Chapter 5

Production of food nanomaterials by specialized equipment

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Contents

Keywords

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Abstract

In the past decade, there has been a great interest in using nanotechnology by different industries, including food, pharmaceutical, and beauty. Nanotechnology provides many advantages to produce functional compounds which tend to be delivered for desired properties, such as protection from the environment or food matrix, controlled release, and increased bioavailability and bioaccessibility (Muhammad et al., 2019, Sedaghat Doost et al., 2019b, Sedaghat Doost et al., 2018c). There is a variety of methods to prepare food nanomaterials. Specialized equipment is frequently employed for the production of efficient nano-delivery systems, which is the focus of this chapter; the basic principle of conventional and recent techniques, as well as their advantages and disadvantages are described.

5.1. Introduction

The size of a carrier system in food materials is one of the most vital factors with a powerful contribution to the physicochemical properties of the system. Nanotechnology refers to the production of nanomaterials, i.e. usually possess a particle size between 10 to 1000 nm (Sedaghat Doost et al., 2020). The nano scale size of these materials have the potential to enhance the bioavailability and improve the controlled release due to their small size. Nano-sized delivery systems remain to be considered as one of the most promising technologies. These systems have many advantages due to their small size and changes in their mechanical, electrical, and optical properties. One of the advantages is their increased surface-to-volume ratio, which improves their reactivity and provides an efficient absorption through cells, controlled release and accurate targeting of bioactive compounds (Prakash et al., 2018). The solubility and thermal stability of encapsulated bioactive compounds can also be enhanced and they can be protected against natural and processing effects, including chemical, enzymatic, and physical instability during processing. Moreover, the incorporation of nano-size delivery systems in food applications can improve their sensory attributes, such as texture, flavor retention, coloring strength, and technological properties such as processibility, and stability during shelf-life (Ferreira and Nunes, 2019, Prakash et al., 2018). Different methods have been proposed for the fabrication of food nanomaterials based on two classifications, including top-down and bottom-up methods. Top-down methods are based on the breakage of a systems into smaller size scales, fo instance, through mechanical size reduction input by applying high energy. On the other hand, bottom-up methods require low energy and the process can be controlled by the intrinsic physicochemical properties (Sedaghat Doost et al., 2019b). These include solvent demixing, self-emulsification (spontaneous emulsification) and phase inversion assays. Top-down methods usually need specialized equipment, including high-pressure, ultrasonication, electrospinning, spray drying, and ball milling (Prakash et al., 2018). Most of these methods have been currently scaled up and industrialized. The reproducibility and large scale production are the considerable advantages of the high pressure techniques while vortex fluidic device (VFD) needs lower cost and its environmental friendly technique.However, there are some drawbacks that may limit the utilization and promote the modification of these methoods or the development of a new technique. The preparation technique can indeed exert a considerable influence on the physicochemical stability as well as desired functionality of the produced materials. For instance, despite the fact that the temperature of the mixture during sonication can be controlled to some extent, the chemical degradation can be induced, specially if the mixture contains a volatile compound, because of the high pressure and temperature of the cavitation effect (Salvia-Trujillo et al., 2014). Another drawback of some of these techniques is high energy consumption, which makes it an expensive processing step for industry. Additionaly, the scaling up and infrastructure required for these technqiues are also rather dear. In this chapter, the basic principle of techniques that need specialized equipment for the production of food nanaomaterials are introduced as well as their advantages and disadavantages.

5.2. High-pressure techniques

5.2.1. Microfluidization

Microfluidic processing has been used for the size reduction of emulsions (Bai and McClements, 2016), nano-dispersions, liposomes (Guldiken et al., 2018), and for preparing nanomaterials (Ganesan et al., 2018). Microfluidization can be used as a high-energy approach for the fabrication of nanoemulsions. Basically, a microfluidizer consists of three main constituents, an intensifier pump, an air motor, and an interaction chamber, as shown in Figure 5-1. For emulsification applications, a coarse emulsion is initially prepared by mixing the oil phase and the aqueous phase containing an emulsifier using a high shear mixer. After that, this pre-mix emulsion is fed into an interaction chamber in the microfluidizer by force. Two streams of the coarse emulsion flow at high velocities through channels with small diameter to the direction of an impingement area. The two streams of the pre-mix emulsion bump into each other and generate rigorous turbulent forces, including cavitation, turbulence, and shear, resulting in the size reduction of the oil droplets (Jafari et al., 2007). A significant advantage of microfluidization is the large scale production with higher reproducibility (Ganesan et al., 2018). It has been reported that microfluidization is more efficient and more successful in the fabrication of emulsions with small droplet sizes than other homogenizers, such as high-pressure jet and rotor-stator devices (Silverson) (Perrier-Cornet et al., 2005). In contrast, Alliod et al. (2019) reported that nanoemulsions produced by microfluidization showed a higher chemical degradation of all-trans retinoic acid compared to other emulsification processes, e.g., ultrasound and premix membrane emulsification. Moreover, microfluidized nanoemulsions were unstable at a 4-fold droplet size enhancement under stress conditions.

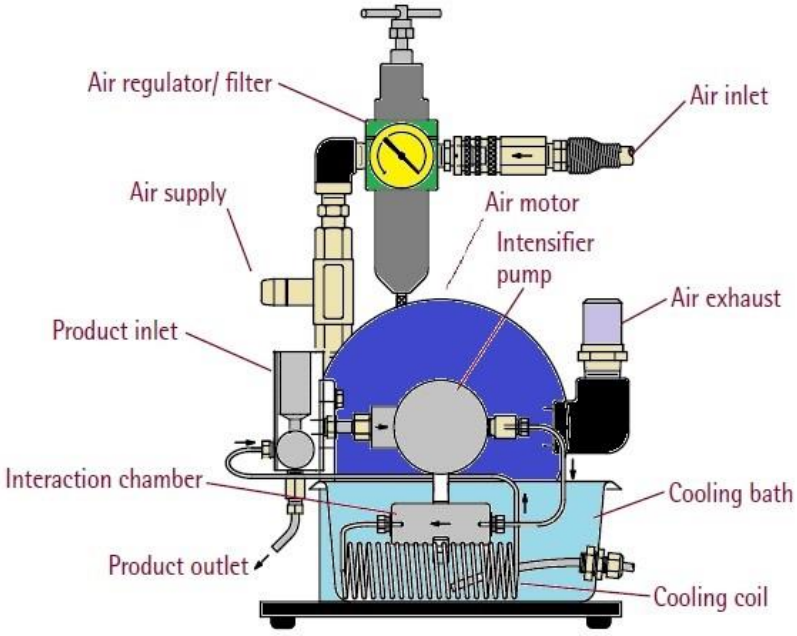

Figure 5-1.Schematic representation of Microfluidizer (redrafted from Microfluidics-M110S manual).

As the coarse emulsions are forced into the microfluidizer through a reservoir with one inlet, conventional microfluidizers are called single-channel devices which have some limitations. One of their limitations is the necessity of a high-shear mixer to fabricate the coarse emulsion which needs extra devices, cost, and time. Furthermore, several cycles of homogenization passes of the coarse emulsion through the chamber are often required. Another limitation of conventional microfluidizers is that due to the requirement of the rinsing before the main preparation, some extent of the pre-mix emulsion is wasted; hence, decreasing the yield. Moreover, the content of the used oil is limited since increasing the oil level results in higher viscosities which may become an obstacle to be forced through the device. Thus, dual-channel microfluidization has been

designed for the efficient fabrication of nanoemulsions in which the oil phase and aqueous phase are separately fed into the device. The advantages of this method in comparison to its conventional single-channel counterpart are lower consumption of time, cost, energy, and labor since the additional step of preparing a coarse pre-emulsion with another equipment is omitted, and one cycle of homogenization could be enough for some cases. Moreover, the separate entering the oil and water phase provides the opportunity of no requirement to feed a pre-mix coarse emulsion, thus there is no limitation for the content of the used oil. Therefore, concentrated nanoemulsions with high oil contents can be produced; thus, boosting its application in food and nutraceutical fields (Ganesan et al., 2018, Bai and McClements, 2016).

The pressure of microfluidization, the number of cycles of the homogenization, oil content, and the emulsifier content are the most cheif process parameters that influence the performance of the apparatus for the fabrication of nanoemulsions (Jafari et al., 2007, Sedaghat Doost et al., 2018a). By increasing the microfluidization pressure, the droplet size of nanoemulsions decreases, as was observed by Uluata et al. (2016). Bai and McClements (2016) reported that the droplet size of nanoemulsions stabilized by polysorbate 80 was lineary log-log related to the homogenization pressure. It has been also suggested in the literature that by increasing the number of passes through the homogenizer as well as an enhancement in surfactant content decreased the droplet size of the nanoemulsion (Sedaghat Doost et al., 2018a, Uluata et al., 2016).
Lv et al. (2018) observed that by increasing the content of vitamin E in the carrier oil (corn oil), the droplet size of the quillaja saponin stabilized nanoemulsions, which were fabricated by a dual-channel microfluidizer, increased. This droplet size increase was triggered by the enhancement in the viscosity of the oil phase. Consequently, these plant-based nanoemulsions creamed faster and showed lower physical stability during storage.
The incorporation of bioactive compounds into microfluidized nanoemulsions is able to improve their efficiency and bioavailability in addition to increase their physical and chemical stability, which is due to their smaller droplet size. For example, in a study conducted by Raviadaran et al. (2018), curcumin-incorporated nanoemulsions were developed applying microfluidization for increasing the bioavailability of the curcumin. Luo et al. (2017) also showed that the water dispersibility and chemical stability of β-carotene could be improved by its incorporation into microfluidized nanoemulsions. In order to increase the functionality and bioavailability of essential oils, microfluidization has been used in different studies to prepare oil-in-water nanoemulsions (Sedaghat Doost et al., 2018b, Sedaghat Doost et al., 2017, Sedaghat Doost et al., 2019e). In addition to conventional nanoemulsions, Pickering nanoemulsions with high stability against coalescence can be fabricated using microfluidization (Schröder et al., 2018).
The disadvantages of the microfluidization approach for the fabrication of nanoemulsions are the high energy input requirement, and its wasting since the emulsification only consumed 0.1% of the input energy, and the remaining part is wasted as thermal energy. Furthermore, several passes are required for obtaining more monodispersed droplets since all droplets are not exposed to an equal shear stress because of their different positions in the interaction chamber. Moreover, the generated heat during the process limits its application for heat-labile materials (Alliod et al., 2019).

Microfluidization can be used for the development of solid lipid nanoparticles (SLNs) without the disadvantages of other fabrication methods such as high-speed homogenization, spray drying, hot homogenization, cold homogenization, ultrasonication, and supercritical technology, which are partitioning of the lipids, weaker stability, and higher consumption of organic solvents. Due to the above-mentioned disadvantages, the development of novel SLNs becomes limited. Microfluidization provides the opportunity to produce SLNs with considerably small particle sizes, which boosts their application as a delivery system. For example, Helgason et al. (2015) fabricated transparent SLNs ranging from 36 to 136 nm by cooling 10 wt% octadecane and 1–5 wt% sodium dodecyl sulfate nanoemulsions homogenized using high-pressure microfluidization (5000–28,500 psi) which are applicable in clear beverages and juices or other transparent food products. Furthermore, the produced SLNs by microfluidization provide higher encapsulation efficiencies for incorporated bioactive compounds. Moreover, the microfluidized SLNs provide higher stability and bioaccessibility for the encapsulated compound because of their small particle size (Arora et al., 2015, Singh et al., 2016).

Nanoliposomes have also been developed using microfluidization with small particle size, high encapsulation efficiency, and sustained release of bioactive components. It has been said that the incorporation of bioactive components into microfluidized nanoliposomes with small size (60-100 nm) provided higher stability and bioaccessibility, and controlled release of tea polyphenols than ultrasonication and high-pressure homogenization (Zou et al., 2014a, Zou et al., 2014b). Guldiken et al. (2018) also developed black carrot extract-loaded nanoliposomes as an antioxidant agent with a particle size lower than 50 nm using this method. Microfluidization can be further used for the deagglomeration of nanoparticle clusters. This method was used by Gavi et al. (2018) for completely breaking up silica nanoparticle clusters into submicron aggregates with a size of 150 nm through erosion; additionally, the effect of the particle content and the viscosity of continuous phase on the deagglomeration of clusters was investigated. More passes or a higher power intensity was required for samples with a higher particle content or the viscosity of continuous phase.

5.2.2. High-pressure homogenizer (HPH)

High-pressure (HP) homogenization is a type of top-down high energy technique which fabricates nanoparticles (Riegger et al., 2018), nanoemulsions (Agarwal et al., 2019, Jasmina et al., 2017), and nanodispersions (Tan et al., 2016b) by producing powerful disruptive forces including shear stress, cavitation, and turbulent flow. The created disruptive force due to the intense energy can disrupt larger particles and oil droplets into the nano-size range as shown in Figure 5-2 (Agarwal et al., 2019). The standard range of hydrostatic pressures (i.e., which is generally used for HP-homogenization) is 150 to 200 MPa; whereas, 350 to 400 MPa is applied for ultra-HP homogenization using intensifier technology (Singha et al., 2016). The requirements of an HP-homogenizer are an HP positive displacement pump and a restriction assembly. Depending on the kind of the pump, and the kind and the number of restrictions, their designs could be different. The HP can be transferred to the fluid using piston-type pumps. The liquid is withdrawn to the pump by its suction valve; then, it is pushed to the pump depletion valve and the homogenizing valve by the forward stroke of the piston. The restriction assembly is another part of an HP-homogenizer which exists in three types: with adjustable valve, with nozzle, and with microchannels. The relative distribution of shear, turbulence, impact, and cavitation varies categorically in the homogenizer based on the type of restriction assembly. The kind of the nozzle is usually a better option among other valves since tunable valves may generate higher variations in different batches (Singha et al., 2016).

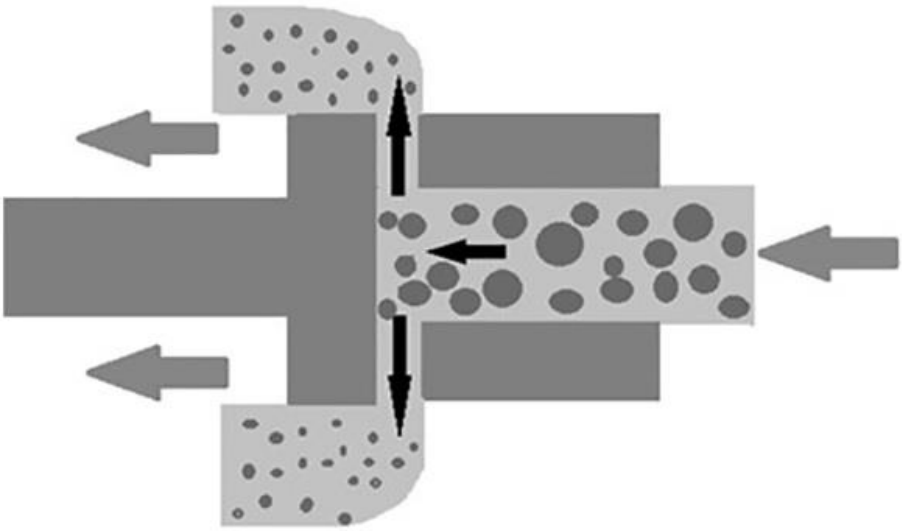

Figure 5-2. A simple homogenization valve. Reprinted from dos Santos Aguilar et al. (2018).

HP homogenizers can be used as a highly efficient nanoemulsification method by flowing the two liquid phases (i.e., including surfactants and co-surfactants) through the small orifice of a piston homogenizer called the homogenizing valve, nozzle, or microchannel, under a high pressure (500-5000 psi) (Li et al., 2018b, Xu et al., 2018). These authors used HP homogenization for the production of nanoemulsions based on soy protein. These researchers reported that HP homogenization improved the functionality of the protein as an emulsifier. It has been reported that the structural changes of the protein after exposure to HP homogenization could improve its functional properties (Sedaghat Doost et al., 2019d).

Several hydrophobic bioactive compounds such as curcumin (Ma et al., 2017), essential oils including pepper oil (Galvão et al., 2018), carotenoids such as β-carotene (Borba et al., 2019) and jackfruit extract (*Artocarpus heterophyllus* Lam) (Ruiz-Montañez et al., 2017), vitamin E (Ozturk et al., 2015), and kenaf seed oil (Cheong and Nyam, 2016) have been incorporated into HP homogenized nanoemulsions.

