Chapter 8
Stability and Release Behavior of Bioactive Compounds (with Antioxidant Activity) Encapsulated by Pickering Emulsion

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8.1 Introduction

Recently, emulsions have attracted tremendous scientific attentions owing to their wide range of useful applications in the field of cosmetics, food, pharmaceuticals and paint, etc. The word "emulsion" is derived from the Latin word mulgeo, mulgere, which means "milk", as milk is a typical example of emulsion containing fat and water, along with other constituents. Emulsions are thermodynamically unstable systems comprising of droplets of a liquid dispersed in another immiscible or partially miscible liquid (Chen et al. 2011). The phase that is present in the form of droplets is known as the dispersed phase, and the phase in which the droplets are suspended is called the continuous phase, whereas the boundary between them is called the "interface". During their passage through the emulsions, these interfaces emit lights which give cloudy appearances to the emulsions (Loi et al. 2019). Common emulsions formed spontaneously are not stable and tend to destabilization because of droplets coalescence. However, the potential applications of emulsions are strongly dependent on their stability, which is to maintain their characteristics as long as possible. Therefore, in order to stabilize these emulsions, the oil and water mixtures require (i) the addition of emulsifiers in the form of amphiphiles which adsorb to the bare oil-water interface, thus preventing droplets coalescence, and (ii) energy input– through exposure to prolong periods of mechanical agitation, stirring, homogenizing or power ultrasound (Kentish et al. 2008). In simple words, it can be stated that an emulsion consists of oil, water and stabilizer (amphiphiles). These emulsions may be of the oil-in-water (O/W) or water-in-oil (W/O) types depending

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on whether the oil is dispersed as droplets in water, or vice versa. If a droplet of the emulsion is dispersed in pure water it is of O/W type, conversely if a droplet is dispersed in pure oil it is regarded as W/O (McClements 2012). Nowadays the most commonly known emulsions used as delivery systems are nano, micro or solid particles stabilized Pickering emulsions. It is important to specify precisely the kind of emulsion used in a particular study, because this affects the most appropriate method used to synthesize them, the foremost factors affecting their stability (such as pH, temperature, presence of salts, etc.) and their physicochemical and functional properties.

Before going to detail about Pickering emulsion, it is important to clarify briefly the confusion between nano and micro emulsions, which are often, miscomprehend due to the prefixes nano and micro relating their droplets size. A nanoemulsion is a conventional surfactant stabilized emulsion with very small particles ($r < 100$ nm) (Tadros et al. 2004). Actually, these kinds of emulsions can be fabricated without surfactants as stabilizer, but practically they will be highly unstable to droplet coalescence and hence surfactants are needed to impart them kinetic stability during storage (McClements 2015). On the other hand, microemulsions are conventional surfactant stabilized emulsions which may also have very small particles ($r < 100$ nm) but are thermodynamically stable contrary to the nanoemulsions which are kinetically stable.

Another important class of emulsions, which are stabilized by solid particles instead of surfactants, is called Pickering emulsions and is discussed in the next section in detail.

8.2 Pickering Emulsions (PEs)

The phenomenon of PE was first introduced one century ago by Ramsden (Ramsden 1904) and later by Pickering (Pickering 1907) Substituting solid particles for traditional surfactants in these emulsions not only make them more stable against coalescence but also impart them many useful properties. For example, some food grade particles as PE stabilizers have lower toxicity, and thus are safe for usage in vivo. In addition, the solid particles confer useful characteristics of enhanced conductivity, responsiveness and porosity. The significant stability of PEs against coalescence can be contributed to the irreversible adsorption of the solid particles onto the interfaces of the dispersed and continuous phases (Low et al. 2017).

The high resistance against coalescence and Oswald ripening makes it possible to preserve the droplets under high concentration of dispersed phase and even they are allowed to dry and re-disperse (Akartuna et al. 2008; Frelichowska et al. 2009). Furthermore, they also have shown enhanced stability against the influence of environmental factors such as pH, temperature, oil composition, ionic strengths and so forth (Shah et al. 2016a). In short, these promising properties make PEs as useful candidates in various disciplines especially in food and nutrition, pharmaceutics and cosmetics where the use of toxic surfactants are undesirable. Therefore, in recent

years scientific community has been paid tremendous attention in the development of cost effective, facile and novel PEs. A simple sketch of the particles stabilized O/W Pickering emulsion has been given in Fig. 8.1.

A wide range of materials has been employed as particulate emulsifier for the fabrication of the PEs including organic particles (e.g. polymer latex and polymer micelle) and inorganic particles (such as silica, hydroxides, and clay particles). To be adsorbed at the interfaces, the particles used should be partially wetted by both the oil and water phases. Depending on the degree of relative wettability of the particles, the emulsions can be classified as either O/W or W/O. The relative wettability of the liquid phases for the solid particles is determined by the three-phase contact angle θ and should be greater than 0° and less than 180°. If the contact angle measured through the aqueous phase is greater than 90°, then the solid particles are relatively more wetted by the oil phase, and in such situations, W/O emulsions are generally formed. When the contact angle θ is less than 90°, the particles are preferentially wetted by the aqueous phase and in such situations, O/W emulsions are formed. In case of θ = 90°, both liquid phases equally wet the particles equally, and in such situations, there is no preferred emulsion O/W or W/O (Fig. 8.2).

Generally, the contact angle is measured through sessile drop method. Briefly, the particles with a specified volume fraction (φ_p) are dispersed in water and are spin-coated onto glass cover slips. The samples are then air-dried overnight before use. Both advancing and receding contact angle measurements are made, and the average used is regarded as the equilibrium contact angle (French et al. 2015).

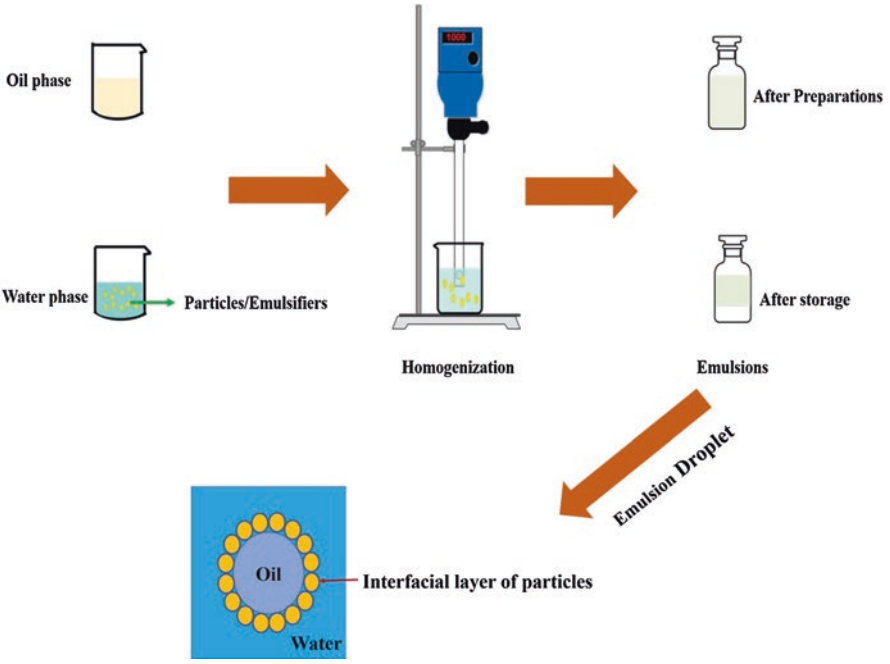

Fig. 8.1 Schematic diagram of the formation of an O/W Pickering

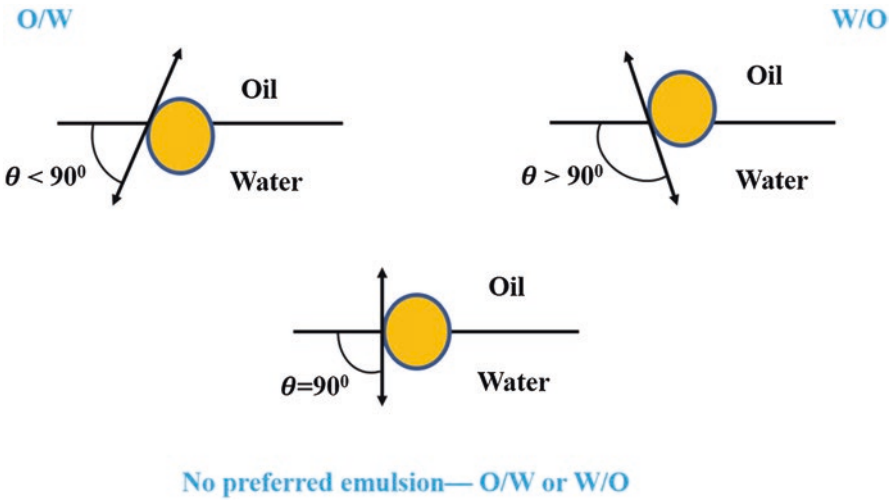

Fig. 8.2 Emulsion types based on wetting conditions of the particles described in terms of contact angle θ between the phases

8.3 Different Types of Particles Used as Stabilizers/ Emulsifiers for PEs

As stated earlier, PEs are the emulsions that are stabilized by solid particles instead of surfactants. These particles are partly wetted by both the phases of PEs i.e. oil and water. Available literature shows that so far various types of particles have been used as emulsifiers to kinetically stabilize the PEs. The particles could be either from inorganic or organic sources and have been discussed below in details.

