Natural Emulsion Stabilizers

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Natural emulsion stabilizers are polymers of amino acid, nucleic acid, carbohydrate, etc., which are derived from microorganisms, bacteria, and other organic materials. Plant and animal proteins are basic sources of natural emulsion stabilizers. Pea protein-maltodextrin and lentil protein feature entrapment capacity up to 88%, (1–10% concentrated), zein proteins feature 74–89% entrapment efficiency, soy proteins in various concentrations increase dissolution, retention, and stability to the emulsion and whey proteins, egg proteins, and proteins from all other animals are applicable in membrane formation and encapsulation to stabilize emulsion/nanoemulsion. In pharmaceutical industries, phospholipids, phosphatidyl choline (PC), phosphatidyl ethanol-amine (PE), and phosphatidyl glycerol (PG)-based stabilizers are very effective as emulsion stabilizers. Lecithin (a combination of phospholipids) is used in the cosmetics and food industries. Various factors such as temperature, pH, droplets size, etc. destabilize the emulsion. Therefore, the emulsion stabilizers are used to stabilize, preserve and safely deliver the formulated drugs, also as a preservative in food and stabilizer in cosmetic products. Natural emulsion stabilizers offer great advantages because they are naturally degradable, ecologically effective, non-toxic, easily available in nature, non-carcinogenic, and not harmful to health.

emulsion stabilizer nanoemulsion emulsion technology biopolymer

1. Emulsion and Emulsion Stabilizer

1.1. Emulsion and Emulsification

In an emulsion, immiscible droplets are dispersed between two liquid phases. An example is the dispersion of water in oil or the dispersion of oil in water when it is stabilized by a suitable surfactant [1]. The substances using stabilizer agents in emulsion and nanoemulsion are called emulsion stabilizers; the general number of biopolymers used as monolayer stabilizers as well as multilayered stabilizers is presented in **Figure 1**. Nanoemulsion and emulsion are two different substances, with significant differences between them. The main differences between emulsion and nanoemulsion are listed in **Table 1**.

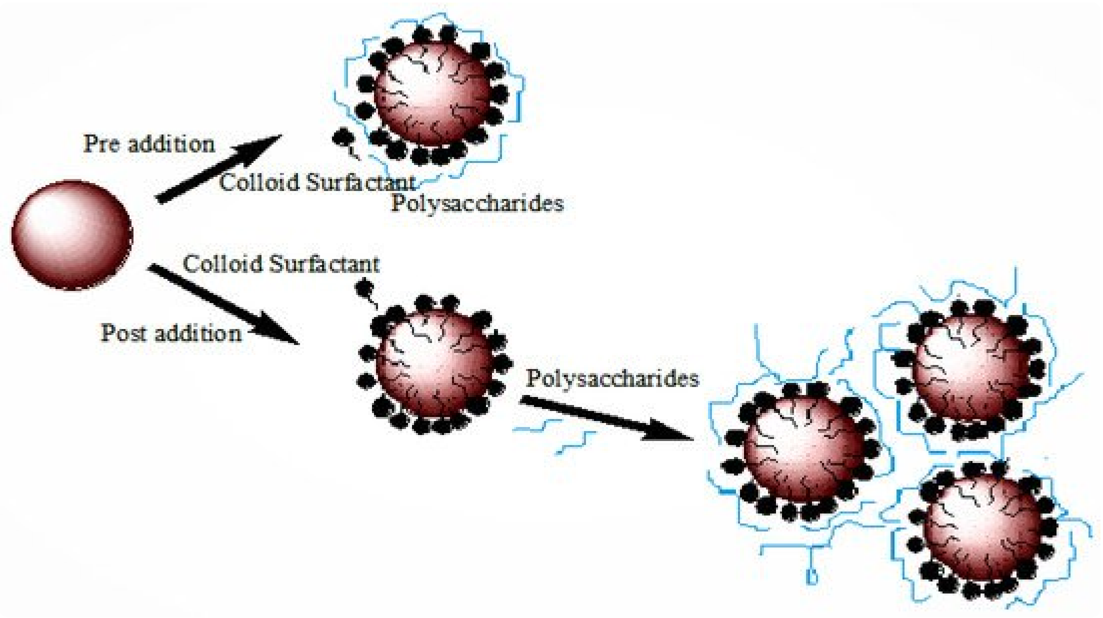

Figure 1. Stabilization of emulsion by using biopolymer stabilizer [2].