Similar to other high energy methods, the parameters that affect the obtained droplet size are energy intensity, holding time of the energy input, interfacial tension, the difference between the viscosity of the phases, type and level of the emulsifier, and emulsifier-to-oil ratio (Karthik et al., 2017, Xu et al., 2018). The influence of the type of emulsifier on the droplet size of HP-homogenized nanoemulsions has been previously investigated. Ozturk et al. (2015) reported that whey protein isolate performed better as an emulsifier at low concentrations in producing smaller droplets than Arabic gum for stabilizing Vitamin E fortified nanoemulsions applying HP-homogenization. By increasing the emulsifier content, homogenization time, or energy input the droplet size of the fabricated nanoemulsions could be decreased (Li et al., 2018b). Silva et al. (2015) reported that an enhacement in the homogenizing pressure decreased the droplet size of nanoemulsions stabilized by different surfactants (polysorbate 20, SDS and DTAB) from 177 to 128 nm. It was also observed that an enhancement in the surfactant level triggered a decrease in the droplet size. Cheong and Nyam (2016) investigated the effect of homogenization pressure in the range of 16,000 to 28,000 psi and number of homogenization cycles of 3 to 5 cycles on the droplet size and stability of kenaf seed oil nanoemulsions stabilized with sodium caseinate, Tween 20, and β-cyclodextrin complexes. It was observed that increasing the homogenizing pressure and the number of passes yeilded a smaller nanoemulsion droplet size and a higher stability. They fabricated nanoemulsions with a particle size of 122 nm, a span of 0.147, and a surface charge of -46.6 mV through the optimum HP-homogenization conditions which were 28,000 psi for 4 cycles. Another effective parameter is the level of the oil phase and its ratio in comparison to the emulsifier. An enhancement in the level of the oil phase, increased the droplet size of HP-homogenized nanoemulsions

incorporating curcumin (Ma et al., 2017). Contrary to these results, Silva et al. (2015) reported that by increasing the portion of oil in comparison to water in nanoemulsions stabilized with nonionic surfactants, the droplet size decreased from 341 to 171 nm.

HP homogenizers can be used for the fabrication of lipid-based nanoparticles such as SLNs and NLCs (Akhavan et al., 2018). HP homogenization associated with hot and cold approaches is one of the most common methods for the fabrication of these lipid-based particles since it provides the opportunity to scale up the production without any requirement for using organic solvents (Akhavan et al., 2018). The hot HP homogenization is the dissolvation of the bioactive compound and the melted lipid in a hot emulsifier solution with the same temperature followed by a pre-homogenization using a high-speed stirrer and then passing through a high-pressure homogenizer. The cold HP homogenization is defined by dispersing the bioactive component in the lipid melt, and their mix is then cooled. The resulting solid is subsequently ground to prepare solid microparticles which are dispersed in a cold emulsifier solution and exposed to HP homogenization (Müller et al., 2002). Different bioactive compounds have been incorporated into lipid-based nanoparticles which were produced using HP-homogenization. For instance, citral into glyceryl monostearate SLNs based on polysorbate 80 and span 80 (Tian et al., 2018). Biopolymer based particles were also fabricated using HP homogenization. Starch nanoparticles were produced through HP homogenization associated with mini-emulsion cross-linking (Ding et al., 2016, Shi et al., 2011). In another study, Riegger et al. (2018) by using 1-7 passes of HP homogenization at 40 MPa fabricated chitosan nanoparticles in the size range of 125 – 250 nm. Nanodispersions can also be prepared using HP-homogenization. High-pressure valve homogenization was used for the formation of lutein nanodispersions based on polysorbate 80 and comparison with their fabricated counterparts with the solvent displacement method by Tan et al. (2016b). It was observed that the particle size and poly dispersity index were not significantly different for both methods, while lutein retention was better in the nanodispersion formed via the solvent displacement technique.

The disadvantage of HP-homogenization like other high energy methods is its high energy consumption which limits its large-scale application in industry. Moreover, the increase in the temperature during the process can be harmful to heat-sensitive compounds. Nevertheless, this is the most common method for the preparation of nanoemulsions (Jasmina et al., 2017).

5.3. Sonication

Sonication is an effective method to prepare various nanomaterials. This method has also been used for different food applications such as the microbial inactivation in liquid food products (Knorr et al., 2004, Piyasena et al., 2003), or extraction (Vilkhu et al., 2008). Ultrasound or power ultrasound is term for the sonic waves, also known as acoustic waves ehich have higher frequencies than those of audible sounds for the human ear (higher than 16 kHz). Based on the frequency and intensity ranges, there are two ultrasound processings: low and high intensity. Low intensity (high- frequency) ultrasound has hardly destructive effects during passing through the medium due to its low power. On the other hand, high intensity (low-frequency) ultrasound can be used for destruction purposes, including depolymerization of macromolecules, breaking down particles and aggregates down to the nanometer size range, emulsification (homogenization), deflocculating droplets, and extracting bioactive compounds from diverse matrices. Cavitation phenomena induced through this method have the ability to stimulate several chemical reactions. Cavitation is the phenomenon that is induced by high-intensity sonic waves in the range of 16 kHz – 100 MHz through the mass of liquid and is determined by the sequential creation of millions of vapor microbubbles or microcavities in the liquid. When these bubbles are nonlinearly collapsed or burst, the concentrated energy within these bubbles is released considerably fast, resulting in hot spots, turbulence, and free radicals, which can be

generated in the cold fluid in a short period of time (Suslick and Price, 1999). A conventional ultrasonication setup consists of different parts, including the electrical supply, a piezoelectric transducer, and an emitter which is typically in the form of a titanium horn (probes) or bath (Suslick and Price, 1999). Nanoparticles based on different food-grade biopolymers have been fabricated via sonication. The generated physical forces, such as shear forces, which are formed by micro-streaming and normal impingement from the water jets at the interfaces of solid and liquid result in breaking down the biopolymers into nanometric range particles or aggregates. Gilca et al. (2015) prepared lignin nanoparticles by ultrasonication. Ultrasonication can not only be used for the fabrication of nanoparticles from biopolymers but can also improve their functional properties and boost their application. Zhang et al. (2018b) reported that ultrasound treatment was able to unfold the conformation of rice bran protein resulting in the exposure of its interior functional groups, which improved its solubility, emulsifying, and foaming properties. Jiang et al. (2019) combined pH-shifting and sonication to prepare and functionalize pea protein nano-aggregates for the fabrication of nanoemulsions and nano complexes as nanocarriers for cholecalciferol (vitamin D3). It has been suggested that ultrasound-treated pea proteins had an improved antioxidant capacity and provided a higher bioavailability for D3. The association of ultrasonication with low hydrostatic pressure and low heat, is called mano-thermo-sonication (MTS) which is able to increase the cavitation activity and can be used for the fabrication and modification of protein nanoparticles. Yildiz et al. (2017) fabricated and functionalized spherical shaped soy protein nanoparticles with a size of 27±1 nm using this process in combination with pH-shifting. Their results revealed that the MTS process enhanced the solubility, emulsifying properties, surface hydrophobicity, and antioxidant activity of the soy protein. The fabricated nanoparticles also showed the ability to stabilize canola oil-in-water nanoemulsions during 21 days of storage.

The ultrasonication process can also be used as an aid for decreasing particle size in other particle fabrication methods. For example, in a study conducted by Feng et al. (2019), ultrasonication was used for further decreasing the size of anti-solvent precipitated zein nanoparticles. Moreover, the surface charge, encapsulation efficiency, and the encapsulation capacity for stigmasterol incorporation of zein nanodispersions significantly increased after exposure to the ultrasonication treatment. Furthermore, ultrasonication can be used as a post-formation process in the final step of the preparation of liposomes for reducing the number of bilayers which helps to fabricate smaller liposomes (Pimentel-Moral et al., 2018).

Sonication has also been used for the fabrication of nanoemulsions. The advantages of this method include lower consumption of energy and surfactant, smaller droplet size and size distribution, and higher stability among other high-energy emulsification methods such as HP homogenization and microfluidization. This process also needs less maintenance and handling time compared to other mechanical methods (Li et al., 2019). Ultrasonication can form nanoemulsions by breaking down the mixture of oil and water, increasing the diffusion rate, and dispersing the aggregates by cavitation (Peshkovsky et al., 2013). This process is schematically represented in Figure 5-3. It has been reported that the ultrasonication was 18 times more energy-efficient in the fabrication of nanoemulsions in comparison to microfluidization (Kumar et al., 2017).

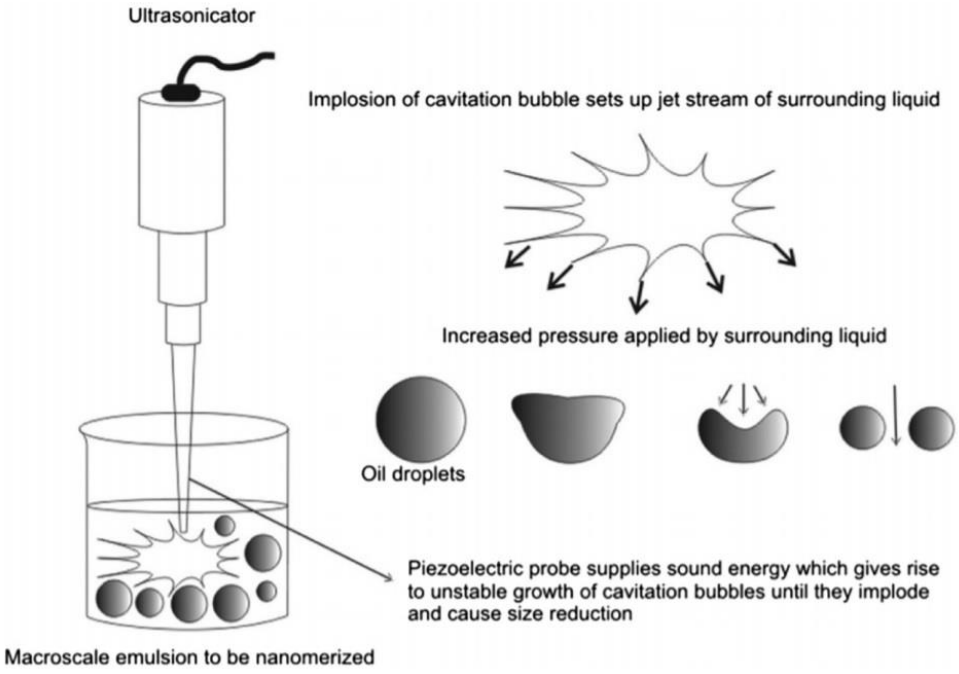

Figure 5-3. Schematic illustration of ultrasonication to produce nanoemulsions taken from Cheaburu-Yilmaz et al. (2019).

The properties of the fabricated nanoemulsions (i.e., including droplet size, optical and rheological stability) depend on the applied emulsification technologies, their process variables, and emulsifier types (Li et al., 2019). The main effective process variables in nanoemulsification through ultrasonication are the sonication time and intensity (Salvia-Trujillo et al., 2017). By increasing the sonication time, the power level, and the emulsifier concentration, the droplet size decreased (Sedaghat Doost et al., 2019f). Tan et al. (2016a) also investigated the effect of ultrasonic parameters including pre-sonication ultrasonic intensity, sonication time, and temperature for the formulation of a valproic acid-loaded nanoemulsion stabilized by lecithin and tween 80 with response surface methodology. Their results displayed that the relation between ultrasonic intensity and time had the most impact on the size of the nanoemulsions. The increase of the ultrasonic intensity decreased the span. Sedaghat Doost et al. (2019f) identified the ultrasonication time and intensity as the most effective variables for the droplet size of nanoemulsions (i.e., fabricated for encapsulation of thymol as a major compound of some essential oils with antimicrobial and antioxidant activity) (Sedaghat Doost et al., 2019c). However, Mehmood et al. (2018) observed that the most effective parameter on the droplet size of β-carotene nanoemulsions obtained by ultrasonication was the emulsifier content, rather than ultrasonic homogenization time and oil content. Using sonication for the fabrication of nanomaterials may have some drawbacks. One of these drawbacks is the temperature increase (in some cases up to 80 °C) due to the hot spots produced during bubble implosion and high shear rates, which may result in deterioration of components susceptible to heat. Moreover, the degradation of lipids due to the hydrolysis or oxidation of triglycerides can occur (Salvia-Trujillo et al., 2017). Free radicals released in acoustic cavitation during the process can also increase the rate of oxidation (Chemat et al., 2004). Another limitation of industrial application of ultrasonication in the fabrication of nanomaterials is the probability of the migration of metal ions or metal particles from the sonication probe into the product as a result of the cavitational abrasion which causes contamination for the food-grade labeled products (Freitas et al., 2006).

5.4. Electrohydrodynamic devices

Electrospinning is a novel and popular top-down method for the fabrication of nanomaterials in the form of nanofibers with dimensions in the range of 40 to 2000 nm from a wide variety of starting materials with different applications (Reneker and Chun, 1996, Sedaghat Doost et al., 2019d). The term “electrospinning”

was coined since 1994 while this technique was used by Anton (1934) for the first time. There has been considerable attension to this method because of being cost-effective, scalable, and straightforward (Schiffman and Schauer, 2008). The basic requirements (Figure 5-4) for this process are a high power voltage supply, which is connected to a capillary tube containing a polymeric solution with a needle or pipette, as well as a collector or target, through electrical wires. The capillary tube can be simply a syringe connected to a pump while the collector could be a copper plate (Schiffman and Schauer, 2007a, Schiffman and Schauer, 2007b), or an aluminum foil, plate, or rotating drum (Chew et al., 2005). By applying a high voltage, a pendant droplet of the solution is altered into a conical shape with an angle of 33.5° called Taylor cone due to the generated electric field between the tip of the syringe needle of the capillary tube and the target, located at a short distance from each other (Taylor, 1969, Yarin et al., 2001). This is because the created electric field reduces the surface tension of the polymer solution, resulting in the creation of a Taylor cone at the tip of the syringe needle which is changed to a straight jet that releases from the cone and reaches the collector when the voltage exceeds a critical value. At this voltage level, the electrostatic repulsion is higher than the surface tension between the solution droplets resulting in stretching them at the needle tip and throwing them out on the collector. Dry micro- or nano-sized electrospun fibers can be collected from the collector in the form of non-woven mats due to solvent evaporation during the process (Kakoria and Sinha-Ray, 2018, Schiffman and Schauer, 2008).

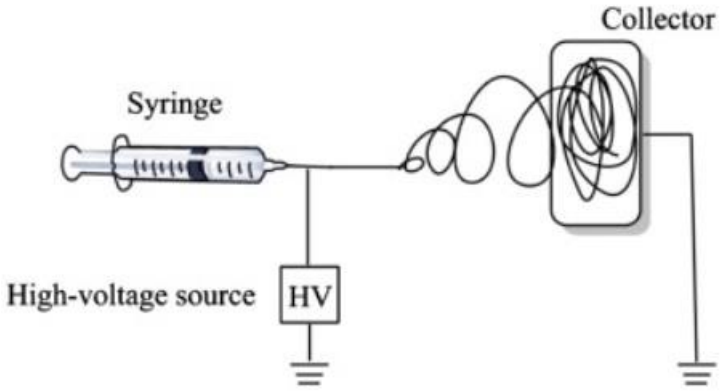

Figure 5-4. Illustration of basic setup for electrospinning (Hu et al., 2014).

The electrospinning process can be influenced by several parameters. Some of these are related to the used components, including their molecular weight (MW), molecular weight distribution, solubility, and glass transition temperature; while some others are related to their solution properties such as concentration, viscosity, viscoelasticity, surface tension, electrical conductivity, and solvent quality, which are not independent of each other. The solution feed rate, field strength, applied voltage, geometry of electrodes and their materials, spinning distance, and vapor pressure of the solvent are effective process parameters. The selection of electrospinnable biopolymer is a critical parameter. Biopolymers with too high or too low MW are hard to electrospin. For example, Pirzada et al. (2019) observed that both native high MW (~2×10^6 Da) and hydrolyzed low MW (~1.6×10^4 Da) guar were not electrospinnable at the applied conditions. Therefore, they used a blend to tune the MW. It is also important to note that polymers with higher MW need a lower concentration in the solution since they are able to deliver a sufficient number of polymer entanglements and appropriate solution viscosity even at low concentrations (Gómez-Mascaraque et al., 2016). The content of the polymer in the solution is also an important parameter in the electrospinning process. Higher concentrations of the biopolymer result in higher viscosities of the solution because of the intensive overlap of polymer chains, which resists the thinning of the solution jet; thus, yielding larger fibers. The viscosity of the solution by itself should be optimized since at too low values, droplets are formed instead

of the Taylor cone while at too high values the ejection of the polymer solution jets and the fiber formation become difficult (Bhardwaj and Kundu, 2010). Surface tension is an effective parameter on the size and morphology of the fabricated nanofibers, especially when low concentrations of polymers or polymers with lower molecular weights are used. More the surface tension of the solution is, more electric field is required for the electrospinning. At too high surface tensions, the jet is unstable and may spray out in the form of droplets instead of fibers (Sunil, 2017). The surface tension of the polymer solutions can be tuned by the addition of surfactants, ionic salts, or electrolytes. These additives have the ability to decrease the surface tension or enhance the net charge density of the solution. Sodium dodecyl sulfate (SDS), dodecyl trimethyl ammonium bromide (DTAB), and Triton X-100 (TX-100) were added to a lignin solution to reduce the surface tension of the spinning dopes for obtaining smooth, beadles, and small nanofibers (Fang et al., 2017). The electrical conductivity of the solutions is another important parameter that is related the used solvent and the used polymer. Solutions with lower electrical conductivity yield fibers with larger diameters due to their shorter stretching of the electrified jet (Bhardwaj and Kundu, 2010). The spinnability of a WPI-maltodextrin blend was observed to be more successful in comparison to an SPI-maltodextrin blend due to its lower electrical conductivity (Kutzli et al., 2019). Fonseca et al. (2019) performed starch phosphorylation to increase the charge density by producing electrostatic charges, which helped it to become electrospinnable. The addition of additives such as salts and surfactants can also be effective to modify the electrical conductivity of the solutions. Salts provide migrating ions which transport charges in the solution and due to the increase in charge density result in higher conductivities (Sunil, 2017). It has been suggested by many researchers that by increasing the voltage, which usually varies between 6 and 30 kV, more larger fibers are electropsun due to the increase in polymer ejection power. On the other hand, some reports revealed that the increased voltage resulted in more electrostatic repulsive forces on the fluid jet, leading to more stretching of the solution.

