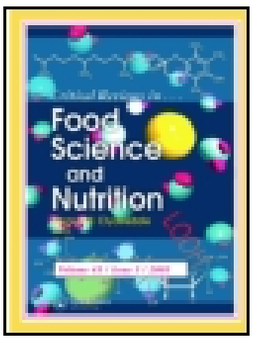

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REVIEW

The influence of nanodelivery systems on the antioxidant activity of natural bioactive compounds

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ABSTRACT

Bioactive compounds may lose their antioxidant activity (e.g., phenolic compounds) at elevated temperatures, enhanced oxidative conditions and severe light exposures so they should be protected by various strategies such as nano/microencapsulation methods. Encapsulation technology has been employed as a proper method for using antioxidant ingredients and to provide easy dispersibility of antioxidants in all matrices including food and pharmaceutical products. It can improve the food fortification processes, release of antioxidant ingredients, and extending the shelf-life and bioavailability of them when ingested in the intestine. In this study, our main goal is to have an overview of the influence of nanoencapsulation on the bioactivity and bioavailability, and cellular activities of antioxidant ingredients in different delivery systems. Also, the effect of encapsulation process conditions, storage conditions, carrier wall materials, and release profile on the antioxidant activity of different natural bioactives are explained. Finally, analytical techniques for measuring antioxidant activity of nanoencapsulated ingredients will be covered.

KEYWORDS

Encapsulation; antioxidant activity; bioactive ingredients; analytical techniques; nanocarriers; biopolymers

Introduction

Recent years have witnessed an increasing interest in the antioxidants for the inhibition of radicals and oxidative stresses, cancer prophylaxis and therapy and longevity (Jafari 2019; Rostami et al. 2019). A number of chemical and physical phenomena can initiate oxidation, which proceed continuously in the presence of suitable substrates, until a blocking defense mechanism occurs (Antolovic et al. 2002; Ming-Hua and Schaich 1996). The initiation, propagation, branching and termination are four crucial properties of a free radical-mediated oxidation reaction. This procedure could be triggered by an external agent (such as light, heat or ionizing radiation) or a chemical initiator like a metallic ion or a metalloprotein (Kanner, German, and Kinsella 1987). Target substances include oxygen, polyunsaturated fatty acids, phospholipids, cholesterol and DNA (Antolovic et al. 2002). Antioxidants can retard or prevent the process of oxidation which takes place under the effect of atmospheric oxygen or due to reactive oxygen species (ROS) (Kalcher et al. 2009). Antioxidants play a major role in the defense mechanism against free radical-induced pathogenic conditions (Litescu et al. 2011).

As described in Table 1, natural antioxidants can be divided into two classes, namely enzymatic antioxidants and nonenzymatic antioxidants (Ramadan-Hassanien 2008; Taghvaei and Jafari 2015). Enzymes, low-molecular weight molecules and enzyme cofactors are several examples of the endogenously secreted antioxidants (Moharram and Youssef 2014). Nonenzymatic antioxidants are mainly obtained from dietary sources that can be classified into various classes; polyphenols present the largest class in this group (Assadpour, Jafari, and Esfanjani 2017; Esfanjani and Jafari 2016). Exogenous antioxidants can be either natural-based or synthetic (Litescu et al. 2011).

Hydrolyzed proteins and bioactive peptides are also considered as exogenous antioxidants (Akbarbaglu et al. 2019; Sarabandi et al. 2018). There are numerous antioxidants in dietary plants (Lindsay and Astley 2002; Ramadan-Hassanien 2008). In human tissues, cellular low molecular weight antioxidants can be attained through different sources. Nicotinamide adenine dinucleotide (reduced form), glutathione (GSH) and carnosine can be derived through the cell; while, bilirubin and uric acid (UA) are classified as the waste products of the cell metabolisms. Tocopherols, ascorbic acid and polyphenols are the dietary-supplied antioxidants (Chance, Sies, and Boveris 1979; Ames et al. 1981; Stocker et al. 1987; Frei, England, and Ames 1989).

Polyphenols can be found in a diverse range of structures. The phenolic ring is the major monomer of polyphenol which can be categorized as phenolic acids and phenolic alcohols. Polyphenols could also be classified according to the strength of their phenolic rings. However, phenolic acids, flavonoids, stiblins, phenolic alcohols, and lignans are among the prominent classes. Polyphenols can be categorized into flavonoids and nonflavonoid groups as well (Piccolella and Pacifico 2015). Flavonoids (such as

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Table 1. Classification of natural antioxidants.

First class	Second class	Third class
Endogenous or enzymatic antioxidants	Primary enzymes	Catalase, peroxidase, glutathione, superoxide dismutase
	Secondary enzymes	Glucose 6-phosphate, glutathione peroxidase, dehydrogenase
Exogenous or nonenzymatic antioxidants	Vitamins	A, C, E, D, K3
	Carotenoids	β-Carotene, lutein, lycopene, zeaxanthin, astaxanthin
	Minerals	Selenium, zinc
	Organosulfur compounds	Indoles, allium, allyl sulfide,
	Uric acid	
	Albumin	
	Metallothioneins	
	Polyphenols	Anthocyanins, flavones, flavonols, isoflavones, flavanones, coumarins, hydroxybenzoic acids, tannins
	Hydrolyzed proteins and bioactive peptides	
	Bilirubin	

flavanones, flavanols, flavonols, isoflavones, flavons, and anthocyanidins) have two benzene rings connected by a three-carbon chain from the neighboring pyran ring. Furthermore, six classes of flavonoids are different in terms of the oxidation state of the central carbon. In flavonols, a double bond can be observed between C3 and C2 while the hydroxyl group is attached to C3. The major backbone of flavonoids is C6–C3–C6 which encompasses two phenolic units (C6) (Abbas et al. 2017). The nonflavonoid polyphenols possess a higher variability and mainly comprise of benzophenones, hydroxycinnamic acid derivatives (e.g., caffeic acid phenyl ester, caffeoyl phenylethanoids, curcumin, rosmarinic acid, and their derivatives), hydrolyzable tannins (gallotannins and ellagitannins), lignans, stilbenes, and xanthones (Piccolella and Pacifico 2015). Cinnamic acid and benzoic acid derivatives possess C1–C6 and C3–C6 backbones, respectively (Abbas et al. 2017).

Bioactive compounds may lose their antioxidant activity (e.g., phenolic compounds) at elevated temperatures, enhanced oxidative conditions and severe light exposures; so they should be protected by encapsulation methods (Khaled, Hatem, and Azza 2018; Taghvaei et al. 2014; Maqsoudlou et al. 2020). Encapsulation technology has been employed as a proper method for using antioxidant food ingredients (Abbasi et al. 2019; Ghorbanzade et al. 2017; Mohammadi et al. 2016). Encapsulation process involves loading the bioactive compounds in a carrier surrounded by diverse food-grade materials. In this way, the wall substances will serve as a shield and protect the incorporated ingredients from various stresses. Moreover, encapsulation can result in controlled and targeted release (Jafari et al. 2008).

Three major methods could be applied to prepare biopolymeric nanostructures: top-down, bottom-up, and their combination. Top-down strategies involve the use of instrumental/high energy processes to decline the size to nanoscale. Nano spray drying, high-pressure homogenization, micro-fluidization, ultrasonication, milling, electrospinning, electrospraying, micro/nanofluidics, and vortex fluidic systems are some of the examples (Jafari 2019). The top-down approaches are benefited from the possibility of mass production, high industrial potentials, and fast processing. In the case of bottom-up techniques, nanomaterials are made by low-energy/formulation-based approaches starting from precursors (Esfanjani, Assadpour, and Jafari 2018, Esfanjani and Jafari 2016). Molecular and atomic self-assembly to nanosized structures, the formation of protein-polysaccharide coacervates, desolvation, layer-by-layer deposition, conjugation, micro-emulsification, precipitation, and templates are some of the examples. Nanoemulsions can be prepared utilizing the internal chemical energy of the systems. This approach can offer smaller droplet sizes in comparison with high-energy ones (Jafari 2019). Higher stability, transparency, energy efficiency, cost-effectiveness, and feasibility are among the advantages of these techniques (Jafari 2019; Esfanjani, Assadpour, and Jafari 2018).

Among encapsulation techniques, spray-drying is a common method for encapsulation of bioactive food ingredients, because it is fast, cheap, and has a high reproducibility (Gharsallaoui et al. 2007; Arpagaus et al. 2018; Assadpour and Jafari 2019). Conventional spray drying can be used to prepare particles at micron scale. The atomization methods can offer large nonuniform droplet diameters (Esfanjani and Jafari 2016). The piezoelectric-driven vibrating mesh atomizer has recently enabled the experimental formation of nanoparticles as small as 100 nm in nano spray dryers. This technique requires droplet dispersion through sonication using the meshes whose size is smaller than the micron mesh window diameter followed by drying at mild conditions within a medium-velocity laminar flow. The dried particles will be then collected in an electrostatic particle collector with high product detainment and yields above 90% (Jafari 2019). There are several advantages for micro/nanoencapsulation of antioxidants which have been depicted briefly in Figure 1.

Although there have been some published papers on the encapsulation of antioxidant compounds in the form of a review article or book chapter, none of them have focused on the various aspects/effects of the encapsulation process on the antioxidant properties with a systematic investigation. In this study, first the influence of encapsulation and the role of different nanocarriers on the antioxidant activity of food bioactives will be explained and then, a brief overview of analytical techniques for measuring the antioxidant activity of nanoencapsulated ingredients is presented.

Figure 1. Importance of nanoencapsulation for antioxidant food ingredients.

The role of encapsulation on retaining the antioxidant activity of food bioactives

Nanoencapsulation of the bioactive ingredients can be considered as an appropriate method to protect their activity (Esfanjani and Jafari, 2017). Nanoparticle synthesis parameters including polymer weight and composition, surfactant, synthesis method, hydrophobicity, surface charge and particle size, directly affect nanoparticle physicochemical properties and antioxidant release rate (Stevanovic and Uskokovic, 2009). The mentioned features could ultimately influence the performance of antioxidants and their application in food and pharmaceutical industries (Pereira et al. 2017).