Table 1. Differences between emulsion and nanoemulsion.

Properties	Emulsions	Nanoemulsions	References
Droplet size	Lager than nanoemulsions	20–200 nm	[3]
Stability	Thermodynamically unstable	Thermodynamically stable	[4]
Formation	By high shear homogenization methods	Micro-fluidization of emulsions	[5]
Viscosity	Higher viscosity than nanoemulsions	Lower viscosity than emulsions	[5]

1.2. Stabilization and Destabilization of Nanoemulsion

Although nanoemulsions feature small droplet sizes, they exhibit long-term stability due to their ability to withstand destabilization processes such as creaming, sedimentation, and coalescence, as shown in **Figure 2**. Nanoemulsions have been used to solubilize and preserve drugs against unpleasant environmental factors in the parenteral form, such as oxidation, pH, and hydrolysis [6], to target special fixed organs by exploiting the increased absorptivity and reservation effect [7] and to evade the reticular endothelial system [8]. Nanoemulsion droplets are large enough to saturate highly hydrophobic drugs and increase their dissolution, resulting in an anticipated increase in their systemic bioavailability [9]. As nanoemulsions partition and diffuse from the oil to the surface-active layer and then into the hydrolyzed stage [10], they offer the possibility of obtaining sustained/controlled release devices. During nanoprecipitation, the drug’s surface area is greatly increased, which ultimately accelerates its dissolution. The Noyes–Whitney equation is used to calculate the dissolution rate. Sedimentation occurs when particles in suspension are trapped in a medium and then settle into it. Therefore, preventing such aggregation may stabilize an emulsion. The suspension is unstable due to the presence of flock-like colloids, known as flocculation. In flocculated systems, the Van der Waal forces are stronger than the repellent forces, which is why droplets tend to stick together. To prevent flocculation, a solution must overcome the attraction between droplets. Electrical double layers can be formed with anionic surfactant to create repelling forces. Emulsions become unstable when two or more droplets coalesce, resulting in coalescence. To reduce coalescence, polysaccharides and polypeptides act as weighting agents.

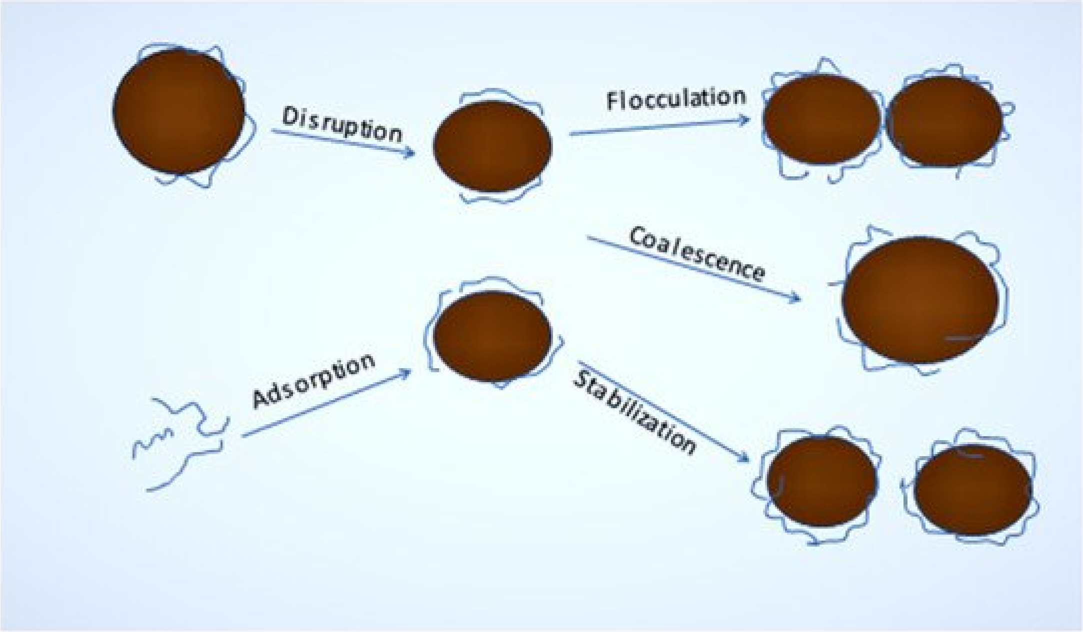

Figure 2. Overall views of instability emulsion [11].