The polymer solution flow rate, which usually varies between 0.01 mL/h and 1 mL/h, is another effective process parameter. An increase in polymer flow rate yields larger fibers with larger pore size with more beads since, at higher flow rates, there is not enough time for the fibers to dry during their travel to the collector. The length of the gap between the tip of the needle and the collector, which generally varies between 10 and 30 cm, is also important and should be optimized because it determines the time for the solvent evaporation and fiber drying before reaching the collector and it is decisive for the number of the formed beads in the fiber structure. A larger distance, which means a larger flight time and more stretching, usually produces thinner fibers with less beaded structures. Therefore, a too-large distance causes less stretching of the fibers and an increase of their diameter because of the reduction of the electrostatic forces and an effective voltage drop. On the other hand, a smaller distance yields beaded structure fibers due to a too strong electrostatic field and jet instability.

Electrospun nanofibers can be used in different fields and applications including drug delivery, tissue engineering, wound dressing materials, , filtration and wastewater treatment, fuel cells, and biosensing. In the food industry, nanofibers fabricated from biopolymers can be used for designing new food ingredients and food additives, as delivery systems of bioactive compounds with sustained release, food novel packaging material, edible food coating, and food sensor as they are non-toxic, edible, and biocompatible. The three-dimensional open porous structure of electrospun nanofibers which is associated with a high specific surface area that enables mass transfer and effective delivery makes them suitable for delivering food bioactive agents with controlled release (Neo et al., 2018).

Since the electrospinning process is a non-thermal process, it is suitable for the encapsulation of biological components that are susceptible to high temperatures. Moreira et al. (2019) suggested that the thermal

stability of phycocyanin, an antioxidant agent extracted from *Spirulina* microalga, increased after encapsulation by LEB 18/poly(ethylene oxide) (PEO) nanofibers.

In addition to use electrospun fibers from proteins and polysaccharides as a bio-material for food packaging, this method also opens a promising route for adding active properties such as antimicrobial (Deng et al., 2017, Kuntzler et al., 2018a, Kuntzler et al., 2018b), antioxidant (Li et al., 2018a), and biosensing activities (Moreira et al., 2018, Neo et al., 2018).

For the encapsulation of bioactive agents, different approaches of electrospinning including blend, co-axial, and emulsion electrospinning and surface modification of the electrospun fiber mats have been used. Blend electrospinning, as the most common encapsulation approach, is the direct addition of the bioactive agent to the biopolymeric solution. In this method, both the bioactive agent and the biopolymer are dissolved in the one solvent. By solidifying the solution jet during the process, the active agent is encapsulated within the polymeric fibers. This method of electrospinning is straightforward and simple while it is not suitable for the encapsulation of sensitive bioactive compounds including proteins, enzymes, and cells. This is because using organic solutions and mechanical stirring, homogenization or ultrasonication for blending can cause conformational changes or destroy their biological integrity.

Coaxial electrospinning (i.e., with the same setup as conventional electrospinning except having a core-shell syringe) has been developed to prepare core and shell fibers which are sufficient for the delivery of food bioactive components that are not soluble in organic solvents. In this process, the polymer and the bioactive component are separately dissolved in their proper solvent and separately ejected through two confocal nozzles as the shell and core solutions, respectively. In this method, the sensitive bioactive agent is concentrated in the core of the fibers providing its effective protection.

Emulsion electrospinning is another method in which the active agent is surrounded by emulsifiers or surfactants and impregnated into a polymeric carrier whereby a controlled encapsulation process with sustained-release is achieved. Hydrophilic and hydrophobic compounds including carotenoids, polyphenols, vitamins, enzymes, peptides, oils, essential oils, flavors, and probiotics, can be encapsulated using this method with W/O and O/W emulsions, respectively. This method of electrospinning fabricates core and shell nanofibers using only a single nozzle. Another advantage of this method is minimizing the need for organic solvents which makes them appropriate for food applications (Zhang et al., 2018a).

The electrospinning equipment and nanofibers are moving forward to commercialization and scaling up to industrialization. Fabricating nanofibers using the electrospinning method, as well as solution bowling, are methods among the other techniques for nanofiber production (such as drawing, template synthesis, self-assembly, and phase separation), that can be used on an industrial scale (Leidy and Maria Ximena, 2019). Donaldson Co., Inc in the United States in the early 1980s introduced the first commercial products of sub-micron sized fibers mainly for air filtration applications. The process scaling-up is still largely an issue. The issues which should be concerned are large volume processing, accuracy and reproducibility, safety and environmental attributes (Persano et al., 2013). Moreover, the electrospinning of food-grade biopolymers is difficult since their high molecular weight distribution and their complex chemical structure interfere with the entanglement necessary for spinnability (Kutzli et al., 2019). The throughput of the electrospinning is also one of its general limitations. This problem can be solved with a novel method known as solution blowing which belongs to the group of melt blowing in which a polymer in molten state is extruded through a spinneret (Kakoria and Sinha-Ray, 2018). Therefore, the solution blowing method is suitable for biopolymers which are sensitive to degradation or denaturation after exposure to high temperatures while melting. Electrospraying, like electrospinning, is an electrohydrodynamic technique that has gained an increased interest in food technologists. Electrospraying, which is a process first described in 1914 (Zeleny, 1914),

requires a setup that is similar to electrospinning. However, in electrospraying small droplets are scattered to the target rather than fibers due to the lower viscosity of the solution. Therefore, instead of micro- or nano-sized fibers, particles are fabricated with a particle size in the range of a few nanometers to 100 µm. Polymer chain entanglement, polymer molecular weight, and the evaporation rate of the polymer-solvent are the effective parameters for the formation of particles in this process. Polymer chain entanglement, which is determined by the polymer concentration, is a key factor in the electrohydrodynamic process. A solution with higher biopolymer concentration would be suitable for electrospinning rather than electrospraying due to its higher chain entanglement and higher viscosity (Niu et al., 2020).

The polymer molecular weight was reported to affect the concentration, viscosity, surface tension, and conductivity in the case of chitosan solutions, which subsequently influenced the morphology and the size of the electrosprayed nanoparticles. The lowest chitosan molecular weight (25 kDa) allowed the highest solution concentration and the highest productivity of nanocapsules for the encapsulation of epigallocatechin gallate (EGCG) (Gómez-Mascaraque et al., 2016). Coaxial electrospraying can be used for the fabrication of multilayer encapsulation structures with food-grade materials as delivery systems for both hydrophilic and hydrophobic active agents with improved encapsulation efficiency in food applications (Gómez-Mascaraque et al., 2019). EGCG as a model hydrophilic component and α-linolenic acid (ALA) as a model hydrophobic agent were encapsulated in zein and gelatin coaxially electrosprayed capsules compared to uniaxially electrosprayed particles. Coaxial ones showed a higher encapsulation efficiency and enhanced bioactivity protection in thermal degradation assays (for ALA), as well as enhanced antioxidant activity after *in-vitro* digestion (for EGCG).

5.4.1. Solution blowing

Solution blowing is a process for fabricating fibers with the size in the range of nanometers to micrometers. This process is similar to electrospinning whereby a high-velocity gas flow is applied instead of an electric field (Figure 5-5). In this method, the polymer solution in the nozzle is pressed out through the orifices by compressed air which is obtained from a high-speed air-supply, and drag out by a high-velocity gas flow. Therefore, a co-axial die is required, consisting of a core nozzle for the polymer solution flow and a shell nozzle for the high-speed air flow. Fibers can be collected on the collector by the evaporation of the solvent. The fiber production rate and the diameter of the fabricated fibers are larger in comparison to electrospinning (Kakoria and Sinha-Ray, 2018). The air flow rate, nozzle dimensions, collecting distance, viscoelasticity of the polymer solution, and ambient temperature are the key parameters that play an important role in controlling the solution blowing process. By increasing the air pressure and temperature, the fiber diameter is decreased. The advantage of this technique is its capabality to blend biopolymers and its scalability (Kolbasov et al., 2015). In a study by Kolbasov et al. (2015), nanofibers with the size of 0.5 and 1.5 µm were fabricated by this method from soy protein isolate solutions containing chitosan, lignin, sodium alginate, or zein, in the range of 900 to 1600 cm^2 in 10 s with a solid weight of 5.1 g by using nozzles of 0.002 inch I.D.

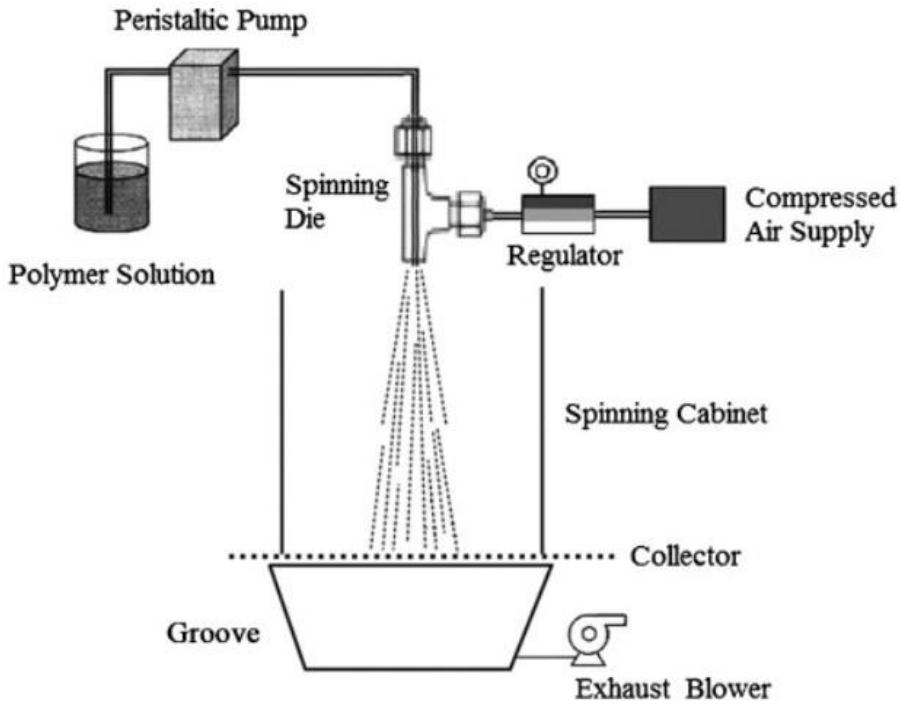

Figure 5-5. Solution blow spinning (Zhuang et al., 2012).

Blowing assisted electro-spinning or electro-blowing is the association of blowing solution and electrospinning. The aerodynamic stretching is associated with the electrostatic force since the nozzle is connected to a high voltage power supply, resulting in the additional stretching of the polymer jets. This method can solve the limitation of polymer solutions with extremely high viscosities which are hard to have successfully electrospun (Wang et al., 2005).

5.5. Spray dryer

Spray drying is a continuous and intensive nanomaterial manufacturing approach. This technique has been used for the preparation of micro/nano-capsules, controlled release particles, composite microparticles, nanoparticles, solid lipid nanoparticles, and liposomes. In this method, the stream of a liquid is transformed into dried particles with a one-step process via spraying in a chamber with a stream of hot air or inert gas, which can be fully automatically controlled (Assadpour and Jafari, 2019a, Masters, 1985). A spray drier set-up comprises several components, including a feed solution container, feed pump, spray nozzle, drying chamber, exhaust filter, cyclone, and collector. A basic illustration of a spray dryer is given in Figure 5-6. Briefly, the feed solution is pumped and then atomized through a nozzle to the drying chamber in which the atomized droplets are exposed to the hot air or inert gas (e.g., nitrogen). By passing the drying chamber, energy-mass transfer occurs at the dynamic droplet surface and eventually the dried powder is separated from the drying air via a cyclone and is collected in a collector (Assadpour and Jafari, 2019a, Masters, 1985). The main purpose of the atomization process is enhancing the surface area over which heat and mass transfer occur. Different types of atomizers can be used, such as rotary, hydraulic (pressure), pneumatic or ultrasonic nozzles, which determines the type of the used pump. Moreover, the viscosity of the feed solution can also affect this selection. For instance, when rotary atomizers or bi-fluid nozzles are applied, low-pressure pumps are suitable, while high-pressure pumps must be used for pressure nozzles. After going through the nozzle, the atomized droplets are dispersed into the drying chamber with a usual height to diameter ratio of 5:1 (tall) or 2:1 (small) to expose to the drying hot air. There are different flow directions of the drying air including co-current, counter-current or mixed flow. The concurrent type is the most common flow type, especially for heat-sensitive components. In this type of flow, the atomized droplets and the drying air (150 to 220 °C)

follow a similar route and the produced powder is exposed to a neigther high nor low temperature (50 to 80 °C) (Shishir and Chen, 2017). The drying air increases the temperature of the atomized droplets, which results in the evaporation of the solvent (water). At the end of the drying chamber separation devices (e.g., scrapping devices including vibratory devices, mechanical brushes, and/or compressed air) are embedded for powder recovery. Since scrappers can have adverse effects on the phase behavior of the dried dispersions due to the generated stress, cyclones may be used instead. The tangential entry of the gas-solid mixture into the cyclone body generates a circular flow whereby the centrifugal force triggers the separation of the two phases. Therefore, the particles in the air/gas, which is passing through the cyclone, get deposited on the cyclone walls due to the centrifugal force. Finally, the particles settle down due to the gravitational force to the bottom of the cyclone and are collected in the collector. Another type of collector generally used for spray driers with ultrasonic atomizers and with the ability to collect even nano-sized particles is the electrostatic particle collector. This device consists of two electrodes: a star electrode and a tubular particle gathering electrode which are defined as a cathode and an anode, respectively. As a result of the high voltage between them particles are collected on the surface of the tubular electrode due to their electrostatic deposition (Arpagaus et al., 2018, Arpagaus et al., 2017).

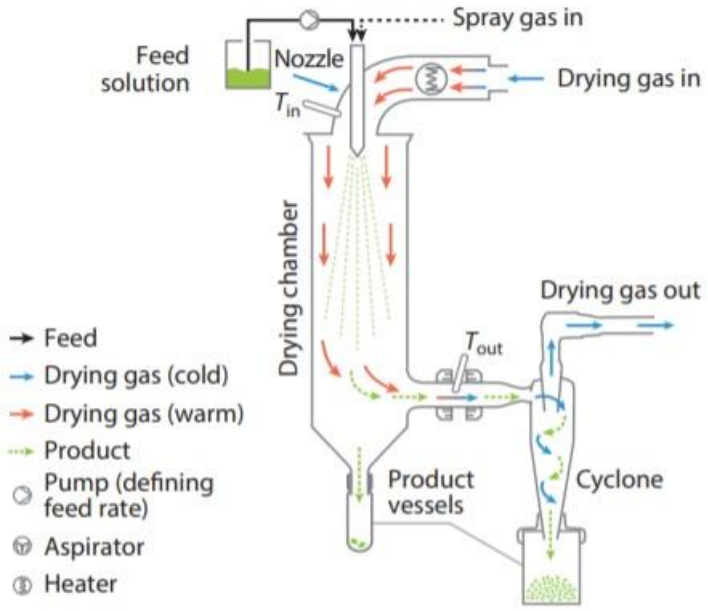

Figure 5-6. Different parts of a spray dryer apparatus (from Arpagaus et al. (2018) with permission from Elsevier).

The morphology (size, shape, structure, and surface attributes) of the obtained particles depends on the material characteristics, feed solution variables such as feed concentration, solution dynamics of the feed, viscosity, bioactive component/polymer ratio, sort and concentration of the carrier agent, and process parameters including inlet temperature, feed rate, drying air/gas flow rate, atomization variables (type of atomizer, speed of atomizer, pressure of atomizer), and outlet temperature (Assadpour and Jafari, 2019a, Shishir and Chen, 2017). Higher inlet temperatures increase the rate of the drying, which result in lower residual moisture in the final particles. Moreover, the applied temperature determines the particle size of the dried powders. Larger particles are fabricated at higher inlet temperatures due to the faster water evaporation without time for the shrinkage of the spheres. Furthermore, at higher temperatures, the bulk density of the powder will be deceased since the larger particles are more porous.

Atomization is considered as the most important part of the spray drying process. Thus, it is called the heart of the spray dryer, since the quality and characteristics of the process and the produced particles depend on this feature. The purpose of atomization is to convert the feed stream into fine droplets to increase the

surface area for preparing the opportunity for better effective and sufficient drying. Higher atomization speeds result in a higher drying rate and a lower residual moisture content. Beck-Broichsitter et al. (2015) reported that reducing the spray rate resulted in a decreased particle size and increased span. Higher atomizer pressures provide smaller particles with a larger surface area. It has also been reported that adding surfactants can be effective in modifying the morphology of the spray-dried particles. Adding surfactants forms a smooth spherical surface on the dried particles due to their ability to tune the surface-to-viscous forces inside the droplets (Arpagaus et al., 2017). Abdel-Mageed et al. (2019) reported that Tween® 80 could be effective in controlling the morphology of spray-dried nanoparticles containing α-amylase.

