composed from 100 to 3000 units of building blocks connected in a rigid and moderately flexible chain, obtaining three natures of blocks: homopolymeric M-blocks, homopolymeric G-blocks and heteropolymeric alternating MG-blocks. This composition and block structure are strongly related to the functional properties of alginate molecules within an encapsulation matrix (Chávarri *et al*., 2012). The composition of the polymer chain will differ in quantity and distribution according to the source, affecting the functional properties of alginate as supporting material (Burgain *et al*., 2011). Sodium alginate is favored for being used as a matrix carrier due to its simplicity, non-toxicity, biocompatibility and low cost (Burgain *et al*., 2011).

This polymer has been used for many purposes, such as coating material, loaded with polyphenols to preserve the quality of fresh Japanese sea bass fillets (Nie *et al*., 2018), as a wall material to made kenaf oil microcapsules (Chew and Nyam, 2016) or to microencapsulate phenolic extracts from flower petals of *Clitoria ternatea* using the extrusion method with alginate and calcium chloride ($CaCl_2$). In the latter case, authors reported a maximum encapsulation efficiency of 84.87%, directly linked to the percentages of extract (5-20%), alginate (1-2%), and $CaCl_2$ (1.5-5%), being the optimized condition of extract-loaded alginate beads: 10% of extract, 1.5% alginate and 3% $CaCl_2$. Under this condition, the authors recorded antioxidant capacities by $DPPH^{\bullet}$, $ABTS^{\bullet+}$ and FRAP assays of 21.2%, 13.2 mg of Trolox equivalent/g beads and 14.3 mg of $FeSO_4$ equivalent/g beads, respectively, as well a total phenolic content of 11.76 mg gallic acid equivalent/g beads. The alginate microcapsules show smooth surface shape with a particle size distribution of 985 μm, proving the absence of chemical interactions with the extract as verified by FT-IR. The use of this wall material lets retain high loads of polyphenols, therefore improving the antioxidant capacity of beads (Pasukamonset *et al*., 2016).

In other way, ethyl cellulose is a water-insoluble commercial thermoplastic or biocompatible polymer used for coating and controlled release applications. The use of ethyl cellulose-based microcapsules has been reported by several authors for the encapsulation of a variety of drugs (Estevinho and Rocha, 2018). This polymer was used in the microencapsulation of bayberry extracts, where the authors reported that the antioxidant activity of bayberry polyphenols could be effectively protected by microencapsulation (89.62% by $DPPH^{\bullet}$ assay), showing stability even under storage and adverse environments. The microcapsules had a smooth surface shape with a particle size distribution of 10-97 μm with a retention rate of 85-99% against different light conditions, 55-90% against different temperatures (90 to 50°C) and 65-85% against different moisture settings (50-10%) (Zheng *et al*., 2011).

One of the most used wall materials in spray drying microencapsulation is maltodextrin, which is prepared from starch by enzymatic depolymerization of an aqueous suspension of potato starch dried after spray-drying. They are low in sweetness and readily digestible, highly soluble, and highly hygroscopic. Maltodextrins have a heterogeneous composition of the mixture of sugars with a wide range of starch depolymerization (Dextrose equivalents, DE), being the maltodextrin with DE > 10 the one recommended as wall material (Bartkowiak *et al*., 2017a). The efficacy of maltodextrin is due to its rapid film or shell forming property and the relatively low water diffusivity in these films (Moser *et al*., 2017); it forms a very good oxygen barrier with low viscosity at high solids content and represents low cost (Fang and Bhandari, 2012).