Bioactivity and bioavailability of nanoencapsulated antioxidant ingredients

Food bioactive ingredients and nutraceuticals must be prevented from digestion when passing through the upper gastrointestinal tract (GIT), (in particular, the stomach). In an ideal situation, they should be released in the intestine as they can easily enter the blood stream, upon crossing the epithelial wall, and finally reach the target organ (Livney 2015). In this regard, nanoencapsulation has been introduced as a promising approach to offer protection for food bioactive ingredients and present a delivery system for nutraceuticals (Assadpour, Jafari, and Esfanjani 2017). Nanoencapsulation of antioxidants can alleviate their bioactivity and bioavailability in addition to free radical removal and anti-disease features. Bioactivity is the specific effect upon exposure to a substance. It includes tissue uptake and the consequent physiological response (e.g., antioxidant, anti-inflammatory, etc.). It also includes information on how the bioactive compounds are transported and reached the target tissue, how they interact with biomolecules, metabolism and biotransformation characteristics, as well as the biomarkers' generation and the consequent physiological responses.

Bioavailability is a measure of the efficiency of bioactive compounds, being the fraction of ingested bioactive amount that becomes available to manifest its bioactivity at the level of body organs and tissues (Dima et al. 2020). Despite their relation, bioavailability and bioaccessibility are two different concepts that could be misunderstood. Bioaccessibility refers to the amount of a compound released from a matrix and becomes accessible for absorption upon the digestion process. On the other hand, bioavailability can be defined as the amount of a compound reaching the systemic circulation and showing its effect after metabolization and tissue distribution (Gonçalves et al., 2019). Therefore, the intended components of a food matrix should be released and be available for absorption into the bloodstream. The

knowledge of diverse mechanisms through which these components cross the epithelium and reach the bloodstream is also of crucial significance (Gonçalves et al., 2019).

In fact, nanoencapsulation can enhance the bioavailability of antioxidant food ingredients by elevating their solubility, absorption and permeation in the body (Maqsoudlou et al. 2020). Compared to their microencapsulated counterparts, the nanoencapsulated antioxidants have a higher stability under stomach conditions (enzymatic reactions and low pH) (Palafox-Carlos, Ayala-Zavala, and GonzáLez-Aguilar 2011). Large surface area and tunable release of the nanoencapsulated antioxidant ingredients can protect them against enzymatic reactions in low-pH stomach (Maqsoudlou et al. 2020). Nanoencapsulation also facilitates the passive absorption of antioxidants from the intestine lumen to the lymphatic and blood circulation. This will enhance their bioavailability (Li et al. 2015; Esfanjani, Assadpour, and Jafari 2018). There are many studies dealing with the influence of encapsulation on the bioactivity and bioavailability of antioxidant ingredients; some of them are listed in Table 2.

As an example, curcumin has been frequently served as a model for natural bioactives (Rafiee et al. 2018). Its absorption from GIT is restricted due to its low solubility after oral administration, giving rise to its reduced bioavailability (Fang and Bhandari 2010). Thus, curcumin encapsulation by sodium caseinate (NaCas) through spray drying enhanced its solubility up to 137 μg/mL (Pan, Zhong, and Baek 2013). According to Sari et al. (2015), curcumin-loaded nanoemulsions possess a higher stability and bioavailability compared with nonencapsulated curcumin. Moreover, the curcumin release kinetic profile from the nanoemulsions in simulated gastrointestinal conditions revealed a slow rate; such a slow release can enhance the curcumin bioavailability. Some other studies have suggested the possibility of improving the bioactivity and bioavailability through loading curcumin into SLNs[1] (Kakkar et al. 2011; Sun-Waterhouse, Wadhwa, and Waterhouse 2013). The antioxidant-loaded SLNs exhibited a higher bioavailability than their free counterparts. In a study by Yadav et al. (2012), curcumin encapsulation in chitosan nanoparticles was addressed. Their results indicated enhanced antioxidant and chelating potential of encapsulated curcumin (at far less dosage) in comparison with free curcumin.

According to Sessa et al. (2011), nanoencapsulation of resveratrol[2] can improve its bioavailability, preventing from chemical degradation and avoiding its fast metabolism. Results indicated that resveratrol encapsulation in oil-in-water (O/W) nanoemulsions (prepared by natural and food grade ingredients only) can resist metabolism during in vitro gastric and intestinal digestions. Furthermore, the formulations with finer average droplet sizes (<200 nm) can retain their physical stability through the digestion procedure; this will let the resveratrol reach the intestinal wall while being entrapped by lipid droplets. In addition, lecithin-based nanoemulsions improved transport across the cell monolayer as well as enhancing the passive transport mechanism because of their structure resemblance to the cellular membrane phospholipid bilayers. Eventually, nanoencapsulation facilitates the continuous release of bioactive substances and avoids their unwanted instantaneous release. The in vitro antioxidant activity retention of nanoencapsulated resveratrol during digestion was evaluated by FRAP and oxygen radical absorption capacity (ORAC). Based on the results, nanoencapsulated resveratrol managed to retain the antioxidant activity as compared to its nonencapsulated peer. *In vitro* digestion led to the decline of antioxidant activity for all formulations; in particular, in the gastric step. This could be attributed to the enlarged droplet size after gastric passage causing a profound decline in the surface area (two orders of magnitude) which can ultimately make resveratrol unavailable by the oil/water interfaces.

The impact of dietary lipids on the GI behavior of tangeretin-loaded zein nanoparticles was assessed by Chen et al. (2014). Tangeretin bioavailability showed an enhancement with fat content elevation in O/W emulsions. Hence, it can be concluded that lipid nanoparticles are capable of improving the bioavailability of hydrophobic bioactive substances (i.e., tangeretin) (Jafari 2019). Catechin encapsulation was achieved by chitosan/γ-poly glycolic acid (PGA) to increase its oral bioavailability, as it shows pH sensitivity within the gastrointestinal media. The release profiles of tea catechin-loaded nanoparticles were highly pH-dependent in the simulated GIT medium. The free radical ((2,2-diphenyl-1-picrylhydrazyl) (DPPH) and 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid (ABTS)) scavenging assays also suggested the antioxidant retention of tea catechins following encapsulation. Owing to their positive surface charge, these nanoparticles are capable of interacting with Caco-2 cells membranes, causing a decline in the epithelial trans-electrical resistance (TEER) and an enhanced permeation (Teng, Li, and Wang 2014; Jafari 2019). Catechin has also been encapsulated in a carbohydrate matrix by Ferreira, Rocha, and Coelho (2007) who managed to prevent its oxidation and improve its bioavailability.

The anthocyanins are an important group of antioxidants with low bioavailability, which can be assigned to their degradation during gastrointestinal digestion. The anthocyanins are usually lost in food production as can be rapidly deteriorated upon exposure to pH, temperature, oxygen, light, and metal ions. The encapsulation approach can enhance the efficiency of these bioactive compounds by raising their solubility, bioavailability, stability, or controlling their release (Li et al. 2015). Some of the studies dealing with the influence of encapsulation on the bioactivity and bioavailability of anthocyanin are shown in Table 2.

Cellular antioxidant activity (CAA) of nanoencapsulated food bioactives

Direct cellular uptake of natural antioxidants increases after nanoencapsulation within micelles and nanoemulsions and has a key role in enhancing the cellular antioxidant features

[1]Solid lipid nanoparticles.
[2]A low soluble polyphenolic entity abundant in peanuts and red grape.

Table 2. Bioactivity and bioavailability of nanoencapsulated antioxidant ingredients.

Bioactive ingredients	Nanocarriers	Purpose	Reference
Capsaicin	Complex of gelatin and acacia	Increasing antioxidant activity, and melting point and improving degradation properties	Jincheng, Xiaoyu, and Sihao (2010)
Curcumin	β-Casein	Increasing the solubility of curcumin and its cytotoxicity to human leukemia cell line K-562 and antioxidant activity	Esmaili et al. (2011)
Curcumin	Chitosan cross-linked with tripolyphosphate	Increasing antioxidant and anticancer activity	Sowasod, Charinpanitkul, and Tanthapanichakoon (2008)
Phenolics, tocopherols and sterols from red fleshed pitaya seed oil	Gum arabic/maltodextrin Gum arabic/lactose Sodium caseinate/maltodextrin Sodium caseinate/lactose Whey protein/maltodextrin	Increasing antioxidant activity	Lim et al. (2012).
Root extract	PLGA nanoparticles	Higher ability to scavenge free radicals of bioactive components	Kumar and Anand (2016)
Quercetin and catechin	PLGA nanoparticles	Enhancing superoxide anion-scavenging activity and the chelating properties	Pool et al. (2012)
Quercetin	Chitosan	Improving the DPPH radical scavenging activity and reducing power	Zhang et al. (2008)
β-Carotene	NLCs	Protection and increasing the bioavailability of β-carotene	Hejri et al. (2013)
β-Carotene	Nanoemulsions with sodium caseinate	Improving the oxidative stability of carotene and decreasing the lipolysis of carotene during the gastric and intestinal digestion	Yi et al. (2014)
Curcumin	Nanoemulsions of MCT oil droplets with whey protein concentrate (WPC) and Tween 80	More bioavailability and stability during gastric and intestinal digestion and DPPH radical scavenging activity	Sari et al. (2015)
Curcumin	Nanoliposome	Enhancing the bioavailability and plasma antioxidant activity	Takahashi et al. (2009)
Epigallocatechin-3-gallate (EGCG)	Stabilized nanoemulsions by ι-carrageenan and β-lactoglobulin	Enhancing *in vitro* antioxidant and anticancer activity	Ru et al. (2010)
Quercetin	Nanoliposomes (cholesterol and egg PSC)	Enhancing bioavailability and anxiolytic and cognitive-enhancing effects	Priprem et al. (2008)
Quercetin	SLNs (glyceryl monostearate and soy lecithin	Enhancement of gastrointestinal absorption	Li et al. (2009a)
Quercetin	NLCs (Imwitor 900 K, mediumchain triglycerides(	Improving bioavailability and stability during gastric and intestinal digestion	Aditya et al. (2014)
Astaxanthin	SLNs (stearic acid, glycerin monostearate, and glycerol stearates(	Enhancing the absorption of astaxanthin in epithelial cells via endocytotic cellular uptake	Li et al. (2015(
Polyphenols	Chitosan	Reversely disrupting tight junctions and increasing the absorption in the epithelial cells by mediating transmembrane tight junction protein CLDN4	Yeh et al. (2011)
Luteolin	Nanoliposome	Enhancement of antitumor efficacy to colorectal carcinoma	Wu et al. (2018)
Cyanidin-3-glucoside (C3G)	Nanoliposome	Improving antioxidant activity and inhibiting cancer cell proliferation was studied with Caco-2 cells	Liang et al. (2017)
Curcumin	Chitosan/poly(lactic acid) using electrospinning	Increasing the DPPH radical scavenging activity; significant reduction of wound area when compared to untreated during *in vivo* wound healing studies on excision and incision wounds created on rat model	Dhurai et al. (2013)
Quercetin and ferulic acid	Amaranth protein isolate and pullulan using electrospinning	Sustaining release of quercetin and ferulic acid through *in vitro* digestion and improving their antioxidant capacity determined using the $ABTS^{\bullet+}$ radical cation method	Aceituno-Medina et al. (2015)
β-carotene	Casein micelles	Increasing the bioavailability of β-carotene.	Chu et al. (2007).
β-carotene	Casein micelles		Yi et al. (2015)

(*continued*)

Table 2. Continued.