Additional elements such as the ability to convert direct para-cellular/transcellular transfer [12][13] extend gastric retention because of mucosal entanglement [14], as well as helping in nanoemulsion-mediated bioavailability improvement. Nanoemulsions have been shown to absorb directly into the lymphatic system, reducing the likelihood of first-pass metabolism and improving the bioavailability of drugs subject to hepatic transformation to a great extent [15]. Across a variety of sectors, including food technology, pharmaceuticals, and agriculture, biopolymers are used to form nanoemulsions to an increasing degree. Colors, flavors, lipids, preservatives, vitamins, and nutraceuticals are among the hydrophobic functional ingredients that food and beverage producers must encapsulate in their products. By encapsulating these functional ingredients, they may be more easily handled, water-dispersible, and chemically stable. Biologically active substances such as vitamin A, D, E, F, lutein, cumin, and coenzyme Q10 can be encapsulated, protected, and delivered effectively by nanoemulsion-based delivery methods [16].

1.3. Synthesis and Application of Nanoemulsion

Nanoemulsions can be made and used in several dosage forms, such as fluids [17], pastes [18], fogs [19], gels [20][21], fine particles of liquid and solid in the air [22][23] and can be equally applied by changing routes such as topical [24], oral [25], intravenous [26], intranasal, pulmonary and ocular [27]. In addition to the cosmetic industry [28] and pesticide industry [29], they also have been used as aqueous mediums for organic deliverables due to their superior solubilization capabilities. We compared the nanoemulsions with their droplet size obtained by different techniques used from various sources, as shown in **Table 2**.

Table 2. Comparison of nanoemulsion with droplet size.

Sources	Emulsification Techniques	Droplet Size	References
Fluids	Ultrasonic emulsification	24.21 ± 0.11 nm	[17]
Pastes	Emulsion inversion point method	<300 nm	[18]
Fogs	High-pressure homogenization	200–600 nm	[19]
Gels	Microfluidization	<100 nm	[20][21]
Fine liquid and solid particles in the air	Vertex mixing	282 nm	[22][23]
Topical	High-pressure homogenization	50–100 nm	[24]
Oral	Microfluidization	22 ± 4.0 nm	[25]
Intravenous	High-pressure homogenization	89.23 ± 7.2 nm	[26]
Intranasal, pulmonary, and ocular	High-pressure homogenization	8.4 ± 12.7 nm	[27]
Cosmetic industry	Ultrasonic emulsification	6–10 nm	[28]
Pesticide industry	Low-energy emulsification	~30 nm	[29]

2. Polysaccharides Chemical Structure and Their Properties

2.1. Synthesis of Polysaccharides Emulsion

Monosaccharide units, also known as glycosyl units, are used in polysaccharides to create larger molecules [30]. A polysaccharide's degree of polymerization is identified by the number of monosaccharide units in it; the degree of polymerization (DP) ranges from 100 to more than 10,000, with the majority falling between 200 and 3000. Homoglycans and heteroglycans are distinct in that they are composed of different sugar monomers. The former, for example, are formed by monomers of the same sugar in starch amylose, while the latter are made up of different monomers. Heteroglycans such as align and guar gum are also found in locust bean gum [31].

To lower its interfacial tension, alkyl polysaccharides are produced against hydrocarbons phases and the use of polysaccharides with ions in personal care products. In shampoo, shower bath, and soap formulations, ionic surfactants produce more foam than non-ionic sugar surfactants.

2.2. Glycosyl with Polysaccharides

The presence of glycosyl units, which contain three hydroxyl groups, makes polysaccharides very hydrating, since water molecules are highly attracted to them. Polysaccharides are hydrated more easily because they can form bonds with water, called hydrogen bonds [32][33].

Furthermore, glycosidic oxygen atoms can form hydrogen bonds with water when the oxygen atom is added to the ring structure. The functional properties of foods such as texture can be modified and controlled by carbohydrates with lower molecular masses by controlling the mobility of water in the food system [34]. It is important to understand that water whose structure has been sufficiently modified by the polymer so that it does not freeze is sometimes called polymer or polymerizing water. The water that is naturally hydrogen-bonded to polysaccharide molecules is called non-freezable water. A chemical scale does not show the molar bonding of these molecules in this water. Regardless of their slowed motion, they are free to exchange with other water molecules and can do so rapidly. There is little water contained in gels and fresh tissue foods other than the water that is essential for hydration. Water is entrapped in gels and tissues in t capillaries and holes of different sizes above the hydration water level. Rather than cryoprotectants, polysaccharides act as cryostabilizers. Their large size and high atomic weight mean that they do not significantly affect water’s osmolality or freezing point, and their colligative properties do not cause the molecules to behave in these ways [35]. When polysaccharide solutions are frozen, crystalline water (ice) and glass, containing perhaps 70% polysaccharide molecules and 30% non-freezable water, are created. Non-freezable water is such a complex mixture of molecules that it is part of a fluid whose molecules feature very little mobility due to its very high viscosity, which is only possible in carbohydrates of lower molecular weight. Others provide cryostabilization by adsorbing to nuclei or active crystal growth sites to limit crystallization by freezing a freeze-concentrated matrix.

