#### REVIEW



# Methods for nanoemulsion and nanoencapsulation of food bioactives

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#### Abstract

Nanoencapsulation is a promising technology allowing miniaturized dosage and administration of valuable volatiles, degradable bioactives and biologicals. The produced nanoparticles display qualities such as a sustained availability of active constituents, targeted delivery and enhanced shelf stability. This review presents methods of nanoencapsulation and nanoemulsion, such as solvent evaporation–emulsification, coacervation, nanoprecipitation, inclusion complexation, electrospraying, electrospinning, freeze drying and spray drying. Those methods are particularly relevant for the pharmaceutical, food and agricultural industries.

Keywords Nanoencapsulation · Bioactives · Encapsulation efficiency · Stability · Bioactive release

# Introduction

Nanoencapsulation is an emerging technique for encapsulation of bioactive compounds prone to degradation by environmental factors, as well as, for site-specific and sustained delivery of the bioactives (Soukoulis and Bohn 2015; Rezaul et al. 2018). This powerful technique is of particular importance in designing novel delivery mechanisms of bioactives in food and therapeutic supplements/ drugs and plays a prominent role in determining the future of 'nanomedicine' (Pereira et al. 2017; Subrot et al. 2018). Off late, numerous methods of nanoencapsulation have been investigated for protection and efficient delivery of biological materials (Fathi et al. 2018). Though these methods are varied, they are quite versatile in their performance and accurately meet their objectives (Iqbal and Sun 2018; Shchukina et al. 2018). The present review collates the findings made by investigators on novel materials of encapsulation of

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bioactives, strategies involved, mode of delivery, and applications. The objective of this disquisition is to present the findings made, with a focus on the methods employed and the areas that need further investigation. This article is an abridged version of the chapter published by Dasgupta and Ranjan (2018) in the series Environmental Chemistry for a Sustainable World (http://www.springer.com/series/11480).

# Liquid-based nanoencapsulation

Liquid-based nanoencapsulation is an efficient technique for site-specific delivery of nutraceuticals, even at a cellular level. In this section, liquid-based methods used by researchers have been discussed, and their detailed findings are made. Figure 1 shows the different techniques for the process.

### Solvent evaporation-emulsification

This technique involves emulsification of a polymer solution in aqueous phase and the subsequent evaporation of the solvent, resulting in precipitation of the polymer as nanoparticles (Ghaderi et al. 2014). Research has shown that nanoencapsulates are spherical, where its size distribution is largely determined by constraints such as viscosity of organic/aqueous phase, stirring rate, temperature, and type as well as amount of the dispersing agent. The polymers which are used frequently are polylactic acid (PLA),

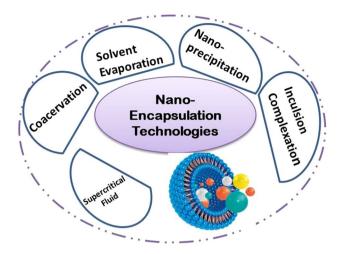


Fig. 1 Techniques of liquid-based encapsulation

polylactic-co-glycolic acid (PLGA), cellulose acetate phthalate, ethyl cellulose, β-hydroxybutyrate, and polycaprolactone (Cavallaro et al. 2015; Fornaguera et al. 2015). These nanospheres are reportedly developed by employing either homogenization or high-speed ultrasonication (Rebolleda et al. 2015; Scholz and Keck 2015). The technique of 'multiple emulsion' has been employed for the encapsulation of curcumin in a network of chitosan cross-linked with tripolyphosphate along with freeze drying, yielding spherical encapsulates of sizes 254-415 nm (Sowasod et al. 2008). In another approach, researchers have studied solvent evaporation technique for encapsulation of curcumin, followed by freeze-drying technique (Li et al. 2015b). The same approach was used by Prajakta et al. (2009) and the curcumin encapsulates (<135 nm) revealed about twofold increase in anticancer activity, vis-à-vis curcumin per se, in HT-29 cell lines (human colon adenocarcinoma). On the other hand, smaller-sized nanospheres (45 nm) have been obtained for curcumin by using PLGA nanospheres, along with higher loading capacity, sustained release of bioactive, and higher anticancer potency on human prostate cancer cell lines (Mukerjee and Vishwanatha 2009; Akl et al. 2016).

In addition, emulsion evaporation technique has produced curcumin encapsulates with in vivo antimalarial activity. High-pressure emulsification has also been found effective in the formation of nanospheres of curcumin in PLGA with a 22-fold improved oral bioavailability than non-encapsulated curcumin (Tsai et al. 2011, 2012; Klippstein et al. 2015), and also, solubility of curcumin was improved 640-fold when entrapped in this technique in the said wall (Xie et al. 2011). Furthermore, the 'single emulsion technique' has been employed for formulation of a blended nanoencapsulate of PLGA and PLGA-PEG blend (< 200 nm) using sonication followed by freeze drying, with the encapsulates having 16 and 55 times higher bioavailability over the

non-encapsulated bioactive (Khalil et al. 2013; Akl et al. 2016). In fact, PLA-based coat in nanoencapsulation in evaporation-emulsification method has revealed 130-nmsized encapsulates with a 97% entrapment of the bioactive (Feng et al. 2018). The release study exhibited an initial burst followed by sustained delivery of bioactive, such as that of quercetin, with 88% release in 72 h and complete release in 96 h (Kumari et al. 2010, 2011). The success of this technique critically depends on the selection of appropriate emulsification and drying procedures. In another study,  $\alpha$ -tocopherol has been encapsulated in nanosphere of size range 90-120 nm and exhibited total shelf life of about 3 months. To further illustrate that the processing parameters and aqueous-to-organic phase ratio do not affect the size of droplet and distribution of fabricated nanodispersion (Cheong et al. 2008; Campardelli and Reverchon 2015). Investigations by other authors have further shown that varied droplet sizes could be achieved for biologicals such as astaxanthin (1101–165 nm) (Anarjan et al. 2011), phytosterols (50–282 nm) (Fun et al. 2011), and  $\beta$ -carotene (9–280 nm) (Hélder et al. 2011).

#### Coacervation

The coacervation technique allows loading of about 99% of bioactive during encapsulation. The process involves the principle of phase separation for differentiation of a single polyelectrolyte and/or mixture of polyelectrolytes from a solution, followed by formation of a coacervate phase, encircling the core. The strength of the coacervate has been observed to increase by including enzymatic/chemical cross-linkers such as transglutaminase or glutaraldehyde (Rathore et al. 2013; Moore et al. 2015; Wang et al. 2016a; Zhang et al. 2016a) This technique variants include simple and complex types using one and multiple types of coats, respectively, and they have been successfully employed for entrapment of sensitive bioactives (Taylor et al. 2008, 2010). Furthermore, the nature and strength of the encapsulate could be determined by variations in type and ratio of the biopolymer (charge, flexibility, and molar mass), pH, ionic strength, along with hydrophobic interaction between biopolymers (Hosseini et al. 2015; Zou et al. 2016).

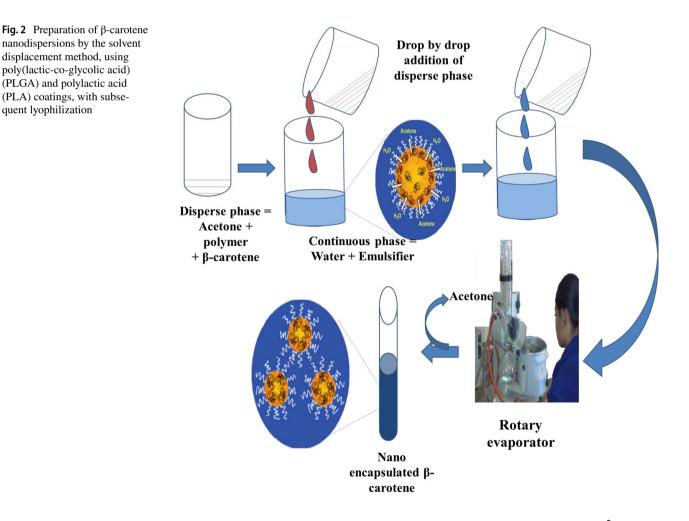
Particularly, upon investigation, complex coacervation has been found to be effective in encapsulating capsaicin in gelatin and acacia, wherein capsaicin was treated with hydrolyzable tannins, followed by cross-linking with glutaraldehyde and subsequent freeze drying. The process permitted high target compound loading, encapsulation efficiency, and a satisfactory release (Xing et al. 2005; Nakagawa and Nagao 2012). A similar observation was made by researchers upon encapsulating bovine serum albumin using polyanion tripolyphosphate (TPP) as coat and chitosan as cross-linker, vielding 200–580-nm-sized nanospheres (Li et al. 2015a; Lomova et al. 2015; Wang et al. 2016b).