8.3.1 Inorganic Particles

Inorganic particles such as silica particles have been used extensively as Pickering emulsifiers due to their simple preparation and modification (Jiang et al. 2020). Besides, these particles are of interest as they are commercially available with desirable characteristics such as varying well-defined sizes, surface areas as well as hydrophobicity. Although, these particles were first used as model emulsifiers in the preparation of non-food grade emulsions (Gautier et al. 2007; Horozov and Binks 2006), later on some studies, they were used as food grade emulsifiers as well (Pichot et al. 2010; Skelhon et al. 2012). Both United States Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) have approved silica and other insoluble forms of silicates as safe food additives (up to 1500 mg SiO_2 per day) (EFSA. 2009; FDA. 1979). However, their inorganic and synthetic origin still left a

huge gap for critics on their suitability for food applications. This provided a turning point to the scientific community for paying substantial attention towards biocompatible and biodegradable organic nutrient-based particles as particulate emulsifiers for stabilizing PEs.

8.3.2 Protein-Based Particles

Various protein-based particles have been successfully applied as emulsifiers for the preparation of O/W PEs (McClements 2004). This includes both plant proteins such as zein or soy protein and animal proteins such as whey protein. Zein is a major food grade protein found in corn and is capable of self-assembling to form nano or micro particles. Zein is insoluble in water but soluble in aqueous alcoholic solutions. Consequently, it was supposed that zein-based colloidal particles hold great potential as stabilizers for PEs without surface modification (de Folter et al. 2012). Unfortunately, PEs stabilized solely by zein were unstable and separation was observed only after 3 days of storage. The reason was attributed to the overly hydrophobic nature of the particles obtained through antisolvent approach that facilitated the formation of agglomerates at the aqueous medium. This behavior hinders the particles to be adsorbed at oil droplet surface. Favorably, the problem was solved by combing zein with other hydrophobic compounds such as sodium stearate, chitosan, sodium caseinates (NaCas) etc. that impart significant stability to the synthesized PEs (Gao et al. 2014), (Feng and Lee 2016; Wang et al. 2016). Similarly, PEs stabilized by soy protein for instance soy protein isolate (SPI) or its principal component glycinin (Liu and Tang 2016; Luo et al. 2013) and whey protein isolate (WPI) based PEs have been reported previously (Wu et al. 2015) .

8.3.3 Lipid-Based Particles

In fact, biomaterials with lower environmental influence are considered better candidates in the synthesis of stable PEs. In this context, lipid nanoparticles (NPs) have found a privileged place in the field. Different lipid-based particles have been reported to be efficient PEs stabilizers (Pawlik et al. 2016). The lipid or lipophilic molecules that used for the formation of particulate emulsifiers generally have one or several polar groups (e.g, phytosterols, flavonoids, glyceryl stearyl citrate, or lactylate). The particles from these molecules in aqueous media can be synthesized by mechanical treatments in same way as emulsification process and sometimes may require high temperatures in the case of lipids with high melting points (Gupta and Rousseau 2012).

Lipid based particles were found to stabilize the emulsions of either type i.e., W/O or O/W. For example, fat crystals stabilized W/O PEs like edible spreads were

prepared by various research groups (Dickinson 2012; Rousseau 2013). Most recently W/O as well as O/W PEs as a delivery systems stabilized by solid lipid NPs were reported (Dieng et al. 2019; Pawlik et al. 2016).

8.3.4 Carbohydrate-Based Particles

Modified starch-based particles comprise a large group of food grade emulsifiers for PEs. Particular attention has been given to these materials owing to their striking advantages of being natural ingredient, ample in nature, renewable, biocompatible, biodegradable, sustainable and comparatively cheaper (Dufresne 2014). In order to use them for stabilizing oil-water interfaces, it is necessary to modify them chemically because starches are originally highly hydrophilic. The chemical modification is aimed to create hydrophobicity in these starches and is mostly achieved by partial hydrophobization with octenyl succinic anhydride (OSA) (Miao et al. 2014; Timgren et al. 2013). Consequently, the wetting properties and affinity of the particles for both phases are improved. Most commonly used carbohydrates-based particles include chitin, cocoa powder and cocoa fibers, cellulose and chitin nanocrystals, chitosan and so forth. Among them, in recent years chitosan (CS) has attracted much attention due to its wide range of useful applications in many fields such as biomedical, pharmaceuticals, metal chelation, food additives, and other industrial applications (Guibal et al. 2001; Kumar et al. 2004; Rabea et al. 2003).

CS is a renewable linear cationic polysaccharide composed of randomly distributed β-(1–4)-linked D-glucosamine and N-acetyl-D- glucosamine units (Fig. 8.3a), produced by the deacetylation of chitin. The degree of deacetylation (DD) and molecular weight of CS are the two main characteristics which have a significant impact on its physical and chemical characteristics such as emulsification capacity, aggregation activity, rheological and solution properties (Bodnar et al. 2005). Furthermore, CS has been known as a pH responsive polymer and its amine groups are protonated and positively charged at low pH, giving CS a water-soluble cationic polyelectrolyte character. On contrary, CS amines are deprotonated at high pH and it loses its charge thereby making it insoluble in aqueous medium. Considering this information, a number of attempts were made to synthesize pH tunable CS-NPs as stabilizers for PEs (Asfour et al. 2017; Liu et al. 2012; Wang and Heuzey 2016). In this regard, another important approach for the synthesis of CS-NPs is ionic gelation that involves the ionic interaction between the positively charged primary amino groups of CS and negatively charged groups of poly anions (Konecsni et al. 2012). As an example, using ionic gelation, tripolyphosphate (TPP) crosslinked CS-NPs were synthesized. These NPs were then used as stabilizers for PEs, the preparation of which was optimized first by preparing the PEs at fixed concentration (5 wt%) of medium chain triglyceride (MCT) and subsequently by increasing MCT content to 10, 20, 30 and 50 wt%. As a result, PEs prepared with CS:TPP ratio of 5:5 (w/w) and 50 wt% MCT showed best qualities in term of stability against the tested parameters such as storage time, salts, pH, etc. (Shah et al. 2016a).

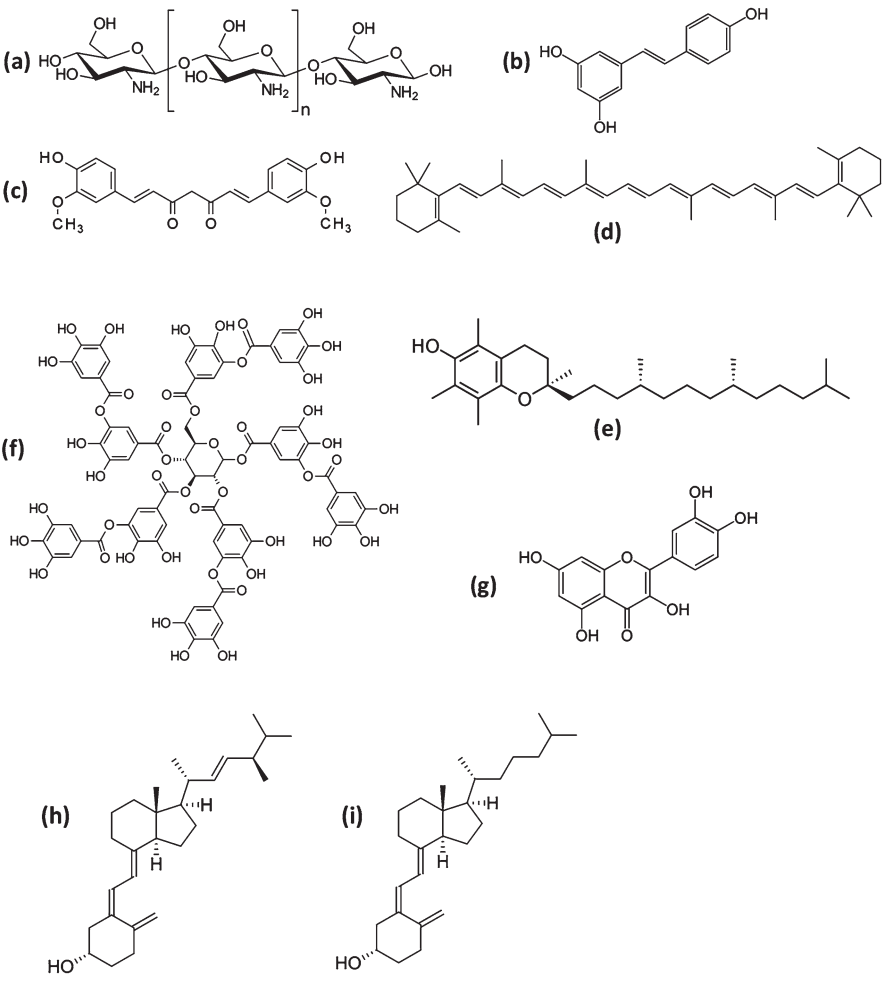

Fig. 8.3 Chemical structures of (**a**) Chitosan, (**b**) Resveratrol, (**c**) Curcumin in Keto form, (**d**) β-carotene, (**e**) α-tocopherol, (**f**) Tannic acid, (**g**) Quercetin, (**h**) vitamina D_2 and (**i**) vitamin D_3