Bioactive ingredients	Nanocarriers	Purpose	Reference
		Decreasing of medium effective dose values of β-carotene against Caco-2 cells	
Curcumin	β-Casein	Increasing the antioxidant activity and decreasing the medium effective dose of curcumin tested on human leukemia cell line K-562	Esmaili et al. (2011)
Curcumin	β-Casein micelles	Increasing the bioavailability and antioxidant activity of curcumin	Esmaili et al. (2011)
Resveratrol	Chitosan/γ-PGA nanoparticles	Increasing the DPPH radical scavenging activity and ferric reducing antioxidant power (FRAP) and improving the stability, and cellular uptake.	Jeon, Lee, and Lee (2016)
Oregano essential oils	β -Cyclodextrin	Increasing the DPPH radical scavenging activity and lower degradation	Arana-Sánchez et al. (2010)
Polyphenols extracted from peels of Egyptian prickly pears fruit	Sodium alginate and chitosan	Increasing the DPPH radical scavenging and reducing power activity	Khaled, Hatem, and Azza (2018)
Curcumin	Water-soluble chitosan nanoparticles	Providing high DPPH radical scavenging activity and chelating potentials	Yadav et al. (2012)
Anthocyanin from black soybean	Chitosan	Increasing th stability of anthocyanin in terms of color and antioxidant activity (DPPH radical scavenging activity and carotene bleaching assay)	Ko et al. (2017)
Anthocyanins from red raspberry	β-Lactoglobulin	Increasing the DPPH radical scavenging activity, increasing the stability in mouth (pH 6.8), simulated gastric (SG, pH = 2), and simulated intestinal (SI, pH = 6.9)	Salah et al. (2020)
Anthocyanins from bilberry extract	Whey protein and citrus pectin	Enhancing the intestinal accessibility upon passing through the small intestine and modulating the formation of the degradation product phloroglucinol aldehyde (PGAL) in human plasma	Mueller et al. (2018)

of bioactive ingredients (Yu et al. 2011). In this regard, cellular antioxidant activity (CAA) assay (please see Section 3.4) is appropriate to evaluate the real bioavailability, uptake, and metabolism of nanoparticles loaded with antioxidants. CAA has been used to measure the antioxidant activity of resveratrol-loaded nanoemulsions and micelle encapsulated curcuminoids (Sessa et al. 2011). Hu et al. (2013) evaluated the antioxidant activity of free (−)-epigallocatechin-3-gallate (EGCG), nanoparticles composed of caseinophosphopeptide and chitosan containing EGCG through the CAA assay. Their study showed an enhanced CAA value for the nanoencapsulated EGCG compared to free EGCG; reflecting their ideal EGCG delivery.

With the help of emulsification–solvent evaporation approach, Mukerjee and Vishwanatha (2009) successfully prepared curcumin-loaded poly lactic-co-glycolic acid (PLGA) nanospheres, which showed enhanced intracellular uptake, CAA and high efficacy in prostate cancer cell lines. In order to orally deliver tea catechins, Tang et al. (2013) introduced a pH-responsive nanoparticle through self-assembly of chitosan and poly γ-glutamic acid (γ-PGA). Positively charged nanoparticles are able to transiently open the strong bonds between Caco-2 cells and hence augment the paracellular transport of tea catechins. Resveratrol encapsulation in nanodelivery systems showed even higher contribution in the cellular uptake enhancement. For instance, nanocarriers were fabricated for pharmaceutical purposes by lipospheres with efficient resveratrol transportation into the cardiovascular system (Fang and Bhandari 2010). Antioxidant behavior of the control (undigested nanocapsules) as well as the digested ones was evaluated by a cell-based antioxidant assay; pretreatment of Caco-2 cells with nanoencapsulated resveratrol was conducted. Owing to the nanoscale size of capsules, they could pass the membrane and enter the cell. According to their results, the mentioned modification prevented the emergence of antioxidant effects outside the cells and limited the measured CAA to the intracellular resveratrol interactions. Besides, resveratrol-containing nanoemulsions exhibited superior cellular antioxidant activity compared to the nonencapsulated ones. In addition, CAA variation during the in vitro digestion procedure was properly good. Nanoscale dimensions of the capsules can also augment their cellular uptake. The digestion had no significant influence on the antioxidant activity of encapsulated resveratrol, reflecting its stability through gastric and intestinal digestion; hence offering its antioxidantly active form to the cells (Sessa et al. 2011).

Although numerous surface active bile salts can displace the emulsifier molecules at the O/W interface, no significant alternation was detected in the efficiency of resveratrol delivery to the cells before and after the GIT digestion. Such phenomenon could be assigned to the dual emulsifier formulation which enhanced the resveratrol protection and its transfer across the biological membranes. Additionally, formulations with the highest physical and chemical stability manifested maximum chemical and CAA compared with the undigested and nonencapsulated resveratrol (Sessa et al. 2011). Polymeric micelles were employed to improve the cell protection ability of resveratrol against oxidative stress and apoptosis (Lu et al. 2009). In this regard, SLNs were applied to enhance the resveratrol uptake of keratinocytes cells (Teskac and Kristl 2010). The explosive release of resveratrol can be declined by alginate/chitosan complexation or water-in-oil (W/O) emulsification-templated Ca alginate which also resulted in the cellular uptake improvement (Min et al. 2018).

Antioxidant activity of lipophilic/hydrophilic bioactives in different nanodelivery systems

The encapsulation process provides the ability to use various bioactive compounds with different chemical structures in various food systems; therefore, antioxidant activity of lipophilic compounds in hydrophilic systems and the antioxidant activity of hydrophilic compounds in lipophilic systems will be increased (Maqsoudlou et al. 2020). Some antioxidant ingredients exhibit a very low water or lipid solubility, making their incorporation into most food systems extremely difficult (Donsì et al. 2010). Despite numerous investigations on the antioxidant activity of phenolic extracts, a limited number of works have addressed the technological aspects of their incorporation into real foods. In particular, their miscibility, stability and interaction with other food components have been mostly neglected. Nanodelivery systems which can protect antioxidant compounds and enhance their activity by the mass transfer facilitation with minimum impact on the organoleptic features of final product (Sessa et al. 2011; Amendola, De Faveri & Spigno, 2010; Nanditha and Prabhasankar 2009).

Possibility of antioxidant encapsulation in different sites (e.g. inside the inner water phase, oil phase, or the outer water phase of double emulsions) allows researchers to develop a single delivery system containing multiple functional components. Moreover, such approach can be exploited to protect them and have a targeted release of aqueous components entrapped within the inner water droplets (Weiss, Takhistov, and Mcclements 2006). Hydrophilic antioxidants are soluble in water but insoluble in lipids and organic solvents. Some of the encapsulated hydrophilic antioxidants are polyphenols, most bioactive peptides, GSH, and vitamin C (Teeranachaideekul, Muller, and Junyaprasert 2007; Dube et al. 2010; Ferreira, Rocha, and Coelho 2007). Lipophilic antioxidants are insoluble in water but soluble in lipids and organic solvents. Encapsulated lipophilic antioxidants include β-carotene, some bioactive peptides, vitamins A and E, lipoic acid, etc. (Heyang et al. 2009; Zimet & Livney 2009).

Based on the solubility of bioactive material, the type of wall material is effective in their stability (Ezhilarasi et al. 2013). Lipids have a leading role in nanoencapsulation of phenolic compounds and antioxidants as these substances can be loaded in lipid matrices of O/W or W/O nanoemulsions, NLCs and SLNs. The lipid phase can also serve as a continuous phase to distribute the water nanodroplets containing phenolics and antioxidants in W/O nanoemulsions (Mcclements 2015). Sun-Waterhouse, Wadhwa, and Waterhouse (2013) found that the type of wall material had a significant impact on the encapsulation efficiency[3] of polyphenols. Antioxidant properties of β-carotene, as a lipophilic antioxidant, also will be preserved, if the encapsulation efficiency is high and it could be maintained well. Typically, polysaccharides (gum Arabic and modified starch) and proteins (whey proteins, sodium caseinate, soy proteins, and gelatin) have been employed as wall materials in spray drying encapsulation. Owing to their profound emulsifying properties, whey proteins have exhibited extraordinary encapsulation features both alone or combined with other biomaterials for encapsulation of oil-soluble antioxidants (Kagami et al. 2003; Keogh et al. 2001). It can also form matrices with tunable sizes with no harmful impacts on the sensory features of final product. Moreover, the functional groups of this protein facilitate its interaction and protection with antioxidant compounds as well as their reversing which could stabilize the food texture (Chen, Remondetto, and Subirade 2006).

Liposomes refer to the colloidal spherical structures surrounded by polar lipids in such a way that the hydrophilic heads are oriented to the water compartment while the lipophilic tails away from the water are directed to the vesicle center. Such structure can simultaneously encapsulate both hydrophilic and lipophilic antioxidants within its water core and lipid section, respectively. Phospholipids are responsible for liposomal production as a bilayer component; thus numerous food resources, such as egg, soy, and milk can be applied for liposomal preparation (Katouzian and Jafari 2016; Mozafari et al. 2008). Ha et al. (2013) employed β-lactoglobulin (β-Lg) and chitosan complex nanoparticles for quercetin nanoencapsulation. The physical characteristics of obtained nanoparticles were under the influence of charged amount of β-Lg and sub-ambient temperature treatment. The mentioned research presented a non-lipid quercetin delivery system for use in food formulations, especially in low-fat and nonfat ones. According to Sessa et al. (2011), nanoemulsion-based delivery systems involving a combination of hydrophilic (sugar ester, defatted soy lecithin, polysorbate 20) and lipophilic emulsifiers (defatted soy lecithin, glycerol monooleate) can be employed for polyphenol encapsulation (i.e. resveratrol and grape marc extracts) and their dispersion in aqueous systems; 10-fold of their therapeutic concentrations.

[3]Encapsulation efficiency (EE%) is the percentage of incorporated materials that is successfully entrapped into the nanocarriers. It is calculated by [(total incorporated material added – free non-entrapped incorporated material) divided by the total incorporated material] multiplied by 100.