#### Nanoprecipitation

quent lyophilization

Nanoprecipitation technique encompasses interfacial deposition of polymers, subsequent to the displacement of a semi-polar solvent miscible with water from a lipophilic solution (Eisner 2015). The method is more facile, less complex, less energy consuming, and is an easy and reproducible method that has been widely used in the preparation of nanoparticles. Common polymers include poly(alkylcyanoacrylate) (PACA), poly(ε-caprolactone) (PCL), polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), and Eudragit (Vuddanda et al. 2014; Bacinello et al. 2015; Cauteruccio et al. 2015; Mahalingam and Krishnamoorthy 2015). Reportedly, this technique has been used for producing nanoparticles (76-560 nm) in PLGA, with poly(L-lysine) and polyvinyl alcohol (PVA) as stabilizers, and subsequent lyophilization. The encapsulates have considerable anticancer effect (with sustained release) in colonogenic assays, with respect to non-encapsulated curcumin. Another study has also used the same coat for encapsulation of curcumin, with PLGA and PEG-5000 as stabilizers. The researchers found enhanced in vitro and in vivo bioavailability of curcumin and increased cellular uptake (Anandharamakrishnan 2014a; Zhu et al. 2014). To improve the functionalities of the core, such as cellular uptake, targeted release and mucoadhesive properties, single or multiple biopolymers have been examined for matrices such as for curcumin (Gou et al. 2011; Suwannateep et al. 2011; Xu et al. 2012; Klippstein et al. 2015).

The solvent displacement method adopted for design of β-carotene encapsulate has reportedly produced smallsized nanoparticles (<80 nm) (Fig. 2), unaltered from coalescence, and ringing (Ribeiro et al. 2008; Paz et al. 2013). The technique has also been employed for encapsulation of astaxanthin (Bhatt et al. 2016) and vitamin E, via membrane contractor technique (Khayata et al. 2012a, b; Hategekimana and Zhong 2015). Authors observed enhanced stability, bioavailability, cellular uptake, and sustained release of the active compound in the said encapsulation technique. The limitation that has been cited is with the use of only organic solvents in the process, disallowing the otherwise spontaneous release of the active compound.



#### Inclusion complexation

Inclusion complexation is another viable method of encapsulation wherein a supramolecular linkage of a ligand and a shell material (a cavity-bearing substrate) is established, with typical entropy-driven hydrophobic effect and van der Waals force or hydrogen bonding (Karoyo and Wilson 2015; Aree and Jongrungruangchok 2016). The approach has been utilized for encapsulation conducted with  $\alpha$  and  $\beta$ -cyclodextrin (structure illustrated in Fig. 3), with yields of 88% and 74%, respectively, (Hădărugă et al. 2006), while an encapsulation efficiency of 99.5% and stability of 4 months (in suspension form) was achieved when usnic acid was encapsulated in  $\beta$ -cyclodextrin (Lira et al. 2009). In fact, compared to encapsulation of the same core in usnic acid liposome, a prolonged release from the encapsulates in inclusion complexation technique was observed (Lira et al. 2009). Similarly, the encapsulation of docohexanoic acid in  $\beta$ -lactoglobulin (with low methoxy pectin) provide 80% improved shelf stability to the core vis-à-vis when free (Zimet and Livney 2009; Ron et al. 2010). Few researchers have even proposed  $\beta$ -lactoglobulins and  $\beta$ -cyclodextrin to be the most appropriate coat materials in the process, particularly for volatile bioactives (Zhu et al. 2014; Hosseini et al. 2015; Perez et al. 2015; Rajendiran et al. 2015; Ha et al. 2016).

#### **Encapsulation using supercritical fluid**

Supercritical fluid has intermediate properties between that of liquid and gas and has unique characteristics such as liquid-like density, gas-like viscosity, higher penetrability, and higher solubility than a gas, and is suitable for encapsulation of thermolabile compounds (Dutta 2017; Kaga et al. 2018). Common supercritical fluids include carbon dioxide, propane, nitrogen, and water, with carbon dioxide being the most popular. For encapsulation, the mixture of active compound and the coat (such as a polymer) is exposed to supercritical fluid and subsequently allowed to expand, through a nozzle (throttling), resulting in entrapment of the active core, owing to the supercritical phase behavior. The process could be assumed to be principally pressure driven, with scope of modification in encapsulation by altering the temperature (Duarte et al. 2015).

Supercritical carbon dioxide encapsulation has been conducted for hydroxypropyl methyl cellulose phthalate (HPMCP), producing 163-219 nm nanoparticles with improved bioavailability and shelf stability of the core (Jin et al. 2009). Phytonutrients such as curcumin have been encapsulated using supercritical antisolvent technology using polymer polyvinylpyrrolidone in a one precipitation-encapsulation step by Alvaro et al. (Londoño 2018). Another study on phytosterol nanoencapsulation using supercritical fluid revealed a particle size < 500 nm and also the influence of the surfactant type and its concentration on the characteristics of nanoencapsulate (Türk and Lietzow 2004; Delgado-Zamarreño et al. 2016). The process is highly efficient, albeit the high capital investment for the supercritical unit is a limitation (Reverchon et al. 2015).

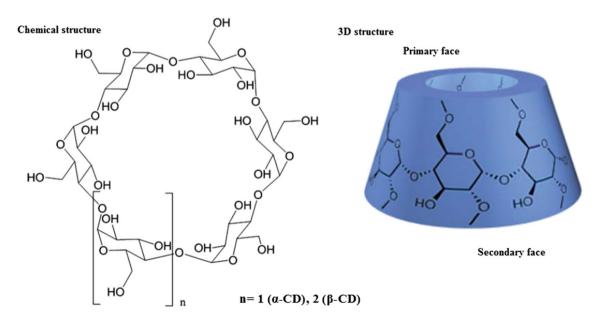


Fig. 3 Structures of cyclodextrins (Zhou and Ritter 2010)

#### Electrospraying and electrospinning

Electrospraying and electrospinning techniques are particularly favored for food and pharmaceutical applications, since these processes produce desirable nanosized particles and fibers for targeted applications. The process employs electrohydrodynamic force to break the liquids into fine droplets for encapsulation (Zhu et al. 2014; Ghorani and Tucker 2015; Lim 2015). Importantly, in electrospraying, the polymer is transformed into nanosized particles, while in electrospinning, the polymer is transformed into continuous nanosized polymer threads (Ceylan et al. 2017; Azarian et al. 2018). Process of encapsulation using the process of electrospinning improves the stability and water solubility (Tu and Id; Beliba 2018). In fact, according to Fung (2015), electrospraying is the modified version of electrospinning. Both of these have been explained in the following section.

# Electrospraying

Electrospraying is one of the most favored methods of nanoencapsulation. In this technique, an electric field acts as the driving force for encapsulation. The core mixed with polymer solution passes through a syringe and is acted upon by the voltage applied across the syringe resulting in a jet stream of the low viscosity mixture, now nanoencapsulated, emanating from the syringe as a fine mist. The emanation from syringe is often termed as Taylor cone (Fig. 4), and the process forms a continuous system of encapsulation once initiated (Jaworek and Sobczyk 2008; Lim 2015; Moghaddam et al. 2015b). The encapsulates fall onto oppositely charged surface, with subsequent evaporation of the solvent; yielding miniaturized dry nanoparticles. Their size depends on the solvent flow rate and charge applied (Chen 2007a; Anandharamakrishnan 2014a, chapter 3; Moghaddam et al. 2015b). The quantum of voltage and duration of electrical exposure are critical in this process and govern the characteristics of the product. The applied voltage determines the force required for pushing the solution and making it a continuous process.