8.4 Factors Influencing Formation and Stability of Pickering Emulsions

In a broader way, emulsion stability denotes the capability of an emulsion to retain its characteristics unchanged over a period of time and against different influencing factors, such as pH, ionic strength, temperature, oil-water ratios, nature of biopolymers and medium, presence of other agents (e.g. surfactants) in the system and charge of biopolymers, etc. Stability of an emulsion is prerequisite for its applications in different industries. Therefore, numerous experimental studies have been conducted on evaluating the stability of PEs to understand the possible physical

mechanisms that prevent droplet coalescence (Frith et al. 2008). This implies that controlling and modification of these procedures will help in enhancing stability and hence significant usage of the PEs. There are various underlying mechanisms corresponding to the destabilization of PEs, which may be influenced by the above-mentioned factors. These mechanisms are as follow:

Gravitational Separation The first common and visually observable mechanism is gravitation separation (GS) of the emulsion into upper cream layer and lower serum layer. The separation occurs because of the difference in density of the continuous and dispersed phases and is explained by Stokes law as below (Eq. 8.1) (Pal 2019):

$$v = \frac{2gr^2\left(\rho_{2-}\rho_1\right)}{9\eta_1}, \tag{8.1}$$

where v is the GS rate (m/s); g is the gravitational acceleration (m/s^2); r is the droplet radius (m); ρ_1 and ρ_2 are the densities of the dispersed and continuous phases (kg/m^3), respectively and η_1 is the continuous phase viscosity (kg/m·s).

From the Stokes equation, certain important presumptions can be withdrawn as follow; (i) depending on the density differences, emulsion droplets will either sediment or cream and (ii) GS rate is directly proportional to the droplet size but inversely proportional to the viscosity of the continuous phase. This means that GS can be slowed down by reducing the droplet size and/or increasing the viscosity of the continuous phase and can be used as a strategy to delay creaming.

Flocculation: is the process of flocs formation that happens due to the aggregation of two or more emulsion droplets, though the droplets maintain their individual identity. It can occur if the attractive forces between dispersed phase droplets overcome the repulsive forces. The droplets stay in close proximity to each other but they do not reach close enough to flocculate by merging into each other. The phenomenon can be explained by Van der Waals interactions/forces, which are always attractive in these dispersions and needs to be counterbalanced by either electrostatic or steric repulsions. The electrostatic interactions can be greatly influenced by the solvent conditions, particularly ionic strength and pH (Mcclements 2007).

Coarsening or Ostwald ripening: is defined as the growth of larger droplets at the expense of smaller ones, either due to the diffusion of disperse phase molecules through the continuous phase or because the solubility of the material within a spherical droplet in the surrounding continuous phase increases as the radius of the droplet decreases. Simply stated, Ostwald ripening is the process of disappearance of small particles or droplets by dissolution and deposition on the larger particles or droplets (Bommana et al. 2019).

Corresponding to the preceding statements, a research group attempted to evaluate the effect of pH, NaCl and oil contents on the PE gels stabilized by wheat protein NPs. In their study, 70% oil content, pH 5.5 and 6.0 in the absence of NaCl were the favorable conditions to obtain a stable PE (Zhu et al. 2018). In another study, it was

found that PEs stabilized by TPP cross linked CS-NPs showed enhanced stability to all the tested parameters including storage time, oil-water ratio, pH and salts (Shah et al. 2016a). Similarly, particle concentration also plays an important role in emulsion stability by preventing Ostwald ripening. One research group defined a minimum particle concentration required to prevent Ostwald ripening, if water-soluble substances are partially in the oil phase. In this study, toluene-in-water emulsions formed at very low concentrations of silanised fumed silica NPs. It was observed that droplets size increased and flocculated together even after gentle rotation of the emulsions. However, increasing the particle concentration to 1 wt%, significantly reduced the rate of droplets coarsening and prevented droplets flocculation. These findings suggested the possible approach for controlling the stability of emulsions formulated with polar, slightly hydrophilic oils at low silica particle concentrations (Juárez and Whitby 2012). Another research group demonstrated similar correlation by describing the influence of particle concentration on the average drop diameter in the emulsion. The particles used in this study were based on partially hydrophobic silica at primary diameter and concentration of 25 nm and 0.7 wt%, respectively. In order to evaluate the effect of particle concentration, all emulsions were prepared by homogenization of the water and oil phases (at an oil volume fraction of 0.33) together for 3 min. The results showed that with increasing particle concentration, emulsion droplet size decreased until a minimum size (≈ 5–20 μm) is reached as the extent of coalescence during drop formation is reduced (Binks and Whitby 2004).

8.5 PEs as Delivery Systems for Bioactive Compounds with Antioxidant Properties

> Antioxidants also called free-radical scavengers (FRS) are substances/compounds that can prevent or slow down oxidation. Oxidation is a chemical process damaging the cells caused by free radicals, unstable molecules that the body produces as a reaction to environmental and other pressures (Lobo et al. 2010).

There are two types of antioxidants i.e. endogenous antioxidants that are produced by the body and exogenous ones, which come from outside the body. In exogenous, particular attention is being paid to natural antioxidants including polyphenols, carotenoids, glucosinolates and different kinds of vitamins such as vitamin E, C, etc.

It is a well-known fact that antioxidants can aid in preventing life threatening pathologies including heart disease, liver disease and some cancers (such as oral, oesophageal, stomach and bowel cancers). Many people have common practice of taking antioxidants in the form of supplements as a defense against these diseases. However, antioxidants available in the form of commercial food additives are prepared synthetically and may contain high contents of preservatives. Several reports claim that synthetic antioxidants, such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and tertiary butyl hydroquinone (TBHQ), can produce toxins or act as carcinogens resulting in the development and progression of cancer

(Nieva-Echevarría et al. 2015). At this point, it is inevitable to discover and rely on vital natural antioxidant sources as an alternative for the synthetic ones to ensure better health. Food is the source of essential nutrients for growth and maintenance; however, other phytochemicals promote health by combating the aging process and preventing disease. Consequently, this provoked the attention of scientific community, food manufacturers, cultivators, and consumers towards the antioxidant constituents from plant materials and their magnificent roles in maintaining human health. Nevertheless, most of these materials based on dietary sources or other phytochemicals have problem concerning their bioavailability implying that they may not be adequately absorbed to stimulate any biological effects (Aqil et al. 2013). This low absorption could most probably because of their hydrophobic nature and therefore, an utmost need was left to develop effective strategies to encapsulate and deliver them to enhance their stability, solubility and bioactivity.

In this regard, biocompatible, biodegradable and food grade materials-based emulsion technology (e.g. PEs) to encapsulate, protect, and release these compounds provided a well-suited platform to accomplish the task. Some examples of the natural lipophilic compounds, which have been known for their potential antioxidants activities encapsulated in PEs, are discussed in the following subsections.

8.5.1 Resveratrol

Resveratrol is a naturally occurring polyphenolic compound (*trans*-3,5,4′-trihydroxystilbene) (Fig. 8.3b) with efficient antioxidant, cardioprotective, anti-inflammatory and anticancer potentials. It is mainly found in red grapes, red wine, white wine, peanuts, blueberries and pistachios.

According to some reports, comparatively peanuts have more resveratrol contents than red grapes which could maybe due to more water contents in red grapes than peanuts (Burns et al. 2002; Sanders et al. 2000). It is believed that low solubility of resveratrol in water (<0.05 mg/mL), caused by its chemical structure affects its absorption in aqueous medium. Moreover, several other problems hindering its biological activities are its photosensitive nature, short biological half-life, and rapid metabolism and elimination. To overcome these issues, numerous resveratrol nano-formulations have been synthesized and evaluated, including liposomes, solid lipid NPs, polymeric NPs and cyclodextrins which have been studied in great detail (Summerlin et al. 2015). However, PEs based formulations to encapsulate and deliver resveratrol demonstrated better outcome among them as hallmarked by several studies.

Similarly, the same research group formulated quinoa starch particles stabilized PEs with a mixture of miglyol and orange oil (in ratio 1:9) as dispersed phase. In comparison to the surfactant (Tween 20) stabilized O/W emulsions, the Pickering emulsions showed higher stability against creaming phenomena and superior encapsulation efficiency (up to 98%), although both types of emulsions had similar droplet sizes. Their formulated system confirmed to be an appropriate resveratrol carrier system for further use in functional food formulations (Matos et al. 2018).