Spray drying has been used for the nanoencapsulation of different types of food bioactive components, such as probiotics (Gong et al., 2019, Su et al., 2018), flavors (Prasad Reddy et al., 2019), PUFA-rich oils (Prasad Reddy et al., 2019), essential fatty acids (Chang and Nickerson, 2018), vitamins (Penalva et al., 2015), antioxidants (Ferreira Nogueira et al., 2019, Khanji et al., 2018, Kritchenkov et al., 2019), antimicrobial agents (Hu et al., 2016, Wang et al., 2019), enzymes (Abdel-Mageed et al., 2019), and natural food colorants (de Boer et al., 2019, Fang et al., 2017). Spray drying is a favorable technique for bioactive components since it transforms a liquid feed into a powder form which is easier to handle, store, transport, and has higher stability (Veneranda et al., 2018). This method can be directly used for the encapsulation of hydrophilic and indirectly for the encapsulation of hydrophobic compounds after emulsification with high encapsulation efficiency. Carbohydrate biopolymers, protein biopolymers, lipids and waxes, polymers, surfactants, emulsifiers, and stabilizers can be used as wall material in the feed solution. Using different emulsifiers for stabilizing the prepared emulsions containing hydrophobic bioactive agents before spray drying can be effective in modifying the properties of the final dried particles.

Nano-spray drying, which is realized by the Büchi Nano Spray Dryer B-90, is a novel technique for the production of nano scale particles that can be used for drug and nutraceuticals delivery (Li et al., 2010). Some modifications should be performed on the set up of conventional spray dryers to prepare a nano-spray dryer. Commonly, ultrasound nozzles are used, and a proper collector such as an electrostatic particle collector is also required since conventional cyclones do not have the ability to collect particles with the size below 2 µm (Arpagaus et al., 2018, Arpagaus et al., 2017). The major advantages of a nano-spray drier over conventional ones are the smaller required sample quantities (minimum 2 ml which is 30 ml for the conventional ones), lower maximum drying temperature (i.e. 120°C which is 220°C for the traditional ones), higher yield, and smaller particle size. However, these nano-spray driers have lower scale-up capability compared to traditional spray dries due to their limited vibrating mesh technology and using an electrical particle collector (Arpagaus et al., 2017). Prasad Reddy et al. (2019) prepared roasted coffee bean oil with whey protein as wall material by both nano- and conventional spray drying and their results showed that the nano-spray dried capsules were approximately 11-fold smaller than the microencapsulates with more uniform particle size distribution and smoother, and more spherical morphology. In another study, zein-sodium caseinate-pectin complex nanoparticles were formed by Veneranda et al. (2018) for the nanoencapsulation of eugenol using nano-spray drying. These nanoparticles loaded with eugenol were spherical and had a small size distribution with a size of 140 nm.

The encapsulation of nutraceuticals and bioactive compounds using spray drying protects them and their active performance against environmental stress conditions with high encapsulation efficiencies. Khanji et al. (2018) reported that the encapsulation of curcumin in casein micelle powder produced by spray-drying protected its antioxidant activity. Kyriakoudi and Tsimidou (2018) also nanoencapsulated saffron extract in maltodextrin wall using a Büchi B-90 nano-spray dryer to improve the thermal and *in-vitro* gastrointestinal stability of saffron apocarotenoids. It has been also shown that the encapsulation of nutraceuticals by spray

drying improves their bioavailability. Penalva et al. (2015) reported that folic acid encapsulation in casein nanoparticles (150 nm), prepared by spray-drying, promoted its oral bioavailability in male adult rats.

There are some reports on food applications of spray-dried particles incorporated with bioactive components. For instance, Moncada et al. (2015) directly incorporated the nano spray-dried sodium chloride in cheese cracker production and compared its sensory and antimicrobial properties with two other salt sizes. The cheese cracker with nano-sized salt on its surface had a significantly higher preferred saltiness and significantly lower yeast counts. Thus, using nano-spray dried salt can be helpful in decreasing sodium consumption in this kind of product.

The first industrial use of spray drying in the milk and detergent manufacturing was reported to be in the 1920s while its application has been spread to various types of food products including egg products, beverages, vegetable proteins, fruit and vegetable extracts, carbohydrates, tea extracts, and yogurt (Masters, 1985). One of the limitations of spray drying, especially in the case of applying conventional atomizers, is the large particle size distribution, high electric energy consumption, and the blockage of the nozzle. Another limitation of spray drying is using high temperatures which can have adverse effects on sensitive components such as PUFA-rich oils, lycopene, β-carotene, anthocyanins, vitamin C, colors and flavors (Assadpour and Jafari, 2019). Living bacterial agents such as lactic acid bacteria and probiotics can also be damaged due to the exposure to high temperatures even for short times and the reduction in the water content. Therefore, there is an increasing interest in association of other methods with spray drying such as ultrasound-assisted spray drying (which is discussed above), vacuum spray drying (Islam et al., 2017), ultrasound-assisted vacuum spray drying (Liu et al., 2019), and dehumidified air spray drying (Jedlińska et al., 2019).

Vacuum spray drying is the combination of vacuum drying and spray drying which applies low temperatures for drying as the process is done under vacuum. Therefore, this technique is suitable for materials that are labile to heat (Shishir and Chen, 2017). Dehumidified air spray drying is a modification of the conventional spray drying for having a better performance in decreasing the stickiness limitations and improving the powder collecting by connecting a dehumidified air drying system to its chamber via the air inlet. The recovered powder in this method contains a lower moisture level and higher bulk density compared to the conventional method. Moreover, because of the lower outlet temperature and moisture content of the drying air, the produced particles have a smooth surface.

5.6. Micro/nanofluidic system

The microfluidic technique was originally developed in the 1950s and firstly used in different chromatographic systems (Golay, 1957). Later on, this technique was used for capillary electrophoresis to improve the separation process. After the 1990s, the use of microfluidic systems boosted and was further studied by several researchers (Khan et al., 2015). The microfluidic and nanofluidic methods (i.e., particularly focused on nano-sized productions) are modern low-energy and bottom-up technologies for the fabrication of nanomaterials. Interestingly, these methods have also been used for the manufacture of nanocarriers as drug delivery systems. However, their application for the nanoencapsulation of food nutraceuticals and bioactive components still require further research and comprehensive study (Ran et al., 2017, Zhang et al., 2019). A microfluidic device has coaxial assemblies of a series of rigid glass capillaries with dimensions of 10-100 µm which are resistant to chemicals. Also, they have a 3D geometry that enables the production of different types of nanomaterials (e.g., nanoemulsions, nanoparticles, and nanoliposomes) (Balbino et al., 2017, Joshi et al., 2016). Moreover, these channels work with significantly small amounts of sample due to their small dimensions. Other advantages of this method are the low energy consumption and low cost of the whole system, in addition to the use of low amounts of sample and ingredients. Furthermore, this is a rapid technique that provides the opportunity to develop in-vitro evaluations. The specific size of the channels makes it possible to fabricate sophisticated nanoparticles with specific sizes and narrow size

distributions. Also, nano- to micro-seconds of mixing, reaction and self-assembly, real-time monitoring or imaging, and direct scale-up, are some favorable properties of this method (Assadpour and Jafari, 2019b, Zhang et al., 2019). The laminar flow in this method (i.e., small Reynolds number) is continuous and controllable. As an emulsification technique, this method does not require high energy inputs; thus, providing a mild process. Besides, there are no temperature fluctuations, making this method suitable for the encapsulation of heat-labile compounds and live microorganisms such as prebiotics and yeasts (Feng and Lee, 2019).

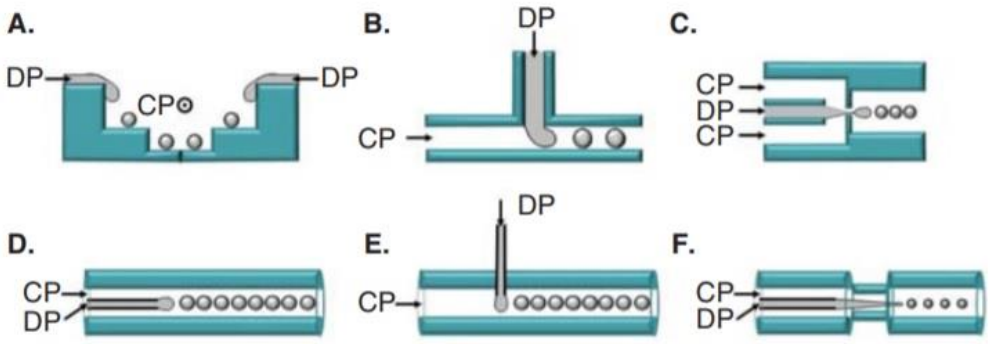

Figure 5-7. Different types of microfluidic devices: A) T-junction, B) flow focusing, C) capillary-based, D) cross-flow, E) flow focusing. CP= Contineous phase and DP = Dispersed phase (Khan et al., 2015).

There are several different types of microfluidic devices, including terrace-like, T-junction, flow-focusing, capillary-based, co-flow, cross-flow, and flow-focusing devices (Figure 5-7). Among them, channel-based and capillary-based devices are the most common. Microchannel-based devices are manufactured through different microfabrication processes such as micro-milling, micromachining, lithography, and mold replication, by applying varied materials (e.g., metal, glass, silicon, or polymer). However, capillary-based systems are usually fabricated from low-cost commercially available parts in less time with the same efficiency as microchannel-based devices (Khan et al., 2013). Therefore, the fabrication and use of capillary-based systems are more time and cost-efficient. Additionally, they can be applied under aggressive chemical conditions. However, it is more difficult to handle and to be paralleled to achieve larger yields in comparison to microchannel-based counterparts.

The microfluidic process is achieved by mixing two phases: a) continuous, and b) dispersed phases. The miscibility of these two phases determines the type of final product. The mixing of miscible fluids enables chemical reactions and can be used for the production of nanoparticles while mixing two immiscible fluids provides the formation of droplets (Feng and Lee, 2019).

The control over the microfluidic process is usually conducted by adjusting the flow rate of both continuous and dispersed phases which can also determine the characteristics of the fabricated nanostructures. The terrace geometry of microfluidic devices is another effective parameter. Y-junction, T-junction, and flow-focusing are three types of terrace geometry that provide different shear rates that determine the size and properties of the final product. Among the mentioned geometries, T-junction geometry provides the highest shear rate which generates emulsions with smaller droplet size distribution. In addition to the terraced geometry, its angle is also an important factor in the mixing efficacy at the joint of two microchannels where the two phases meet (Feng and Lee, 2019, Zhang et al., 2019).

The microfluidic devices have been used as a novel technology for the fabrication of particles. Biopolymeric particles are usually fabricated through nanoprecipitation effect and by an anti-solvent process. In this process, the stream of biopolymer solution is merged with the stream of anti-solvent solution where the two microchannels meet; whereby, the diffusion of solvents results in achieving equilibrium in the concentrations

of solvent and anti-solvent. At this point, the biopolymer-based nanoparticles are formed with precise control over size and characteristics (Feng and Lee, 2019). It has been reported by Abstiens and Goepferich (2019) that the microfluidic nanoprecipitation results in smaller nanoparticles with monodisperse size distribution in comparison to the bulk nanoprecipitation method. The type and rate of the flow are the most effective factors on the size and properties of the final nanoparticles. For example, turbulent flows result in larger particle size distributions due to its chaotic condition and various shear rate distribution. However, laminar flows can form more homogenous particles. Microfluidics provides the opportunity of preparing Janus particles in a simpler and more accurate way compared to other conventional methods. Two different polymers within two channels are merged at the junction to fabricate Janus particles which consisted of two distinct segments that are chemically and physically amphiphilic or bipolar (Zhang et al., 2017). Different biopolymers have been used for the fabrication of nanoparticles using microfluidic techniques including chitosan (Pessoa et al., 2017), polylactic acid (Othman et al., 2015), and zein (Olenskyj et al., 2017). Electrostatic complexes can also be prepared using microfluidic devices. For instance, β-lactoglobulin/gum arabic complexes were assembled using this new technique by Amine et al. (2017). SLNs can also be produced using this method with particle sizes significantly smaller than those of biopolymeric nanoparticles. For example, Chen et al. (2016) fabricated SLNs using this method with a final particle size of 27 nm.

Food nutraceuticals and bioactive compounds can be encapsulated within the self-assembled nanostructures using the microfluidic technique as a novel nanoencapsulation method. Joshi et al. (2016) simultaneously encapsulated either or both water-soluble and water-insoluble drugs using microfluidic fabricated nanoliposomes with a final particle size ranging between 90-300 nm.

The microfluidic devices can be used for the fabrication of nanoemulsions by injecting the dispersed phase into another immiscible or partially immiscible liquid phase. Due to the competition between the shear stress imposed by the flow of the continuous phase and the interfacial force at the junction where the two phases meet, the droplets are exposed to shear stress while their droplet size is reduced (Khan et al., 2015, Shaddel et al., 2019). Also, the spontaneous emulsification process (i.e., mechanism of emulsification) uses a microfluidic system based on Laplace pressure differences in the dispersed phase on the terrace and in the channel. Usually, the microfluidic device is used for further reduction in the droplet size of pre-mixed emulsions (Feng and Lee, 2019).

Another limitation of this method is the low production per hour due to the low capacity of the channels. This issue can be solved by parallelizing droplet generators (Khan et al., 2015, Khan et al., 2013). For scaling-up the microfluidic process, the best option for the terraced geometry is the Y-junction due to its control over the droplet size (Feng and Lee, 2019). Another limitation of the application of this technique in the field of food industry is the heterogeneity of food ingredients which may result in the clogging of the microfluidic channels. This problem can be solved by an auto-cleaning system; nevertheless, it requires an additional cost (Feng and Lee, 2019).

5.7. Vortex Fluidic Device (VFD)

The vortex fluidic device (VFD) is a relatively new processing platform used in thin-film microfluidics and thin-film flow chemistry. The processing efficiency of VFD is improving. Thus, it is applicable in many fields of scientific research and industry, including the synthesis of small molecules, processing in pharmaceutical industry, and manipulating single-cell organisms. Some of the problems of traditional batch approaches include limited mixing and heat transfer, both of which are solved in VFD (Yasmin et al., 2013). The vortex fluidic device consists of a rotating glass tube tilted at an angle θ relative to the horizontal position (Figure 5-8).

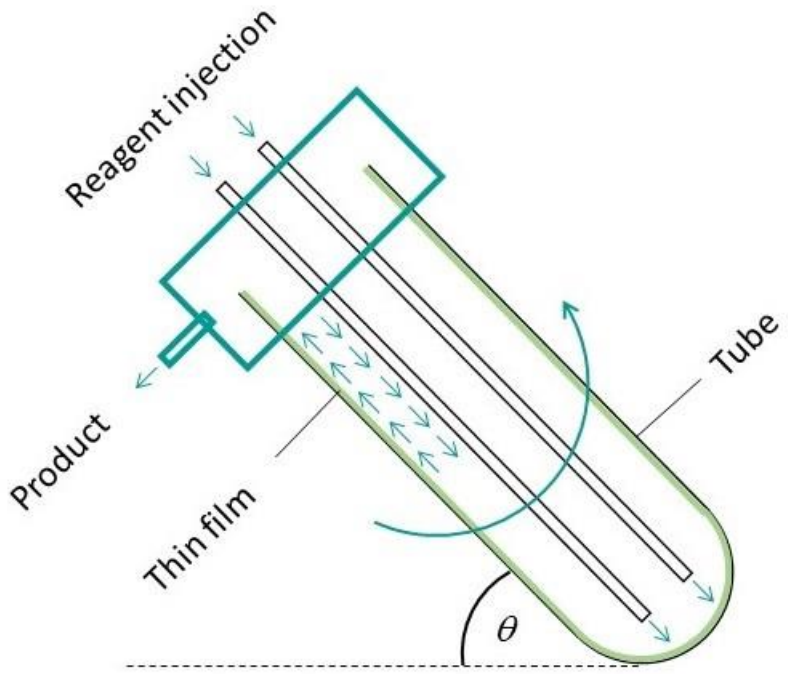

Figure 5-8.Schematic representation of the vortex fluidic device (Sitepu et al., 2018).

The movement of the tube causes the liquid inside to accelerate upwards and form Stewartson/Ekman layers on the sides, whereby the rotation causes the formation of a dynamic film (Kumari et al., 2016). VFD can operate in confined mode and continuous flow mode. The confined mode is used when the volume of reactants is finite. The speed, which can be controlled within 1 rpm, has to be sufficient to ensure that a vortex is maintained to the base of the tube, but the liquid must not fall out of the tube. Alternatively, in the continuous flow mode, liquid is continuously delivered to the base or a specific points in a tube, while the products are collected from the top. The conversion rate is affected by the residence time of the liquid in the tube. Thickness of the film depends on the volume of the liquid in the tube (which under continuous flow depends on the flow rate), the speed of rotation and angle θ. For a fixed tilt angle and rotational speed, the residence time can be expressed as the ratio of the fluid volume retained in the device to the incoming fluid flow rate. The optimization of the parameters is crucial for the successful use of the VFD since even small alterations can have significant consequences for the final result. For instance, Britton and Raston (2014) used the VFD for room-temperature, catalyst-free conversin of sunflower oil to biodiesel. They found that the percentage of conversion dropped from 100 to 80% when they increased the flow rate from 1 mL/min to 5 mL/min. Furthermore, Sitepu et al. (2018) used the VFD to transesterificate wet microalgae biomass to biodiesel and reported an increase in the conversion efficiency from 30 to 90% when the speed of rotation increased from 4000 to 8000 rpm. Also, in the confined mode, when using the base catalyst, the conversion efficiency dropped for the speed of rotation less than 6000 rpm. Generally, VFD shows the optimal performance for the speed of rotation from 2000 to 9000 rpm and tilt angles $\theta > 0°$, whereby a tilt angle of 45° is most commonly used. Jones and Raston (2017) reported that, for a specific speed along the tube, the film thickness decreases towards the exit and also decreases with speed, with an average thickness 530 μm at 6000 rpm and 294 μm at 8000 rpm.