This polymer is wide reported with different technologies, such as freeze drying or spray drying. It is reported in the microencapsulation of potassium norbixinate and curcumin by freeze drying. In this case, a maltodextrin DE20 was used, evaluating the microcapsules for exposition to light, air, different pH, water solubility, and in food applications (Sousdaleff *et al*., 2013). The best results were obtained with a ratio of 1:20 of potassium norbixinate with 1.2 g of initial charge and 20 g of maltodextrin, having color retention of 78% and same ratio for curcumin with 1.1 g of initial charge and 20 g of maltodextrin, having color retention of 71%. According with micrography the size of both microcapsule systems were smaller than 50μm. Differential scanning calorimetry and thermogravimetry showed evidences of interaction between encapsulated compounds and maltodextrin. With this work, it was clear that maltodextrin can be used to encapsulate those compounds, providing an enhancement on their solubility.

Maltodextrin was effective in the microencapsulation of laurel infusions (LI) (*Listea glaucescens*) with initial values of phenolic content of 42.1 mg gallic acid equivalent (GAE)/g of laurel and EC_{50} of 0.40 mg LI/mL of DPPH$^{\bullet}$. Microparticles showed defined morphologies with sizes of 6-40 μm, total phenolic content of 10.2 to 20.2 mg GAE/g of laurel and EC_{50} of 0.40 mg LI/mL of DPPH$^{\bullet}$. Microcapsules also showed encapsulation yields of 47.6 to 62.3% and efficiency of about 70%, being the best conditions of encapsulation at 160°C of inlet temperature and 8 mL/min of feed rate. With the initial data, percentage of retention was calculated around 48% (Medina-Torres *et al*., 2016).

Maltodextrin is also used with gum arabic, which is a highly water-soluble polymer, produced by acacia (*Acacia senegal*) as a tree secretion; it is considered as one of the most important encapsulating agents in the food industry due to its solubility, low viscosity, emulsification characteristics, and its good retention of volatile compounds. Gum arabic is a complex branched polysaccharide, composed of two fractions, one formed of sugar units (D-galactose, L-arabinose, L-rhamnose, D-glucuronic acid), and a protein content; it is found as a mixed calcium, magnesium, and potassium salt of a polysaccharide acid (Estevinho and Rocha, 2018). This combination was used to encapsulate phenolic compounds from grape pomace by spray drying. There were used different DE maltodextrins (DE_{4-} and DE_{17-20}) and gum arabic at different ratios of core and wall materials (10:0, 8:2 and 6:4) and different inlet temperatures (120, 140, 160 and 180°C). All microcapsules had a size of 1-10 μm, where the better particles were obtained with an 8:2 ratio of maltodextrin-gum arabic at 140°C inlet temperature, and a powder yield of 42.6-59.5%. At 120°C, microcapsules with the 8:2 ratio had the highest total phenolic content ~15 mg GAE/g of powder and DPPH$^{\bullet}$ inhibition of 28-30%. The encapsulation efficiency was about 98.8 % and 99.1% for core:coating ratios of 1:1 and 1:2, respectively. (Tolun *et al*., 2016).

Another report of microencapsulation of bioactive compounds extracted from blackberry (*Rubus fruticosus*) by spray-drying, used gum arabic (10%) and polydextrose (15%) at inlet temperatures of 140 to 160°C. In this case, authors (Rigon and Zapata-Norena, 2016) reported that encapsulation conditions did not affect hygroscopicity, and the morphology of microcapsules presented smooth surfaces with some concavities and some brightness at particle sizes of 5-10 μm according to micrographies. Results showed that the inlet temperature at 140°C and 15% of gum arabic were the best encapsulation conditions. The anthocyanins retention inside microcapsules was 878.3-1300.8 mg/100g, and the total phenolic content was 2106.6-2429.2 mg (GAE)/100g. The antioxidant activity was measured with DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ assays with values between 31.3 to 40.3% and 27 to 45.2%, respectively.

4.1.2 Proteins

Proteins are biological polymers formed of smaller units named amino acids. The amino acid chains give place to a variety of different general structures: fibrous, random coil, and globular proteins. They are good choices to be used as wall materials, especially in the microencapsulation by spray-drying, because they have the ability to form thermally permanent gels above 70°C (Bartkowiak *et al*., 2017a). Thus, to select the appropriate protein or combination as a wall material, some factors must be considered. For example, it is important to know the specific physicochemical characteristics of the proteins to be used. That is thermal denaturation and transition temperatures, isoelectric points, sensitivities to monovalent or multivalent ions, also the susceptibility to specific enzyme or chemical crosslinking or degradation reactions (Estevinho and Rocha, 2018).