Effect of encapsulation process conditions on the antioxidant activity of bioactives

Some of antioxidants significantly decreased upon exposure to the encapsulation process. Ferreira et al. (2015) reported that all-*trans*-*β*-carotene and all-*trans*-α-carotene mainly constituted the carotenoids content of crude palm oil before and after encapsulation. The DPPH radical inhibitory ability of palm oil showed a significant reduction by encapsulation which might be explained by peroxide content enhancement since the latter is indicative of greater oil oxidation degree; this observation could also be attributed to decrease of antioxidant contents (e.g., vitamin E) (Ramadan, Amer, and Sulieman 2006). Despite the fact that total carotenoids remained unchanged, the heat applied by spray dryer can further promote *trans*-carotenoids isomerization to their less common, *cis*, forms. *Trans*-carotenoid isomerization will lead to a slight color loss in the pro-vitamin A which will eventually reduce the antioxidant activity. However, the encapsulation process does not always reduce the antioxidant activity; for instance, encapsulation of oregano essential oil was conducted by Arana-Sánchez et al. (2010) which caused an enhancement in DPPH radical scavenging activity of the oil as lower degradation was observed. Khaled, Hatem, and Azza (2018) indicated the positive impact of nanoencapsulation process on the antioxidant activity of Egyptian prickly pears fruit. Nanoencapsulation also enhanced the quality and stability of bioactive compounds. In general, various factors during encapsulation process may affect the antioxidant capacity of bioactive compounds, and it depends on the applied encapsulation technique. These factors can be controlled to maintain their antioxidant activity.

Temperature is one of these critical factors particularly in spray drying encapsulation of natural antioxidants. Decreasing the antioxidant activity of sensitive compounds such as polyphenols due to high temperatures of spray drying encapsulation process is one of the negative effects and some strategies have been anticipated to solve this problem (Suhag and Nanda 2016). In this regard, the operation temperature is one of the crucial factors in spray drying of heat-sensitive substances. Suhag and Nanda (2015) reported a decline in total phenolic content (TPC) of acai (*Euterpe oleracea Mart.*) juice following the spray drying at inlet/outlet temperatures of 140/78 °C when different carrier agents were added. They also examined the TPC of honey enriched by spray-dried encapsulated anola and basil extract. Accordingly, the inlet temperature significantly and negatively affected TPC in a linear manner which could be due to decomposition of phenolic compounds or variation in their molecular structure in elevated temperatures. The impact of spray drying on the phenolic compound preservation in bayberry juice was addressed by Fang and Bhandari (2011). They reported 96% TPC retention after drying which could be assigned to the reduced thermal stress by ultrafast evaporation technique.

Regarding the role of oxidation in degradation during drying process, binding the intended compounds to an encapsulant polymer could result in protective effects (Sun-Waterhouse, Wadhwa, and Waterhouse 2013). Samborska et al. (2019) studied the impact of low-temperature spray drying by dehumidified air on the phenolic compound and antioxidant capacity of rapeseed honey. In comparison with the pure honey, modified samples exhibited enhanced TPC. It was hypothesized that application of lower heat during the dehumidified-air spray drying can protect the phenolic compounds. Further heat transfer by traditional spray drying however may diminish the honey bioactivity. According to Sun-Waterhouse and Waterhouse (2015), use of warm feed for spray-drying could inactivate the polyphenol oxidase and facilitate the anthocyanins retention which in turn may decrease the feed viscosity and decline the nozzle clogging and enhance the spray-drying efficiency.

Temperature is also an effective and important factor during spray-drying of some oil soluble antioxidants such as *β*-carotene, as operation at temperatures above the melting point is accompanied with the risk of antioxidant melt down (Desobry, Netto, and Labuza 1997). As Leach, Oliveira, and Morais (1998) reported use of *D. salina* (natural algae known for its high *β*-carotene production) along with maltodextrin (MD) and gum Arabic at the air inlet temperature of 200 °C will enhance the storage stability; since such spray-drying procedure can reduce the oxygen exposure by establishing a barrier for oxygen diffusion. Regarding the influence of inlet temperature on the spray-drying evaporation rate, it should be optimized to avoid the agglomeration, poor fluidity and high water content in the produced powders (Gharsallaoui et al. 2007). Air flow rate could affect the moisture content of the resulting powder; as increasing air flow significantly decreases moisture content; therefore, the structural degradation of bioactive compounds is prevented during storage (Donhowe and Kong 2014).

With the help of high-pressure homogenization procedure, Yuan et al. (2008) managed to formulate *β*-carotene nanoemulsions (O/W) and evaluated the impact of emulsifying conditions on the nanoemulsions stability and features. They observed a decline in physical stability of nanoemulsions by the temperature rise while it showed an enhancement with pressure augmentation (up to 100 MPa) and homogenization cycle (up to three cycles). Furthermore, *β*-carotene degradation after four weeks occurred with greater loss when stored at 25 °C. Wang et al. (2008b) concluded that high-pressure homogenization will result in smaller droplet curcumin nanoemulsions (80 nm) and enhanced antioxidant behavior as compared with high-speed homogenization approach (619 nm). Chemical stability of nanoencapsulated resveratrol during high-pressure homogenization was also assessed by Sessa et al. (2011). Results showed that the stability of *trans*-resveratrol (a highly photosensitive substance with considerable susceptibility toward oxidative degradation) was maintained during nanoencapsulation procedure. The high performance liquid chromatography (HPLC) retention time and ultraviolet–visible (UV–Vis) spectra of nanoencapsulated and nonencapsulated resveratrol were similar reflecting lack of chemical alternation during nanoencapsulation.

Table 3. Effect of storage conditions on the antioxidant activity of nanoencapsulated bioactives.

Bioactive ingredients	Nanocarriers	Purpose	Reference
β-carotene	Zein nanoparticles	Improving stability and enhancing antioxidant activity of β-carotene	Chuacharoen and Sabliov (2016)
Carotene from pequi oil	Whey protein isolate (WPI) and maltodextrin	Enhancing thermal stability and improving protective impact on the oil antioxidative capacity	Oliveira et al. (2017)
β-carotene	PLA and PLGA	Increasing the stability against destroying during storage	Ribeiro et al. (2008)
(+) catechin and (−)epigallocatechin gallate (EGCG)	Chitosan–tripolyphosphate	Protecting catechin and EGCG from degradation and prevention of changes in the antioxidant activity during storage	Dube et al. (2010)
Anthocyanins	Alginate and inulin	Increased antioxidants protective properties, improved stability over long storage	Waterhouse et al. (2017)
Jujube pulp and seed extracts	Chitosan nanoparticles	Enhancing antioxidant activity and storage stability	Han et al. (2015)
β-Carotene	O/W nanoemulsions stabilized by WPI	Good stability against environmental stresses during storage	Mao et al. (2009)
Curcuminoids	SLNs (stearic acid, glyceryl monostearate, and Poloxamer 188)	Increasing the antioxidant activity, prolonged release and maintaining the physical and chemical stability during storage	Tiyaboonchai, Tungpradit, and Plianbangchang (2007)
Lutein	NLCs	Protecting lutein from environmental stresses	Mitri et al. (2011)
Piperine-rich black pepper extracts	Soy phosphatidyl choline/Tween 80 nanoliposomes	Higher antioxidant potency and better storage stability	Dutta and Bhattacharjee (2017)
β-Sitosterol	NLCs [Precirol (lipid), Miglyol (oil)]	Increasing the antioxidant activity and storage stability	Bagherpour et al. (2017)
Green tea extract	Nanoliposome	Improving antioxidant activity and storage stability	Naghavi et al. (2016)
Curcumin	Casein-soy polysaccharide	Maintaining antioxidant activity, extending storage stability and controlling the release	Wu and Wang (2017); Xu, Wang, and Yao (2017)
Curcumin	Casein-zein complex, casein-zein-pectin complex	Maintaining antioxidant activity and extending storage stability	Chang et al. (2017)
Curcumin	Casein-dextran conjugate	Maintaining antioxidant activity, extending storage stability and improving oral bioavailability	Wu and Wang (2017)
Resveratrol	Cyclodextrins	Increasing bioavailability and stability	Lucas-Abellan et al. (2007)

Effect of storage conditions on the antioxidant activity of nanoencapsulated bioactives

There are many studies dealing with the influence of storage conditions on the antioxidant activity of nanoencapsulated bioactives; some of them are listed in the Table 3.

Khaled, Hatem, and Azza (2018) reported that nanoencapsulation of bioactive compounds of prickly pears peel fruit by chitosan and sodium alginate preserved their bioactive compounds during various storage periods (120 days). Supplementation of guava juice with these nanoencapsulated ingredients explains its resistance toward high temperatures and pasteurization procedure (Khaled, Hatem, and Azza 2018). Storage stability of enriched guava juice samples were assessed based on total antioxidant capacity. Koç et al (2015) examined the oxidative stability of encapsulated extra virgin olive oil powder prepared under optimal conditions which was encapsulated by 92% MD, 7% whey protein isolate (WPI), and 1% Tween 20. At 1st day of storage, peroxide value of encapsulated powder was below the acceptable level which then showed a sharp enhancement at day 15; further storage did not induce a significant variation in peroxide content. Furthermore, when olive oil is converted into powder, its surface area will be enhanced which in turn can augment its oxidation sensitivity. Nonetheless, at similar temperature, final powders exhibited declined peroxide value and enhanced oxidation stability in comparison to the liquid olive oil.

Sessa et al. (2011) measured the chemical stability of nanoencapsulated resveratrol at accelerated storage conditions. UV-C exposure resulted in creation of *cis*-forms in the nonencapsulated resveratrol, whereas nanoencapsulated sample exhibited slower *trans*-resveratrol degradation rate and fewer *cis*-resveratrol. Nanoencapsulated resveratrol also had a high stability at refrigeration condition (4 °C) and 30 °C. In contrast, the nonencapsulated resveratrol behaved differently, as the active resveratrol was better protected at elevated temperatures. Such observation can be attributed to augmented oxidative degradation arisen from enhanced water solubility of oxygen at lower temperatures. Thus, higher stability of encapsulated compound at lower temperatures implies the preserving tendency of nanoencapsulation process against chemical degradation; since it effectively protected resveratrol exposure to dissolved oxygen molecules (Lucas-Abellan et al. 2007).

Sessa et al. (2011) employed high pressure homogenization to encapsulate grape marc polyphenols by a nanoemulsion-based delivery system. The sunflower oil-based nanoemulsion systems could effectively preserve grape marc polyphenols against degradation after 14 days of storage. Contrarily, palm oil-based systems showed lower efficiency, with a subtle decline in the absorbance peak after 14 days of

storage indicating the release of encapsulated substances and their degradation. β-carotene was successfully encapsulated by casein/gum tragacanth complex coacervation in a work by Jain et al. (2016), which presented stability improvement throughout a three-month storage course when compared with their nonencapsulated peers.