Encapsulation of chitosan micro-/nanospheres loaded with ampicillin has been verified by the findings of researchers who optimized the process parameters and recommended 26 g of needle gauge and 7 cm working distance to obtain an efficiency of 80% and zeta potential of 128.2 mV, besides higher stability compared to nonencapsulated counterpart (Arya et al. 2008). In a similar study, docosahexaenoic acid with ultrathin zein has been encapsulated with the product's high shelf stability (Torres-giner et al. 2010). While, for encapsulation of whey

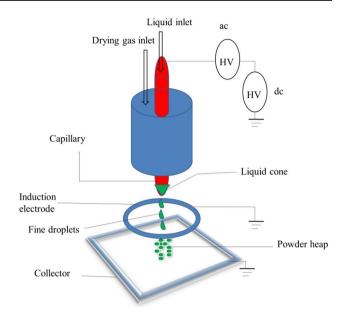


Fig. 4 Depiction of nanoencapsulation by electrospraying (Taylor cone indicated encircled). HV high voltage, ac alternating current, dc direct current

by this method has shown influence on concentration of whey proteins, additional component such as glycerol, and pH too have effects in determining the capsule morphology and size (Sanchez et al. 2009; López-rubio and Lagaron 2012). When curcumin with zein was elctrosprayed, nanoparticles of 175–250 nm were obtained which had 85–90% of the active core, and showed improved dispersibility and shelf stability of the same (Gomez-Estaca et al. 2012, 2015).

#### Electrospinning

Another widely used technique of late is electrospinning, capable of producing nanofibers of size about 100 nm, and is reportedly employed in food, drug, and tissue engineering especially for neural, vasculature, tendon/ligament, and bone (Danie Kingsley et al. 2013a; Jayaraman et al. 2015). Akin to electrospray, this process also involves electrical current for generation of nanoparticles, but at a higher voltage, allowing solidification of the liquid when emanated from the syringe, and subsequent fiber generation of the polymer used for encapsulation. The prime regulators of the process are solute concentration, polymer type, flow rate of solution, nozzle to ground distance, and applied voltage (Chen 2007a; Anandharamakrishnan 2014b; Moghaddam et al. 2015c). The effects of process parameters and characteristics of the solution are presented in Table 1.

In this technique, mainly the fiber holds the core within, and therefore, it is critical to determine the stability and release characteristics of the core. Besides, the conventional

Table	Table 1 Dependence of fiber morphology on different process parameters and solution characteristics	leters and solution characteristics	
S. no.	Process parameters	Fiber morphology	References
Basis:	Basis: process parameters		
1	At constant electric potential, flow rate, and concentration	Fiber diameter is inversely proportional to screen distance (cm)	Chen (2007b), Sill and von Recum (2008), Danie Kingsley et al. (2013a, b), Anandharamakrishnan (2014c), Jayaraman
7	At constant flow rate, screen distance, and concentration	Fiber diameter is inversely proportional to electric potential (kV)	et al. (2015) and Moghaddam et al. (2015a, b)
ŝ	At constant electric potential and screen distance and concentration	Fiber diameter is directly proportional to flow rate (mL/h)	
4	At constant electric potential and screen distance and flow rate	Fiber diameter is directly proportional to the concentration (wt $\%$ )	
5	Increase in applied voltage	Fiber diameter increases initially and then decreases	Chen (2007a, b), Sill and von Recum (2008), Danie Kingsley
9	Increase in flow rate	Fiber diameter increases <i>Note:</i> beaded morphologies occur if the flow rate is too high	et al. (2013a, b), Anandharamakrishnan (2014a, b, c), Jayaraman et al. (2015) and Moghaddam et al. (2015a, b)
L	Increase in distance between capillary and collector	Fiber diameter increases <i>Note</i> : beaded morphologies occur if the distance between the capillary and collector is too short	
×	Addition of cartenoids (tomato peel extract)	Fiber diameter and conductivity increased with homog- enously distributed carotenoids.	Tu and Id
Basis:	Basis: solution characteristics		
1	Polymer concentration	Directly proportional to viscosity and surface tension	Chen (2007a, b), Sill and von Recum (2008), Danie Kingsley
7	Solvent volatility	Influences solvent evaporation between the tip and collector	et al. (2013a, b), Anandharamakrishnan (2014a, b, c),
б	Solvent volatility	Influences phase separation during the flight of the solvent	Jayaraman et al. (2015) and Mognaddam et al. (2015a, b)
4	Solution conductivity	Directly affects the tensile strength of the fiber produced	
5	Increase in polymer viscosity or concentration	Fiber diameter increases	Chen (2007a, b), Sill and von Recum (2008), Danie Kingsley
9	Increase in solution conductivity	Fiber diameter decreases	et al. $(2013a, b)$ , Anandharamakrishnan $(2014a, b, c)$ ,
2	Solvent volatility	Fibers exhibit microtexture, i.e., pores on their surfaces, which increase the surface area	Jayaraman et al. (2013) and Mognaudam et al. (2013a, D)

electrospinning, two-phase electrospinning has also been found to be effective for encapsulation of bioactives. In this method, the aqueous solution of the core bioactive is mixed with an organic-polymer solution and subjected to electrospinning, forming nanoencapsulates within the polymer fiber. This approach has been effective in encapsulation of growth factors, hormones, cytochrome C and proteins in a biocompatible polymer (Dong et al. 2009). Bovine serum albumin has also been electrospun into biodegradable PCL by coaxial electrospinning for medical applications (Zhang et al. 2006). Encapsulation of bovine serum albumin and fluorescent-labeled epidermal growth factor was too conducted into the same coat prepared from poly(lactic-co-glycolic acid) and tecophilic polyurethane (Chen et al. 2009). Ultrathin PVA electrofibers (<150 nm droplet size) have also displayed higher protection to bifidobacteria, with regard to bacterial concentration and a concomitant higher shelf life, when electrospun (Sanchez et al. 2009; Lópezrubio and Lagaron 2012).

Notably, electrospun curcumin in zein (310 nm) has shown enhanced antioxidant activity, entrapment efficiency and sustained release of the bioactive (Brahatheeswaran et al. 2012). Improved stability of curcumin in cellulose acetate nanofibers (314-340 nm) has also been demonstrated throughout the 4-month study (Suwantong et al. 2007, 2008, 2010; Suwannateep et al. 2011). In another work, researchers reportedly utilized electrospinning and formulated nanoencapsulated curcumin loaded in β-cyclodextrin and PVA (250-350 nm) by inclusion complexation. Interestingly, PVA/complex fibers showed comparatively faster release than PVA/curcumin (Sun et al. 2013b). Parallely, β-carotene in ultrafine fibers of zein prolamine was exposed to encapsulation, and the encapsulate (1.140 mm) had improved thermal and luminous stability (Fernandez et al. 2009). In fact, vanillin/cyclodextrin inclusion complex in PVA (nanoparticles of 120-230 nm) provided significant stability to vanillin than when free (Kayaci and Uyar 2012; Kayaci et al. 2013).

#### Nanoencapsulation and drying techniques

In order to have the flexibility of application, storage, shipment, and easy dispersion in aqueous medium of encapsulates, drying is preferable. Among the techniques available, freeze drying and spray drying are mostly applied.

## **Freeze drying**

Freeze drying or lyophilization is a method of evaporation of moisture from the frozen substrate by sublimation of moisture from the same. The process is favorably suited for thermolabile compounds and is preferred over dehydration (Rey and May 2004; Anandharamakrishnan 2014a; Ishwarya 2014). The four main steps in freeze drying are freezing, primary drying, secondary drying, and final treatments.

Curcumin has been subjected to emulsion-diffusion-evaporation technique, along with lyophilization, to form nanoparticles (264 nm) with 77% efficiency, 15% active compound loading, achieving a stability of 3 months, and a nine times higher bioavailability (Shaikh et al. 2009). Similar constructive effects of the said technique have also been reported for curcumin-loaded O-carboxymethyl chitosan nanoparticles which have shown controlled and sustained release of curcumin from the nanocapsules. These nanoparticles also exhibited enzyme-triggered degradation and release in the presence of lysozyme; having a toxic behavior against cancer cell lines (Anitha et al. 2011a, b, 2012, 2017). In another study, curcumin has been entrapped in chitosan-gpoly(N-vinylcaprolactam), by ionic cross-linking using tripolyphosphate and freeze drying, and the encapsulates have shown anticancer activity on cell lines (Anitha et al. 2011a, 2012; Rejinold et al. 2011). Volatile bioactives such as fish oil (Bejrapha et al. 2010; Choi et al. 2010), capsicum oleoresin (Quintanar-Guerrero et al. 1998; Surassmo et al. 2010, 2011; Bejrapha et al. 2011; Hebbalalu et al. 2013), miglyol 829 oil (Abdelwahed et al. 2006; Roca and Cited 2006; Sun et al. 2013a; Frank et al. 2015; Zhang et al. 2016b) (+)-catechin and (-)-epigallocatechin gallate (EGCG) (Dube et al. 2010; Gadkari and Balaraman 2015), tocopherol (Luo et al. 2012; Hosseini et al. 2013), have also been encapsulated by the said technique. However, lyophilization is energy and time incentive and requires usage of cryo-protectants (such as sucrose, trehalose) to prevent aggregation of the dried substrate (Clark and Doona 2015; Ezhilarasi et al. 2013; Anandharamakrishnan 2014b) adding to the cost.