8.5.2 β-Carotene

The term carotenoids is collectively applied to a class of natural coloring agents generally found in fruits and vegetables, and have been used in various food, cosmetic, and pharmaceutical products so far. Besides their role as colorants, carotenoids are also well-appreciated for their health benefits as pro-vitamin A, as well as antioxidants to prevent many chronic diseases, such as cancer, cardiovascular disease, macular degeneration (Rodriguez-Amaya 2015).

Among different carotenoids, β-carotene (Fig. 8.3d) has attracted special attention, due to its abundance and potential bioactive nature. However, the applicability of naturally occurring β-carotene is detained by its highly hydrophobic characteristics as consequence of its unsaturated structure, which makes it insoluble in water and liable to degradation. Furthermore, β-carotene commonly participates in making protein complexes, which hinder its adsorption by human body, thereby significantly lowering its bioavailability. The discussion implies that incorporation of β-carotene into food systems is no doubt challenging but a mandatory job (Rodriguez-Amaya 2015). Therefore, intensive research work has thus been performed in recent years to incorporate β-carotene into functional foods by encapsulating it in PEs in particular, to fulfil its health potentials. In this context, two kinds of PEs stabilized by different concentrations of either whey protein isolate (WPI) or sodium caseinate (NaCas) (0.1 to 2.0 wt%) in 30 wt% sucrose aqueous solution were synthesized with the aim of seeing their comparative protective effects on β-carotene. The outcome of the study showed that the system formulated with 0.8 wt% concentrations of protein had high β-carotene stability. Nevertheless, NaCas provided a better barrier than WPI, probably due to the different amino acid composition and interface structure which significantly reduced β-carotene degradation rate (Cornacchia and Roos 2011). In line with this study, other researchers synthesized O/W PEs based on pea protein isolate (PPI) at pH 3.0 to be used as a delivery system for β-carotene. The required emulsions were produced by microfluidization at a specified protein concentration of 6.0% (w/v) and varying oil fractions (ϕ) between 0.2–0.6. The same procedure was used to prepare β-carotene-loaded PPI emulsions, but the oil phase used here contained β-carotene (30 wt%) which was directly mixed with preheated (~ 45 °C) soy oil to a final concentration of 0.2 wt%. The results demonstrated that increasing ϕ favored the gel-like network strengthening of these emulsions. Most importantly, by conducting the in vitro simulated digestion analysis, it was found that the release of β-carotene during the intestinal digestion of these emulsions was controllable by changing ϕ. The gel-like emulsion at higher oil fractions ($\phi = 0.6$) showed much lower release of β-carotene, but higher stability towards degradation during the digestion, than that at $\phi = 0.3$. The authors concluded that the reported formulation could be an important tool for the design of novel delivery systems for lipophilic bioactive components in general and for the development of plant protein-based formulations in particular (Shao and Tang 2016).

The same research group in another study prepared an O/W emulsion stabilized by soy glycinin particles as a delivery system for β-carotene. They evaluated the release behavior of β-carotene under simulated intestinal conditions. Their findings suggested that β-carotene in the PE was released at a much lower rate than that in a conventional emulsion, and β-carotene was rather stable during the digestion process (Liu and Tang 2016). Most recently, β-carotene was encapsulated in wheat gluten nanoparticles (WGNP) or wheat gluten nanoparticle-xanthan gum (WGNP-XG) complexes. Comparing the two formulations, it was found that the WGNP-XG emulsions had larger initial mean particle diameters (23.9 μm) than the WGNP ones (9.4 μm), but they were still stable against aggregation in wide range of pH values (4–8) and ionic strengths (0–1000 mM NaCl). Furthermore, these PEs demonstrated enhanced protection of the encapsulated β-carotene from chemical degradation during storage, with around 94.3% and 70.1% of the carotenoids being retained after one-month storage at 25 and 37 °C, respectively. Conducting the in vitro digestion experiment, it was found that that β-carotene had a higher bioaccessibility in the WGNP-XG emulsions than in the WGNP ones (Fu et al. 2019).

8.5.3 Curcumin

Curcumin, is a natural and typical flavonoid compound extracted from turmeric *Curcuma longa*, predominantly exists in keto-enol form (1,7-bis(4-hydroxy-3-methoxyphenyl)1,6-heptadiene-3,5-dione) (Fig. 8.3c).

Curcumin is widely used as a spice and food coloring agent in different cuisines and food products as well as in traditional medicine for many centuries in countries such as India and China. Over the past decades, numerous research studies have signified the importance of curcumin as antioxidant, anti-inflammatory, antiarthritic, anti-amyloid, hepatoprotective, thrombo-suppressive, anti-HIV, antimicrobial and antitumor agent (Patra and Sleem 2013).

Although the exact mechanism(s) through which curcumin performs these activities is still unknown, the antioxidant ability of this yellow pigment appears to be an indispensable constituent underlying its pleiotropic biological activities. In fact, curcumin has been reported to hinder lipid peroxidation and to efficiently scavenge superoxide anion and hydroxyl radicals (Ruby et al. 1995). Besides its inherent ability to attenuate the reactivity of oxygen free radical species, curcumin has been shown in vivo to enhance the activities of detoxifying enzymes such as glutathione-S-transferase (Piper et al. 1998). Furthermore, curcumin has established potent inducing effect on heme oxygenase-1 (HO-1), which is one of the genes encoding for proteins having antioxidant characteristics. This pathway supported the enhanced heme oxygenase activity to be an important pillar in curcumin-mediated cytoprotection against oxidative stress (Motterlini et al. 2000).

However, the clinical advancement of curcumin is hindered by its low water solubility (i.e. 0.0004 mg mL^{-1} at pH 7.3) and degradation under physiological conditions. To improve its solubility and hence bioavailability, encapsulation and

delivery approaches based on nanotechnology have been remained the fundamental interest of scientific community from time to time. A wide range of particles have been used for encapsulation of curcumin including liposome, silk fibroin and chitosan, chitosan, β-cyclodextrin inclusion complex, PLGA NPs, nanospheres, phospholipids, cyclodextrin, silica particles and polymeric NPs, etc. (Patra and Sleem 2013; Zhao et al. 2012). Among different formulations, PEs have been shown to efficiently fulfill the duties of encapsulation and delivery. A research group evaluated stability and release behavior of curcumin encapsulated in silica NPs stabilized PEs during storage and simulated gastric and intestinal digestion. Stability and release kinetics of curcumin were characterized describing encapsulated curcumin with stability approximately 100 fold higher than the stability of curcumin suspended in distilled water. Furthermore, the steady release profile confirmed sustained release of over 80% of the encapsulated curcumin in 36 h. During simulated gastric digestion model experiment (2 h), above 80% of the encapsulated curcumin was retained. In addition, incubation in simulated intestinal environment resulted in destabilization of the emulsion and approximately 60% of the encapsulated curcumin was released within 2 h of incubation. Overall, these results demonstrated that PEs has a potential for effective delivery of bioactive compounds (Tikekar et al. 2013). In another report, preparation of TPP crosslinked CS-NPs stabilized PEs for the encapsulation and delivery of curcumin was reported. The preparation of the PEs was optimized, and the emulsions showed enhanced stability during storage and against different pH ranges and salts concentration. The in vitro release profile of the encapsulated curcumin form the PEs confirmed its sustained release over extended period, thereby supporting these PEs as efficient delivery vehicles for curcumin and other bioactive compounds (Shah et al. 2016a). Similarly, in another study, curcumin encapsulated PEs or nanoemulsions were prepared by dissolving curcumin at a concentration of 0.1 wt% either in MCT or LCT (long chain triglyceride) such as corn oil. PE was prepared by homogenizing the aqueous phase containing TPP crosslinked CS-NPs and the oil phase at a speed of 10,000 rpm for 3 min. On the other hand, curcumin encapsulated nanoemulsions were prepared using nonionic surfactants (Span80 and Tween80 at ratio of 1.5:8.5) and the oil phase (5 wt% MCT or LCT) at surfactant to oil ratio (SOR) of 2:1. Results demonstrated slower rate of digestion and consequently lower bioaccessibility values of curcumin in PEs than for nanoemulsions. The authors also indicated that in comparison to the free curcumin, curcumin encapsulated in PEs had higher radical scavenging potentials, which acknowledged the protective effect of the emulsion systems on antioxidant activity of curcumin (Shah et al. 2016b). Another research group synthesized gel-like PE (50%, v/v, oil) stabilized by zein/Tannic acid (TA) complex colloidal particles as a new encapsulation system for lipophilic ingredients such as curcumin. Compared with NaCas-stabilized emulsions and bulk oil, the emulsions stabilized by zein/TA exhibited enhanced shielding effects on the chemical stability of the encapsulated curcumin after exposure to UV light, where the lipid oxidation rate also decreased significantly in these emulsions. It was postulated that the zein particle layers loaded with TA around the oil droplets could protect them versus severe gastric environment, decelerating the release of free

fatty acids (FFA) and curcumin at the time of in vitro simulated digestion. The authors concluded that zein/TA stabilized PEs are promising encapsulating agent to protect bioactive compounds from degradation and control their release during digestion, which can further enhance the bioavailability of these ingredients (Zou et al. 2017). Most recently, PEs stabilized by milled starch particles were fabricated to enhance the bioaccessibility of curcumin via controlling the digestion of lipids in the human gastrointestinal (GI) tract. Through obtaining data from two different evaluating techniques, it was found that the bioaccessibility of encapsulated curcumin in PEs was 27.6% and 50.7%, respectively, in comparison to free curcumin suspended in bulk oil phase, which was 22.1% and 7.8%, respectively. Based on this huge difference in bioaccessibilities of encapsulated and free curcumin, the synthesized PEs were regarded as potential delivery systems for lipophilic bioactive compounds such as curcumin (Lu et al. 2019).