The possibility of controlling the reactivity and selectivity, as well as the ability of simple and efficient preparation of complex molecules resulted in various chemical transformations being performed using the VFD. Britton et al. (2016) demonstrated the acceleration of enzymatic catalysis for four enzymes using the VFD and established a method to make biocatalysis more practical. Vimalanathan et al. (2017) reported a

surfactant-free, one-step method for the controlled growth of stable nanotubules of fullerene C_{60} within the VFD as a thin film microfluidic platform, avoiding the incorporation of solvent molecules. The VFD tube surface can be easily altered to increase the efficiency of micro-mixing or covalent attachment. Furthermore, it is possible to control the surface contact angle in order to change the fluid's viscous drag. Incorporation of field effects is also achievable, including light sources and lasers. Besides the fact that the product characteristics can be modified by changing the processing parameters, the main advantages of the VFD lie in its low environmental impact and low cost. A possible limitation of the VFD is the use of highly viscous liquids in continuous flow mode, where clogging of the system can happen.

In food technology, the encapsulation of fish oil using VFD has been researched. He et al. (2019) studied the nano-encapsulation of fish oil in the presence of phospholipids. They also compared the results obtained using VFD with those obtained using conventional homogenization. It was reported that the diameter of the encapsulated particles changed significantly; spheroidal particles from 50 to 250 nm in diameter were generated in the VFD, while conventional homogenization yielded particles with diameters ranging from 2 µm to 4 µm. Smaller particles could potentially exhibit better absorption of fish oil. Additional benefits of VFD include elimination of organic solvents and a smaller number of processing steps. Furthermore, the utility of a VFD thin-film microfluidic platform for enzymatic hydrolysis, pasteurization, and encapsulation was explored (He et al., 2019). It was found that the processing time of enzymatic hydrolysis shortens from about 2 to 3 h to 20 min when using the VFD. Additionally, the usage of VFD reduced the processing time of standard pasteurization of raw milk from 30 min to 10 min. VFD was also effective in reducing the size of curcumin particles encapsulated with fish oil and sucrose monolaurate from approximately 1000 nm to less than 100 nm, while avoiding the need for expensive homogenization equipment. Although the VFD is just starting to be used in food processing, these preliminary results show that it has a great potential in the food industry.

5.8. Ball milling

A ball mill is a type of grinder which belongs to the group of tumbling mills, which are divided into few categories, with respect to the type of grinding media and feed particle's size. Besides ball mills, there are pebble mills, autogenous mills, rod mills, and tube mills, which work on the same principle.

Tumbling mills consist of a hollow rotating cylinder, which is usually horizontal but it can also be tilted at a small angle. The length of the cylinder is usually 1 to 1.5 times the cylinder diameter and it contains the grinding media and the particles that need to be broken. As it rotates, the mass inside the mill initially moves up the wall of the cylinder and acquires potential energy. When the force of gravity surpasses the friction and centrifugal forces, it falls into the "toe" of the mill, as potential energy becomes kinetic. This type of movement causes collisions between the grinding media and the mill wall, as well as between the grinding media themselves. The ultimate result is grinding of the particles which are caught in those collisions.

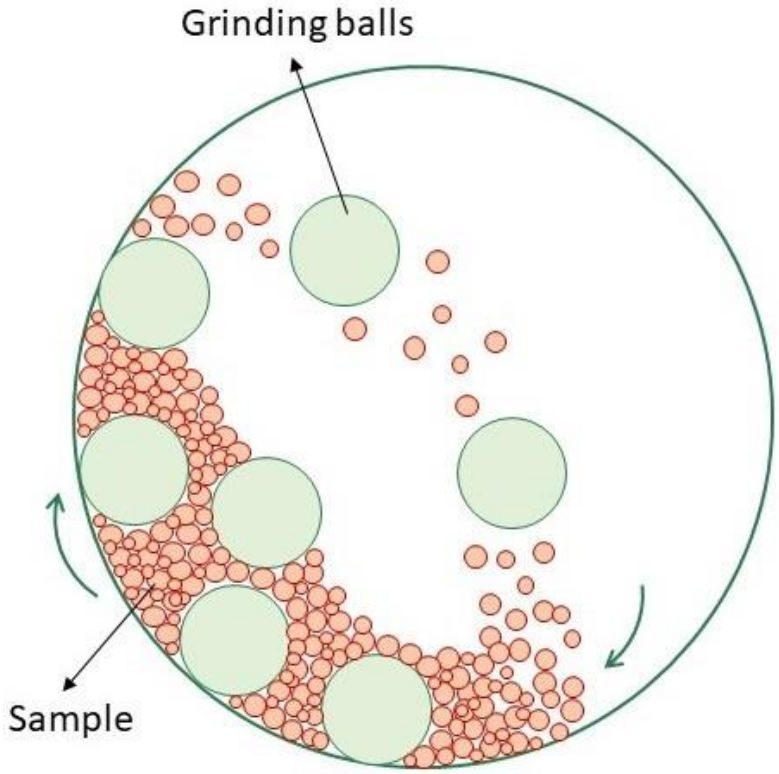

Figure 5-9. Schematic representation of the working principle of ball milling process.

There are two general types of movements that occur during the grinding process in a mill. Cataracting is a process in which grinding balls rise higher inside the cylinder and detach from the interior walls, describing an approximately parabolic trajectory. Cascading implies rolling of the balls one on top of another without falling (Figure 5-9). When a ball mill is working, those movements are combined and they are determined by the friction, centrifugal and gravitational forces, as well as the mutual effect of the lining of the mill and the grinding bodies. The resultant of the gravitational and centrifugal forces cause the occurrence of a centrifugal force field. The center of that field is at a distance of $Y = g/\omega^2$ above the mill axis. When that distance is equal to the radius of the mill shell, the gravitational and centrifugal forces are in equilibrium at the top of the mill shell. At this point, the peripheral speed of the mill is so great that instead of falling, the grinding balls adhere to the mill shell and stay on the perimeter of the mill for a complete revolution, thus causing no further grinding, and the mill starts acting like a centrifuge. This speed is called the critical speed (n_c) and is equal to:

$$n_c = \frac{42.3}{\sqrt{D}} \text{ rpm}$$

where D is the inside diameter in meters. The operational speed (expressed in rpm) is usually given as a percentage of the critical speed. Although there have been instances in which ball mills have been successfully operated at speeds ranging from 60 to 90 percent of their critical speed, it is a common practice to run the mills at speeds between 65 and 80 percent of their critical speed. A cascading movement (Figure 5-10) occurs always, while a cataracting movement depends on the grinding body charge and a friction coefficient, which can be influenced by the shape of the liner plates (Bellopede et al., 2009). Cascading causes finer grinding than cataracting, which is why the mill charge should be bigger for coarser grinding. Ball mills are more applicable for cataracting purposes since the weight effect is well accomplished by spherical bodies.

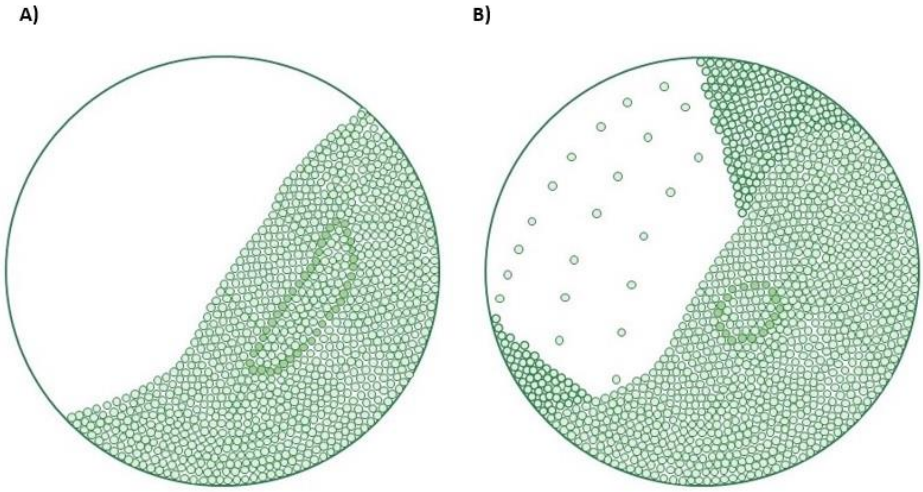

Figure 5-10. Cascading (a) and cataracting movement (B) in a rotary cylinder (Bellopede et al., 2009).

Some parameters need to be considered to get the best possible results. One is the sample to media ratio, which is critical because too much powder will limit the milling efficiency due to the poor media-media contact, resulting in less effective tumbling. Furthermore, the rotation speed must be well adjusted. If it is too fast, the centrifugal force will cause the grinding balls to stick to the sides of a mill. On the other hand, if it is too slow, the balls will only roll around the bottom since there will not be sufficient force to lift them. The right choice of the grinding media is crucial when designing an experiment. Among the materials used as grinding balls, ceramic or steel balls are the most common. The balls should be denser and their size should considerably exceed that of the largest pieces of the sample to be ground. They must be durable enough to grind the particles for a significant amount of time but not so tough that they cause damage to the tumbler. Possible interactions of grinding media and the sample have to be considered. For example, iron can react with corrosive substances, so ceramic or stainless-steel grinding media need to be used. Flammable samples can become explosive as they become smaller. This can be circumvented by selecting balls made from ceramic or lead, which don't produce sparks on impact, and by filling the cylinder with inter gas, which prevents explosive reactions with air.

The main advantage of ball milling is the low cost of installation and grinding media (Takacs, 2002). It is applicable for a variety of materials, with a possibility of open as well as closed circuit grinding. Ball mills can produce powders with average particle sizes less than 1 μm. Also, ball mills are powerful tools in mechanochemistry where the procedure usually offers one-pot, solvent-free reaction routes with large yields, making it environmentally friendly. The milling process can be carried out using dry or wet samples

making this procedure possible for a wide variety of materials. Wet milling requires additional caution because the liquid medium must be removed when the process is complete which can cause the formation of agglomerates.

A possible disadvantage is the fact that the final product may be contaminated from the wear of the grinding balls or the container. To prevent that, the grinding media and container can be coated with hard-wearing ceramic materials such as zirconia. If only the grinding balls are coated, a polymer container must be used. Also, after the completion of the milling process, the sample must be withdrawn. Although there are methods for efficient draining of the mill, it is common that the material remains sticking on the cylinder wall and the surface of the grinding balls. These residues can be washed out, and a part of the sample can be lost.

Planetary ball mill (Figure 5-11) is a special type of ball mill which consists of two or more jars mounted on a disc which is sometimes called the sun wheel. The jars are rotating at an angular velocity *w* around their axis, opposite of the movement of the disc (ratio -2:1 or -1:1), which subjects the grinding balls in the jars to centrifugal and Coriolis forces, which ultimately results in a reduction of the particle size. Compared to common ball mills, planetary ball mills are smaller in size and are mainly used in laboratories for grinding sample materials since this alternative offers a higher degree of energy to create finer or more homogenous size distributions.

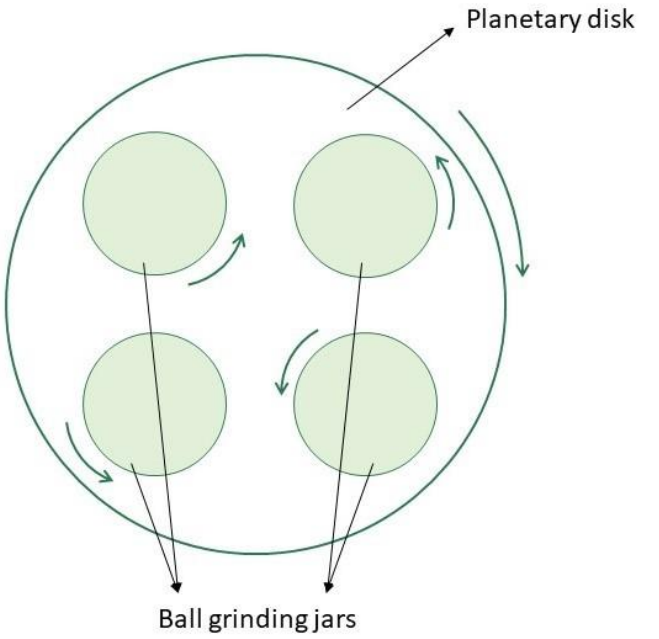

Figure 5-11.Schematic representation of a planetary ball mill (Chauruka et al., 2015).

Recently, a great deal of interest for particle size reduction emerged in the field of food science and biotechnology (Chen et al., 2018). That is mainly due to the altered physical and chemical characteristics of compounds when their size is sufficiently reduced. A smaller size of the particles means that they have a larger surface area which causes better water absorption and solubility. Kim et al. (2001) used ball milling under to convert native potato starch to the relaxed glassy state at ambient temperature and to induce its transition from the glassy to the rubbery state. They showed that the process of ball milling can accelerate enthalpy relaxation and provide an alternative way to make glassy starches of different states. He et al. (2014) studied the physicochemical properties of maize starch subjected to ball milling. It was found that after the ball milling, the surface morphology of starch granules is altered compared to their native state, which causes an increase in their surface area. Furthermore, the transparency and cold-water solubility of starch increased

as well. Those results are consistent with the ones obtained by Huang et al. (2008). Besides maize starch, they also studied cassava starch and concluded that the gelatinization temperature and the enthalpy of gelatinization decrease after ball milling, while their apparent amylose content, cold water solubility, and transparency increase. When compared to milled maize starch, milled cassava starch showed a lower amylose content and a greater cold-water solubility and transparency. Ball milling increased the amorphous regions of the starch granules and decreased their crystalline regions. In addition to starch, the effect of milling on the physicochemical properties was investigated using the peels of root and tuber crops, including yam (*Dioscorea alata* L.), taro (*Colocasia esculenta* L.) and sweet potato (*Ipomea batatas* L.) (Huang et al., 2010). The ball milling process resulted in a redistribution of fibre components from insoluble to soluble, decreased the bulk density and increased the solubility and water-holding capacity of the micronized peels.

5.9. Membrane technology

Membrane technology has been widely used as both processing and separation methods in the food industry. Generally, this technology is used as an alternative to conventional techniques or as an advanced technology for processing foods and production of new ingredients (Dhineshkumar and Ramasamy, 2017). Membranes are semipermeable barriers that allow the separation of certain species by a combination of sieving and diffusion mechanisms into two fractions: a) filtrate or permeate (i.e., fraction passing through the membrane), and b) concentrate or retentate (fraction retained by the membrane).

Depending on the driving force, there are mainly two types of membrane technologies used in the food industry. Membranes based on pressure-driven process, in which the main driving force for separation is transmembrane pressure to overcome natural osmotic pressure (Dhineshkumar and Ramasamy, 2017, Kotsanopoulos and Arvanitoyannis, 2015). These pressure-driven membrane processes include microfiltration, ultrafiltration, nanofiltration, and reverse osmosis. Conversely, electrodialysis (ED) enables separation based on an electrical potential difference as a driving force.

Depending on the specific applications, membrane materials can be hydrophilic or hydrophobic. They could be made of various organic and inorganic materials, providing different properties as a function of the desired separation process. Polymeric membranes are extensively used in the food industry and can be found in a wide range of pore sizes (Dhineshkumar and Ramasamy, 2017). Compared to the inorganic membranes (e.g., ceramic membranes with different metal oxides coatings as active layers), polymeric membranes are significantly cheaper and offer high packing densities. Nevertheless, polymeric membranes are not as mechanically resistant as their inorganic counterparts. They can only work at certain ranges of temperatures, pH, and transmembrane pressures. Inorganic membranes are mainly applied in more extreme industrial conditions but they are considerably expensive. Membranes are packed in membrane modules of different types: plate-and-frame, tubular, hollow-fiber, spiral-wound, or membrane cassette. These modules differ in price and packing density (Dhineshkumar and Ramasamy, 2017). Hollow-fiber and spiral-wound modules have the largest packing density, while plate-and-frame and tubular modules have the lowest packing density. One of the main advantages of membrane technology in the food industry is its green technology approach. Briefly, membrane technology aims to reduce the negative ecological impact of the processes in the food industry. Membrane technology is also considered as a cold process since it does not increase the temperature during process, which allows the natural taste of food products to be preserved (Dhineshkumar and Ramasamy, 2017, Trägårdh, 1991).