#### Spray drying

Spray drying is a versatile and widely applied drying technique for food and pharmaceuticals, wherein the feed (solution of core and coat) is fed to the drier, exposed to hot air at regulated inlet air temperature and sprayed from an atomizer, producing a fine mist of the feed, resulting in generation of encapsulates when dried (Jafari et al. 2008) (Fig. 5). This requires less time and energy, (compared with lyophilization) thus produces microparticles (Bayu et al. 2011; Murugesan and Orsat 2012). Choice of wall materials include maltodextrin, gum acacia, modified starch, polysaccharides (alginate, carboxymethylcellulose, guar gum), and proteins (whey proteins, soy proteins, and sodium caseinate), to name a few (Dutta and Bhattacharjee 2016; Ghosh et al. 2017; Singh et al. 2018). Mechanism of this technique is discussed in Fig. 6.

Nanoencapsulation has also been attempted by the said technique lately, wherein nanoemulsions are subjected to spray drying (Kyriakoudi and Tsimidou 2018). Authors

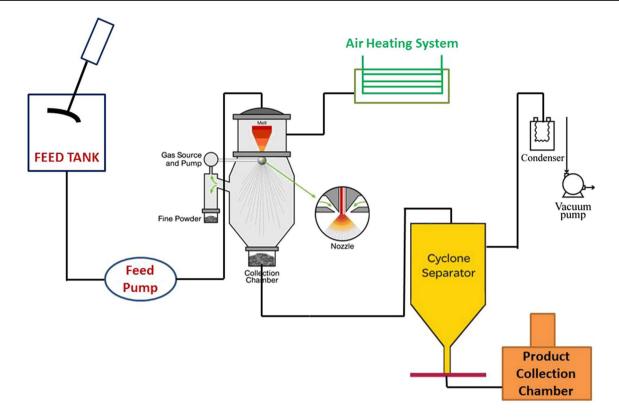
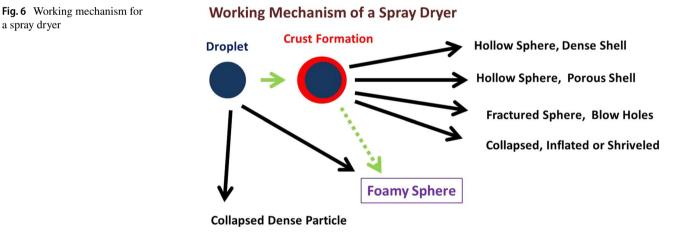


Fig. 5 Steps of spray-drying process. (1) Atomization, (2) spray-hot air contact, (3) evaporation of moisture, (4) product separation Adopted with permission from: Clark and Doona (2015) and Anandharamakrishnan and Ishwarya (2015)



have reported suitability of modified starch (Hi-Cap) and whey protein for nanoentrapment of various bioactives (Taylor et al. 2007; Jafari et al. 2008, 2016; Mahdi et al. 2008). Apart from all, a compiled review about all omega-3-fatty acid-rich oil by spray drying for encapsulation has been studied and elaborately reported by Chang et al. (Nickerson 2018). Also, research has revealed catechin nanoparticles (80 nm diameter) being formed by spray drying in a carbohydrate coat matrix, rendering enhanced bioavailability and stability to the core material (Ferreira

a spray dryer

et al. 2007; Majeed et al. 2015). Duet of emulsification evaporation and spray drying has also been explored by the said authors for encapsulation of  $\beta$ -carotene in n-octenyl succinate starch, forming encapsulates with particle size of 300-600 nm having about 90% entrapment efficiency. Pharmaceutical drugs are encapsulated using spray-drying technique for better stability, penetrating efficiency without any structural change of the molecule, as reported by Cordin et al. (Arpagaus et al. 2018).

#### Conclusion

Nanoencapsulation has played a key role in determining the path for the advancement of administration of bioactives including therapeutic supplements in food, pharma, and allied fields, during recent times. The approach particularly benefits from the nanoscale size of the particles which can penetrate the target sites, be in the case of drugs, nutraceuticals or generic food and therapeutic supplements. The research conducted so far has been overwhelming and the opinion is that in near future more avenues of versatile applications of nanoparticles with specific objectives would be explored, which aids utilization of the potential of the bioactives to their best. Future researchers are advised to focus more on effective entrapment and release of the bioactives, which are otherwise difficult to work with, owing to their unstable nature.

# References

- Abdelwahed W, Degobert G, Fessi H (2006) Pharmaceutical nanotechnology a pilot study of freeze drying of poly(epsilon-caprolactone) nanocapsules stabilized by poly(vinyl alcohol): formulation and process optimization. Int J Pharm 309:178–188. https://doi.org/10.1016/j.ijpharm.2005.10.003
- Akl MA, Kartal-Hodzic A, Oksanen T et al (2016) Factorial design formulation optimization and in vitro characterization of curcumin-loaded PLGA nanoparticles for colon delivery. J Drug Deliv Sci Technol 32:10–20. https://doi.org/10.1016/j.jddst .2016.01.007
- Anandharamakrishnan C (2014a) Techniques for nanoencapsulation of food ingredients. Springer, New York
- Anandharamakrishnan C (2014b) Techniques for nanoencapsulation of food ingredients. In: Techniques for nanoencapsulation of food ingredients, pp 43–49. https://doi. org/10.1007/978-1-4614-9387-7
- Anandharamakrishnan C (2014c) Electrospraying and electrospinning techniques for nanoencapsulation. In: Techniques for nanoencapsulation of food ingredients. Springer, pp 43–49
- Anandharamakrishnan C, Ishwarya P (2015) Spray drying technique for food ingredient encapsulation, 1st edn. IFT Press, London
- Anarjan N, Mirhosseini H, Baharin BS, Tan CP (2011) Effect of processing conditions on physicochemical properties of sodium caseinate-stabilized astaxanthin nanodispersions. LWT Food Sci Technol 44:1658–1665. https://doi.org/10.1016/j. lwt.2011.01.013
- Anitha A, Deepagan VG, Rani VVD et al (2011a) Preparation, characterization, in vitro drug release and biological studies of curcumin loaded dextran sulphate-chitosan nanoparticles. Carbohydr Polym 84:1158–1164. https://doi.org/10.1016/j.carbp ol.2011.01.005
- Anitha A, Maya S, Deepa N et al (2011b) Efficient water soluble O -carboxymethyl chitosan nanocarrier for the delivery of curcumin to cancer cells. Carbohydr Polym 83:452–461. https:// doi.org/10.1016/j.carbpol.2010.08.008
- Anitha A, Rejinold NS, Bumgardner JD et al (2012) Approaches for functional modification or cross-linking of chitosan. https:// doi.org/10.1002/9781119962977.ch7