8.5.4 α-Tocopherol

Vitamin E is a collective name used for a group of fat-soluble vitamins that have been known for their distinctive antioxidant activities. Various sources of vitamin E include dietary sources (nuts, such as almonds, peanuts and hazelnuts and vegetable oils such as sunflower, wheat germ, safflower, corn and soybean oils). Some leafy vegetables such as spinach and broccoli also contain vitamin E. Naturally vitamin E occurs in 8 different forms, with 4 tocopherols (alpha, beta, gamma and delta) and 4 tocotrienols. Among these, alpha- (or α-) tocopherol (Fig. 8.3e) is the most common and most potent form that is recognized to meet human requirements (Alqahtani et al. 2015). Substantial evidences acknowledge that daily intake of α-tocopherol may benefit human health due to its antioxidant potency and ability to inhibit various diseases. However, being a strongly hydrophobic molecule, making it difficult to disperse directly into foods and beverages that have an aqueous continuous phase. Additionally, exposure to light, heat, and oxygen promotes the chemical degradation of α-tocopherol during storage, leading to a reduction in its biological activity and nutritional benefits. To overcome these challenges, α-tocopherol can be encapsulated and protected using colloidal delivery systems such as PEs. A research group fabricated WPI stabilized O/W emulsion for the encapsulation and delivery of both α-tocopherol and β-carotene. Summarizing their results, they concluded that highly concentrated O/W emulsions were synthesized with oil fractions of up to 60%. Encapsulation of α-tocopherol and β-carotene did not affect stability of the emulsions rather interestingly confirmed enhanced protection of the encapsulants i.e. α-tocopherol and β-carotene against degradation most likely by the protein layer surrounding the oil droplets (Gaspar et al. 2017).

8.5.5 Vitamin D

Vitamin D is a lipophilic compound, which not only contributes in maintaining normal calcium metabolism, but also plays a vital role in a wide range of non-classic actions. Previous studies have shown that vitamin D has both anti-inflammatory and antiperoxidative activity (Ke et al. 2016). Normally, vitamin D accumulates in adipose tissues and it is believed that a typical adult adipose contain sufficient amounts equivalent to its several months of daily reference intake (DRI) (Hengist et al. 2019). There are two main forms of this vitamin, namely vitamin D_2 (ergocalciferol) (Fig. 8.3h) and vitamin D_3 (cholecalciferol) (Fig. 8.3i). Although foods such as beef liver, dairy products, egg yolk and fish contain small amounts of vitamin D, the main source is sunlight which is needed to modify its precursor 7-dehydrocholesterol into a bio-functional form known as vitamin D_3 (Borel et al. 2015). This implies that people who have little exposure to sunlight or have underlying pathological conditions such as obesity, hyperparathyroidism or gastrointestinal diseases are at high risk of vitamin D_3 deficiency (Cashman 2019). Therefore, there is an intense need to formulate vitamin D_3 enriched functional foods with particular focus on emulsions based encapsulated systems to overcome its oxidative instability as well as to enhance its bioavailability in aqueous environments (Winuprasith et al. 2018). In this regard, in a study O/W PE stabilized by nanofibrillated cellulose (NFC) extracted from mangosteen was developed to encapsulate vitamin D_3. The formulated emulsions contained 10 wt% oil (0.01 wt% vitamin D_3 and 9.99 wt% soybean oil) and 1 wt% NFC as emulsifier. In order to evaluate the impact of NFC on lipid digestion and vitamin bioaccessibility, the in vitro gastrointestinal (GIT) environment consisted of all the three phases i.e. mouth, stomach and small intestine was simulated. The authors observed that an increase in NFC concentration led to a decrease in lipid digestion and vitamin bioaccessiblity. In addition, the results indicated that mangosteen fiber can be used as potential stabilizer for an O/W PE, that exhibited minor effect on lipid digestion and encapsulated vitamin D_3 bioaccessibility when used at relatively low levels (Winuprasith et al. 2018). One year later, a similar study was conducted by the same authors, in which vitamin D_3 was encapsulated in 10% wt soybean O/W PEs stabilized by either NFC or WPI at 0.3 wt%, 0.5 wt% and 0.7 wt%. Stability of the prepared vitamin D_3-loaded emulsions were tested against temperature (30 °C to 90 °C), pH (2 to 8), and ionic strength (0 to 500 mM NaCl). Based on the obtained results, it was concluded that NFC can be used as an efficient emulsifier for producing vitamin enriched emulsions with good long-term stability (Mitbumrung et al. 2019). In a very recent study, vitamin D_3 fortified PEs stabilized by nanochitin (NCh) were prepared. The authors evaluated the effect of emulsifier format (molecular vs particles) on the GIT fate of the emulsions by examining their physicochemical properties, microstructure, digestibility, and bioaccessibility using an in vitro human GIT model. PEs were prepared by homogenization of a 90 wt% aqueous NCh (0.11 wt%) suspension with a 10 wt% oil phase (2 wt% vitamin D_3 in corn oil). The final stock PE contained 0.1 wt% NCh and 10.0 wt% oil. The behavior of these emulsions was compared to those of a

Tween 80-stabilized emulsion, as well as to emulsions containing a combination of nanochitin and Tween 80. After analyzing the results, it was found that the NCh-emulsions experienced much more droplet aggregation within the simulated GIT as compared to the Tween 80-stabilized ones. Vitamin D_3 bioaccessibility was 45% less and lipid digestion was 30% less and for the NCh-emulsions than for the Tween 80-stabilized ones. In conclusion, their findings proposed that NCh decelerate lipid digestion, which may be useful for developing high-satiety foods, however, on the other hand as it also decrease vitamin D_3 bioaccessibility, it could be a bottleneck of the current system from nutritional point of view (Zhou et al. 2020).

8.5.6 Tannic Acid

Tannic acid (TA), is a specific form of tannin and is a naturally occurring plant polyphenol, composed of a central glucose molecule derivatized at its hydroxyl groups with one or more galloyl residues (Gülçin et al. 2010) (Fig. 8.3f). It can be found in practically all aerial plant tissues but mostly in tea, nettle, wood, berries, Chinese galls and oak is believed to be its richest source (Robles 2014). Early studies have shown that TA inhibited skin, lung and forestomach tumors induced by polycyclic aromatic hydrocarbon carcinogens and N-methyl-N-nitrosourea in experimental mice models (Bance and Teel 1989). Furthermore, a line of reports have described that TA has antimutagenic and anticarcinogenic, antihypertensive activities which could be related in part to its antioxidant potential, being a polyphenol (Andrade Jr. et al. 2005). To confirm this claim, the antioxidant and radical scavenging properties of TA with different analytical methodology such as DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) and ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) assays were studied. It was concluded that TA has significant antioxidant potential compared with standard antioxidant compounds e.g. BHA, BHT, tocopherol and trolox (Gülçin et al. 2010). The addition of TA to conventional emulsions can also improve the chemical stability of lipophilic bioactives, which was again attributed to the antioxidant properties of TA (Li et al. 2019; Liu et al. 2020). In this context, some researchers incorporated TA in the formulation of PEs, for example in one of pioneering studies, zein/TA colloidal particles were synthesized based on the hydrogen-bonding interaction between zein and TA in aqueous ethanol solution. Then using these particles at different concentrations (0.25–1.5 wt %), stable PE gels with high corn oil volume fraction (> 50%) were prepared (Zou et al. 2015). Rheological behavior of these PE gels, formulated over a wide range of zein/TA particle concentration (1–5%, w/v) and oil fractions (5–60%, v/v), was investigated as well. Based on the obtained results, it was concluded that the microstructure and rheological properties of the synthesized PE can be switched by altering both the particle concentration as well as the oil content (Zou et al. 2018). In another study, PEs stabilized by zein/TA NPs with weight ratios of zein to TA of 4:1, 2:1 and 1:1

with varying zein concentrations (0.1%, 0.2% or 0.3%, w/v) were prepared. Where the optimum ratio was found to be 0.3% concentration of zein and zein to TA of 1:1. And the emulsion formed at this ratio showed dramatically improved the oxidative stability as compared to others (Zhou et al. 2019).