Caseins are a group of proteins that conform 80% of milk proteins. The main caseins are αs1, αs2, β and κ-casein that have an open and flexible structure and consist of hydrophilic and hydrophobic segments. They have so many functional properties, like foaming, thickening, emulsification, texture, stabilizer, self-assembly, excellent gelation and water binding capacity under defined conditions. Therefore, those physical properties and their behavior in both individual caseins and casein micelles enable them as good candidates for wall material in microcapsules (Ranadheera *et al*., 2016). Casein has been used to protect phenolic compounds from leaves of oak trees. *Quercus resinosa* infusions were microencapsulated by spray drying using lactose and sodium caseinate (Rocha-Guzmán *et al*., 2010). Three lactose-caseinate blends (110:40, 90:60 and 70:80 g/L) were tested at different homogenization pressures. The obtained capsules had sizes of 138.1 to 269.8 nm that were able to retain the good antioxidant capacities of the initial infusions. The highest value of total phenolic content was found in the group of blends of 70:80 with up to 55 GAE/g of sample.

The term whey proteins have been used to describe the group of milk proteins that remain soluble in milk serum or whey after precipitation of caseins at pH 4.6 and 20°C. The major characterized components of this fraction are β-lactoglobulin (50%), α-lactoalbumin, serum albumin, immunoglobulin, and proteose-peptone fractions (Farrel *et al*., 2004). Whey protein has been used in blends with soy protein as carrier agents to microencapsulate phenolic compounds in powdered BRS Violeta grape juice (Moser *et al*., 2017). The results showed that those combinations preserved almost all anthocyanins content inside microcapsules.

Another protein used is gelatin that is produced from collagens by destruction of their secondary and higher structures. Collagen is obtained from bones and skin of pigs and cattle. In the industry there are two forms to produce gelatins; one is by acid treatment, producing gelatin type A, and the other, type B, by alkaline treatment. Gelatin is a heterogeneous mixture of polypeptides of 300-4000 amino acids each, conforming a helix structure every third unit in all chains, presenting glycine, then proline and 4-hydroxyproline as commonly occurring residues (Bartkowiak *et al*., 2017b). An example on the use of gelatin in microencapsulation processes is the encapsulation of black raspberry water extracts rich in anthocyanins (770.2 mg cyanidin-3-glucoside equivalent (CGE)/100 g) (Shaddel *et al*., 2018). The results showed microcapsules with lower moisture, hygroscopicity and solubility values than the free presentation of dried anthocyanins, with average sizes of 35.3 to 80.2 μm and high loading capacity (29.7-38.5%). Those microcapsules exposed the characteristic intense red color along storage time, implying the effectiveness of the method and the wall material chosen to preserve anthocyanins.

4.1.3 Lipids

Lipids is a group of diverse compounds that have the property of being soluble in organic solvents, but insoluble in water due to their low polarity. They are classified like acylglycerols, fatty acids, phospholipids, carotenoids, phytosterols, and oil-soluble vitamins. Lipids can also be used as a carrier for lipophilic compounds, for example in the production of liposomes (Fang and Bhandari, 2012).

In the case of phospholipids, they have important properties like self-organization in water systems that have the ability to produce structures with high entrapment efficiency of both lipophilic and hydrophilic compounds. An example of the use of lipids is the microencapsulation of rutin by liposomes using egg yolk phospholipids (Bernardo *et al*., 2019). Microcapsules obtained were smaller than 140 nm with a microencapsulation efficiency of about 87%.