Jeon, Lee, and Lee (2016) synthesized chitosan/γ-PGA nanoparticles using ionic gelation technique to enhance the resveratrol solubility, stability, and cellular uptake. Optimized chitosan/γ-PGA ratio showed improved entrapment efficiency and a higher UV protection in comparison to the nonencapsulated compound. A strong effect on the apparent solubility of resveratrol was exerted by the nanoencapsulation since the solubility increased 3.2 and 4.2 times before and after lyophilization of the carriers, respectively, in comparison to the control sample. Enhanced solubility and antioxidant activity were sustained during storage; the latter was assessed by DPPH and ferric reducing antioxidant power (FRAP) assays. In the case of nonencapsulated resveratrol, however, the antioxidant activity showed a significant decline within 15 days of storage. Chitosan/γ-PGA nanoencapsulation also substantially elevated the resveratrol uptake in Caco-2 cell monolayer (Jeon, Lee, and Lee 2016).

Lo Nostro et al. (2007) addressed the antioxidant activity of vitamin C derivative surfactant (8ASC10) in nanostructured organogels. According to their findings, these organogels maintained the parent vitamin C antioxidant features at a higher level (>90%) after one-month storage consistence with native ascorbic acid and esters. Hao et al. (2017) succeeded in quercetin encapsulation within chitosan-coated nanoliposomes with a small particle size (even with coating layer) and proper encapsulation efficiency (71.14%). In comparison with free quercetin, the encapsulated sample exhibited enhanced quercetin antioxidant activity and storage stability (at ambient and refrigerator temperatures in dark and natural lights). Shin et al. (2013) reported a greater particle size and zeta potential for chitosan-coated curcumin-loaded nanoliposomes. They also claimed that chitosan increased the muco-adhesive characteristics of nanoliposomes resulting in higher absorption of encapsulated curcumin within GIT; moreover, it increased the storage stability of curcumin-loaded nanoliposomes at 4 and 25 °C in 40-day storage (Shin et al. 2013). In another study, Mosquera et al. (2014) encapsulated peptides extracted from collagen of a sort of bream scales through use of liposomal nanocarriers and reported sustained antioxidant features in the encapsulated peptides after 8 days of storage at 4 °C.

Waterhouse et al. (2017) used alginate and inulin to produce anthocyanin-rich powder products with favorable reconstitution features in water or milk employing the blueberry wastes. The alginate-formulated powder exhibited greater preserving potentials for the anthocyanin content of blueberry wastes in comparison to inulin-encapsulated powders. Different storage stabilities could be due to anthocyanins interactions with their environmental components (the type and amount of coexisting constituents may vary depending on the extraction and encapsulation processes during spray-drying). For prolonged storage periods, anthocyanins will polymerize in addition to being decomposed resulting in lower monomeric anthocyanins. Anthocyanins may also break down to phloroglucinaldehyde and benzoic acid derivatives (e.g. syringic acid or 4-hydroxybenzoic acid) (Patras et al. 2010). Such processes may contribute to the temporal variation of total phenolics. The phenolic compounds originated from anthocyanins degradation or polymerization can compensate the anthocyanins decline upon TPC analyses (Sadilova, Carle, and Stintzing 2007).

The stability of jujube nanoparticle was studied by Han et al. (2015). As storage time increased, TPC of nonencapsulated jujube pulp and seed extracts rapidly decreased. Although the TPC of jujube pulp and seed extract-loaded nanoparticles also decreased significantly, it was more slowly than nonencapsulated extracts which could be due to the gelation and protective impact of chitosan nanoencapsulation process. Such a difference in antioxidant activity became more evident by prolonging the storage time. From 9th to 12th day, the antioxidant activity of nonencapsulated jujube pulp and seed extracts was merely 53–58% of the jujube nanoparticles. Tang et al. (2013) also reported similar outcomes; they indicated improved protease stability for different storage times, temperatures, and pH values through chitosan nanoencapsulation. The impact of nanoencapsulation was more profound on antioxidant activity rather than TPC which could be attributed to diversity of bioactive materials (i.e., vitamins and saponins) in jujube as it might affect the antioxidant behavior of jujube nanoparticles.

Effect of carrier wall materials on the antioxidant activity of nanoencapsulated bioactives

Maximization of encapsulation efficiency will prevent the core materials from oxidation and loss of volatile compounds; this process can also prolong the product shelf life. The type of wall material plays a key role in encapsulation efficiency of bioactives. Therefore, the formulation process must be optimized to achieve minimal surface core materials on the powder particles (Tonon, Grosso, and Hubinger 2011). The wall material used may affect the antioxidant properties of final carriers. Depending on the ability of wall materials for donating the electron or hydrogen, they can participate in antioxidant reactions; therefore, antioxidant activity of encapsulated food ingredients will be increased.

There are several reports on nanoencapsulation of antioxidant compounds with various wall materials, which indicate the effect of wall materials on the antioxidant properties of final carriers (Table 4). For example, Khaled, Hatem, and Azza (2018) used sodium alginate and chitosan to nanoencapsulate antioxidants extracted from peels of Egyptian prickly pears fruit. They evaluated DPPH radical scavenging activity assay, total antioxidant capacity, reducing power capacity, and TPC to determine the antioxidant activity of nanoencapsulated antioxidant extracts. Results showed that DPPH radical scavenging and reducing power activity increased after nanoencapsulation process depending on the extract concentration and wall material. The extracts

Table 4. Effect of carrier wall materials on the antioxidant activity of nanoencapsulated bioactives.

Bioactive ingredients	Nanocarriers	Purpose	Reference
(−)-Epigallocatechin-3-gallate (EGCG)	β-Lactoglobulin	Reserving the antioxidant activity	Li et al. (2012)
EGCG	Caseinophosphopeptide and chitosan	Stronger free radical scavenging of nanoencapsulated EGCG	Hu et al. (2013)
Anthocyanins	WPI/pectin	Preventing changes in antioxidant activity	Stănciuc et al. (2017)
Catechin	Chitosan/poly (γ-glutamic acid)	Enhancing the transport and antioxidant activity	Tang et al. (2013)
Essential oils (EOs)	Zein nanoparticles	Increasing the water solubility without hindering their ability to scavenge free radicals	Wu, Luo, and Wang (2012)
Capsaicin	Gelatin cross-linked with glutaraldehyde	Improving melting point and antioxidant activity	Wang et al. (2008)
β-carotene	O/W nanoemulsions of orange oil droplets stabilized by β-lactoglobulin and Tween 20	Increasing the stability of β-carotene against chemical degradation	Qian et al. (2012)
Quercetin	Chitosan nanoparticles	Maintaining the quercetin antioxidant activity	Zhang et al. (2008)
Grape marc polyphenols	Sunflower oil and palm oil-based O/W nanoemulsions	Higher antioxidant activity in case of ORAC	Sessa et al. (2014(
Olive leaf phenolic extracts	W/O/W multiple emulsions of soybean oil stabilized by WPC and pectin.	Increasing the antioxidant activity, stability and sustained-release	Mohammadi et al. (2016)
Quercetin	Nanoliposomes	Enhancing antioxidant capabilities	Cadena et al. (2013)
Bioactive peptides from enzymatic hydrolysis of rainbow trout skin gelatin	Chitosan-coated nanoliposomes	Maintaining their antioxidant activities	Ramezanzade, Hosseini, and Nikkhah (2017)
Sea bream-extracted collagen peptidic fractions	Nanoliposomes composed of partly-purified soy-derived phosphatidylcholine	Retaining the radical scavenging ability	Mosquera et al. (2014)
Enzymatic antioxidant (CAT)	SLNs	Protecting against proteolysis and regular releasing	Qi et al. (2012)
Resveratrol	Peanut oil and sunflower oil-based nanoemulsions	Protecting resveratrol from chemical changes	Sessa et al. (2011)
Resveratrol	Nanoemulsions by Tween 80	Protecting against degradation	Davidov-Pardo and Mcclements (2015)
Resveratrol	Nanoliposomes (cholesterol and diacetyl phosphate)	Enhancing antioxidant activity	Kristl et al. (2009)
Olive leaf phenolics	Nanoliposome	Improving the antioxidant properties	Tavakoli et al. (2019)
Folic acid	Whey protein concentrate and a commercial resistant starch using nano-spray dryer	Physicochemical stability and preventing the degradation	Shekarforoush et al. (2018)
Superoxide dismutase	Poly (lactic acid) (PLLA) by electro-spinning	Controlled release system	Chen et al. (2010)
Curcumin	Poly (ε caprolactone)/gum tragacanth using electrospinning technique	Increasing antioxidant activity	Ranjbar-Mohammadi and Bahrami (2016)
Gallic acid	Zein using electro-spinning	Preserving phenolic character	Neo et al. (2013)
β-Carotene	Casein micelles	Protecting the degradation of β-carotene	Semo et al. (2007).
Curcumin	Cyclodextrins	Improved water solubility and better antioxidant activity	Yallapu, Jaggi, and Chauhan (2012)
Rutin, tannic acid, catechin, and gallic acid	Casein based films	Producing radical-scavenging films, applicable to food products that are susceptible to oxidation	Helal et al. (2012)
Usnic acid	β-Cyclodextrin incorporated into liposomes	Providing a targeted delivery system	Lira et al. (2009)
Catechin	β-Cyclodextrin	Increasing antioxidant activity	Krishnaswamy, Orsat, and Thangavel (2012)
Catechin	β-Casein	Increasing water solubility and maintaining antioxidant activity	Haratifar and Corredig (2014)
Naringenin	β-Casein	Enhancing solubility and stability	Moeiniafshari, Zarrabi, and Bordbar (2015)
Curcumin	Nanofibers based on almond gum/PVA and almond gum/PVA/β-cyclodextrin	Preserving hydrophobic antioxidants	Rezaei and Nasirpour (2018)
β-Carotene	β-Casein micelles	High stability against common food processes	Sálz-Abajo et al. (2013)
Pequi oil and its carotene	WPI, maltodextrin and inulin	Higher thermal stability and improved protective features for the oil antioxidative capacity	Oliveira et al. (2017)

nanoencapsulated by chitosan showed the highest DPPH scavenging activity, which may be due to their ability for donating the electron. Radical-scavenging properties of the extract did not significantly differ from that of alginate and chitosan-encapsulated extracts. Moreover, alginate-encapsulated extract exhibited a significantly lower DPPH

scavenging ability compared to other formulations. It was reported that the reducing power of nanoencapsulated extract by chitosan and mixture of chitosan and alginate was probably due to their hydrogen donating ability which might explain its higher amount of chitosan than in other formula. When combined with sodium alginate, chitosan can exhibit higher protective impacts on the bioactive ingredients. Owing to their degradation-protective behavior, alginate and chitosan have been extensively employed in encapsulation of antioxidants (Mokhtari, Jafari, and Assadpour 2017). Usually, chitosan is coated or used in combination with alginate beads to inhibit the gel erosion and chelator-induced (Han et al. 2008). Moreover, the choice of gelation method (ionotropic, external, and internal) can significantly affect the physical properties and chemical stability of the obtained carriers (Donhowe and Kong 2014).