8.5.7 Quercetin

Quercetin, is an another important representative of polyphenols (Fig. 8.3g), which is mainly found in a variety of human foods including red onions, grapes, apples, berries, cherries, broccoli, citrus fruits, tea (*Camellia sinensis*) and at considerable high concentrations (180 mg per 100 g) in capers and lovage. Quercetin has shown a wide range of biological benefits such as antioxidant activity in radical scavenging, lowering of blood pressure and ameliorating hyperglycemia-related diseases (Bischoff 2008). In aim to enhance the efficacy of the quercetin by enhancing its stability and accessibility, quercetin was encapsulated in W/O PEs stabilized by an interfacial complex of water-insoluble polyphenol crystals and protein. The outcomes found that polyphenol crystals of either curcumin or quercetin absorb at the interface and stabilized water droplets for several days when used alone; however, when WPI was added to the polyphenols, the water-oil interface exhibited a significant improvement in the stabilization of the system (Zembyla et al. 2019). Quercetin was also encapsulated in olive oil in SPI/Pectin-stabilized O/W emulsion. To fabricate the desired emulsions, first SPI/pectin complex particle dispersions were prepared by blending SPI aqueous dispersions (5.0% protein w/w) with specified concentrations of pectin samples (1.0% w/v) in SPI/pectin ratio of 1/1(v/v). Thereafter, this SPI/pectin complex particle suspension was homogenized with oil phase (olive oil 50%) by ultrasonic for 6 min to obtain the required O/W emulsions. The same procedure was applied to formulated quercetin loaded emulsions where 2.0 mL quercetin (0.1 mg/mL) was first dissolved in the oil phase and added to the preceding SPI/pectin complex and was homogenized as mentioned above to prepare the ultimate SPI/pectin complex particle stabilized emulsions with encapsulated quercetin. Stability of the prepared emulsions against pH was further evaluated in different conditions (pH 3.0 to pH 9.0). The results showed that emulsion at pH 3.0 exhibited enhanced stability stable after storage for 30 days' at 4 °C and also showed best freeze-thaw stability after 3 cycles. Moreover, rheological measurements of these emulsions revealed a broad viscoelasticity zone and had the best viscoelasticity stability. In vitro intestinal digestion experiment was performed too and quercetin availability reached 15.94% at pH 7.0 and 7.8% at pH 3.0. Regarding these values for availability, the authors concluded that quercetin can be consumed in a green and healthful way, being encapsulated in SPI/Pectin-stabilized emulsions (Wang et al. 2020).

8.6 Conclusion

Since long time ago, plant-based compounds have been a great source of materials used in beneficial medical treatments. Many plant extracts have been shown antioxidant potentials thereby aiding in treatment and prevention of pathologies like cardiovascular diseases, liver diseases, cancers and other related conditions. However, issues of poor oral bioavailability of these compounds hinder their clinical advancements, and hence need delivery systems to ensure their efficient delivery.

Synthesis of these delivery vehicles are principally aimed to protect the encapsulants from harsh environments e.g. human gut and also to ensure their targeted delivery. Furthermore, most importantly, by maintaining their sustained and controlled release, these systems are supposed to enhance bioavailability of the encapsulated hydrophobic bioactive compounds which have low solubility in aqueous medium that hinder their potential applications in food, pharmaceutical and cosmetic industries. These advantages can be significantly achieved if the synthesized system is of better quality in terms of long-term stability during storage and against different influencing factors such as pH, salts, heat and so on, as well as have reduced toxicity towards the organisms.

In this perspective, among different formulations, PEs have shown to perform the duties proficiently due to their better qualities in terms of long-term stabile and non-toxic nature as compared to the others. PEs are actually-stabilized by biodegradable components derived from different nutrients (e.g. polymers, proteins, fats etc.), differing them from conventional emulsions which are stabilized by surfactants where toxicity is an issue. On these grounds, therefore, in the current chapter we particularly focused on the PEs, firstly on their synthesis, characterization and factors influencing their stability, and thereafter their vital role for encapsulating and delivery of bioactive compounds with well-known antioxidant potentials.

References

Akartuna I, Studart AR, Tervoort E, Gonzenbach UT, Gauckler LJ (2008) Stabilization of oil-in-water emulsions by colloidal particles modified with short amphiphiles. Langmuir 24:7161–7168. https://doi.org/10.1021/la800478g

Alqahtani S et al (2015) Cellular uptake, antioxidant and antiproliferative activity of entrapped α-tocopherol and γ-tocotrienol in poly (lactic-co-glycolic) acid (PLGA) and chitosan covered PLGA nanoparticles (PLGA-Chi). J Colloid Interface Sci 445:243–251. https://doi.org/10.1016/j.jcis.2014.12.083

Andrade RG Jr, Dalvi LT, Silva JMC Jr, Lopes GK, Alonso A, Hermes-Lima M (2005) The antioxidant effect of tannic acid on the in vitro copper-mediated formation of free radicals. Arch Biochem Biophys 437:1–9. https://doi.org/10.1016/j.abb.2005.02.016

Aqil F, Munagala R, Jeyabalan J, Vadhanam MV (2013) Bioavailability of phytochemicals and its enhancement by drug delivery systems. Cancer Lett 334:133–141. https://doi.org/10.1016/j.canlet.2013.02.032

Asfour MH, Elmotasem H, Mostafa DM, Salama AAA (2017) Chitosan based Pickering emulsion as a promising approach for topical application of rutin in a solubilized form intended for wound healing: in vitro and in vivo study. Int J Pharm 534:325–338. https://doi.org/10.1016/j.ijpharm.2017.10.044

Bance R, Teel R (1989) Effect of tannic acid on rat liver S9 mediated mutagenesis, metabolism and DNA binding of benzo [a] pyrene. Cancer Lett 47:37–44. https://doi.org/10.1016/0304-3835(89)90174-2

Binks BP, Whitby CP (2004) Silica particle-stabilized emulsions of silicone oil and water: aspects of emulsification. Langmuir 20:1130–1137. https://doi.org/10.1021/la0303557

Bischoff SC (2008) Quercetin: potentials in the prevention and therapy of disease. Curr Opin Clin Nutr Metab Care 11:733–740. https://doi.org/10.1097/MCO.0b013e32831394b8

Bodnar M, Hartmann JF, Borbely J (2005) Preparation and characterization of chitosan-based nanoparticles. Biomacromolecules 6:2521–2527. https://doi.org/10.1021/bm0502258

Bommana MM, Kirthivasan B, Gupta SS, Shikhar A, Shah A (2019) Nanostructures in pharma: elixir to oral medicine. In: Nanoparticles in pharmacotherapy. Elsevier, Cambridge, MA, pp 23–44. https://doi.org/10.1016/B978-0-12-816504-1.00001-6

Borel P, Caillaud D, Cano N (2015) Vitamin D bioavailability: state of the art. Crit Rev Food Sci Nutr 55:1193–1205. https://doi.org/10.1080/10408398.2012.688897

Burns J, Yokota T, Ashihara H, Lean ME, Crozier A (2002) Plant foods and herbal sources of resveratrol. J Agric Food Chem 50:3337–3340. https://doi.org/10.1021/jf0112973

Cashman KD (2019) Vitamin D deficiency: defining, prevalence, causes, and strategies of addressing. Calcif Tissue Int:1–16. https://doi.org/10.1007/s00223-019-00559-4

Chen J, Vogel R, Werner S, Heinrich G, Clausse D, Dutschk V (2011) Influence of the particle type on the rheological behavior of Pickering emulsions. Colloids Surf A Physicochem Eng Asp 382:238–245. https://doi.org/10.1016/j.colsurfa.2011.02.003

Cornacchia L, Roos YH (2011) Stability of β-carotene in protein-stabilized oil-in-water delivery systems. J Agric Food Chem 59:7013–7020. https://doi.org/10.1021/jf200841k

de Folter JW, van Ruijven MW, Velikov KP (2012) Oil-in-water Pickering emulsions stabilized by colloidal particles from the water-insoluble protein zein. Soft Matter 8:6807–6815. https://doi.org/10.1039/C2SM07417F

Dickinson E (2012) Use of nanoparticles and microparticles in the formation and stabilization of food emulsions. Trends Food Sci Technol 24:4–12. https://doi.org/10.1016/j.tifs.2011.09.006

Dieng SM et al (2019) Pickering nano-emulsions stabilized by solid lipid nanoparticles as a temperature sensitive drug delivery system. Soft Matter. https://doi.org/10.1039/C9SM01283D

Dufresne A (2014) Crystalline starch based nanoparticles. Curr Opin Colloid Interface Sci 19:397–408. https://doi.org/10.1016/j.cocis.2014.06.001

EFSA (2009) Scientific opinion of the panel on food additives and nutrient sources added to food on calcium silicate, silicon dioxide and silicic acid gel added for nutritional purposes to food supplements following a request from the European Commission. EFSA J 1132:1–24. https://doi.org/10.2903/j.efsa.2009.1132