Another material reported is stearic acid (octadecanoic acid) that is a saturated fatty acid with 18 carbons (C_{18}) with a hydrophobic aliphatic chain of carbons obtained from animal fats and vegetal oils (McMurry, 2012). However, there are few papers describing the use of stearic acid, because this material has not been widely used in the microencapsulation of polyphenols (Zhang *et al*., 2007). These authors prepared particles varying the concentrations of stearic acid from 150 to 240 mg, surfactant (Brij 78) from 80 to 170 mg and silibinin from 10 to 40 mg, being the samples with 210 mg of stearic acid the highest encapsulation efficiency. The results showed microcapsule sizes of 178.9-387.0 nm, with high encapsulation efficiencies (94.8 to 98.94%) and encapsulation loadings of 3.17-12.43%.

According with these examples, the use of lipid wall materials could be a good option to explore microencapsulation of polyphenols, starting from the idea that these microcapsules may be absorbed orally the same way as the food lipids are (Pandita *et al*., 2014).

5 Novel polymers, new options

In the food and pharmaceutical industry, "novel" products are those that were not used in significant quantities before May 15th, 1997 for human food in the European Union, in accordance with Regulation (EC) N° 258/1997. Those products must meet with one or more requirements. First, foods or food ingredients must have a new or intentionally modified primary molecular structure and they could be microorganisms, fungi or algae, vegetables or the ingredients obtained from them, and they will not imply a health risk (Parlamento Europeo, 2009). According to this, polysaccharides with novel or improved properties may be obtained by modifying the microbial cultivation conditions (Lourenço *et al*., 2017), or obtained from agroindustrial wastes.

5.1 Mucilages and gums

Mucilage is a high molecular weight polysaccharide that behaves as a polyelectrolyte. It is present in a

variety of plants such as nopal, chia, Aloe vera and plantago, and it has been used as a carrier material for microencapsulation processes (Kaewmanee *et al*., 2014). They have functional properties like water binding, texture modifier, and gelling, emulsifying, or foaming agents, and as wall materials in bioactive compounds microencapsulation.

In the case of nopal mucilage, it is extracted from cladodes of *Opuntia ficus-indica*. The mucilage comes from the degradation of pectin substances that have a molecular structure of up to 30,000 units of different sugars. Nopal mucilage contains residues of arabinose, galactose, galacturonic acid, rhamnose and xylose. It is known for the ability to form molecular networks that can retain large amounts of water (Medina-Torres *et al*., 2000). Nopal mucilage has been used in the microencapsulation of gallic acid (Medina-Torres *et al*., 2013) and as a wall material for microencapsulation of fruit pulp extracts and skin pigments from *Escontria chiotilla* and *Stenocereus queretaroensis* by spray drying processes. The microcapsules showed smooth and spherical morphologies with sizes smaller than 10 μm and concentration of betalains from 0.37 to 4.64 mg/g, attaining over 90% in their retention after three months of storage. The yields of microencapsulated betalains varied from 53 to 73 %, for the pulp extract, and from 42 to 82 % for skin betalains (Soto-Castro *et al*., 2019).

Psyllium husk mucilage is obtained from the seed of *Plantago psyllium* plant that is cultivated mainly because of its mucilage content, which is a white fibrous material with hydrophilic properties. This mucilage can be obtained by mechanical milling or grinding. Psyllium is an anionic polysaccharide of L-arabinose, D-xylose and D-galacturonic acid and its mucilage consists of arabinoxylans (arabinose 22.6%, xylose 74.6%) (Kumar *et al*., 2018). This mucilage has been used combining its purification with simultaneous microencapsulation of curcumin. In this technique the mucilage was extracted with water and purified with ethanol, while an ethanolic solution of curcumin was added. The arabinoxylan precipitation (mucilage) promoted incorporation of 56% of the curcumin in solution, while the mucilage interacted with curcumin, improving its thermal stability. The size of obtained microcapsules was about 10 μm according with SEM images, having a microencapsulation efficiency of 22.9 mg/g. Compared with other studies, this process had a low encapsulation yield (10.2%). Interestingly, the presence of curcumin did not interfere in the production of precipitated arabinoxylan. The authors observed the interaction between polysaccharide and curcumin (Álvares-Monge-Neto *et al*., 2017) and proved that the mucilage was effective in shielding curcumin from thermal degradation. Therefore, as the mucilage is non-toxic and biodegradable, it has the potential to be used in food processing and as a wall material for encapsulations.