In the food industry, one of the most common uses of membrane technology is in the dairy industry. For instance, milk consists of a wide variety of particles of different charges and sizes which enables the use of membranes for an efficient selective separation (Ahmad and Ahmed, 2014). Additional use of membrane technology includes the preparation of food nanomaterials. Membrane emulsification can be used for the

fabrication of nanoemulsions whereby the dispersed phase is converted into fine droplets after passing by force under pressure through the membrane into the continuous phase containing surfactant. The small droplets are surrounded immediately after formation by surfactants present in the continuous phase. The characteristics of the dispersed and continuous phases can have noticeable influences on the droplet size of the membrane emulsified nanoelumsions as well as the properties of the membrane such as its pore size, pore size distribution, pore shape, and hydrophobicity and the type and concentration of surfactant (Charcosset, 2016, Vladisavljević, 2018). The properties of the dispersed phase such as its viscosity play an important role on the membrane emulsification process since it should be passed through the pores of the membrane. In the case of dispersed phased with high viscosities, the process faces troubles. Pre-mix membrane emulsification technique could be an alternative in such situations since the initial coarse emulsion has lower viscosity in comparison to the dispersed phase and make the process easier (Gehrmann and Bunjes, 2017, Charcosset, 2016). For example, Alliod et al. (2018) used pre-mix membrane emulsification for the fabrication of nanoemulsions, which were stable for nine months with an average droplet size of 260 nm. By increasing the pore size, the droplet size of the final produced nanoemulsions increases. Narrow pore-size distribution membranes result in monondispersed nanoemulsions. It has been reported that the distance between the pores of the membrane have also effect on the properties of the fabricated nanoemulsions. The membranes with a higher porosity yielded nanoemulsions with the higher risk of droplets coalescence since the pores are placed close to each other. The type and content of surfactant are also effective parameters on the droplet size. Different types of nanoemulsions have been fabricated using this method applying different types of membranes. For instance, oil-in-water nanoemulsions are emulsified using hydrophilic membranes and water-in-oil nanoemulsions are fabricated using hydrophobic conterparts. Multiple emulsions including water-in-oil-in-water and oil-in-water-in-oil can also be prepared by the membrane emulsification method (Charcosset, 2016, Vladisavljević, 2018).

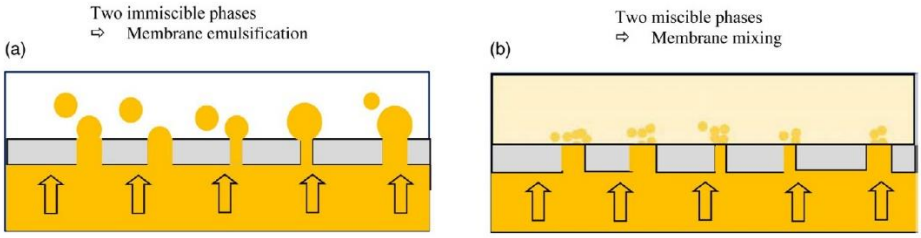

Figure 5-12. Schematic illustration of memebrane emulsification (a) and membrane mixing (b) (Charcosset, 2016).

The membrane mixing method is another technique (Figure 5-12) which has been reported for the preparation of different colloidal systems such as nanocapsules, nanoparticles, nanoliposomes and SLNs with a high efficiency by introducing one solution into another. It has been found that nanoemulsions can also be prepared using membrane mixing method in addition to membrane emulsification method. In this method, in contrast to the membrane emulsification method, there may be a reaction between the two solutions (Charcosset, 2016). Yedomon et al. (2013) prepared nano scale bovine serum albumin particles (139 nm) with a narrow particle size distribution using the membrane mixing method associated with antisolvent method. This protein was first dissolved in ethanol and then passed through the membrane.

For the preparation of nanoliposomes using membrane technique, at first large-size liposomes are formed in the dispersed phase and then their mixture is passed through the membrane pores. This method is called membrane extrusion method, which is a straightforward, efficient and reproducible method for the preparation of nanoliposomes with high encapsulation efficiency. The properties of the formed nanoliposomes depend on the pore size of the membrane as well as the used pressure and tempreture during the process. Membrane mixing method can also be used for the preparation of nanoliposmes, which is based

on the ethanol injection method whereby the bioactive component and the lipids are passed through a membrane under pressure generated by a pump after being dissolved in ethanol.

The process of fabricating SLNs is the same as emulsions using membrane technology while in the preparation of SLNs, the lipid before passing through the membrane is heated at higher temperature of its melting point. The advantage of the preparation of SLNs using the membrane method is the possibility of tuning their size by adjusting the process parameters. Moreover, scaling-up can be achieved easiliy by using membranes with a larger surface.

5.10. Conclusions and future perpective

Food nanomaterials have attracted great interest due to their uniqe characteristics. Among different approaches that exist to produce the nano scale systems, the techniques which require specialized equipment were briefly highlighted in this chapter. Despite the fact that some conventional approaches are expensive to scale up or they use high energy, the reproducibility and the insutrial scale production make them usefull. On the other hand, there is an increasing interest for new methods such as electrospinning, vortex fluidic or micro/nanofluidic devices. These methods are not yet insudtrilized but much of the reaserch has been conducted on them to study different aspects, i.e. optimization of the process. It seems that the novel techniques need an in-depth knowledge to understand the utilization possibility for different food ingredients as variable features such as viscosity, sensitivity to heat, solvent limitation, or size may limit their utilization.

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References

ABDEL-MAGEED, H. M., FOUAD, S. A., TEAIMA, M. H., ABDEL-ATY, A. M., FAHMY, A. S., SHAKER, D. S. & MOHAMED, S. A. 2019. Optimization of nano spray drying parameters for production of α-amylase nanopowder for biotheraputic applications using factorial design. *Drying Technology,* 37**,** 1-9.

ABSTIENS, K. & GOEPFERICH, A. M. 2019. Microfluidic manufacturing improves polydispersity of multicomponent polymeric nanoparticles. *Journal of Drug Delivery Science and Technology,* 49**,** 433-439.

AGARWAL, S., VIVEKANANDAN, S., DAVID, T., MITRA, M., PALANIVELU, J. & CHIDAMBARAM, R. 2019. Nanoemulsions: Industrial Production and Food-Grade Applications. *In:* GUTIÉRREZ, T. J. (ed.) *Polymers for Agri-Food Applications.* Cham: Springer International Publishing.

AHMAD, S. & AHMED, S. K. M. 2014. Application of Membrane Technology in Food Processing. *In:* MALIK, A., ERGINKAYA, Z., AHMAD, S. & ERTEN, H. (eds.) *Food Processing: Strategies for Quality Assessment.* New York, NY: Springer New York.

AKHAVAN, S., ASSADPOUR, E., KATOUZIAN, I. & JAFARI, S. M. 2018. Lipid nano scale cargos for the protection and delivery of food bioactive ingredients and nutraceuticals. *Trends in Food Science & Technology,* 74**,** 132-146.

ALLIOD, O., ALMOUAZEN, E., NEMER, G., FESSI, H. & CHARCOSSET, C. 2019. Comparison of Three Processes for Parenteral Nanoemulsion Production: Ultrasounds, Microfluidizer, and Premix Membrane Emulsification. *Journal of Pharmaceutical Sciences*.

ALLIOD, O., VALOUR, J.-P., URBANIAK, S., FESSI, H., DUPIN, D. & CHARCOSSET, C. 2018. Preparation of oil-in-water nanoemulsions at large-scale using premix membrane emulsification and Shirasu Porous Glass (SPG) membranes. *Colloids and Surfaces A: Physicochemical and Engineering Aspects,* 557**,** 76-84.

AMINE, C., BOIRE, A., DAVY, J., MARQUIS, M. & RENARD, D. 2017. Droplets-based millifluidic for the rapid determination of biopolymers phase diagrams. *Food Hydrocolloids,* 70**,** 134-142.

ANTON, F. 1934. Process and apparatus for preparing artificial threads. Google Patents.

ARORA, R., KUHAD, A., KAUR, I. P. & CHOPRA, K. 2015. Curcumin loaded solid lipid nanoparticles ameliorate adjuvant-induced arthritis in rats. *European Journal of Pain,* 19**,** 940-952.

ARPAGAUS, C., COLLENBERG, A., RÜTTI, D., ASSADPOUR, E. & JAFARI, S. M. 2018. Nano spray drying for encapsulation of pharmaceuticals. *International Journal of Pharmaceutics,* 546**,** 194-214.

ARPAGAUS, C., JOHN, P., COLLENBERG, A. & RÜTTI, D. 2017. 10 - Nanocapsules formation by nano spray drying. *In:* JAFARI, S. M. (ed.) *Nanoencapsulation Technologies for the Food and Nutraceutical Industries.* Academic Press.

ASSADPOUR, E. & JAFARI, S. M. 2019a. Advances in spray-drying encapsulation of food bioactive ingredients: from microcapsules to nanocapsules. *Annual review of food science and technology,* 10**,** 103-131.

ASSADPOUR, E. & JAFARI, S. M. 2019b. Chapter 3 - Nanoencapsulation: Techniques and Developments for Food Applications. *In:* LÓPEZ RUBIO, A., FABRA ROVIRA, M. J., MARTÍNEZ SANZ, M. & GÓMEZ-MASCARAQUE, L. G. (eds.) *Nanomaterials for Food Applications.* Elsevier.

BAI, L. & MCCLEMENTS, D. J. 2016. Development of microfluidization methods for efficient production of concentrated nanoemulsions: Comparison of single- and dual-channel microfluidizers. *Journal of Colloid and Interface Science,* 466**,** 206-212.

BALBINO, T. A., SERAFIN, J. M., RADAIC, A., DE JESUS, M. B. & LUCIMARA, G. 2017. Integrated microfluidic devices for the synthesis of nanoscale liposomes and lipoplexes. *Colloids and Surfaces B: Biointerfaces,* 152**,** 406-413.

BECK-BROICHSITTER, M., STREHLOW, B. & KISSEL, T. 2015. Direct fractionation of spray-dried polymeric microparticles by inertial impaction. *Powder Technology,* 286**,** 311-317.

BELLOPEDE, R., CLERICI, C., MARINI, P. & ZANETTI, G. 2009. Rocks with Asbestos: Risk Evaluation by Means of an Abrasion Test. *American Journal of Environmental Sciences,* 5.

BHARDWAJ, N. & KUNDU, S. C. 2010. Electrospinning: a fascinating fiber fabrication technique. *Biotechnology advances,* 28**,** 325-347.

BORBA, C. M., TAVARES, M. N., MACEDO, L. P., ARAÚJO, G. S., FURLONG, E. B., DORA, C. L. & BURKERT, J. F. M. 2019. Physical and chemical stability of β-carotene nanoemulsions during storage and thermal process. *Food Research International,* 121**,** 229-237.

BRITTON, J., MENEGHINI, L. M., RASTON, C. L. & WEISS, G. A. 2016. Accelerating Enzymatic Catalysis Using Vortex Fluidics. *Angewandte Chemie International Edition,* 55**,** 11387-11391.

BRITTON, J. & RASTON, C. L. 2014. Continuous flow vortex fluidic production of biodiesel. *RSC Advances,* 4**,** 49850-49854.

CHANG, C. & NICKERSON, M. T. 2018. Encapsulation of omega 3-6-9 fatty acids-rich oils using protein-based emulsions with spray drying. *Journal of Food Science and Technology,* 55**,** 2850-2861.

CHARCOSSET, C. 2016. 2 - Preparation of nanomaterials for food applications using membrane emulsification and membrane mixing. *In:* GRUMEZESCU, A. M. (ed.) *Emulsions.* Academic Press.

CHAURUKA, S. R., HASSANPOUR, A., BRYDSON, R., ROBERTS, K. J., GHADIRI, M. & STITT, H. 2015. Effect of mill type on the size reduction and phase transformation of gamma alumina. *Chemical Engineering Science,* 134**,** 774-783.

CHEABURU-YILMAZ, C. N., KARASULU, H. Y. & YILMAZ, O. 2019. Chapter 13 - Nanoscaled Dispersed Systems Used in Drug-Delivery Applications. *In:* VASILE, C. (ed.) *Polymeric Nanomaterials in Nanotherapeutics.* Elsevier.

CHEMAT, F., GRONDIN, I., SING, A. S. C. & SMADJA, J. 2004. Deterioration of edible oils during food processing by ultrasound. *Ultrasonics Sonochemistry,* 11**,** 13-15.

CHEN, S., TAM, Y. Y. C., LIN, P. J. C., SUNG, M. M. H., TAM, Y. K. & CULLIS, P. R. 2016. Influence of particle size on the in vivo potency of lipid nanoparticle formulations of siRNA. *Journal of Controlled Release,* 235**,** 236-244.

CHEN, T., ZHANG, M., BHANDARI, B. & YANG, Z. 2018. Micronization and nanosizing of particles for an enhanced quality of food: A review. *Critical Reviews in Food Science and Nutrition,* 58**,** 993-1001.

CHEONG, A. M. & NYAM, K. L. 2016. Improvement of physical stability of kenaf seed oil-in-water nanoemulsions by addition of β-cyclodextrin to primary emulsion containing sodium caseinate and Tween 20. *Journal of Food Engineering,* 183**,** 24-31.

CHEW, S. Y., WEN, J., YIM, E. K. F. & LEONG, K. W. 2005. Sustained release of proteins from electrospun biodegradable fibers. *Biomacromolecules,* 6**,** 2017-2024.

DE BOER, F. Y., IMHOF, A. & VELIKOV, K. P. 2019. Encapsulation of colorants by natural polymers for food applications. *Coloration Technology,* 135**,** 183-194.

DENG, L., KANG, X., LIU, Y., FENG, F. & ZHANG, H. 2017. Effects of surfactants on the formation of gelatin nanofibres for controlled release of curcumin. *Food Chemistry,* 231**,** 70-77.

DHINESHKUMAR, V. & RAMASAMY, D. 2017. Review on membrane technology applications in food and dairy processing. *Journal of Applied Biotechnology & Bioengineering,* 3**,** 399-407.

DING, Y., ZHENG, J., ZHANG, F. & KAN, J. 2016. Synthesis and characterization of retrograded starch nanoparticles through homogenization and miniemulsion cross-linking. *Carbohydrate Polymers,* 151**,** 656-665.

DOS SANTOS AGUILAR, J. G., CRISTIANINI, M. & SATO, H. H. 2018. Modification of enzymes by use of high-pressure homogenization. *Food Research International,* 109**,** 120-125.

FANG, W., YANG, S., YUAN, T.-Q., CHARLTON, A. & SUN, R.-C. 2017. Effects of Various Surfactants on Alkali Lignin Electrospinning Ability and Spun Fibers. *Industrial & Engineering Chemistry Research,* 56**,** 9551-9559.

FENG, S., ZHENG, X., LUAN, D., SHAO, P. & SUN, P. 2019. Preparation and characterization of zein-based phytosterol nanodispersions fabricated by ultrasonic assistant anti-solvent precipitation. *LWT,* 107**,** 138-144.

FENG, Y. & LEE, Y. 2019. Microfluidic assembly of food-grade delivery systems: Toward functional delivery structure design. *Trends in Food Science & Technology,* 86**,** 465-478.

FERREIRA, C. D. & NUNES, I. L. 2019. Oil nanoencapsulation: development, application, and incorporation into the food market. *Nanoscale research letters,* 14**,** 9.

FERREIRA NOGUEIRA, G., MATTA FAKHOURI, F. & DE OLIVEIRA, R. A. 2019. Incorporation of spray dried and freeze dried blackberry particles in edible films: Morphology, stability to pH, sterilization and biodegradation. *Food Packaging and Shelf Life,* 20**,** 100313.

FONSECA, L. M., DE OLIVEIRA, J. P., DE OLIVEIRA, P. D., DA ROSA ZAVAREZE, E., DIAS, A. R. G. & LIM, L.-T. 2019. Electrospinning of native and anionic corn starch fibers with different amylose contents. *Food research international,* 116**,** 1318-1326.

FREITAS, S., HIELSCHER, G., MERKLE, H. P. & GANDER, B. 2006. Continuous contact-and contamination-free ultrasonic emulsification—a useful tool for pharmaceutical development and production. *Ultrasonics Sonochemistry,* 13**,** 76-85.

GALVÃO, K. C. S., VICENTE, A. A. & SOBRAL, P. J. A. 2018. Development, characterization, and stability of O/W pepper nanoemulsions produced by high-pressure homogenization. *Food and bioprocess technology,* 11**,** 355-367.

GANESAN, P., KARTHIVASHAN, G., PARK, S. Y., KIM, J. & CHOI, D.-K. 2018. Microfluidization trends in the development of nanodelivery systems and applications in chronic disease treatments. *International journal of nanomedicine,* 13**,** 6109-6121.

GAVI, E., KUBICKI, D., PADRON, G. A. & ÖZCAN-TAŞKıN, N. G. 2018. Breakup of nanoparticle clusters using Microfluidizer M110-P. *Chemical Engineering Research and Design,* 132**,** 902-912.

GEHRMANN, S. & BUNJES, H. 2017. Preparation of Nanoemulsions by Premix Membrane Emulsification: Which Parameters Have a Significant Influence on the Resulting Particle Size? *Journal of Pharmaceutical Sciences,* 106**,** 2068-2076.

GILCA, I. A., POPA, V. I. & CRESTINI, C. 2015. Obtaining lignin nanoparticles by sonication. *Ultrasonics Sonochemistry,* 23**,** 369-375.

GOLAY, M. 1957. Vapor phase chromatography and telegrapher's equation. *Analytical Chemistry,* 29**,** 928-932.

GÓMEZ-MASCARAQUE, L. G., SANCHEZ, G. & LÓPEZ-RUBIO, A. 2016. Impact of molecular weight on the formation of electrosprayed chitosan microcapsules as delivery vehicles for bioactive compounds. *Carbohydrate Polymers,* 150**,** 121-130.