- Anitha A, Maya S, Deepa N et al (2017) Curcumin-loaded N,Ocarboxymethyl chitosan nanoparticles for cancer drug delivery. J Biomater Sci Polym Ed 23:1381–1400. https://doi. org/10.1163/092050611x581534
- Aree T, Jongrungruangchok S (2016) Crystallographic evidence for β-cyclodextrin inclusion complexation facilitating the improvement of antioxidant activity of tea (+)-catechin and (–)-epicatechin. Carbohydr Polym 140:362–373
- Arpagaus C, Collenberg A, Rütti D et al (2018) Nano spray drying for encapsulation of pharmaceuticals. Int J Pharm 546:194– 214. https://doi.org/10.1016/j.ijpharm.2018.05.037
- Arya N, Chakraborty S, Dube N, Katti DS (2008) Electrospraying: a facile technique for synthesis of chitosan-based micro/ nanospheres for drug delivery applications. J Biomed Mater Res Part B, Appl Biomater 88:17–31. https://doi.org/10.1002/ jbm.b.31085
- Azarian MH, Ahmad W, Mahmood K et al (2018) Nanoencapsulation of intercalated montmorillonite-urea within PVA nanofibers: hydrogel fertilizer nanocomposite. J Appl Polym Sci 45957:1– 10. https://doi.org/10.1002/app.45957
- Bacinello D, Garanger E, Taton D et al (2015) Tailored drugrelease from multi-functional polymer-peptide hybrid vesicles. Eur Polym J 62:363–373. https://doi.org/10.1016/j.eurpo lymj.2014.09.001
- Bayu A, Nandiyanto D, Okuyama K (2011) Progress in developing spray-drying methods for the production of controlled morphology particles: from the nanometer to submicrometer size ranges. Adv Powd Technol 22:1–19. https://doi.org/10.1016/j. apt.2010.09.011
- Bejrapha P, Min S-G, Surassmo S, Choi M-J (2010) Physicothermal properties of freeze-dried fish oil nanocapsules frozen under different conditions. Dry Technol 28:481–489. https://doi. org/10.1080/07373931003613684
- Bejrapha P, Surassmo S, Choi M-J et al (2011) Studies on the role of gelatin as a cryo-and lyo-protectant in the stability of capsicum oleoresin nanocapsules in gelatin matrix. J Food Eng 105:320–331
- Beliba KB (2018) Nanoencapsulation by electrospinning to improve stability and water solubility of carotenoids extracted from tomato peels. Food Chem 268:86–93. https://doi.org/10.1016/j. foodchem.2018.06.017
- Bhatt PC, Srivastava P, Pandey P et al (2016) Nose to brain delivery of astaxanthin-loaded solid lipid nanoparticles: fabrication, radio labeling, optimization and biological studies. RSC Adv 6:10001–10010. https://doi.org/10.1039/C5RA19113K
- Brahatheeswaran D, Mathew A, Aswathy RG et al (2012) Hybrid fluorescent curcumin loaded zein electrospun nanofibrous scaffold for biomedical applications. Biomed Mater 7:45001. https://doi. org/10.1088/1748-6041/7/4/045001
- Campardelli R, Reverchon E (2015) α-Tocopherol nanosuspensions produced using a supercritical assisted process. J Food Eng 149:131–136. https://doi.org/10.1016/j.jfoodeng.2014.10.015
- Cauteruccio S, Bartoli C, Carrara C et al (2015) A nanostructured PLGA system for cell delivery of a tetrathiahelicene as a model for helical DNA intercalators. ChemPlusChem 80:490–493
- Cavallaro G, Craparo EF, Sardo C et al (2015) PHEA–PLA biocompatible nanoparticles by technique of solvent evaporation from multiple emulsions. Int J Pharm 495:719–727. https://doi. org/10.1016/j.ijpharm.2015.09.050
- Ceylan Z, Sengor GFU, Yilmaz MT (2017) Nanoencapsulation of liquid smoke/thymol combination in chitosan nanofibers to delay microbiological spoilage of sea bass (*Dicentrarchus labrax*) fillets. J Food Eng 229:43–49. https://doi.org/10.1016/j.jfood eng.2017.11.038
- Chen M (2007a) Development and parametric studies of carbon nanotube dispersion using electrospraying. Theses

- Chen M-J (2007b) Development and parametric studies of carbon nanotube dispersion using electrospraying
- Chen J, Dong X, Zhao J, Tang G (2009) In vivo acute toxicity of titanium dioxide nanoparticles to mice after intraperitioneal injection. J Appl Toxicol 29:330–337. https://doi.org/10.1002/jat.1414
- Cheong JN, Tan CP, Man YBC, Misran M (2008) α-Tocopherol nanodispersions: preparation, characterization and stability evaluation. J Food Eng 89:204–209. https://doi.org/10.1016/j.jfood eng.2008.04.018
- Choi MJ, Ruktanonchai U, Min SG et al (2010) Physical characteristics of fi sh oil encapsulated by β-cyclodextrin using an aggregation method or polycaprolactone using an emulsion-diffusion method. Food Chem 119:1694–1703. https://doi.org/10.1016/j. foodchem.2009.09.052
- Clark JP, Doona CJ (2015) (Institute of Food Technologists Series) Anandharamakrishnan C, Ishwarya, S (2015) Padma-spray drying techniques for food ingredient encapsulation. Wiley-Blackwell, Hoboken
- Danie Kingsley J, Ranjan S, Dasgupta N, Saha P (2013a) Nanotechnology for tissue engineering: need, techniques and applications. J Pharm Res 7:200–204. https://doi.org/10.1016/j.jopr.2013.02.021
- Danie Kingsley J, Ranjan S, Dasgupta N, Saha P (2013b) Nanotechnology for tissue engineering: need, techniques and applications. J Pharm Res 7:200–204. https://doi.org/10.1016/j.jopr.2013.02.021
- Dasgupta N, Ranjan S (2018) Food engineering for developing foodgrade nanoemulsions. In: An introduction to food grade nanoemulsions. Springer, pp 83–103
- Paz E De, Pressure H, Group P (2013) Production of water-soluble  $\beta$ -carotene formulations by high pressure processes, pp 1–6
- Delgado-Zamarreño MM, Fernández-Prieto C, Bustamante-Rangel M, Pérez-Martín L (2016) Determination of tocopherols and sitosterols in seeds and nuts by QuEChERS-liquid chromatography. Food Chem 192:825–830. https://doi.org/10.1016/j.foodc hem.2015.07.083
- Dong B, Smith ME, Wnek GE (2009) Encapsulation of multiple biological compounds within a single electrospun fiber. Small 5:1508–1512. https://doi.org/10.1002/smll.200801750
- Duarte JL, Rafael J, Amado R (2015) Evaluation of larvicidal activity of a nanoemulsion of *Rosmarinus officinalis* essential oil. Rev Bras Farmacogn 25(2):189–192. https://doi.org/10.1016/j. bjp.2015.02.010
- Dube A, Ng K, Nicolazzo JA, Larson I (2010) Effective use of reducing agents and nanoparticle encapsulation in stabilizing catechins in alkaline solution. Food Chem 122:662–667. https://doi. org/10.1016/j.foodchem.2010.03.027
- Dutta S (2017) Enzyme-assisted supercritical carbon dioxide extraction of active principles of black pepper and small cardamom and applications of the extracts for design of nutraceutical foods and supplements. Jadavpur University, Kolkata
- Dutta S, Bhattacharjee P (2016) Microencapsulation of enzymeassisted supercritical carbon dioxide extract of small cardamom by spray drying. J Food Meas Charact 11:310–319. https://doi. org/10.1007/s11694-016-9398-9
- Eisner M (2015) In the Labyrinth of the Library: Petrarch's Cicero, Dante's Virgil, and the historiography of the renaissance. Renaiss Q 67:755–790. https://doi.org/10.1086/678774
- Ezhilarasi PN, Karthik P, Chhanwal N, Anandharamakrishnan C (2013) Nanoencapsulation techniques for food bioactive components: a review. Food Bioprocess Technol 6:628–647. https://doi. org/10.1007/s11947-012-0944-0
- Fathi M, Donsi F, McClements DJ (2018) Protein-based delivery systems for the nanoencapsulation of food ingredients. Compr Rev Food Sci Food Saf 17:1–17. https://doi.org/10.1111/1541-4337.12360
- Feng J, Yang G, Zhang S et al (2018) Fabrication and characterization of β-cypermethrin-loaded PLA microcapsules prepared

by emulsion-solvent evaporation: loading and release properties. Environ Sci Pollut Res 25(4):13525–13535. https://doi. org/10.1007/s11356-018-1557-6