Another interesting material with attractive potential applications is Aloe vera mucilage, which comes from *Aloe barbadensis* Miller among other related species. It contains 99.4% of water and 0.6% of solids, where important proportions of D-glucose and D-mannose, uronic acid and polysaccharides of high molecular weight are present as well. Acemannan, a bioactive polymer rich in mannose, glucose, and galactose units is also in Aloe mucilage (Cervantes-Martínez *et al*., 2014). This mucilage can be used in high thermal processing as the spray-drying process because it is able to maintain its internal structure and functional properties (Medina-Torres *et al*., 2018).

This mucilage has been used in the microencapsulation by spray-drying of lactic acid bacteria, specifically *Weissella confusa* (Serna-Cock *et al*., 2012), and *Lactobacillus plantarum* (Ceja *et al*., 2019). Recently, it has been tested as a wall material in the microencapsulation of curcumin (at 0.56%) by spray drying, showing yields of 7.22 to 9.48%, obtaining quasi-spherical particles (10-25 μm) according to SEM images and verifying the encapsulation of the antioxidant by FT-IR analysis. The control (i.e., spray-dried curcumin) showed a total phenolic content of 0.105 μm GAE/mg and antioxidant capacity by ORAC assay of 934.4 μmol Trolox/mg. The obtained microcapsules displayed comparable phenolic content (0.047-0.122 μm GAE/mg) and antioxidant activity (847.3- 938 μmol Trolox/mg) (Medina-Torres *et al*., 2018).

Finally, another novel material reported is the chia mucilage, which is a tetra saccharide with 4-O-methyl-α-D-glucuronopyranosyl residues occurring as branches of β-D-xylopyranosyl residues in the main chain, consisting of (1→4)-β-D-xylopyranosyl-(1→4)-α-D-glucopyranosyl-(1→4)-β-D-xylopyranosyl units. Its high carbohydrate and fiber contents favor its encapsulating properties since the mucilage tends to form gels. Chia mucilage was used together with mesquite gum in the microencapsulation of lemon essential oil (LEO). The blends of chia mucilage (CM) and mesquite gum (MG) were in a 90:10 and 80:20 ratios (MG:CM). The particle size obtained for these ratios were 13.80 and 49.6 μm, respectively. The encapsulation efficiency was

98.3 and 98.6%, respectively, while the volatile oil retention was 49.6 and 51.5, respectively. The microcapsules provided better protection to lemon oil against oxidation than those formed just with mesquite gum. This study demonstrated that use of chia mucilage mixed with mesquite gum effectively improves the oxidative stability of LEO (Cortés-Camargo *et al*., 2018).

In the case of gums, mesquite gum is an exudate (MW 2.12×10^6 Da.) from *Prosopis* trees formed by a branched complex of heteropolyelectrolyte that upon hydrolysis with diluted mineral acid yields L-arabinose, β-D-galactose and 4-O-methyl-D-glucuronic acid. This gum has been used and can be recommended as encapsulating agent (Vernon-Carter *et al*., 2000). The *Prosopis* species (mesquite tree) is native from México, distributed along America, including south USA as well as Argentina, Chile, Brazil and Bolivia (González-Quijano *et al*., 2019).

Mesquite gum has been used mixed with nopal mucilage at different concentrations (25:75, 50:50 and 75:25) in the microencapsulation of lemon essential oil by spray drying. Good encapsulation efficiencies (70.0-90.6%), particle sizes (11.9-44.4 μm) and volatile oil retentions (45.9 to 74.4%) were obtained. Emulsions with higher amount of mesquite gum had smaller droplet sizes due to its more compressed conformation than nopal mucilage; those microcapsules had smaller particle sizes with the highest volatile oil retention, but lower protective effect against LEO oxidation. This may be due to contraction of microcapsules during the drying process (Cortes-Camargo *et al*., 2017).