Polysaccharides differ in their properties based on their molar mass, electrical double layers, hydro-basicity, polarity, and branching degree. Glycoproteins or glycolipids covalently bound to polysaccharides improve their emulsification performance.

3. Food Protein and Food Protein Emulsions

3.1. Animal Protein and Plant Protein

Proteins, which are widely used in food, are most often extracted from animal sources to be used in pharmaceutical applications, such as microencapsulation. Despite various appealing properties of animal protein for microencapsulation, such as smooth/high solubility, lower molecular mass, flexibility (and, hence, greater stabilizing), entrapment, and oxidation-resistant properties compared to plant-based proteins, plant proteins command more attention from consumers as animal products raise the question to food safety due to some health-related controversies related to animal products. One example is the risk of Bovine Spongiform Encephalopathy (BSE) (also called transmissible spongiform encephalopathies (TSE)), a fatal neurodegenerative disease affecting humans and animals, caused by the abnormal formation of a cell protein called prion protein (PrP)). In comparison with animal proteins, plant proteins are more economical and readily available. There is also the possibility of allergy to plant proteins. Therefore, reducing allergenicity requires careful selection of the plant protein (for example, pulse proteins).

A microencapsulation experiment on sweet orange oil [36] utilized Soy Protein Isolate-Gum Arabic (SPI-GA) coacervates to find the different effective factors, such as ionic character, the ratio of SPI/GA, pH, basic elemental load, and introducing sucrose and maltodextrin in the composite and effectiveness of microencapsulation. Eventually, in 4.0, 0 mol/l NaCl pH with a 1:1 ratio of SPI to GA and a 10% loading core materials were found to produce the maximum coacervate yield and encapsulation of basic microelements. Moreover, microencapsulation yields increased dramatically when sucrose was coupled with SPI (sucrose: SPI ratio 1:1). According to previous research [37], the spray-drying of soybean oil produced SPI microencapsulation was a factor influencing retention ability, re-distribution or dissolution properties, and stability in store. Core–wall ratios of 1:1 or higher negatively affect redispersion characteristics, while a 1:1 wall to core ratio exerts a higher positive effect on them.

3.2. Effectiveness of Plant Protein

The non-modified status of pulse proteins has, along with their reduced risk for allergens, made them a popular alternative to soy because they are considered a superior replacement. By using a complex coacervation process, Ducel et al. examined pea globulin used as a wall material in the microencapsulation of model oil. They also studied and compared a cereal protein (alpha-gliadin) and a leguminous protein (pea globulin). The effect of pH and the protein–anionic chemical ratio value were the main topics of investigation for them [38]. In a similar study by Gharsallaoui et al. in pea protein microcapsules with Miglyol 812 N = 5%, pea protein = 0.25%, and maltodextrin = 11% in pH = 2.4 with the addition of spray-dryer, then recalculated at pH = 2.4, as a model oil, stability-to-droplet aggregation was enhanced when the pectin coating was applied after drying. In addition to maintaining oil droplets in suspension, pectin also increased steric repulsion [39].

3.3. Pea Protein Entrapment Efficiency

Karaca et al. found that spritz-dried pea protein-maltodextrin and lentil protein capsules featured maximum entrapment capacities of 88% and 86%, respectively, and released 37% and an additional 47% of the closed flaxseed oil after 2 h and 3 h, respectively [40]. From using freeze-drying, 35.5% maltodextrin-DE9 and 10.5% oil was found to be an optimal wall formulation that accorded good entrapment ability about 83%, the smallest surface oil of about 3%, and a suitable average globule width of about ~3 mm [40]. Furthermore, as the emulsion oil content expanded, the diameter of the oil globule and the surface area of the oil content increased, whereas entrapment efficiency decreased.