- Fernandez A, Torres-Giner S, Lagaron JM (2009) Novel route to stabilization of bioactive antioxidants by encapsulation in electrospun fibers of zein prolamine. Food Hydrocolloids 23:1427–1432. https://doi.org/10.1016/j.foodhyd.2008.10.011
- Ferreira I, Rocha S, Coelho M (2007) Encapsulation of antioxidants by spray-drying. Chem Eng Trans 11:713–717
- Fornaguera C, Dols-Perez A, Caldero G et al (2015) PLGA nanoparticles prepared by nano-emulsion templating using low-energy methods as efficient nanocarriers for drug delivery across the blood-brain barrier. J Controlled Release 211:134–143. https:// doi.org/10.1016/j.jconrel.2015.06.002
- Frank LA, Contri RV, Beck RCR et al (2015) Improving drug biological effects by encapsulation into polymeric nanocapsules. Wiley Interdiscip Rev Nanomed Nanobiotechnol 7:623–639
- Fun W, Che YB, Ming O et al (2011) Effect of sucrose fatty acid esters on the particle characteristics and flow properties of phytosterol nanodispersions. J Food Eng 104:63–69. https://doi. org/10.1016/j.jfoodeng.2010.11.028
- Fung WY (2015) Electrospinning and electrospraying: production of nanofibers and microparticles for nutraceutical/pharmaceutical applications. Universiti Sains Malaysia
- Gadkari PV, Balaraman M (2015) Catechins: sources, extraction and encapsulation: A review. Food Bioprod Process 93:122–138. https://doi.org/10.1016/j.fbp.2013.12.004
- Ghaderi S, Ghanbarzadeh S, Mohammadhassani Z, Hamishehkar H (2014) Formulation of gammaoryzanol-loaded nanoparticles for potential application in fortifying food products. Adv Pharm Bull 4:549–554. https://doi.org/10.5681/apb.2014.081
- Ghorani B, Tucker N (2015) Fundamentals of electrospinning as a novel delivery vehicle for bioactive compounds in food nanotechnology. Food Hydrocolloids 51:227–240. https://doi. org/10.1016/j.foodhyd.2015.05.024
- Ghosh PK, Bhattacharjee P, Das S (2017) Microencapsulation of supercritical carbon dioxide extract of tuberose flowers (*Polian-thes Tuberosa* Linn.): process optimization and stability studies. World J Pharm Pharm Sci 6:1014–1045. https://doi.org/10.20959 /wjpps20171-8365
- Gomez-Estaca J, Balaguer MP, Gavara R, Hernandez-Munoz P (2012) Formation of zein nanoparticles by electrohydrodynamic atomization: effect of the main processing variables and suitability for encapsulating the food coloring and active ingredient curcumin. Food Hydrocolloids 28:82–91. https://doi.org/10.1016/j.foodh yd.2011.11.013
- Gómez-Estaca J, Gavara R, Hernández-Muñoz P (2015) Encapsulation of curcumin in electrosprayed gelatin microspheres enhances its bioaccessibility and widens its uses in food applications. Innov Food Sci Emerg Technol 29:302–307. https://doi.org/10.1016/j. ifset.2015.03.004
- Gou M, Men K, Shi H et al (2011) Curcumin-loaded biodegradable polymeric micelles for colon cancer therapy in vitro and in vivo. Nanoscale 3:1558–1567. https://doi.org/10.1039/c0nr00758g
- Ha H-K, Jeon N-E, Kim JW et al (2016) Physicochemical characterization and potential prebiotic effect of whey protein isolate/inulin nano complex. Korean J Food Sci Anim Resour 36:267
- Hădărugă NG, Hădărugă DI, Păunescu V et al (2006) Thermal stability of the linoleic acid/ $\alpha$ - and  $\beta$ -cyclodextrin complexes. Food Chem 99:500–508
- Hategekimana J, Zhong F (2015) Degradation of vitamin E in nanoemulsions during storage as affected by temperature, light and darkness. Int J Food Eng 11:199–206. https://doi.org/10.1515/ ijfe-2014-0256
- Hebbalalu D, Lalley J, Nadagouda MN, Varma RS (2013) Greener techniques for the synthesis of silver nanoparticles using plant

extracts, enzymes, bacteria, biodegradable polymers, and microwaves. ACS Sustain Chem Eng 1:703–712

- Hélder DS, Cerqueira MA, Souza BWS et al (2011) Nanoemulsions of β-carotene using a high-energy emulsification–evaporation technique. J Food Eng 102:130–135. https://doi.org/10.1016/j. jfoodeng.2010.08.005
- Hosseini SF, Zandi M, Rezaei M, Farahmandghavi F (2013) Two-step method for encapsulation of oregano essential oil in chitosan nanoparticles: preparation, characterization and in vitro release study. Carbohydr Polym 95:50–56. https://doi.org/10.1016/j. carbpol.2013.02.031
- Hosseini SMH, Emam-Djomeh Z, Sabatino P, Van der Meeren P (2015) Nanocomplexes arising from protein-polysaccharide electrostatic interaction as a promising carrier for nutraceutical compounds. Food Hydrocolloids 50:16–26. https://doi.org/10.1016/j.foodh yd.2015.04.006
- Iqbal K, Sun D (2018) Synthesis of nanoencapsulated Glauber's salt using PMMA shell and its application on cotton for thermoregulating effect. Cellulose 25:2103–2113. https://doi.org/10.1007/ s10570-018-1692-8
- Ishwarya SP (2014) Spray-freeze-drying: a novel process for the drying of foods and bioproducts. Trends Food Sci Technol 41:161–181. https://doi.org/10.1016/j.tifs.2014.10.008
- Jafari SM, Assadpoor E, He Y, Bhandari B (2008) Encapsulation efficiency of food flavours and oils during spray drying. Dry Technol 26:816–835. https://doi.org/10.1080/07373930802135972
- Jafari M, Akhavan P, Rezaee Nour J (2016) An application of factor analysis for change resolution: the preliminaries of knowledge management establishment. Int J Knowl Cult Change Manag Annu Rev 7:89–102. https://doi.org/10.18848/1447-9524/cgp/ v07i05/50366
- Jaworek A, Sobczyk AT (2008) Electrospraying route to nanotechnology: an overview. J Electrostat 66:197–219. https://doi. org/10.1016/j.elstat.2007.10.001
- Jayaraman P, Gandhimathi C, Venugopal JR et al (2015) Controlled release of drugs in electrosprayed nanoparticles for bone tissue engineering. Adv Drug Deliv Rev 94:77–95
- Jin H, Xia F, Jiang C et al (2009) Nanoencapsulation of lutein with hydroxypropylmethyl cellulose phthalate by supercritical antisolvent. Chin J Chem Eng 17:672–677. https://doi.org/10.1016/ S1004-9541(08)60262-1
- Kaga K, Honda M, Adachi T et al (2018) Nanoparticle formation of PVP/astaxanthin inclusion complex by solution-enhanced dispersion by supercritical fluids (SEDS): effect of PVP and astaxanthin Z-isomer content. J Supercrit Fluids 136:44–51. https://doi. org/10.1016/j.supflu.2018.02.008
- Karoyo A, Wilson L (2015) Nano-sized cyclodextrin-based molecularly imprinted polymer adsorbents for perfluorinated compounds—a mini-review. Nanomaterials 5:981–1003. https://doi.org/10.3390/ nano5020981
- Kayaci F, Ertas Y (2013) Uyar T (2013) Enhanced thermal stability of eugenol by cyclodextrin inclusion complex encapsulated in electrospun polymeric nanofibers. J Agric Food Chem 61(34):8156–8165
- Kayaci F, Uyar T (2012) Encapsulation of vanillin/cyclodextrin inclusion complex in electrospun polyvinyl alcohol (PVA) nanowebs: prolonged shelf-life and high temperature stability of vanillin. Food Chem 133:641–649. https://doi.org/10.1016/j.foodc hem.2012.01.040
- Khalil NM, do Nascimento TCF, Casa DM et al (2013) Pharmacokinetics of curcumin-loaded PLGA and PLGA-PEG blend nanoparticles after oral administration in rats. Colloids Surf, B 101:353– 360. https://doi.org/10.1016/j.colsurfb.2012.06.024
- Khayata N, Abdelwahed W, Chehna MF et al (2012a) Stability study and lyophilization of vitamin E-loaded nanocapsules prepared

by membrane contactor. Int J Pharm 439:254–259. https://doi. org/10.1016/j.ijpharm.2012.09.032