5.2 Inulin

The inulin is a polymer made of linear chains of fructosyl groups bonded by β-2,1 glycosidic linkages, with the reducing end terminated by an α-D-1,2 glucopyranoside ring group. In general, inulins derived from plants have chains containing 2 to 100 or more units of fructose (Bartkowiak *et al*., 2017b).

This polymer was used mixed with 1.5% (w/v) alginate in the microencapsulation of chokeberry (*Aronia melanocarpa*) extract (2.55 mg GAE/ml), which is a rich source of polyphenols with confirmed health benefits. In order to get microcapsules, an electrostatic extrusion process was used (Ćujić *et al*., 2016). The microcapsules had regular shapes with sizes from 800 to 1340 μm. Those obtained with different needle diameter (18, 20 and 22 gauges) and the mix alginate-inulin ratio of 1.5-0.5% showed the best results to release its content with the best encapsulation retention (9.41%), although it was lower compared with other techniques. Higher amounts of polyphenols were presented in particles obtained with inulin (0.23 mg GAE/g) than without it (0.19-0.21 mg GAE/g). Scanning electron microscopy confirmed that inulin improved the final properties of the microcapsules.

In another study, it was confirmed the retention of phenolic compounds during spray-drying of *Cyclopia subternata* extract using corn syrup solids and inulin separately (Pauck *et al*., 2017). The results showed that both microencapsulations were very similar; in the case of the phenolic compounds, specifically the thermolabile ones mangiferin, isomangiferin and iriflophenone 3-C-β-D-glucopyranoside, the spray drying had not affect, probably due to both wall materials used. In this study, inulin was proposed because the polymer is a reduced-kilocalorie carrier that can be safely ingested by diabetics. The initial phenolic content was of 297.2 g GAE/100 g and antioxidant activity of 2342 μmol Trolox/g by DPPH$^\bullet$ assay. Researchers obtained microcapsules (5-10 μm) with comparable values of 292.2-315.2 g of GAE/100 g and 2452-2277 μmol Trolox/g, respectively. All power yields varied from 613 to 652 g/kg. Lastly, it was confirmed the potential use of inulin as wall material with the possibility of being added in the formulation of low energy healthy products and beverages.

5.3 Zein

Zein is a storage protein obtained from corn or maize seeds (*Zea mays* L.). It represents 35 to 60% of the total proteins present in corn. Commercial zein is separated from corn gluten meal, milling, and as a mixture of at least four types of proteins: α-, β-, γ-, and δ-zein. Each protein has different amino acid sequence, molecular weight, and solubility properties (Bartkowiak *et al*., 2017a).

Zein has been used in the microencapsulation of green tea catechins with electrospray (Gómez-Mascaraque *et al*., 2017; Bhushani *et al*., 2017). In the latter study, zein at 5% produced spherical monodisperse particles with diameter of 157.5 nm at different encapsulation efficiencies for epigallocatechin (94.7-97.4%), epicatechin (86.8-89.7%), epigallocatechin gallate (90.0-95.6%) and epicatechin gallate (90.7-95.6%). The capsules were tested *in vitro*, where encapsulated catechins had significantly improved *in vitro* gastrointestinal

stability and Caco-2 cell monolayer permeability compared to non-encapsulated catechins (Bhushani *et al*., 2017).