Based on a study by Mosquera et al. (2014), collagen peptide-loaded nanoliposomes exhibited two-fold higher ABTS radical scavenging performance compared to the free peptides, which could be due to ABTS radical scavenging ability of nanoliposomes constructed by partially purified phosphatidylcholine from industrial soy byproduct. PLGA nanoparticles were also fabricated by Pereira et al. (2017) to deliver guabiroba fruit phenolic extract (GPE) with improved functional features. They employed a modified emulsion-evaporation encapsulation method and analyzed the antioxidant performance of samples to assess their encapsulation efficiency. Based on their results, GPE-loaded PLGA nanoparticles exhibited enhanced antioxidant features when compared with the free GPE. ABTS method was employed by Soares Alves, Mainardes, and Khalil (2016) to assess the antioxidant activity of PLGA nanoparticles or gallic acid-containing PS80-coated PLGA nanoparticles. Their report was indicative of the enhancement in prolonged release of gallic acid from PS80-coated nanoparticles, thus reflecting their lower antioxidant activity compared with PLGA nanoparticles. Samborska et al. (2019) applied MD and Nutriose as the honey powder carriers. Furthermore, skimmed milk substituted the water feed solution. In comparison with the pure honey, encapsulated samples exhibited enhanced TPC. The decline of carrier content decelerated the TPC enhancement reported as per honey solids. This observation suggests the effective role of carriers. The values determined for the encapsulated honey were significantly greater than those of pure honey. This observation cannot be assigned to the contribution of MD and nutriose as these values were reported per mass of honey solids. In addition, application of MD sounds to act in favor of the transformations giving rise to enhanced electron donation ability of the antioxidants (greater reducing capability).

Effect of release profile on the antioxidant activity of nanoencapsulated bioactives

The use of coating in wall materials that can delay the release of core materials has an effect on the severity and duration of antioxidant activity. Since antioxidant ingredients loaded in coated nanoparticles confront an additional barrier to be released, presenting prolonged release, therefore their antioxidant activity will be decreased (Moharram and Youssef 2014). As an example, Soares Alves, Mainardes, and Khalil (2016) prepared poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NP) coated or not coated with polysorbate 80 (PS80) containing gallic acid (NP-PLGA-GA and NP-PLGA/PS80-GA) produced by emulsion solvent evaporation method. Scavenging behavior of gallic acid was higher in all the studied concentrations; only at lower contents, it exhibited a declined activity after 48 h. For high gallic acid concentrations, NP-PLGA-GA presented radical inhibitory impacts similar to that of free gallic acid after 2 h which was maintained for 24 h. The initial antioxidant activity can be understood through the burst effect of PLGA nanoparticles. In the case of gallic acid, its slow release rate failed to cause the activity the same as the free gallic acid; this can justify the decline in antioxidant activity after 48 h. The NP-PLGA/PS80-GA possessed the least antioxidant activity compared with NP-PLGA-GA and free gallic acid. Such a minimum antioxidant activity assessed by colorimetric measurement of (ABTS•+), is consistent with its considerably slow release. Therefore, when gallic acid is loaded in coated nanoparticles, it faces further release barriers which will result in prolonged release compared to uncoated PLGA nanoparticles; hence, its antioxidant activity may be decreased. Soares Alves, Mainardes, and Khalil (2016) said that despite the *in vitro* findings, better in vivo results are expected from the drug-loaded nanoparticles, as the nanoparticles are able to enhance the biopharmaceutical and pharmacokinetic features of drug-loading, giving rise to more apparent pharmacological responses compared to the free drug. *In vivo* assays are essential for confirmation and examination of the possible antioxidant and neuroprotective impacts.

Despites its highest antioxidant delivery efficiency, oral administration can result in low bioavailability of some antioxidant ingredients (Maqsoudlou et al. 2020). This can be mostly assigned to the poor stability and intestinal absorption of the mentioned ingredients (Chow et al. 2003; Lambert, Sang, and Yang 2007). As a result, only a minor portion of the antioxidants could find its way into the bloodstream and arrive into the intended sites. Therefore, using of nanostructured biomaterials for encapsulation of antioxidants is preferred to overcome their limitation and enhance the bioavailability of corresponding phytochemicals (Leonarduzzi et al. 2010; Shutava et al. 2009). Chitosan and alginate were considered as suitable encapsulating materials for hydrophobic antioxidant compounds (for instance β-carotene) through a complete release during simulated intestinal digestion condition and minimal release during simulated gastric digestion condition (Han et al. 2008). Roman, Burri, and Singh (2012) reported almost zero β-carotene in the micelle phase; and so, a complete release, however, it is not essentially accompanied by full antioxidant transformation to the micellar phase during the intestinal digestion. Their observation can be assigned to the inhibitory effect of a soluble fiber like alginate toward the micelle formation. They suggested micelle formation

Table 5. Analytical techniques for measuring the antioxidant activity of nanoencapsulated food ingredients.

Spectroscopic techniques	Electrochemical techniques	Chromatographic techniques		Cellular antioxidant activity
FRAP	Amperometric technique	HPLC		
DPPH	Cyclic voltammetric technique	GC		
ABTS	Biamperometric technique	TLC	Qualitative Semi quantitative	
ORAC	Biosensors technique			
HORAC				
TRAP				
CUPRAC				
PFRAP				
Folin–Ciocalteu method				
Flourimetry				

structures to shed more light on the bioavailability of encapsulated β-carotene.

Release of GPE from PLGA nanoparticles was assessed by Pereira et al. (2017). Both PLGA nanoparticles exhibited similar phenolic compound release profiles. Their profile started with an initial burst effect in the first hour, accompanied with a slow decrease of cumulative release in the next hours. The initial burst of PLGA 65:35 was more pronounced as it showed ~73% release of phenolic compounds just in 15 min. During the same period of time, PLGA 50:50 reached to 57% release; both nanoparticles however exhibited the same amount of release after 30 min, gradually decreasing to 42% and 32% phenolic compounds release by the end of 12 h, respectively. Then, the release showed a steady condition during the studied 72 h. Since they studied an extract, the release from nanoparticles was evaluated by TPC; hence, the cumulative release profiles were dependent on polarity of each phenolic compound (some of which could possess more affinity for the polymeric matrix, while the others may have higher tendency to the release environment). The free guabiroba fruit extract had a TPC of 18.6 ± 0.9 g of gallic acid equivalents (GAEs)/100 g GPE dry basis. GPE compounds are often hydrophilic. Therefore, the burst effect could be assigned to rapid release of hydrophilic substances on nanoparticle surface or close to that (Gomes, Moreira, and Castell-Perez 2011; Zigoneanu, Astete, and Sabliov 2008). In this content, greater initial burst from PLGA 65:35 can be related to the weaker hydrophilic compound-polymer interactions, as it possesses less glycolic acid content making it more hydrophobic.

Reverse results could be detected in the case of PLGA 50:50 regarding its enhanced hydrophilicity (Wischke and Schwendeman 2008). The gradual decline of cumulative release can be assigned to the phenolics content of GPE which are labile under release conditions; suggesting their degradation. Epicatechin, gallic acid, ellagic acid, ferulic acid, and p-coumaric acid are among the main phenolic compounds of GPE (Hass 2011); these compounds have shown sensitivity toward oxidation, light and pH variation; moreover, they can be easily oxidized by free radicals at a pH $>$ 6.5 (Fang and Bhandari 2010). Free GPE was also tested in the same release environment and at similar conditions to check its stability; the results showed that its TPC sharply declined to undetectable levels within the first few hours of experiment. Thus, encapsulation preserved 30% and 40% of the phenolic compounds for up to 12 h in PLGA 65:35 and 50:50, respectively.

Different techniques to measure antioxidant activity of nanoencapsulated ingredients

There are various analytical methods for the determination of total antioxidant capacity (TAC) which can be categorized in different groups (Ahmad et al. 2014), as shown in Table 5.

Based on their mechanisms of action, antioxidants and their activity can be analyzed by two major assays: hydrogen atom transfer (HAT) and single electron transfer (SET) assays (Frankel and Finley 2008). The majority of SET-based assays involve the simulation of antioxidant action by a proper redox-potential probe. In such assays, antioxidants will interact with a fluorescent or colored probe (oxidizing agent) rather than a peroxyl radical. Spectrophotometry-based SET assays evaluate the oxidant-reducing capability of an antioxidant through its color variations. The HAT mechanisms of antioxidant action in which the hydrogen atom (H) of a phenol (Ar–OH) is transferred to a ROO· radical can be summarized by the following reaction:

$$\mathrm{ROO}\cdot + \mathrm{AH/ArOH} \rightarrow \mathrm{ROOH} + \mathrm{A}\cdot/\mathrm{ArO}\cdot$$

In which, the aryloxy radical (ArO·) formed through the antioxidant phenol reaction with peroxyl radical can be stabilized by resonance. The protected phenolic antioxidant and biomolecule are also donated by ArOH and AH species, respectively. In order to protect free radicals against oxidation, the effective phenolic antioxidants should react faster than biomolecules. Regarding the fact that in an HAT-based antioxidant assay, ROO· reacts with fluorescent probe and antioxidants, the antioxidant activities can be examined by investigating the competitive kinetics through the fluorescence decay measurements in the presence or absence of antioxidants (Moon and Shibamoto 2009; Carocho and Ferreira 2013).

Spectroscopic techniques

Spectroscopic approaches rely on the radical reactions, radical cation or forming a complex with a hydrogen-donating antioxidant molecule (Giardi, Rea, and Berra 2010; Brand-Williams, Cuvelier, and Berset 1995; Chong and Olsher 2007). There are several assays for spectroscopic techniques.

FRAP technique

The FRAP (ferric reducing antioxidant power) method is based on the reduction of complex ferric ion-TPTZ (2,4,6-tri (2-pyridyl)-1,3,5-triazine) by the antioxidants. When Fe^{2+} binds with a ligand, a navy blue color is generated (Pellegrini et al. 2003). The absorbance measurements could be employed to quantify the amount of reduced iron which has a correlation with the antioxidant content. Trolox or ascorbic acid can be applied as references (Thaipong et al. 2006; Gil et al. 2002).