FDA (1979) Select Committee on GRAS Substances (SCOGS) Opinion: silicon dioxides. SCOGS Rep 61, US Food Drug Admin

Feng Y, Lee Y (2016) Surface modification of zein colloidal particles with sodium caseinate to stabilize oil-in-water pickering emulsion. Food Hydrocoll 56:292–302. https://doi.org/10.1016/j.foodhyd.2015.12.030

Frelichowska J, Bolzinger M-A, Valour J-P, Mouaziz H, Pelletier J, Chevalier Y (2009) Pickering w/o emulsions: drug release and topical delivery. Int J Pharm 368:7–15. https://doi.org/10.1016/j.ijpharm.2008.09.057

French DJ, Taylor P, Fowler J, Clegg PS (2015) Making and breaking bridges in a Pickering emulsion. J Colloid Interface Sci 441:30–38. https://doi.org/10.1016/j.jcis.2014.11.032

Frith W, Pichot R, Kirkland M, Wolf B (2008) Formation, stability, and rheology of particle stabilized emulsions: influence of multivalent cations. Ind Eng Chem Res 47:6434–6444. https://doi.org/10.1021/ie071629e

Fu D et al (2019) Encapsulation of β-carotene in wheat gluten nanoparticle-xanthan gum-stabilized Pickering emulsions: enhancement of carotenoid stability and bioaccessibility. Food Hydrocoll 89:80–89. https://doi.org/10.1016/j.foodhyd.2018.10.032

Gao Z-M, Yang X-Q, Wu N-N, Wang L-J, Wang J-M, Guo J, Yin S-W (2014) Protein-based pickering emulsion and oil gel prepared by complexes of zein colloidal particles and stearate. J Agric Food Chem 62:2672–2678. https://doi.org/10.1021/jf500005y

Gaspar RB, Nele M, Ferraz HC (2017) Encapsulation of α-tocopherol and β-carotene in concentrated oil-in-water beverage emulsions stabilized with whey protein isolate. J Dispers Sci Technol 38:89–95. https://doi.org/10.1080/01932691.2016.1144196

Gautier F et al (2007) Pickering emulsions with stimulable particles: from highly-to weakly-covered interfaces. Phys Chem Chem Phys 9:6455–6462. https://doi.org/10.1039/B710226G

Guibal E, Sweeney NVO, Zikan M, Vincent T, Tobin J (2001) Competitive sorption of platinum and palladium on chitosan derivatives. Int J Biol Macromol 28:401–408. https://doi.org/10.1016/S0141-8130(01)00130-1

Gülçin İ, Huyut Z, Elmastaş M, Aboul-Enein HY (2010) Radical scavenging and antioxidant activity of tannic acid. Arab J Chem 3:43–53. https://doi.org/10.1016/j.arabjc.2009.12.008

Gupta R, Rousseau D (2012) Surface-active solid lipid nanoparticles as Pickering stabilizers for oil-in-water emulsions. Food Funct 3:302–311. https://doi.org/10.1039/C2FO10203J

Hengist A et al (2019) Mobilising vitamin D from adipose tissue: the potential impact of exercise. Nutr Bull 44:25–35. https://doi.org/10.1111/nbu.12369

Horozov TS, Binks BP (2006) Particle-stabilized emulsions: a bilayer or a bridging monolayer? Angew Chem Int Ed 45:773–776. https://doi.org/10.1002/ange.200503131

Jiang H, Sheng Y, Ngai T (2020) Pickering emulsions: versatility of colloidal particles and recent applications. Curr Opin Colloid Interface Sci 49:1–15. https://doi.org/10.1016/j.cocis.2020.04.010

Juárez JA, Whitby CP (2012) Oil-in-water Pickering emulsion destabilisation at low particle concentrations. J Colloid Interface Sci 368:319–325. https://doi.org/10.1016/j.jcis.2011.11.029

Ke C-Y et al (2016) Vitamin D3 reduces tissue damage and oxidative stress caused by exhaustive exercise. Int J Med Sci 13:147. https://doi.org/10.7150/ijms.13746

Kentish S, Wooster TJ, Ashokkumar M, Balachandran S, Mawson R, Simons L (2008) The use of ultrasonics for nanoemulsion preparation. Innov Food Sci Emerg Technol 9:170–175. https://doi.org/10.1016/j.ifset.2007.07.005

Konecsni K, Low N, Nickerson M (2012) Chitosan–tripolyphosphate submicron particles as the carrier of entrapped rutin. Food Chem 134:1775–1779. https://doi.org/10.1016/j.foodchem.2012.03.070

Kumar MR, Muzzarelli RA, Muzzarelli C, Sashiwa H, Domb A (2004) Chitosan chemistry and pharmaceutical perspectives. Chem Rev 104:6017–6084. https://doi.org/10.1021/cr030441b

Li R et al (2019) Bioaccessibility and stability of β-carotene encapsulated in plant-based emulsions: impact of emulsifier type and tannic acid. Food Funct 10:7239–7252. https://doi.org/10.1039/C9FO01370A

Liu F, Tang C-H (2016) Soy glycinin as food-grade Pickering stabilizers: part. I. Structural characteristics, emulsifying properties and adsorption/arrangement at interface. Food Hydrocoll 60:606–619. https://doi.org/10.1016/j.foodhyd.2015.04.025

Liu H, Wang C, Zou S, Wei Z, Tong Z (2012) Simple, reversible emulsion system switched by pH on the basis of Chitosan without any hydrophobic modification. Langmuir 28:11017–11024. https://doi.org/10.1021/la3021113

Liu Y et al (2020) Enhancement of beta-carotene stability by encapsulation in high internal phase emulsions stabilized by modified starch and tannic acid. Food Hydrocoll 109:106083. https://doi.org/10.1016/j.foodhyd.2020.106083

Lobo V, Patil A, Phatak A, Chandra N (2010) Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn Rev 4:118. https://doi.org/10.4103/0973-7847.70902

Loi CC, Eyres GT, Birch EJ (2019) Protein-stabilised emulsions. In: Melton L, Shahidi F, Varelis P (eds) Encyclopedia of food chemistry. Academic, Oxford, pp 404–409. https://doi.org/10.1016/B978-0-08-100596-5.22490-6

Low LE, Tey BT, Ong BH, Chan ES, Tang SY (2017) Palm olein-in-water Pickering emulsion stabilized by Fe3O4-cellulose nanocrystal nanocomposites and their responses to pH. Carbohydr Polym 155:391–399. https://doi.org/10.1016/j.carbpol.2016.08.091

Lu X, Zhu J, Pan Y, Huang Q (2019) Assessment of dynamic bioaccessibility of curcumin encapsulated in milled starch particle stabilized Pickering emulsions using TNO's gastrointestinal model. Food Funct 10:2583–2594. https://doi.org/10.1039/C8FO02495B

Luo L-J, Liu F, Tang C-H (2013) The role of glycinin in the formation of gel-like soy protein-stabilized emulsions. Food Hydrocoll 32:97–105. https://doi.org/10.1016/j.foodhyd.2012.11.031

Matos M, Laca A, Rea F, Iglesias O, Rayner M, Gutiérrez G (2018) O/W emulsions stabilized by OSA-modified starch granules versus non-ionic surfactant: stability, rheological behaviour and resveratrol encapsulation. J Food Eng 222:207–217. https://doi.org/10.1016/j.jfoodeng.2017.11.009

McClements DJ (2004) Protein-stabilized emulsions. Curr Opin Colloid Interface Sci 9:305–313. https://doi.org/10.1016/j.cocis.2004.09.003

Mcclements DJ (2007) Critical review of techniques and methodologies for characterization of emulsion stability. Crit Rev Food Sci Nutr 47:611–649. https://doi.org/10.1080/10408390701289292

McClements DJ (2012) Nanoemulsions versus microemulsions: terminology, differences, and similarities. Soft Matter 8:1719–1729. https://doi.org/10.1039/C2SM06903B

McClements DJ (2015) Food emulsions: principles, practices, and techniques. CRC Press, Boca Raton

Miao M, Li R, Jiang B, Cui SW, Zhang T, Jin Z (2014) Structure and physicochemical properties of octenyl succinic esters of sugary maize soluble starch and waxy maize starch. Food Chem 151:154–160. https://doi.org/10.1016/j.foodchem.2013.11.043

Mitbumrung W, Suphantharika M, McClements DJ, Winuprasith T (2019) Encapsulation of vitamin D3 in Pickering emulsion stabilized by Nanofibrillated Mangosteen cellulose: effect of environmental stresses. J Food Sci 84:3213–3221. https://doi.org/10.1111/1750-3841.14835

Motterlini R, Foresti R, Bassi R, Green CJ (2000) Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. Free Radic Biol Med 28:1303–1312. https://doi.org/10.1016/S0891-5849(00)00294-X