GÓMEZ-MASCARAQUE, L. G., TORDERA, F., FABRA, M. J., MARTÍNEZ-SANZ, M. & LOPEZ-RUBIO, A. 2019. Coaxial electrospraying of biopolymers as a strategy to improve protection of bioactive food ingredients. *Innovative Food Science & Emerging Technologies,* 51**,** 2-11.

GONG, P., DI, W., YI, H., SUN, J., ZHANG, L. & HAN, X. 2019. Improved viability of spray-dried Lactobacillus bulgaricus sp1.1 embedded in acidic-basic proteins treated with transglutaminase. *Food Chemistry,* 281**,** 204-212.

GULDIKEN, B., GIBIS, M., BOYACIOGLU, D., CAPANOGLU, E. & WEISS, J. 2018. Physical and chemical stability of anthocyanin-rich black carrot extract-loaded liposomes during storage. *Food Research International,* 108**,** 491-497.

HE, S., JOSEPH, N., LUO, X. & RASTON, C. 2019. Continuous flow thin film microfluidic mediated nano-encapsulation of fish oil. *LWT,* 103**,** 88-93.

HE, S., QIN, Y., WALID, E., LI, L., CUI, J. & MA, Y. 2014. Effect of ball-milling on the physicochemical properties of maize starch. *Biotechnology Reports,* 3**,** 54-59.

HELGASON, T., SALMINEN, H., KRISTBERGSSON, K., MCCLEMENTS, D. J. & WEISS, J. 2015. Formation of transparent solid lipid nanoparticles by microfluidization: Influence of lipid physical state on appearance. *Journal of Colloid and Interface Science,* 448**,** 114-122.

HU, Q., GERHARD, H., UPADHYAYA, I., VENKITANARAYANAN, K. & LUO, Y. 2016. Antimicrobial eugenol nanoemulsion prepared by gum arabic and lecithin and evaluation of drying technologies. *International Journal of Biological Macromolecules,* 87**,** 130-140.

HU, X., LIU, S., ZHOU, G., HUANG, Y., XIE, Z. & JING, X. 2014. Electrospinning of polymeric nanofibers for drug delivery applications. *Journal of Controlled Release,* 185**,** 12-21.

HUANG, C.-C., CHEN, Y.-F. & WANG, C.-C. R. 2010. Effects of micronization on the physico-chemical properties of peels of three root and tuber crops. *Journal of the Science of Food and Agriculture,* 90**,** 759-763.

HUANG, Z.-Q., XIE, X.-L., CHEN, Y., LU, J.-P. & TONG, Z.-F. 2008. Ball-milling treatment effect on physicochemical properties and features for cassava and maize starches. *Comptes Rendus Chimie,* 11**,** 73-79.

ISLAM, M. Z., KITAMURA, Y., KOKAWA, M., MONALISA, K., TSAI, F.-H. & MIYAMURA, S. 2017. Effects of micro wet milling and vacuum spray drying on the physicochemical and antioxidant properties of orange (Citrus unshiu) juice with pulp powder. *Food and Bioproducts Processing,* 101**,** 132-144.

JAFARI, S. M., HE, Y. & BHANDARI, B. 2007. Optimization of nano-emulsions production by microfluidization. *European Food Research and Technology,* 225**,** 733-741.

JASMINA, H., DŽANA, O., ALISA, E., EDINA, V. & OGNJENKA, R. 2017. Preparation of nanoemulsions by high-energy and lowenergy emulsification methods. *CMBEBIH 2017.* Springer.

JEDLIŃSKA, A., SAMBORSKA, K., WIECZOREK, A., WIKTOR, A., OSTROWSKA-LIGĘZA, E., JAMRÓZ, W., SKWARCZYŃSKA-MAJ, K., KIEŁCZEWSKI, D., BŁAŻOWSKI, Ł., TUŁODZIECKI, M. & WITROWA-RAJCHERT, D. 2019. The application of dehumidified air in rapeseed and honeydew honey spray drying - Process performance and powders properties considerations. *Journal of Food Engineering,* 245**,** 80-87.

JIANG, S., YILDIZ, G., DING, J., ANDRADE, J., RABABAHB, T. M., ALMAJWALC, A., ABULMEATYC, M. M. & FENG, H. 2019. Pea Protein Nanoemulsion and Nanocomplex as Carriers for Protection of Cholecalciferol (Vitamin D3). *Food and Bioprocess Technology,* 12**,** 1031-1040.

JONES, D. B. & RASTON, COLIN L. 2017. Improving oxidation efficiency through plasma coupled thin film processing. *RSC Advances,* 7**,** 47111-47115.

JOSHI, S., HUSSAIN, M. T., ROCES, C. B., ANDERLUZZI, G., KASTNER, E., SALMASO, S., KIRBY, D. J. & PERRIE, Y. 2016. Microfluidics based manufacture of liposomes simultaneously entrapping hydrophilic and lipophilic drugs. *International Journal of Pharmaceutics,* 514**,** 160-168.

KAKORIA, A. & SINHA-RAY, S. 2018. A review on biopolymer-based fibers via electrospinning and solution blowing and their applications. *Fibers,* 6**,** 45.

KARTHIK, P., EZHILARASI, P. N. & ANANDHARAMAKRISHNAN, C. 2017. Challenges associated in stability of food grade nanoemulsions. *Critical reviews in food science and nutrition,* 57**,** 1435-1450.

KHAN, I. U., SERRA, C. A., ANTON, N. & VANDAMME, T. 2013. Microfluidics: a focus on improved cancer targeted drug delivery systems. *Journal of controlled release,* 172**,** 1065-1074.

KHAN, I. U., SERRA, C. A., ANTON, N. & VANDAMME, T. F. 2015. Production of nanoparticle drug delivery systems with microfluidics tools. *Expert Opinion on Drug Delivery,* 12**,** 547-562.

KHANJI, A. N., MICHAUX, F., PETIT, J., SALAMEH, D., RIZK, T., JASNIEWSKI, J. & BANON, S. 2018. Structure, gelation, and antioxidant properties of curcumin-doped casein micelle powder produced by spray-drying. *Food & Function,* 9**,** 971-981.

KIM, Y. J., SUZUKI, T., HAGIWARA, T., YAMAJI, I. & TAKAI, R. 2001. Enthalpy relaxation and glass to rubber transition of amorphous potato starch formed by ball-milling. *Carbohydrate Polymers,* 46**,** 1-6.

KNORR, D., ZENKER, M., HEINZ, V. & LEE, D.-U. 2004. Applications and potential of ultrasonics in food processing. *Trends in Food Science & Technology,* 15**,** 261-266.

KOLBASOV, A., SINHA-RAY, S., JOIJODE, A., HASSAN, M. A., BROWN, D., MAZE, B., POURDEYHIMI, B. & YARIN, A. L. 2015. Industrial-scale solution blowing of soy protein nanofibers. *Industrial & Engineering Chemistry Research,* 55**,** 323-333.

KOTSANOPOULOS, K. V. & ARVANITOYANNIS, I. S. 2015. Membrane Processing Technology in the Food Industry: Food Processing, Wastewater Treatment, and Effects on Physical, Microbiological, Organoleptic, and Nutritional Properties of Foods. *Critical Reviews in Food Science and Nutrition,* 55**,** 1147-1175.

KRITCHENKOV, A. S., EGOROV, A. R., DUBASHYNSKAYA, N. V., VOLKOVA, O. V., ZABODALOVA, L. A., SUCHKOVA, E. P., KURLIUK, A. V., SHAKOLA, T. V. & DYSIN, A. P. 2019. Natural polysaccharide-based smart (temperature sensing) and active (antibacterial, antioxidant and photoprotective) nanoparticles with potential application in biocompatible food coatings. *International Journal of Biological Macromolecules,* 134**,** 480-486.

KUMAR, R., KAUR, K., UPPAL, S. & MEHTA, S. K. 2017. Ultrasound processed nanoemulsion: A comparative approach between resveratrol and resveratrol cyclodextrin inclusion complex to study its binding interactions, antioxidant activity and UV light stability. *Ultrasonics Sonochemistry,* 37**,** 478-489.

KUMARI, H., KLINE, S. R., KENNEDY, S. R., GARVEY, C., RASTON, C. L., ATWOOD, J. L. & STEED, J. W. 2016. Manipulating three-dimensional gel network entanglement by thin film shearing. *Chemical Communications,* 52**,** 4513-4516.

KUNTZLER, S. G., COSTA, J. A. V. & MORAIS, M. G. D. 2018a. Development of electrospun nanofibers containing chitosan/PEO blend and phenolic compounds with antibacterial activity. *International Journal of Biological Macromolecules,* 117**,** 800-806.

KUNTZLER, S. G., DE ALMEIDA, A. C. A., COSTA, J. A. V. & DE MORAIS, M. G. 2018b. Polyhydroxybutyrate and phenolic compounds microalgae electrospun nanofibers: A novel nanomaterial with antibacterial activity. *International journal of biological macromolecules,* 113**,** 1008-1014.

KUTZLI, I., GIBIS, M., BAIER, S. K. & WEISS, J. 2019. Electrospinning of whey and soy protein mixed with maltodextrin – Influence of protein type and ratio on the production and morphology of fibers. *Food Hydrocolloids,* 93**,** 206-214.

KYRIAKOUDI, A. & TSIMIDOU, M. Z. 2018. Properties of encapsulated saffron extracts in maltodextrin using the Büchi B-90 nano spray-dryer. *Food Chemistry,* 266**,** 458-465.

LEIDY, R. & MARIA XIMENA, Q.-C. 2019. Use of electrospinning technique to produce nanofibres for food industries: A perspective from regulations to characterisations. *Trends in Food Science & Technology,* 85**,** 92-106.

LI, L., WANG, H., CHEN, M., JIANG, S., JIANG, S., LI, X. & WANG, Q. 2018a. Butylated hydroxyanisole encapsulated in gelatin fiber mats: Volatile release kinetics, functional effectiveness and application to strawberry preservation. *Food Chemistry,* 269**,** 142-149.

LI, X., ANTON, N., ARPAGAUS, C., BELLETEIX, F. & VANDAMME, T. F. 2010. Nanoparticles by spray drying using innovative new technology: The Büchi Nano Spray Dryer B-90. *Journal of Controlled Release,* 147**,** 304-310.

LI, Y., JIN, H., SUN, X., SUN, J., LIU, C., LIU, C. & XU, J. 2019. Physicochemical Properties and Storage Stability of Food Protein-Stabilized Nanoemulsions. *Nanomaterials,* 9**,** 25.

LI, Y., WU, C.-L., LIU, J., ZHU, Y., ZHANG, X.-Y., JIANG, L.-Z., QI, B.-K., ZHANG, X.-N., WANG, Z.-J. & TENG, F. 2018b. Soy protein isolate-phosphatidylcholine nanoemulsions prepared using high-pressure homogenization. *Nanomaterials,* 8**,** 307.

LIU, S., ZHU, W., BAI, X., YOU, T. & YAN, J. 2019. Effect of ultrasonic energy density on moisture transfer during ultrasound enhanced vacuum drying of honey. *Journal of Food Measurement and Characterization,* 13**,** 559-570.

LUO, X., ZHOU, Y., BAI, L., LIU, F., DENG, Y. & MCCLEMENTS, D. J. 2017. Fabrication of β-carotene nanoemulsion-based delivery systems using dual-channel microfluidization: Physical and chemical stability. *Journal of Colloid and Interface Science,* 490**,** 328-335.

LV, S., GU, J., ZHANG, R., ZHANG, Y., TAN, H. & MCCLEMENTS, D. J. 2018. Vitamin E Encapsulation in Plant-Based Nanoemulsions Fabricated Using Dual-Channel Microfluidization: Formation, Stability, and Bioaccessibility. *Journal of Agricultural and Food Chemistry,* 66**,** 10532-10542.

MA, P., ZENG, Q., TAI, K., HE, X., YAO, Y., HONG, X. & YUAN, F. 2017. Preparation of curcumin-loaded emulsion using high pressure homogenization: Impact of oil phase and concentration on physicochemical stability. *LWT,* 84**,** 34-46.

MASTERS, K. 1985. Spray drying handbook. *Spray drying handbook.*

MEHMOOD, T., AHMED, A., AHMAD, A., AHMAD, M. S. & SANDHU, M. A. 2018. Optimization of mixed surfactants-based β-carotene nanoemulsions using response surface methodology: An ultrasonic homogenization approach. *Food Chemistry,* 253**,** 179-184.

MONCADA, M., ASTETE, C., SABLIOV, C., OLSON, D., BOENEKE, C. & ARYANA, K. J. 2015. Nano spray-dried sodium chloride and its effects on the microbiological and sensory characteristics of surface-salted cheese crackers. *Journal of Dairy Science,* 98**,** 5946-5954.

MOREIRA, J. B., LIM, L.-T., ZAVAREZE, E. D. R., DIAS, A. R. G., COSTA, J. A. V. & MORAIS, M. G. D. 2019. Antioxidant ultrafine fibers developed with microalga compounds using a free surface electrospinning. *Food Hydrocolloids,* 93**,** 131-136.

MOREIRA, J. B., TERRA, A. L. M., COSTA, J. A. V. & MORAIS, M. G. D. 2018. Development of pH indicator from PLA/PEO ultrafine fibers containing pigment of microalgae origin. *International Journal of Biological Macromolecules,* 118**,** 1855-1862.

MUHAMMAD, D. R. A., SEDAGHAT DOOST, A., GUPTA, V., DONA BIN SINTANG, M., VAN DE WALLE, D., VAN DER MEEREN, P. & DEWETTINCK, K. 2019. Stability and functionality of xanthan gum–shellac nanoparticles for the encapsulation of cinnamon bark extract. *Food Hydrocolloids***,** 105377.

MÜLLER, R. H., RADTKE, M. & WISSING, S. A. 2002. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Advanced drug delivery reviews,* 54**,** S131-S155.

NEO, Y. P., RAY, S. & PERERA, C. O. 2018. Chapter 4 - Fabrication of Functional Electrospun Nanostructures for Food Applications. *In:* GRUMEZESCU, A. M. & HOLBAN, A. M. (eds.) *Role of Materials Science in Food Bioengineering.* Academic Press.

NIKBAKHT NASRABADI, M., GOLI, S. A. H., SEDAGHAT DOOST, A., DEWETTINCK, K. & VAN DER MEEREN, P. 2019a. Bioparticles of flaxseed protein and mucilage enhance the physical and oxidative stability of flaxseed oil emulsions as a potential natural alternative for synthetic surfactants. *Colloids and Surfaces B: Biointerfaces,* 184**,** 110489.

NIKBAKHT NASRABADI, M., GOLI, S. A. H., SEDAGHAT DOOST, A., ROMAN, B., DEWETTINCK, K., STEVENS, C. V. & VAN DER MEEREN, P. 2019b. Plant based Pickering stabilization of emulsions using soluble flaxseed protein and mucilage nano-assemblies. *Colloids and Surfaces A: Physicochemical and Engineering Aspects,* 563**,** 170-182.

NIU, B., SHAO, P., LUO, Y. & SUN, P. 2020. Recent advances of electrosprayed particles as encapsulation systems of bioactives for food application. *Food Hydrocolloids,* 99**,** 105376.

OLENSKYJ, A. G., FENG, Y. & LEE, Y. 2017. Continuous microfluidic production of zein nanoparticles and correlation of particle size with physical parameters determined using CFD simulation. *Journal of Food Engineering,* 211**,** 50-59.

OTHMAN, R., VLADISAVLJEVIĆ, G. T., HEMAKA BANDULASENA, H. C. & NAGY, Z. K. 2015. Production of polymeric nanoparticles by micromixing in a co-flow microfluidic glass capillary device. *Chemical Engineering Journal,* 280**,** 316-329.

OZTURK, B., ARGIN, S., OZILGEN, M. & MCCLEMENTS, D. J. 2015. Formation and stabilization of nanoemulsion-based vitamin E delivery systems using natural biopolymers: Whey protein isolate and gum arabic. *Food Chemistry,* 188**,** 256-263.

PENALVA, R., ESPARZA, I., AGÜEROS, M., GONZALEZ-NAVARRO, C. J., GONZALEZ-FERRERO, C. & IRACHE, J. M. 2015. Casein nanoparticles as carriers for the oral delivery of folic acid. *Food Hydrocolloids,* 44**,** 399-406.

PERRIER-CORNET, J. M., MARIE, P. & GERVAIS, P. 2005. Comparison of emulsification efficiency of protein-stabilized oil-in-water emulsions using jet, high pressure and colloid mill homogenization. *Journal of Food Engineering,* 66**,** 211-217.

PERSANO, L., CAMPOSEO, A., TEKMEN, C. & PISIGNANO, D. 2013. Industrial upscaling of electrospinning and applications of polymer nanofibers: a review. *Macromolecular Materials and Engineering,* 298**,** 504-520.

PESHKOVSKY, A. S., PESHKOVSKY, S. L. & BYSTRYAK, S. 2013. Scalable high-power ultrasonic technology for the production of translucent nanoemulsions. *Chemical Engineering and Processing: Process Intensification,* 69**,** 77-82.

PESSOA, A. C. S. N., SIPOLI, C. C. & DE LA TORRE, L. G. 2017. Effects of diffusion and mixing pattern on microfluidic-assisted synthesis of chitosan/ATP nanoparticles. *Lab on a Chip,* 17**,** 2281-2293.