DPPH technique

Owing to its delocalized free electron, DPPH· (2,2-diphenyl-1-picrylhydrazyl) can be classified as a stable free radical. The delocalization of DPPH· molecule is accompanied with a purple color showing a characteristic absorption band at 520 nm. Upon reaction with a hydrogen donor species, DPPH· will be reduced (DPPH) giving rise to disappearance of the violet color with a linear dependence on the antioxidant content. Trolox plays the role of standard antioxidant (Thaipong et al. 2006; Pisoschi, Cheregi, and Danet 2009; Brand-Williams, Cuvelier, and Berset 1995).

ABTS technique

This assay relies on the formation of ABTS (2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid)) cation radical (ABTS·+) upon loss of an electron by its nitrogen atom which will be manifested by an absorption at 743 nm (emergence of a bluish-green color) at the presence of peroxidase. At the presence of Trolox, the N atoms will quench the hydrogen, resulting in a de-colorized solution. (Pellegrini et al. 2003; Thaipong et al. 2006; Marc et al. 2004).

Hydroxyl radical averting capacity (HORAC) technique

Hydroxyl radical averting capacity (HORAC) technique employs a Co(II) complex to evaluate the inhibitory effects against the hydroxyl radical formation. Fluorescein is incubated with the intended sample followed by addition of Fenton mixture (generating hydroxyl radicals). The initial fluorescence will be assessed followed by readings in one-minute interval after shaking. With the help of a gallic acid solution, the standard curve can be measured (Denev et al. 2010; Ou et al. 2002).

ORAC technique

The ORAC assay evaluates the AAPH[4]-induced antioxidant scavenging activities against the peroxyl radical, at 37 °C in which fluorescein is employed as the fluorescent probe. Reaction with the peroxyl radical will cause the loss of fluorescence which can be considered as a decomposition indicator (Thaipong et al. 2006). (Caldwell 2001).

[4]2,2′-Azobis-(2-amidino-propane) dihydrochloride.

Total radical trapping antioxidant parameter (TRAP) technique.

TRAP stands for total peroxyl radical trapping antioxidant parameter (Cízová et al. 2004). TRAP has been applied in human plasma (Badarinath et al. 2010). The luminol-enhanced chemiluminescence (CL) can be applied in monitoring the peroxyl radical reactions. A CL signal can be obtained through luminol-derived radical production as the consequence of AAPH thermal decomposition. In TRAP assay, the plasma-induced lag-phase is compared with the one induced by Trolox in the similar plasma sample (Huang, Ou, and Prior 2005).

Cupric ion reducing antioxidant capacity (CUPRAC) technique

CUPRAC assay is a newly developed method based on hydroxyl radical scavenging antioxidant activity test. *p*-Aminobenzoate, 2,4- and 3,5-dimethoxybenzoate probes can be exploited as the facile and cost-effective substitutes to detect the hydroxyl radicals produced from the equivalent mixture of Fe(II) + EDTA with hydrogen peroxide. The resultant hydroxyl radicals can simultaneously invade the probe and the water soluble antioxidants at 37 °C upon 2-h incubation. $CuSO_4$ and neocuproine are mixed with standard antioxidants or extracts. After 30 min, the absorbance is read at 450 nm. In this assay, Cu(II) will be reduced to Cu(I) due to electron donation of the antioxidants. The results are recorded as milligrams of Trolox per liter of extract (Apak et al. 2004). A rate constant can be defined for the scavenger-hydroxyl radical reaction by studying the color formation dynamics.

Potassium ferricyanide reducing ability parameter (PFRAP) technique

PFRAP method is based on potassium ferricyanide reducing ability and is categorized as a colorimetric method which evaluates the reduction power of plasma toward strong blue ferric tripyridyltriazine complex to convert it into the ferrous form. The mentioned reaction will cause a change in the absorbance (Meng et al. 2011; Jayaprakasha, Girennavar, and Patil 2008; Benzie and Strain 1999). The antioxidant will react with potassium ferricyanide giving rise to potassium ferrocyanide which will further react with ferric trichloride leading to formation of blue-colored ferric ferrocyanide whose maximal absorbance can be detected at 700 nm. The enhancement in the absorbance is proportional to the reducing power of antioxidants or antioxidative extracts (Pisoschi and Negulescu 2011).

Folin–Ciocalteu method

As an electron transfer-based assay, Folin–Ciocalteu assesses the reduction power of an antioxidant. Folin–Ciocalteu results correlate with those obtained with other antioxidant assays such as ORAC, ABTS, and DPPH (Prior, Wu, and Schaich 2005; Stankovic 2011; Vallverdú-Queralt, et al., 2011, 2013, 2014, 2015). Aqueous extracts of phenolic

compounds react with the Folin-Ciocalteu reagent[5] at the presence of sodium carbonate which will result in a bluish complex and its color intensity has a direct relationship with the reactive phenolic content of the sample. Assessment of TPC is achievable through evaluating the sample absorbance at 765 nm and its comparison with gallic acid calibration curve (Kupina et al. 2018; Lamuela-Raventós 2018).

Fluorimetry

Fluorescence is defined as the light emission from a material exposed to electromagnetic radiation possessing the different wavelength (Pisoschi and Negulescu 2011; Ahmad et al. 2014). Fluorescence spectroscopy can measure the antioxidant properties of samples through various principles including oil solubilization in an aqueous buffer, labeling the resultant emulsion with a proper fluorophore[6] (reflecting the lipid oxidation) and continuous decomposition monitoring (Fruhwirth et al. 2003).Upon excitation at ∼310 nm, the fluorescence emission can be read in the range of 320–800 nm. By adding butyl hydroxyanisole (BHA) and/or TBHQ, a fluorescence band will emerge at ∼330 nm (Olsher and Chong 2008).

Electrochemical techniques

Amperometric technique

Amperometric method refers to quantification of the current intensity of passing between a working and a reference electrode under a constant (applied) potential. In this method, an electroactive analyte is oxidized/reduced giving rise to a current. The potential (relative to the reference electrode) can be fixed at a given level (Milardovic, Ivekovic, and Grabaric 2006). Amperometric antioxidant activity assessment relies on the DPPH· reduction at the surface of a glassy carbon electrode. The proposed approach can be used to evaluate the antioxidant behavior of several water/ethanol-soluble antioxidants including tea, wine and other beverages (Pisoschi and Negulescu 2011; Ahmad et al. 2014).

Cyclic voltammetric (CV) technique

Cyclic voltammetric (CV) is categorized as a potentiodynamic electrochemical approach; which involves linear ramping of a working electrode potential against time (Bard and Faulkner 2001). In contrary with the linear sweep voltammetry, upon reaching to the set potential, the potential of a CV working electrode will be ramped in an opposite direction until returning to the initial point. Such ramping cycles might be repeated as many times as required (Nicholson and Irving 1964). The cyclic voltammogram could be achieved through plotting the working electrode current as a function of the applied voltage (i.e. the working electrode potential). The general use of CV is examination of electrochemical features of an analyte or a molecule adsorbed on an electrode (Heinze 1984; Elgrishi et al., 2018). CV results are often compared with spectrophotometric or HPLC data (Martinez et al. 2006). CV technique has been successfully employed to assess the antioxidant activity of red wine, chocolate and hops (Brcanović et al. 2013; Masek et al. 2014).

Biamperometric technique

In a biamperometric method, the current is measured between two identical working electrodes which are polarized by a tiny potential difference and immersed in a solution including a reversible redox couple. Indirect biamperometric method works on the basis of analyte reaction with the redox couple; and its selectivity depends on the reaction specificity of oxidized or reduced forms of the redox pair and the analyte. Fe^{3+}/Fe^{2+}, $I2/I^{-}$, $Fe(CN)63^{-}/Fe(CN)64^{-}$ are redox couples commonly used in biamperometric measurements (Tougas, Jannetti, and Collier 1985). A common redox pair used in biamperometric studies is DPPH·/DPPH. Upon the antioxidants reaction with DPPH· (radical form), DPPH (reduced form) will be formed where the resultant current intensity is proportional to DPPH· content remained after reaction with the analyte (antioxidant) (Milardovic et al. 2005; Pisoschi, Cheregi, and Danet 2009). The DPPH·/DPPH method has been applied in the determination of total antioxidant capacity in fruit juices, tea, wine, and coffee (Milardovic et al. 2005; Ahmad et al. 2014).

Biosensors technique

Biosensors could be employed to monitor superoxide radical (O2·−), nitric oxide (NO), GSH and uric acid as well as ascorbic acid or phenolic compounds quantification (Mello and Kubota 2007). Owing to their excellent electron transfer ability during catalysis, oxidoreductase enzymes have been widely applied in biosensing purposes (Pisoschi and Negulescu 2011). Some enzyme-based amperometric biosensors have been introduced to detect the phenolic compounds which mainly employed tyrosinase, laccase or peroxidase (Bonanni et al. 2007; Gil and Rebelo 2010). Regarding the effect of tyrosinase on hydroxyl groups of the phenolic compounds, the total –OH groups content of the red wine can be determined by the enzyme electrodes. Results can be presented as GAE as mg/L (Lopez et al. 2001). In order to determine the polyphenol content of vegetable extracts, an amperometric horseradish peroxidase-based biosensor was developed (Mello, Sotomayor, and Kubota 2003).

Chromatographic methods

Chromatographic techniques are more employed for antioxidant separation and detection prior to the spectrophotometric or electrochemical evaluation of total antioxidant capacity (Pisoschi and Negulescu 2011).

[5]Complex mixture of heteropolyphosphotungstatemolybdate.

[6]A fluorophore or fluorochrome is an active fluorescent compound e of reemitting light upon excitation by light. These compounds generally encompass several aromatic rings, or planar or cyclic molecules with several π bonds.