3.4. Other Plant Protein and Entrapment Efficiency

Other plant proteins rarely employed as encapsulating agents are cereal grain proteins. Researchers have studied how to enhance the properties of these proteins. Using a highly concentrated zein protein extract from corn gluten, a spray drying process was used to encapsulate tomato oleoresin. Zein concentrations of 1 to 10% (*w/v*) increased entrapment efficiency from 74% to 89%, but no further increase in entrapment efficiency was observed at 14% [41].

Wang et al. encapsulated fish oil using barley protein taken as a microfluidizer in proteins = 15% and using oil protein ratio = 1:1, followed by spritz dryness processing (at 150 °C), with loading efficiencies of 50% [42]. Jiang et al. changed the initial soy proteins structure by acid pre-treating in pH 1.5 to 3.5 and in alkaline solutions with a pH = 10–12 for many repetitions (0–4 h); the results showed an increase in surface hydrophobicity in the form of a protein-adjusted, liquefied droplet-type configuration, and beneficial changes to its emulsifying characters [43]. Augustin et al. identified that increased temperature-time reactions were necessary to increase the stability of fish oil microcapsules after emulsification. They also observed that heat treatment increases entrapment efficiencies [44].

3.5. Modification of Protein into Functional Components

There are many ways to modify plant proteins chemically or enzymatically. The controlled deamidation and glycosylation of rice endosperm protein emulsion were achieved by Paraman et al. [45]. A denaturation process during protein synthesis could contribute to increasing protein hydration. A methanol-alkali deamidation improvement of rice endosperm protein’s emulsifying properties was found to be the most effective. Wong et al. found that many locations of conjugation and dextran were dependent on the dextran size in wheat protein-dextran Maillard conjugates prepared using the deamidation method [46]. In comparison with the adsorption of protein alone, the complexes were shown to create a deep interfacial, coverage providing greater steric stabilization. Glycation enhanced the emulsifying properties of kidney bean vicilins in the presence of glucose described by tertiary conformation unfolding and rearrangement, and increased quaternary flexibility [47]. Polysaccharides have been found to enhance emulsion stability when used in a mixture with proteins in emulsion [48] by raising the durability of the interfacial thin layer dividing the globules and reducing the droplets’ movement rate, altering the viscosity of the regular phase. Maltodextrins are favored as subsidiary wall materials or additional elements of microencapsulation to upgrade the drying capacities of microcapsules because they possess fine solvability and lower viscousness in maximum solid content [49].

4. The Stability Factors of Proteins Nanoemulsions

Many factors contribute to emulsion stability, such as fluctuating temperature and pH, storing age, ionic strength, and processing technology [50], where temperature and time are the two main determinants. Temperature and time significantly affect the increase in the size of particles, the retention of β-carotene, and the rate of potential decrease with storage temperature as well as time [51]. In addition to droplet collisions in storage, the liquid phase separation rate of nanoemulsions is affected by Brownian motion at higher temperatures. This behavior leads to an increase in the size of the particle due to mass transfer kinetics between the water and oil phases [52][53]. A qualitative study showed that protein emulsifiers inhibit lipid oxidation more effectively than small-molecule surfactants [54]. The food industry will be able to make better use of that antioxidant by utilizing carotenoids, which include β-carotene. In an experiment conducted by [50], a glucamine-based trisiloxane surfactant was obtained through the green synthesis technique. Studying various physicochemical characteristics of the compound, including its surface functioning, accumulation, and wetting properties, HAG (4-S-Glutathionyl-5-Pentyl-Tetrahydro-Furan-2-Ol) was reported to feature a relatively lower surface tension (γ = 19.04 mN/m) and to interact readily with surfaces. It has also been demonstrated that HAG reduces surface tension with remarkable efficiency. A highly assemblable microdevice can also be used for encapsulating drugs and delivering them, as well as a microreactor, as evidenced by TEM and dye encapsulation experiments. Additionally, it could be used as an adjuvant, a cleaning agent, a coating, or a home care product. In total, 99% of HAG can be biodegraded within a week using primary biodegradation experiments.