- Khayata N, Abdelwahed W, Chehna MF et al (2012b) Preparation of vitamin E loaded nanocapsules by the nanoprecipitation method: from laboratory scale to large scale using a membrane contactor. Int J Pharm 423:419–427. https://doi.org/10.1016/j.ijpha rm.2011.12.016
- Klippstein R, Wang JTW, El-Gogary RI et al (2015) Passively targeted curcumin-loaded PEGylated PLGA nanocapsules for colon cancer therapy in vivo. Small 11:4704–4722. https://doi. org/10.1002/smll.201403799
- Kumari A, Kumar S, Pakade YB et al (2010) Development of biodegradable nanoparticles for delivery of quercetin. Colloids Surf B Biointerfaces 80:184–192. https://doi.org/10.1016/j.colsu rfb.2010.06.002
- Kumari A, Kumar S, Pakade YB et al (2011) Nanoencapsulation and characterization of *Albizia chinensis* isolated antioxidant quercitrin on PLA nanoparticles. Colloids Surf B Biointerfaces 82:224–232. https://doi.org/10.1016/j.colsurfb.2010.08.046
- Kyriakoudi A, Tsimidou MZ (2018) Properties of encapsulated saffron extracts in maltodextrin using the Büchi B-90 nano spraydryer. Food Chem 266:458–465. https://doi.org/10.1016/j.foodc hem.2018.06.038
- Li H, Yan K, Shang Y et al (2015a) Folate-bovine serum albumin functionalized polymeric micelles loaded with superparamagnetic iron oxide nanoparticles for tumor targeting and magnetic resonance imaging. Acta Biomater 15:117–126
- Li J, Lee IW, Shin GH et al (2015b) Curcumin-Eudragit<sup>®</sup> e PO solid dispersion: a simple and potent method to solve the problems of curcumin. Eur J Pharm Biopharm 94:322–332. https://doi. org/10.1016/j.ejpb.2015.06.002
- Lim L-T (2015) Encapsulation of bioactive compounds using electrospinning and electrospraying technologies. In: Nanotechnology and functional foods, pp 297–317
- Lira MCB, Ferraz MS, da Silva DGVC et al (2009) Inclusion complex of usnic acid with β-cyclodextrin: characterization and nanoencapsulation into liposomes. J Incl Phenom Macrocycl Chem 64:215–224. https://doi.org/10.1007/s10847-009-9554-5
- Lomova MV, Brichkina AI, Kiryukhin MV et al (2015) Multilayer capsules of bovine serum albumin and tannic acid for controlled release by enzymatic degradation. ACS Appl Mater Interfaces 7:11732–11740
- Londoño J (2018) Encapsulation of curcumin using supercritical antisolvent (SAS) technology to improve its stability and solubility in water. Food Chem 258:156–163. https://doi.org/10.1016/j.foodc hem.2018.02.088
- López-rubio A, Lagaron JM (2012) Whey protein capsules obtained through electrospraying for the encapsulation of bioactives. Innov Food Sci Emerg Technol 13:200–206. https://doi.org/10.1016/j. ifset.2011.10.012
- Luo Y, Teng Z, Wang Q (2012) Development of zein nanoparticles coated with carboxymethyl chitosan for encapsulation and controlled release of vitamin D3. J Agric Food Chem 60:836–843. https://doi.org/10.1021/jf204194z
- Mahalingam M, Krishnamoorthy K (2015) Fabrication and optimization of camptothecin loaded Eudragit S 100 nanoparticles by Taguchi L4 orthogonal array design. Int J Pharm Investig 5:147
- Mahdi S, Assadpoor E, Bhandari B, He Y (2008) Nano-particle encapsulation of fish oil by spray drying. Food Res Int 41:172–183. https://doi.org/10.1016/j.foodres.2007.11.002
- Majeed H, Bian Y, Ali B et al (2015) Essential oil encapsulations: uses, procedures, and trends. RSC Adv 5:58449–58463. https://doi. org/10.1039/C5RA06556A
- Moghaddam MK, Mortazavi SM, Khayamian T (2015a) Preparation of calcium alginate microcapsules containing n-nonadecane

by a melt coaxial electrospray method. J Electrostat 73:56–64. https://doi.org/10.1016/j.elstat.2014.10.013

- Moghaddam MK, Mortazavi SM, Khaymian T (2015b) Micro/nanoencapsulation of a phase change material by coaxial electrospray method. Iran Polym J 24:759–774
- Moghaddam MK, Mortazavi SM, Khaymian T (2015c) Micro/nanoencapsulation of a phase change material by coaxial electrospray method. Iran Polym J (Engl Ed) 24:759–774. https://doi. org/10.1007/s13726-015-0364-x
- Moore S, Kailasapathy K, Phillips M, Jones MR (2015) Development of a viability standard curve for microencapsulated probiotic bacteria using confocal microscopy and image analysis software. J Microbiol Methods 114:16–22. https://doi. org/10.1016/j.mimet.2015.04.002
- Mukerjee A, Vishwanatha JK (2009) Formulation, characterization and evaluation of curcumin-loaded PLGA nanospheres for cancer therapy. Anticancer Res 29:3867–3875
- Murugesan R, Orsat V (2012) Spray drying for the production of nutraceutical ingredients—a review. Food Bioprocess Technol 5:3–14. https://doi.org/10.1007/s11947-011-0638-z
- Nakagawa K, Nagao H (2012) Microencapsulation of oil droplets using freezing-induced gelatin–acacia complex coacervation. Colloids Surf A Physicochem Eng Asp 411:129–139. https:// doi.org/10.1016/j.colsurfa.2012.07.010
- Nickerson CCMT (2018) Encapsulation of omega 3-6-9 fatty acidsrich oils using protein- based emulsions with spray drying. J Food Sci Technol 55:2850–2861. https://doi.org/10.1007/ s13197-018-3257-0
- Pereira MC, Oliveira DA, Hill LE et al (2017) Effect of nanoencapsulation using PLGA on antioxidant and antimicrobial activities of guabiroba fruit phenolic extract. Food Chem 240:396–404. https://doi.org/10.1016/j.foodchem.2017.07.144
- Perez AA, Sponton OE, Andermatten RB et al (2015) Biopolymer nanoparticles designed for polyunsaturated fatty acid vehiculization: protein-polysaccharide ratio study. Food Chem 188:543–550. https://doi.org/10.1016/j.foodchem.2015.05.043
- Prajakta D, Ratnesh J, Chandan K et al (2009) Curcumin loaded pH-sensitive nanoparticles for the treatment of colon cancer. J Biomed Nanotechnol 5:445–455. https://doi.org/10.1166/ jbn.2009.1038
- Quintanar-Guerrero D, Allémann E, Fessi H, Doelker E (1998) Preparation techniques and mechanisms of formation of biodegradable nanoparticles from preformed polymers. Drug Dev Ind Pharm 24:1113–1128. https://doi.org/10.3109/0363904980 9108571
- Rajendiran N, Sankaranarayanan RK, Saravanan J (2015) Nanochain and vesicles formed by inclusion complexation of 4,4'-diaminobenzanilide with cyclodextrins. J Exp Nanosci 10:880–899
- Rathore S, Desai PM, Liew CV et al (2013) Microencapsulation of microbial cells. J Food Eng 116:369–381. https://doi. org/10.1016/j.jfoodeng.2012.12.022
- Rebolleda S, Sanz MT, Benito JM et al (2015) Formulation and characterisation of wheat bran oil-in-water nanoemulsions. Food Chem 167:16–23. https://doi.org/10.1016/j.foodchem.2014.06.097
- Rejinold NS, Muthunarayanan M, Divyarani VV et al (2011) Curcumin-loaded biocompatible thermoresponsive polymeric nanoparticles for cancer drug delivery. J Colloid Interface Sci 360:39–51. https://doi.org/10.1016/j.jcis.2011.04.006
- Reverchon E, Adami R, Campardelli R et al (2015) Supercritical fluids based techniques to process pharmaceutical products difficult to micronize: palmitoylethanolamide. J Supercrit Fluids 102:24–31. https://doi.org/10.1016/j.supflu.2015.04.005
- Rey L, May JC (2004) Freeze drying/lyophilization of pharmaceutical and biological products. https://www.crcpress.com/Freeze-Dryin gLyophilization-of-Pharmaceutical-and-Biological-Products/ Rey/p/book/9781439825754