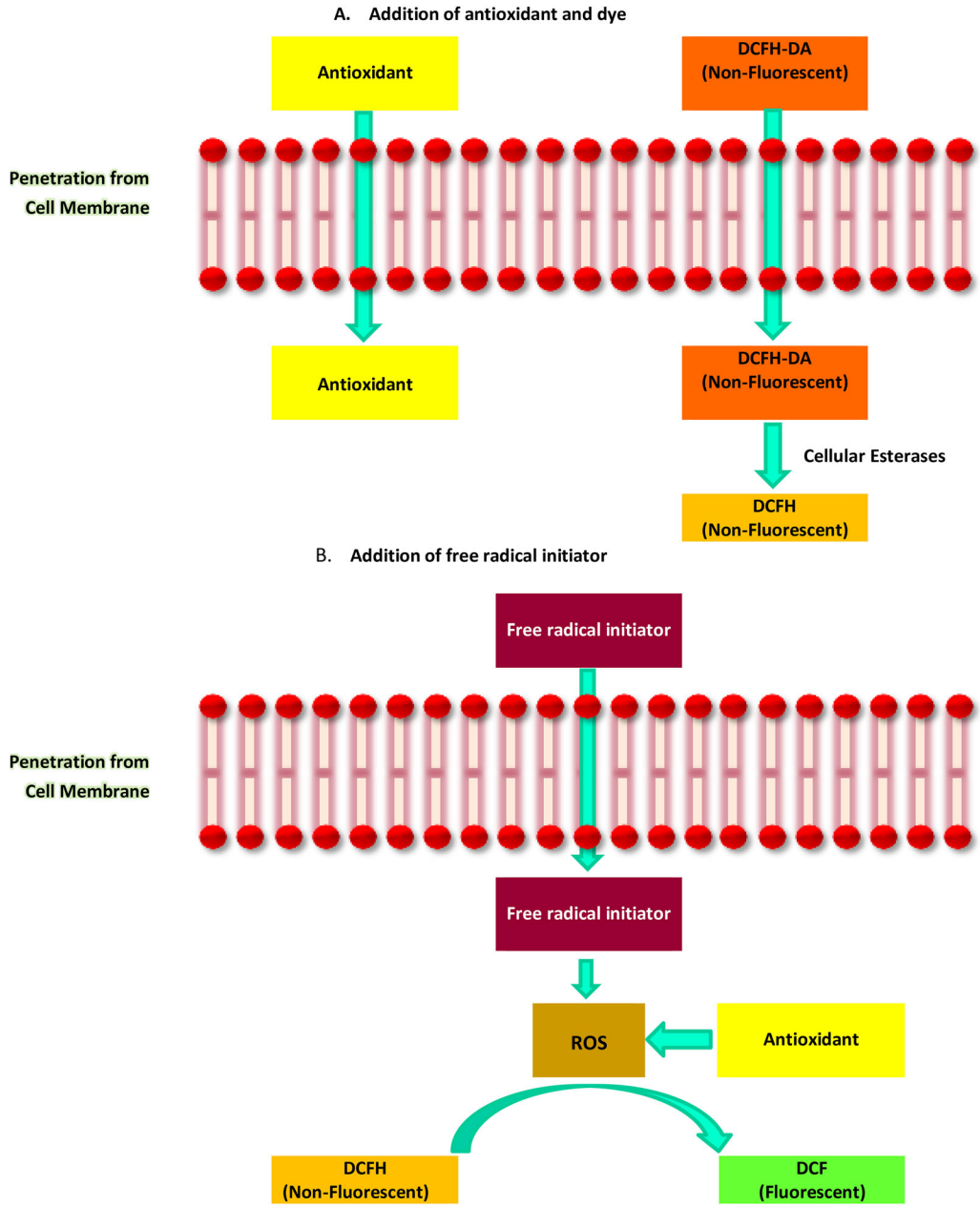

Figure 2. Mechanism of cellular antioxidant activity assay.

HPLC

During HPLC, the analyte and the mobile phase are passed through a shorter-length column containing small stationary phase particles at higher pressures (utilizing a pump) giving rise to separation of cogent. Detector evaluates the retention time (Moharram and Youssef 2014). Normal phase HPLC employs a nonaqueous and nonpolar mobile phase and a polar stationary phase for efficient separation of nonpolar species. On the other hand, reversed phase HPLC applies aqueous and a relatively polar mobile phase combined with a nonpolar stationary phase. The antioxidant activities can be on-line determined through use of a post column. The eluted products are then exposed to a photodiode array detector followed by their mixing with ABTS for absorbance reading at a given wavelength. Upon quenching the radicals, the ABTS bluish color will fade giving rise to a negative peak. Total antioxidant activity can be determined by summing all the individual peaks (Stalmach et al. 2006).

Gas chromatography (GC)

Gas chromatography (GC) has been extensively applied for the separation and analysis of substances capable of decomposition-free vaporization. In this method, the liquid stationary phase and the mobile gas phase of mixture will be separated. The mobile phase is often an inert gas (e.g., helium) or a nonreactive gas (like nitrogen). The stationary phase encompasses a microscopic liquid or polymer layer deposited on the inert solid support (Halvorsen et al. 2002). Antioxidant behavior of turmeric oil was studied using this method through a GC and a mass spectrometer. A flame ionization detector was also applied. The GC results were

then compared by reductive approaches such as carotene linoleate system and phosphor molybdenum method (Jayaprakasha, Girennavar, and Patil 2008).

TLC autography technique

The plant extracts profile can be easily, effectively and rapidly evaluated by thin layer chromatography (TLC) autography technique. This method requires no sample purification since this approach simultaneously separates and measures the radical scavenging activity of plant extract antioxidants (Peiwu et al. 1999).

Qualitative analysis. One of the methods that can be done using this technique is DPPH. The DPPH free radical scavenging capacity can be assessed by TLC technique in which the yellow or white spots on the purple background are recognized as antioxidants (Yrojonen et al. 2003; Weatherby 2007).

Semi-quantitative analysis. The size and intensity of the yellow spots are highly dependent on the solution concentration. Moreover, R_f values could be calculated according to the photographs. Using this technique, 40 µg is equivalent to 50 µg of rutin antioxidant characteristics (Yrojonen et al. 2003).

CAA

CAA is a cell-based technique to study the antioxidant properties of phytochemicals in the cells within a standard cell culture environment. Such an environment provides the temperature, pH, uptake and metabolic aspects of the antioxidants as well as their efficacy (Liu and Finley 2005; Brand-Williams, Cuvelier, and Berset 1995). During a CAA assay, the cells should be first cultured in a 96-well black fluorescence cell culturing plate till confluent. They are then preincubated with the cell-permeable diacetate form of 2,7-dichlorodihydrofluorescein (DCFH-DA) fluorescence probe and the bioflavonoid quercetin, or the intended antioxidant sample. The cells are washed following a short period of incubation; when the reaction is triggered free radical imitators addition which form free radicals capable of converting the probes to highly fluorescent dichlorofluoresceins (DCFs). Depending on its concentration, the quercetin also prevents creation of free radicals, and hence DCF emergence. Fluorescence measurements would be carried out in definite time intervals using the standard microplate fluorimetery. The fluorescence results are correlated with the quenching ability of quercetin toward the free radicals. The antioxidant capacity can be determined by comparison with quercetin (Wolf and Liu 2007). Schematic of the CCA mechanism can be seen in Figure 2.

Conclusions

Encapsulation technology is a promising and important approach for using antioxidants and food ingredients to overcome all the restrictions; it can improve the food fortification process, storage and release of the antioxidant food ingredients in a controlled manner, extending the efficiency of antioxidants when ingested in the intestine undergoing a series of physiological conditions. Studies have suggested that DPPH, TPC, ABTS, ORAC, and CUPRAC techniques are used more than other antioxidant activity techniques to evaluate the bioactivity of nano/microencapsulated food ingredients, since these techniques are simpler, more effective, and more quick than others to study the antioxidant activity. Direct cellular uptake of nanostructures has a key role in enhancing the cellular antioxidant features of antioxidant food ingredients upon their nanoencapsulation by micelles and nanoemulsions. Antioxidant activity of lipophilic compounds in hydrophilic systems and the antioxidant activity of hydrophilic compounds in lipophilic systems will be increased with encapsulation process because of possibility of using various bioactive compounds with different chemical structures in different food systems by appropriate type of wall materials. Decreasing the antioxidant activity of sensitive compounds such as polyphenols due to high temperature of spray dryer during encapsulation process is one of the negative effects that some strategies have been anticipated to solve this problem. The operation temperature is one of the crucial factors in spray drying of heat-sensitive substances. Nanoencapsulation can preserve the bioactive compounds during various storage periods. The wall material used may affect the antioxidant properties of final carriers. Depending on the ability of wall materials for donating the electron or hydrogen and participating in antioxidant reactions, antioxidant activity of encapsulated antioxidant ingredients can be increased. Antioxidant activity maybe decreased by using of coating in the wall materials that can lead to delay the release of core materials; in fact, antioxidants loaded in coated nanoparticles confront additional barrier to be release, presenting prolonged release, therefore their antioxidant activity will be decreased. Single wall material cannot provide all the features of an ideal encapsulation agent. In this content, various approaches have been developed to improve the encapsulation of bioactive food ingredients, most of which are concentrated on carbohydrate–protein mixtures. By forming a thick viscoelastic film at droplet-emulsion interface and preventing from the structural destruction of core material.

Abbreviations

ABTS	2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid)
BHA	Butyl hydroxyanisole
BHT	Butyl hydroxytoluene
β-Lg	*β*-Lactoglobulin
CAA	Cellular antioxidant activity
CL	Chemiluminescence
CUPRAC	Cupric ion reducing antioxidant capacity
CV	Cyclic voltammetry
DCF	Dichlorofluorescein
DCFH	2,7-Dichlorodihydrofluorescein
DCFH-DA	Diacetate form of 2,7-dichlorodihydrofluorescein
DPPH	2,2-Diphenyl-1-picrylhydrazyl
EGCG	(−)-Epigallocatechin-3-gallate
FRAP	Ferric reducing antioxidant power
GA	Gallic acid
GAE	Gallic acid equivalent

GC	Gas chromatography
GIT	Gastrointestinal tract
GPE	Guabiroba fruit phenolic extract
GSH	Glutathione
HAT	Hydrogen atom transfer
HORAC	Hydroxyl radical averting capacity
HPLC	High performance liquid chromatography
MD	Maltodextrin
NP	Nanoparticle
ORAC	Oxygen radical absorption capacity
O/W	Oil-in-water
O/W/O	Oil-in-water-in-oil
PFRAP	Potassium ferricyanide reducing ability parameter
PGA	Poly(glycolic acid)
PLGA	Poly (lactic-co-glycolic acid)
ROS	Reactive oxygen species
SET	Single electron transfer
SLNs	Solid lipid nanoparticles
TAC	Total antioxidant capacity
TEER	Epithelial *trans*-electrical resistance
TLC	Thin layer chromatography
TPC	Total phenolic content
TRAP	Total radical trapping antioxidant parameter
UA	Uric acid
UV–Vis	Ultraviolet–visible
W/O	Water-in-oil
W/O/W	Water-in-oil-in-water
WPC	Whey protein concentrate
WPI	Whey protein isolate

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