4.1. Encapsulation and Encapsulation Efficiency

Various delivery systems for multifunctional drugs, e.g., nanoparticles [55], liposomes [56][57], nanogels [58], nano-capsules [59], and copolymer micelles [60][61][62] have been extensively explored in doxorubicin (a chemotherapy drug called anthracycline, which blocks topoisomerase 2, which cancer cells need to divide and grow) delivery systems to increase antitumor efficiency for a few decades. Polymeric micelles have been attracted to enhancing attention in the form of beneficial nano-carriers for transporting antitumor drugs owing to their superior characteristics, such as self-assembling into micelles in solution, greater consistency besides the reduction of blood density, extended reservation, and superior tumor assembly [63][64][65][66]. A similar study on assorted micelles of Dox@FA-BSP-SA/TPGS regulated under the supervision of Liu et al. [67] reported that the cytotoxicity environment and anti-tumor effectiveness in vivo outcome of Dox@FA-BSPSA/TPGS micelles was ranked than that of doxorubicin-free and Dox@FA-BSP-SA individual micelles, suggesting that it is a promising candidate as a drug delivery carrier for cancer chemotherapy. FA-BSP-SA/TPGS combined micelles presented higher biocompatibility, with a moderate elemental size of 147.3 nm, a load capacity (LC) = 14.4%, and a encapsulation efficiency (EE) = 91.9% for doxorubicin, with a weight ratio of 3:1.

4.2. Emulsifying Properties of Proteins

The protein, or polysaccharide, plays an important role as an encapsulating agent. Such encapsulating agents protect sensitive elements from harmful environmental agents such as oxygen, temperature, pH, moisture, etc., as well as preventing unpleasant smells and flavors, helping to uniformly disperse the active ingredients, and simplifying the handling of the active ingredients [68]. The oils containing *n*-3 polyunsaturated fatty acids, such as linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid, have been entrapped; these oils receive the most attention because they feature healthy characteristics in infant growth, minimizing the possibility of heart and blood vessel-related diseases, and preventing swelling [69][70][71]. When plant protein ingredients are used, they feature less solubility, reduced emulsifying abilities, and decreased reactivity to crosslinking factors relative to proteins formulated from animals, such as whey and casein. Some protein-emulsifying properties are as follows:

(a) Surface hydrophobicity: The percentage of hydrophobic proteins exposed on the surface of proteins measures how much of the protein can adsorb to the oil phase. The presence of hydrophobic sites buried inside proteins can be revealed by partial denaturation, which can increase their emulsifying ability [72].

(b) The flexibility of proteins: It is a self-rearrangement property of proteins, when it is adsorbed at the oil–water (O/W) interface, most of the hydrophilic mass favors the watery parts and the hydrophobic mass favors the oily parts by reducing the attractive force between two liquids [73]. According to the composition of protein, hydrophilic loops of amino acids may enlarge away from the O/W interface in the form of waterish parts, slowing the reaction [73].

(c) The dimension of the protein molecules may affect their movement on the O/W interface emulsification process, and the film formation capacities of the protein. Luyten et al. (2004) [74] reported that smaller proteins are more effective for diffusion at the interface than larger proteins [72].

(d) When encapsulating, a high solubility of proteins is preferable in order to allow higher movement in the O/W interface and higher continuous phase viscosities [72].

(e) The factor influences in the protein solubility are the pH of the solvent, the ionic character, and the attractive or repulsive forces between closer globules showing emulsion instability or stability. When the solvent pH is not near the isoelectric point of proteins or when ionic conditions are low, charge repulsion can enhance emulsion stability [75].

In a study by Liu et al., four major macromolecular proteins with emulsifying abilities were studied, which included peanut protein isolate, whey protein isolate, rice bran protein isolate, and soy protein isolate [76].

4.3. Protein from Rice Bran as an Emulsifier

Rice bran protein (RBP) features high surface activity and good hydrophilicity [77]. Therefore, it is suitable for emulsifiers to stabilize nanoemulsions. Based on one experiment, rice bran protein-based nanoemulsions feature the lowest globule dimension and are highly stable at RBP = 3% and pH = 9.0. When quercetin was added to nanoemulsions, the resulting nanoparticles were smaller and more organic. In an alkaline medium with low concentrated salt ion, the rice bran protein-based nanoemulsion was stable. The use of RBP NEs resulted in a 12.70 ± 0.12% increase in quercetin bioavailability after in vitro digestion and cell piercing observation. In addition to reducing quercetin's toxicity to cells, nanoemulsion-encapsulated quercetin increased the degree of penetration into cells, reaching $4.93 \pm 0.01 \times 10^{-6}$ cm/s. The RBP NEs and QE-RBP nanoemulsions both feature a 14 day preservation period. RBP NEs can be used to carry biologically active molecules, according to this study [77].

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