Nieva-Echevarría B, Manzanos MJ, Goicoechea E, Guillén MD (2015) 2, 6-Di-tert-butylhydroxytoluene and its metabolites in foods. Compr Rev Food Sci Food Saf 14:67–80. https://doi.org/10.1111/1541-4337.12121

Pal R (2019) Modeling of sedimentation and creaming in suspensions and pickering emulsions. Fluids 4:186. https://doi.org/10.3390/fluids4040186

Patra D, Sleem F (2013) A new method for pH triggered curcumin release by applying poly (l-lysine) mediated nanoparticle-congregation. Anal Chim Acta 795:60–68. https://doi.org/10.1016/j.aca.2013.07.063

Pawlik A, Kurukji D, Norton I, Spyropoulos F (2016) Food-grade Pickering emulsions stabilised with solid lipid particles. Food Funct 7:2712–2721. https://doi.org/10.1039/C6FO00238B

Pichot R, Spyropoulos F, Norton I (2010) O/W emulsions stabilised by both low molecular weight surfactants and colloidal particles: The effect of surfactant type and concentration. J Colloid Interface Sci 352:128–135. https://doi.org/10.1016/j.jcis.2010.08.021

Pickering SU (1907) Cxcvi.—emulsions. J Chem Soc Transactions 91:2001–2021

Piper JT, Singhal SS, Salameh MS, Torman RT, Awasthi YC, Awasthi S (1998) Mechanisms of anticarcinogenic properties of curcumin: the effect of curcumin on glutathione linked detoxification enzymes in rat liver. Int J Biochem Cell Biol 30:445–456. https://doi.org/10.1016/S1357-2725(98)00015-6

Rabea EI, Badawy ME-T, Stevens CV, Smagghe G, Steurbaut W (2003) Chitosan as antimicrobial agent: applications and mode of action. Biomacromolecules 4:1457–1465. https://doi.org/10.1021/bm034130m

Ramsden W (1904) Separation of solids in the surface-layers of solutions and 'suspensions'(observations on surface-membranes, bubbles, emulsions, and mechanical

coagulation).—preliminary account. Proc R Soc London 72:156–164. https://doi.org/10.1098/rspl.1903.0034
Robles H (2014) Tannic acid. In: Wexler P (ed) Encyclopedia of toxicology, 3rd edn. Academic, Oxford, pp 474–475. https://doi.org/10.1016/B978-0-12-386454-3.00542-X
Rodriguez-Amaya DB (2015) Nomenclature, structures, and physical and chemical properties. Food Carotenoids: Chemistry, Biology, and Technology. Chichester: John Wiley & Sons, Ltd. 1–23
Rousseau D (2013) Trends in structuring edible emulsions with Pickering fat crystals. Curr Opin Colloid Interface Sci 18:283–291. https://doi.org/10.1016/j.cocis.2013.04.009
Ruby AJ, Kuttan G, Babu KD, Rajasekharan K, Kuttan R (1995) Anti-tumour and antioxidant activity of natural curcuminoids. Cancer Lett 94:79–83. https://doi.org/10.1016/0304-3835(95)03827-j
Sanders TH, McMichael RW, Hendrix KW (2000) Occurrence of resveratrol in edible peanuts. J Agric Food Chem 48:1243–1246. https://doi.org/10.1021/jf990737b
Shah BR et al (2016a) Preparation and optimization of Pickering emulsion stabilized by chitosan-tripolyphosphate nanoparticles for curcumin encapsulation. Food Hydrocoll 52:369–377. https://doi.org/10.1016/j.foodhyd.2015.07.015
Shah BR, Zhang C, Li Y, Li B (2016b) Bioaccessibility and antioxidant activity of curcumin after encapsulated by nano and Pickering emulsion based on chitosan-tripolyphosphate nanoparticles. Food Res Int 89:399–407. https://doi.org/10.1016/j.foodres.2016.08.022
Shao Y, Tang C-H (2016) Gel-like pea protein Pickering emulsions at pH 3.0 as a potential intestine-targeted and sustained-release delivery system for β-carotene. Food Res Int 79:64–72. https://doi.org/10.1016/j.foodres.2015.11.025
Skelhon TS, Grossiord N, Morgan AR, Bon SA (2012) Quiescent water-in-oil Pickering emulsions as a route toward healthier fruit juice infused chocolate confectionary. J Mater Chem 22:19289–19295. https://doi.org/10.1039/C2JM34233B
Summerlin N, Soo E, Thakur S, Qu Z, Jambhrunkar S, Popat A (2015) Resveratrol nanoformulations: challenges and opportunities. Int J Pharm 479:282–290. https://doi.org/10.1016/j.ijpharm.2015.01.003
Tadros T, Izquierdo P, Esquena J, Solans C (2004) Formation and stability of nano-emulsions. Adv Colloid Interface Sci 108:303–318. https://doi.org/10.1016/j.cis.2003.10.023
Tikekar RV, Pan Y, Nitin N (2013) Fate of curcumin encapsulated in silica nanoparticle stabilized Pickering emulsion during storage and simulated digestion. Food Res Int 51:370–377. https://doi.org/10.1016/j.foodres.2012.12.027
Timgren A, Rayner M, Dejmek P, Marku D, Sjöö M (2013) Emulsion stabilizing capacity of intact starch granules modified by heat treatment or octenyl succinic anhydride. Food Sci Nutr 1:157–171. https://doi.org/10.1002/fsn3.17
Wang L-J, Yin S-W, Wu L-Y, Qi J-R, Guo J, Yang X-Q (2016) Fabrication and characterization of Pickering emulsions and oil gels stabilized by highly charged zein/chitosan complex particles (ZCCPs). Food Chem 213:462–469. https://doi.org/10.1016/j.foodchem.2016.06.119
Wang Q, Wei H, Deng C, Xie C, Huang M, Zheng F (2020) Improving stability and accessibility of Quercetin in olive oil-in-soy protein isolate/pectin stabilized O/W emulsion. Foods 9:123. https://doi.org/10.3390/foods9020123
Wang XY, Heuzey MC (2016) Chitosan-based conventional and Pickering emulsions with long-term stability. Langmuir 32:929–936. https://doi.org/10.1021/acs.langmuir.5b03556
Winuprasith T, Khomein P, Mitbumrung W, Suphantharika M, Nitithamyong A, McClements DJ (2018) Encapsulation of vitamin D3 in Pickering emulsions stabilized by nanofibrillated mangosteen cellulose: impact on in vitro digestion and bioaccessibility. Food Hydrocoll 83:153–164. https://doi.org/10.1016/j.foodhyd.2018.04.047
Wu J et al (2015) Pickering emulsions stabilized by whey protein nanoparticles prepared by thermal cross-linking. Colloids Surf B Biointerfaces 127:96–104. https://doi.org/10.1016/j.colsurfb.2015.01.029

Zembyla M, Murray BS, Radford SJ, Sarkar A (2019) Water-in-oil Pickering emulsions stabilized by an interfacial complex of water-insoluble polyphenol crystals and protein. J Colloid Interface Sci 548:88–99. https://doi.org/10.1016/j.jcis.2019.04.010

Zhao L, Du J, Duan Y, Zhang H, Yang C, Cao F, Zhai G (2012) Curcumin loaded mixed micelles composed of Pluronic P123 and F68: preparation, optimization and in vitro characterization. Colloids Surf B Biointerfaces 97:101–108. https://doi.org/10.1016/j.colsurfb.2012.04.017

Zhou B, Gao S, Li X, Liang H, Li S (2019) Antioxidant Pickering emulsions stabilised by zein/tannic acid colloidal particles with low concentration. Int J Food Sci Technol 55:1924–1934. https://doi.org/10.1111/ijfs.14419

Zhou H et al (2020) Nanochitin-stabilized Pickering emulsions: influence of nanochitin on lipid digestibility and vitamin bioaccessibility. Food Hydrocoll 106:105878. https://doi.org/10.1016/j.foodhyd.2020.105878

Zhu YQ, Chen X, McClements DJ, Zou L, Liu W (2018) Pickering-stabilized emulsion gels fabricated from wheat protein nanoparticles: effect of pH NaCl and oil content. J Dispers Sci Technol 39:826–835. https://doi.org/10.1080/01932691.2017.1398660

Zou Y, Guo J, Yin S-W, Wang J-M, Yang X-Q (2015) Pickering emulsion gels prepared by hydrogen-bonded zein/tannic acid complex colloidal particles. J Agric Food Chem 63:7405–7414. https://doi.org/10.1021/acs.jafc.5b03113

Zou Y, Zhong J, Pan R, Wan Z, Guo J, Wang J, Yin S, Yang X (2017) Zein/tannic acid complex nanoparticles-stabilised emulsion as a novel delivery system for controlled release of curcumin. International Journal of Food Science & Technology 52:1221–1228

Zou Y, Yang X, Scholten E (2018) Rheological behavior of emulsion gels stabilized by zein/tannic acid complex particles. Food Hydrocoll 77:363–371. https://doi.org/10.1016/j.foodhyd.2017.10.013