PIMENTEL-MORAL, S., TEIXEIRA, M. C., FERNANDES, A. R., ARRÁEZ-ROMÁN, D., MARTÍNEZ-FÉREZ, A., SEGURA-CARRETERO, A. & SOUTO, E. B. 2018. Lipid nanocarriers for the loading of polyphenols–A comprehensive review. *Advances in colloid and interface science,* 260**,** 85-94.

PIRZADA, T., FARIAS, B. V. D., CHU, H. M. A. & KHAN, S. A. 2019. Fabrication of Guar-Only Electrospun Nanofibers by Exploiting a High- and Low-Molecular Weight Blend. *ACS Omega,* 4**,** 10767-10774.

PIYASENA, P., MOHAREB, E. & MCKELLAR, R. C. 2003. Inactivation of microbes using ultrasound: a review. *International journal of food microbiology,* 87**,** 207-216.

PRAKASH, A., BASKARAN, R., PARAMASIVAM, N. & VADIVEL, V. 2018. Essential oil based nanoemulsions to improve the microbial quality of minimally processed fruits and vegetables: A review. *Food Research International,* 111**,** 509-523.

PRASAD REDDY, M. N., PADMA ISHWARYA, S. & ANANDHARAMAKRISHNAN, C. 2019. Nanoencapsulation of roasted coffee bean oil in whey protein wall system through nanospray drying. *Journal of Food Processing and Preservation,* 43**,** e13893.

RAN, R., SUN, Q., BABY, T., WIBOWO, D., MIDDELBERG, A. P. J. & ZHAO, C.-X. 2017. Multiphase microfluidic synthesis of micro- and nanostructures for pharmaceutical applications. *Chemical Engineering Science,* 169**,** 78-96.

RAVIADARAN, R., CHANDRAN, D., SHIN, L. H. & MANICKAM, S. 2018. Optimization of palm oil in water nano-emulsion with curcumin using microfluidizer and response surface methodology. *LWT,* 96**,** 58-65.

RENEKER, D. H. & CHUN, I. 1996. Nanometre diameter fibres of polymer, produced by electrospinning. *Nanotechnology,* 7**,** 216.

RIEGGER, B. R., KOWALSKI, R., HILFERT, L., TOVAR, G. E. M. & BACH, M. 2018. Chitosan nanoparticles via high-pressure homogenization-assisted miniemulsion crosslinking for mixed-matrix membrane adsorbers. *Carbohydrate polymers,* 201**,** 172-181.

RUIZ-MONTAÑEZ, G., RAGAZZO-SANCHEZ, J. A., PICART-PALMADE, L., CALDERÓN-SANTOYO, M. & CHEVALIER-LUCIA, D. 2017. Optimization of nanoemulsions processed by high-pressure homogenization to protect a bioactive extract of jackfruit (Artocarpus heterophyllus Lam). *Innovative Food Science & Emerging Technologies,* 40**,** 35-41.

SALVIA-TRUJILLO, L., ROJAS-GRAÜ, M. A., SOLIVA-FORTUNY, R. & MARTÍN-BELLOSO, O. 2014. Impact of microfluidization or ultrasound processing on the antimicrobial activity against Escherichia coli of lemongrass oil-loaded nanoemulsions. *Food Control,* 37**,** 292-297.

SALVIA-TRUJILLO, L., SOLIVA-FORTUNY, R., ROJAS-GRAÜ, M. A., MCCLEMENTS, D. J. & MARTÍN-BELLOSO, O. 2017. Edible Nanoemulsions as Carriers of Active Ingredients: A Review. *Annual Review of Food Science and Technology,* 8**,** 439-466.

SCHIFFMAN, J. D. & SCHAUER, C. L. 2007a. Cross-linking chitosan nanofibers. *Biomacromolecules,* 8**,** 594-601.

SCHIFFMAN, J. D. & SCHAUER, C. L. 2007b. One-step electrospinning of cross-linked chitosan fibers. *Biomacromolecules,* 8**,** 2665-2667.

SCHIFFMAN, J. D. & SCHAUER, C. L. 2008. A review: electrospinning of biopolymer nanofibers and their applications. *Polymer reviews,* 48**,** 317-352.

SCHRÖDER, A., SPRAKEL, J., SCHROËN, K., SPAEN, J. N. & BERTON-CARABIN, C. C. 2018. Coalescence stability of Pickering emulsions produced with lipid particles: A microfluidic study. *Journal of Food Engineering,* 234**,** 63-72.

SEDAGHAT DOOST, A., AKBARI, M., STEVENS, C. V., SETIOWATI, A. D. & VAN DER MEEREN, P. 2019a. A review on nuclear overhauser enhancement (NOE) and rotating-frame overhauser effect (ROE) NMR techniques in food science: Basic principles and applications. *Trends in Food Science & Technology,* 86**,** 16-24.

SEDAGHAT DOOST, A., DEVLIEGHERE, F., DIRCKX, A. & VAN DER MEEREN, P. 2018a. Fabrication of Origanum compactum essential oil nanoemulsions stabilized using Quillaja Saponin biosurfactant. *Journal of Food Processing and Preservation,* 42**,** e13668.

SEDAGHAT DOOST, A., DEWETTINCK, K., DEVLIEGHERE, F. & VAN DER MEEREN, P. 2018b. Influence of non-ionic emulsifier type on the stability of cinnamaldehyde nanoemulsions: A comparison of polysorbate 80 and hydrophobically modified inulin. *Food Chemistry,* 258**,** 237-244.

SEDAGHAT DOOST, A., KASSOZI, V., GROOTAERT, C., CLAEYS, M., DEWETTINCK, K., VAN CAMP, J. & VAN DER MEEREN, P. 2019b. Self-assembly, functionality, and in-vitro properties of quercetin loaded nanoparticles based on shellac-almond gum biological macromolecules. *International Journal of Biological Macromolecules,* 129**,** 1024-1033.

SEDAGHAT DOOST, A., MUHAMMAD, D. R. A., STEVENS, C. V., DEWETTINCK, K. & VAN DER MEEREN, P. 2018c. Fabrication and characterization of quercetin loaded almond gum-shellac nanoparticles prepared by antisolvent precipitation. *Food Hydrocolloids,* 83**,** 190-201.

SEDAGHAT DOOST, A., NIKBAKHT NASRABADI, M., KASSOZI, V., DEWETTINCK, K., STEVENS, C. V. & VAN DER MEEREN, P. 2019c. Pickering stabilization of thymol through green emulsification using soluble fraction of almond gum – Whey protein isolate nano-complexes. *Food Hydrocolloids,* 88**,** 218-227.

SEDAGHAT DOOST, A., NIKBAKHT NASRABADI, M., KASSOZI, V., NAKISOZI, H. & VAN DER MEEREN, P. 2020. Recent advances in food colloidal delivery systems for essential oils and their main components. *Trends in Food Science & Technology,* 99**,** 474-486.

SEDAGHAT DOOST, A., NIKBAKHT NASRABADI, M., WU, J., A'YUN, Q. & VAN DER MEEREN, P. 2019d. Maillard conjugation as an approach to improve whey proteins functionality: A review of conventional and novel preparation techniques. *Trends in Food Science & Technology,* 91**,** 1-11.

SEDAGHAT DOOST, A., SINNAEVE, D., DE NEVE, L. & VAN DER MEEREN, P. 2017. Influence of non-ionic surfactant type on the salt sensitivity of oregano oil-in-water emulsions. *Colloids and Surfaces A: Physicochemical and Engineering Aspects,* 525**,** 38-48.

SEDAGHAT DOOST, A., STEVENS, C. V., CLAEYS, M. & VAN DER MEEREN, P. 2019e. Fundamental Study on the Salt Tolerance of Oregano Essential Oil-in-Water Nanoemulsions Containing Tween 80. *Langmuir,* 35**,** 10572-10581.

SEDAGHAT DOOST, A., VAN CAMP, J., DEWETTINCK, K. & VAN DER MEEREN, P. 2019f. Production of thymol nanoemulsions stabilized using Quillaja Saponin as a biosurfactant: Antioxidant activity enhancement. *Food Chemistry,* 293**,** 134-143.

SHADDEL, R., AKBARI-ALAVIJEH, S. & JAFARI, S. M. 2019. Chapter Five - Encapsulation of food ingredients by Pickering nanoemulsions. *In:* JAFARI, S. M. (ed.) *Lipid-Based Nanostructures for Food Encapsulation Purposes.* Academic Press.

SHI, A.-M., LI, D., WANG, L.-J., LI, B.-Z. & ADHIKARI, B. 2011. Preparation of starch-based nanoparticles through high-pressure homogenization and miniemulsion cross-linking: Influence of various process parameters on particle size and stability. *Carbohydrate Polymers,* 83**,** 1604-1610.

SHISHIR, M. R. I. & CHEN, W. 2017. Trends of spray drying: A critical review on drying of fruit and vegetable juices. *Trends in food science & technology,* 65**,** 49-67.

SILVA, H. D., CERQUEIRA, M. A. & VICENTE, A. A. 2015. Influence of surfactant and processing conditions in the stability of oil-in-water nanoemulsions. *Journal of Food Engineering,* 167**,** 89-98.

SINGH, N., KHULLAR, N., KAKKAR, V. & KAUR, I. P. 2016. Hepatoprotective effects of sesamol loaded solid lipid nanoparticles in carbon tetrachloride induced sub-chronic hepatotoxicity in rats. *Environmental toxicology,* 31**,** 520-532.

SINGHA, S., BHATTACHARYA, B. & BASU, S. 2016. 20 - Process technology of nanoemulsions in food processing. *In:* GRUMEZESCU, A. M. (ed.) *Encapsulations.* Academic Press.

SITEPU, E. K., CORBIN, K., LUO, X., PYE, S. J., TANG, Y., LETERME, S. C., HEIMANN, K., RASTON, C. L. & ZHANG, W. 2018. Vortex fluidic mediated direct transesterification of wet microalgae biomass to biodiesel. *Bioresource Technology,* 266**,** 488-497.

SU, Y., ZHENG, X., ZHAO, Q., FU, N., XIONG, H., WU, W. D. & CHEN, X. D. 2018. Spray drying of Lactobacillus rhamnosus GG with calcium-containing protectant for enhanced viability. *Powder Technology*.

SUNIL, A. K. 2017. Biopolymer Electrospinning. *Advances in Physicochemical Properties of Biopolymers (Part 2)***,** 410.

SUSLICK, K. S. & PRICE, G. J. 1999. Applications of ultrasound to materials chemistry. *Annual Review of Materials Science,* 29**,** 295-326.

TAKACS, L. 2002. Self-sustaining reactions induced by ball milling. *Progress in Materials Science,* 47**,** 355-414.

TAN, S. F., MASOUMI, H. R. F., KARJIBAN, R. A., STANSLAS, J., KIRBY, B. P., BASRI, M. & BASRI, H. B. 2016a. Ultrasonic emulsification of parenteral valproic acid-loaded nanoemulsion with response surface methodology and evaluation of its stability. *Ultrasonics Sonochemistry,* 29**,** 299-308.

TAN, T. B., YUSSOF, N. S., ABAS, F., MIRHOSSEINI, H., NEHDI, I. A. & TAN, C. P. 2016b. Comparing the formation of lutein nanodispersion prepared by using solvent displacement method and high-pressure valve homogenization: Effects of formulation parameters. *Journal of Food Engineering,* 177**,** 65-71.

TAYLOR, G. I. 1969. Electrically driven jets. *Proceedings of the Royal Society of London. A. Mathematical and Physical Sciences,* 313**,** 453-475.

TIAN, H., LU, Z., LI, D. & HU, J. 2018. Preparation and characterization of citral-loaded solid lipid nanoparticles. *Food Chemistry,* 248**,** 78-85.

TRÄGÅRDH, G. 1991. Membrane Applications in the Food Industry. *Polymer Journal,* 23**,** 521-529.

ULUATA, S., DECKER, E. A. & MCCLEMENTS, D. J. 2016. Optimization of Nanoemulsion Fabrication Using Microfluidization: Role of Surfactant Concentration on Formation and Stability. *Food Biophysics,* 11**,** 52-59.

VENERANDA, M., HU, Q., WANG, T., LUO, Y., CASTRO, K. & MADARIAGA, J. M. 2018. Formation and characterization of zein-caseinate-pectin complex nanoparticles for encapsulation of eugenol. *LWT,* 89**,** 596-603.

VILKHU, K., MAWSON, R., SIMONS, L. & BATES, D. 2008. Applications and opportunities for ultrasound assisted extraction in the food industry—A review. *Innovative Food Science & Emerging Technologies,* 9**,** 161-169.

VIMALANATHAN, K., SHRESTHA, R. G., ZHANG, Z., ZOU, J., NAKAYAMA, T. & RASTON, C. L. 2017. Surfactant-free Fabrication of Fullerene C60 Nanotubules Under Shear. *Angewandte Chemie International Edition,* 56**,** 8398-8401.

VLADISAVLJEVIĆ, G. T. 2018. Chapter 10 - Fabrication of Nanoemulsions by Membrane Emulsification. *In:* JAFARI, S. M. & MCCLEMENTS, D. J. (eds.) *Nanoemulsions.* Academic Press.

WANG, J., OUSSAMA KHELISSA, S., CHIHIB, N.-E., DUMAS, E. & GHARSALLAOUI, A. 2019. Effect of drying and interfacial membrane composition on the antimicrobial activity of emulsified citral. *Food Chemistry,* 298**,** 125079.

WANG, X., UM, I. C., FANG, D., OKAMOTO, A., HSIAO, B. S. & CHU, B. 2005. Formation of water-resistant hyaluronic acid nanofibers by blowing-assisted electro-spinning and non-toxic post treatments. *Polymer,* 46**,** 4853-4867.

XU, J., MUKHERJEE, D. & CHANG, S. K. C. 2018. Physicochemical properties and storage stability of soybean protein nanoemulsions prepared by ultra-high pressure homogenization. *Food Chemistry,* 240**,** 1005-1013.

YARIN, A. L., KOOMBHONGSE, S. & RENEKER, D. H. 2001. Bending instability in electrospinning of nanofibers. *Journal of applied physics,* 89**,** 3018-3026.

YASMIN, L., CHEN, X., STUBBS, K. A. & RASTON, C. L. 2013. Optimising a vortex fluidic device for controlling chemical reactivity and selectivity. *Scientific Reports,* 3**,** 2282.

YEDOMON, B., FESSI, H. & CHARCOSSET, C. 2013. Preparation of Bovine Serum Albumin (BSA) nanoparticles by desolvation using a membrane contactor: A new tool for large scale production. *European Journal of Pharmaceutics and Biopharmaceutics,* 85**,** 398-405.

YILDIZ, G., ANDRADE, J., ENGESETH, N. E. & FENG, H. 2017. Functionalizing soy protein nano-aggregates with pH-shifting and mano-thermo-sonication. *Journal of Colloid and Interface Science,* 505**,** 836-846.

ZAMINDAR, N., BASHASH, M., KHORSHIDI, F., SERJOUIE, A., SHIRVANI, M. A., ABBASI, H. & SEDAGHATDOOST, A. 2017. Antioxidant efficacy of soybean cake extracts in soy oil protection. *Journal of Food Science and Technology,* 54**,** 2077-2084.

ZELENY, J. 1914. The electrical discharge from liquid points, and a hydrostatic method of measuring the electric intensity at their surfaces. *Physical Review,* 3**,** 69.

ZHANG, C., FENG, F. & ZHANG, H. 2018a. Emulsion electrospinning: Fundamentals, food applications and prospects. *Trends in Food Science & Technology,* 80**,** 175-186.

ZHANG, J., GRZYBOWSKI, B. A. & GRANICK, S. 2017. Janus particle synthesis, assembly, and application. *Langmuir,* 33**,** 6964-6977.

ZHANG, L., PAN, Z., SHEN, K., CAI, X., ZHENG, B. & MIAO, S. 2018b. Influence of ultrasound-assisted alkali treatment on the structural properties and functionalities of rice protein. *Journal of Cereal Science,* 79**,** 204-209.

ZHANG, Y., LIU, D., ZHANG, H. & SANTOS, H. A. 2019. Chapter 7 - Microfluidic mixing and devices for preparing nanoparticulate drug delivery systems. *In:* SANTOS, H. A., LIU, D. & ZHANG, H. (eds.) *Microfluidics for Pharmaceutical Applications.* William Andrew Publishing.

ZHUANG, X., YANG, X., SHI, L., CHENG, B., GUAN, K. & KANG, W. 2012. Solution blowing of submicron-scale cellulose fibers. *Carbohydrate Polymers,* 90**,** 982-987.

ZOU, L.-Q., LIU, W., LIU, W.-L., LIANG, R.-H., LI, T., LIU, C.-M., CAO, Y.-L., NIU, J. & LIU, Z. 2014a. Characterization and Bioavailability of Tea Polyphenol Nanoliposome Prepared by Combining an Ethanol Injection Method with Dynamic High-Pressure Microfluidization. *Journal of Agricultural and Food Chemistry,* 62**,** 934-941.

ZOU, L.-Q., PENG, S.-F., LIU, W., GAN, L., LIU, W.-L., LIANG, R.-H., LIU, C.-M., NIU, J., CAO, Y.-L., LIU, Z. & CHEN, X. 2014b. Improved in vitro digestion stability of (−)-epigallocatechin gallate through nanoliposome encapsulation. *Food Research International,* 64**,** 492-499.