- Rezaul M, Shishir I, Xie L et al (2018) Food technology and equipment, key laboratory for agro-products postharvest handling. Trends Food Sci Technol 1:2. https://doi.org/10.1016/j.tifs.2018.05.018
- Ribeiro HS, Chu B, Ichikawa S, Nakajima M (2008) Preparation of nanodispersions containing β-carotene by solvent displacement method. Food Hydrocolloids 22:12–17. https://doi.org/10.1016/j. foodhyd.2007.04.009
- Roca SF, Cited R (2006) (12) United States Patent. 2:0–5. https://doi. org/10.1038/incomms1464
- Ron N, Zimet P, Bargarum J, Livney YD (2010) Beta-lactoglobulin e polysaccharide complexes as nanovehicles for hydrophobic nutraceuticals in non-fat foods and clear beverages. Int Dairy J 20:686–693. https://doi.org/10.1016/j.idairyj.2010.04.001
- Sanchez E, Sanz Y, Lagaron JM (2009) Encapsulation of living bifidobacteria in ultrathin PVOH electrospun fibers. Biomacromolecules 10:2823–2829
- Scholz P, Keck CM (2015) Nanoemulsions produced by rotor-stator high speed stirring. Int J Pharm 482:110–117. https://doi. org/10.1016/j.ijpharm.2014.12.040
- Shaikh J, Ankola DD, Beniwal V et al (2009) Nanoparticle encapsulation improves oral bioavailability of curcumin by at least 9-fold when compared to curcumin administered with piperine as absorption enhancer. Eur J Pharm Sci 37:223–230. https://doi. org/10.1016/j.ejps.2009.02.019
- Shchukina EM, Graham M, Zheng Z, Shchukin DG (2018) Nanoencapsulation of phase change materials for advanced thermal energy storage systems. Chem Soc Rev 47:4156–4175. https:// doi.org/10.1039/c8cs00099a
- Sill TJ, von Recum HA (2008) Electrospinning: applications in drug delivery and tissue engineering. Biomaterials 29:1989–2006
- Singh H, Kumar C, Singh N, Paul S, Jain SK (2018) Nanoencapsulation of docosahexaenoic acid (DHA) using a combination of food grade polymeric wall materials and its application for improvement in bioavailability and oxidative stability. Food Funct 9(4):2213–2227. https://doi.org/10.1039/c7fo01391d
- Soukoulis C, Bohn T (2015) A comprehensive overview on the microand nano-technological encapsulation advances for enhancing the chemical stability and bioavailability of encapsulation of carotenoids. Crit Rev Food Sci Nutr 58:37–41. https://doi. org/10.1080/10408398.2014.971353
- Sowasod N, Charinpanitkul T, Tanthapanichakoon W (2008) Nanoencapsulation of curcumin in biodegradable chitosan via multiple emulsion/solvent evaporation. Int J Pharm 347:93–101
- Subrot S, Irshaan P, Sivapratha S, Preetam S (2018) Nanoencapsulation strategies for lipid-soluble vitamins. Chem Pap 73:1–6. https:// doi.org/10.1007/s11696-018-0559-7
- Sun J, Bi C, Man H et al (2013a) Curcumin-loaded solid lipid nanoparticles have prolonged in vitro antitumour activity, cellular uptake and improved in vivo bioavailability. Colloids Surf B Biointerfaces 111:367–375. https://doi.org/10.1016/j.colsu rfb.2013.06.032
- Sun XZ, Williams GR, Hou XX, Zhu LM (2013b) Electrospun curcumin-loaded fibers with potential biomedical applications. Carbohydr Polym 94:147–153. https://doi.org/10.1016/j.carbp ol.2012.12.064
- Surassmo S, Min SG, Bejrapha P, Choi MJ (2010) Effects of surfactants on the physical properties of capsicum oleoresin-loaded nanocapsules formulated through the emulsion-diffusion method. Food Res Int 43:8–17. https://doi.org/10.1016/j.foodres.2009.07.008
- Surassmo S, Min S-G, Bejrapha P, Choi M-J (2011) Efficacy of capsicum oleoresin nanocapsules formulation by the modified emulsion-diffusion method. J Nanosci Nanotechnol 11:642–646. https ://doi.org/10.1166/jnn.2011.3276
- Suwannateep N, Banlunara W, Wanichwecharungruang SP et al (2011) Mucoadhesive curcumin nanospheres: biological activity, adhesion to stomach mucosa and release of curcumin into

- Suwantong O, Opanasopit P, Ruktanonchai U, Supaphol P (2007) Electrospun cellulose acetate fiber mats containing curcumin and release characteristic of the herbal substance. Polymer 48:7546– 7557. https://doi.org/10.1016/j.polymer.2007.11.019
- Suwantong O, Ruktanonchai U, Supaphol P (2008) Electrospun cellulose acetate fiber mats containing asiaticoside or *Centella asiatica* crude extract and the release characteristics of asiaticoside. Polymer 49:4239–4247. https://doi.org/10.1016/j.polym er.2008.07.020
- Suwantong O, Ruktanonchai U, Supaphol P (2010) In vitro biological evaluation of electrospun cellulose acetate fiber mats containing asiaticoside or curcumin. J Biomed Mater Res Part A 94:1216– 1225. https://doi.org/10.1002/jbm.a.32797
- Taylor P, Jafari SM, Jafari SM et al (2007) Encapsulation of nanoparticles of d-limonene by spray drying : role of emulsifiers and emulsifying techniques. Dry Technol Int J 25:1069–1079. https ://doi.org/10.1080/07373930701396758
- Taylor P, Wang JC, Chen SH et al (2008) Synthesis and properties research on the nanocapsulated capsaicin by simple coacervation method synthesis and properties research on the nanocapsulated capsaicin by simple coacervation method. J Dispers Sci Technol 29:37–41. https://doi.org/10.1080/01932690701756651
- Taylor P, Jincheng W, Xiaoyu Z, Sihao C (2010) Preparation and properties of nanocapsulated capsaicin by complex coacervation method. Chem Eng Commun 197:99–933. https://doi. org/10.1080/00986440903249700
- Torres-giner S, Martinez-abad A, Ocio MJ, Lagaron JM (2010) Stabilization of a nutraceutical omega-3 fatty acid by encapsulation in ultrathin electrosprayed zein prolamine. J Food Sci 75:N69–N79. https://doi.org/10.1111/j.1750-3841.2010.01678.x
- Tsai Y, Chien C, Lin L, Tsai T (2011) Curcumin and its nano-formulation: the kinetics of tissue distribution and blood-brain barrier penetration. Int J Pharm 416:331–338. https://doi.org/10.1016/j. ijpharm.2011.06.030
- Tsai Y-M, Chang-Liao W-L, Chien C-F et al (2012) Effects of polymer molecular weight on relative oral bioavailability of curcumin. Int J Nanomed 7:2957–2966. https://doi.org/10.2147/IJN.S32630
- Tu H, Id O This article is protected by copyright. All rights reserved
- Türk M, Lietzow R (2004) Stabilized nanoparticles of phytosterol by rapid expansion from supercritical solution into aqueous solution. Aaps Pharmscitech 5:36–45
- Vuddanda PR, Mishra A, Singh SK, Singh S (2014) Development of polymeric nanoparticles with highly entrapped herbal hydrophilic drug using nanoprecipitation technique: an approach of quality by design. Pharm Dev Technol 20:1–9. https://doi. org/10.3109/10837450.2014.908302
- Wang L, Yang S, Cao J et al (2016a) Microencapsulation of ginger volatile oil based on gelatin/sodium alginate polyelectrolyte complex. Chem Pharm Bull 64:21–26

- Wang Y, Xu S, Xiong W et al (2016b) Nanogels fabricated from bovine serum albumin and chitosan via self-assembly for delivery of anticancer drug. Colloids Surf B Biointerfaces 146:107–113
- Xie X, Tao Q, Zou Y et al (2011) PLGA nanoparticles improve the oral bioavailability of curcumin in rats: characterizations and mechanisms. J Agric Food Chem 59:9280–9289
- Xing F, Cheng G, Yi K, Ma L (2005) Nanoencapsulation of capsaicin by complex coacervation of gelatin, acacia, and tannins. J Appl Polym Sci 96:2225–2229. https://doi.org/10.1002/app.21698
- Xu H, Liu C, Chen C et al (2012) Easy alignment and effective nucleation activity of ramie fibers in injection-molded poly(lactic acid) biocomposites. Biopolymers 97(10):825–839. https://doi. org/10.1002/bip.22079
- Zhang YZ, Wang X, Feng Y et al (2006) Coaxial electrospinning of (fl uorescein isothiocyanate-conjugated bovine serum albumin)encapsulated poly(ε-caprolactone) nanofi bers for sustained release. Biomacromolecules 7:1049–1057
- Zhang H, Wang Z, Liu O (2016a) Simultaneous determination of kolliphor HS15 and miglyol 812 in microemulsion formulation by ultra-high performance liquid chromatography coupled with nano quantity analyte detector. J Pharm Anal 6:11–17
- Zhang H, Wang Z, Liu O (2016b) Simultaneous determination of kolliphor HS15 and miglyol 812 in microemulsion formulation by ultra-high performance liquid chromatography coupled with nano quantity analyte detector. J Pharm Anal 6:11–17. https:// doi.org/10.1016/j.jpha.2015.11.004
- Zhou J, Ritter H (2010) Cyclodextrin functionalized polymers as drug delivery systems. Polym Chem 1:1552–1559. https://doi. org/10.1039/c0py00219d
- Zhu X, Shan W, Zhang P et al (2014) Penetratin derivative-based nanocomplexes for enhanced intestinal insulin delivery. Mol Pharm 11:317–328. https://doi.org/10.1021/mp400493b
- Zimet P, Livney YD (2009) Beta-lactoglobulin and its nanocomplexes with pectin as vehicles for u -3 polyunsaturated fatty acids. Food Hydrocolloids 23:1120–1126. https://doi.org/10.1016/j.foodh yd.2008.10.008
- Zou L, Zhang Z, Zhang R et al (2016) Encapsulation of protein nanoparticles within alginate microparticles: impact of pH and ionic strength on functional performance. J Food Eng 178:81–89. https ://doi.org/10.1016/j.jfoodeng.2016.01.010

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