5.4 FucoPol

FucoPol is an exopolysaccharide that was tasted recently as an encapsulation matrix in spray drying microencapsulation techniques in order to protect gallic acid and oregano essential oil (Lourenço *et al*., 2017). FucoPol is a biopolymer (viz., heteropolysaccharide) produced by the bacterium *Enterobacter* A47 that has a high molecular weight and is composed of neutral sugars such as fucose, glucose and galactose and an acidic sugar like glucuronic acid. The researchers obtained spherical capsules having smooth surface of variable diameters (0.5 to 26.7 μm) and thin walls. Initial values from samples of gallic acid were 13.9 and 16.6 μmol/g of bioactive compounds (BC) for DPPH$^{\bullet}$ and FRAP assays, respectively; while values after encapsulation were 20.8 μmol/g of BC for DPPH$^{\bullet}$ and 22.2 μmol/g of BC for FRAP assays. FucoPol as wall material has preserved the antioxidant activity of the bioactive compounds after the microencapsulating process, reason why it could be suggested as a good and promising wall material for use as encapsulating agent of polyphenol compounds (Lourenço *et al*., 2017).

Conclusions

Polyphenols are becoming important phytochemicals as major promoters of health in nutraceutical formulations, so their appropriate handling is a key a factor for their use and commercialization. This review showed an update of the most used and recommended microencapsulation techniques for the protection of polyphenols, including some novel polymers that could represent sustainable options. Within the revised techniques, the most selected for large-scale processes is still spray drying because it is a profitable method, representing low operating costs, high product yields and good storage stability compared to others. However, it should be still at the criteria of every user and application to choose the technique that suits better to every particular need. Unfortunately, there is not yet a universal method to facilitate the appropriate loading of polyphenols in the core of microcapsules for all systems.

In the case of wall materials there is also a variety of them, having different chemical properties and being recently studied in the protection of polyphenols with the named novel polymers. These materials represent value-added and natural possibilities, because they might be economically attractive and obtained mostly from conventional and non-conventional agricultural resources and wastes versus traditional synthetic choices. Novel polymers have been tested as good options due to their compatibility with polyphenols and good encapsulation yields, although their current use at large scale is still limited. This is the case of natural mucilages, gums and proteins such as aloe vera, mesquite and zein.

Additionally, combining wall materials seems to be a recommendable practice to experiment and scaling up. Thus, the study and use of novel polymers is an area of opportunity to be explored, particularly in discrete mixtures with established materials such as maltodextrin. Therefore, important advances would be obtained when optimizing wall material proportions with hydrophobic ingredients that may guarantee particles of smooth surface, more resistance to relatively high levels of moisture and oxygen, and still being productively and economically viable.

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Nomenclature

ABTS$^{\bullet+}$	2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid
bar	bars
$CaCl_2$	calcium chloride
CAPE	caffeic acid phenethyl ester
CD	cyclodextrins
CMC	carboxymethylcellulose
Da	Dalton
DE	dextrose equivalents
DPPH$^{\bullet}$	2,2-diphenyl-1-picrylhydrazyl
DSC	differential scanning calorimetry
EC_{50}	half maximal effective concentration
EC	epicatechin
ECG	epicatechin gallate
EGC	epigallocatechin
EGCG	epigallocatechin gallate
EHDA	Electrohydrodynamic Atomization

FRAP	Ferric Reducing Antioxidant Power
FT-IR	Fourier-transform infrared spectroscopy
g	gram
G	α-L-guluronic acid
GAE	gallic acid equivalent
GTE	green tea extract
GUV	giant unilamellar vesicles
h	hours
HP-β-CD	hydroxypropyl-β-cyclodextrins
LI	laurel infusions
LEO	lemon essential oil
LUV	large unilamellar vesicles
M	β-D-mannuronic acid
mg	milligram
min	minute
mL	milliliter
MLV	multilamellar vesicles
mm	millimeter
mV	millivolts
MVV	multivesicular vesicles
MW	molecular weight
nm	nanometer
NMR	nuclear magnetic resonance
PBS	phosphate buffered saline
SEM	scanning electron microscope
SUV	small unilamellar vesicles
ULV	unilamellar vesicles
UV	ultraviolet light
w/v	weight/volume
w/w	weight/weight
α	alpha
β	beta
γ	gamma
δ	delta
μL	microliters
μm	micrometer
°C	Celsius degree
%	percent

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