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Research progress on natural bio-based encapsulation system of curcumin and its stabilization mechanism

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Abstract

Turmeric is a natural active substance extracted from the Zingiberaceae plant, containing a variety of derivatives, the main component being curcumin. Curcumin has a wide range of sources, low cost, and has strong antioxidant, anti-inflammatory, anti-cancer, antibacterial and other physiological functions, but it has problems such as poor water solubility, poor stability, and low bioavailability. There are certain interactions (hydrophobic interactions, electrostatic interactions, hydrogen bonds, etc.) between curcumin and bio-based proteins or polysaccharides, which can be combined to form different encapsulation systems, which can effectively improve the poor water solubility, poor stability and intestinal problems such as low bioavailability. This article focuses on the types of natural bio-based encapsulation systems (emulsion, liposome, micelle, nanoparticles, gels, and microcapsules), mechanisms and their applications in the food field of curcumin.

Keywords: curcumin; emulsion; solid particle; mechanism; application.

Practical Application: Application of curcumin encapsulation system.

1 Introduction

Turmeric has a history of thousands of years in my country. The Tang Dynasty pharmacology monograph "Tang Materia Medica" first recorded that turmeric has the effect of promoting Qi, breaking blood stasis, clearing the meridian and relieving pain. It is an important Chinese herbal medicine. Turmeric is also mostly used as a kitchen spice. In 1815, scientists isolated curcumin from the root of turmeric, and in 1949, it was proved by scientists that it has antibacterial activity, and the research and exploration of curcumin officially began. Uğur et al. (2022) used different polyphenol-rich herbal teas to study the effect of curcumin on glycemic index. Explored the inhibitory effect and mechanism of curcumin on the growth of human hepatocellular carcinoma (HCC) HepG2 xenografts in nude mice, and the results showed that curcumin could significantly increase the inhibition of cisplatin on the growth of HCC HepG2 xenografts in nude mice effect. As shown in Figure 1, in recent years, the number of research papers has shown a steady upward trend year by year. Curcumin is an active polyphenolic compound extracted from the rhizomes of Zingiberaceae, a lipophilic substance (Chen et al., 2007; Rauf et al., 2018). Turmeric contains a variety of turmeric derivatives, the main components of which are curcumin (77%), demethoxycurcumin (17%), double demethoxycurcumin (3%) and cyclocurcumin (Goel et al., 2008; Heger et al., 2013), Which yellow-orange (Sabet et al., 2021). As shown in Figure 2, the molecular formula of curcumin is $C_{21}H_{20}O_6$, and the molecule contains phenolic hydroxyl, carbonyl and double bond groups, and has a regular crystal structure. Its seven-carbon chain is connected by a β -diketone, α , β -unsaturated moiety Two phenolic o-methoxy-OH groups are composed of aromatic rings (Sahne et al., 2016), has a strong reactivity.

Curcumin exists in three forms, as shown in Figure 2. The keto-enol tautomers of curcumin will transform each other under different pH conditions, mainly in the form of enol under alkaline conditions, and in the form of ketone under acidic or neutral conditions (Anand et al., 2007; Bernabé-Pineda et al., 2004). As shown in Figure 3, curcumin will show different colors under acidic and alkaline conditions, which are based on the hydroxyl groups at both ends of its molecular structure, reddish-brown under alkaline conditions, and bright yellow in varying shades under acidic and neutral conditions.

Curcumin has a wide range of sources, low cost, and has strong antioxidant, anti-inflammatory, anti-cancer, antibacterial and other physiological functions, but it has problems such as poor water solubility, poor stability, and low bioavailability. The encapsulation system is an effective means to improve these problems of curcumin. This article introduces the structure, properties, types of natural bio-based encapsulation systems of curcumin (emulsion, liposomes, micelles, nanoparticles, gels, and microcapsules), mechanisms and their applications in the food field.

2 Physiological properties of curcumin

2.1 Physiological activity of curcumin

Curcumin has a variety of physiological activities. Other researchers have found that the β -diketone moiety also has a role in antioxidant properties (Jovanovic et al., 1999). In addition, curcumin has anti-inflammatory (Ahmadabady et al., 2021), neurodegenerative (Ghosh et al., 2015), cardiovascular disease

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Figure 1. The number of curcumin research papers in the Web of science (SCIE) database.

(Hasan et al., 2014), Gastrointestinal diseases (Morsy & El-Moselhy, 2013), etc., curcumin also has anticancer activity, such as the treatment of breast cancer (Liu & Ho, 2018), sarcoma (Singh et al., 2010) investigated the effects of synthetic and natural food colorings on biochemical and immune parameters, Shakoor et al. (2022) showed that the intake of ADI and food coloring at doses up to 10 times ADI adversely affected immune responses and altered biochemical parameters.

2.2 Properties that limit the application of curcumin's biological activity

- I. Hydrophobicity. With a log octanol/water partition coefficient (logP) value of 3.2, curcumin is practically insoluble in water and highly soluble in lipids (Jamwal, 2018). Its water solubility will be affected by the pH value of the environment in which it is located. When the pH is less than 8, curcumin is highly hydrophobic, and the water solubility is about 24 mg/L. When the ambient pH > 11, curcumin becomes hydrophilic (Mahesh, 2019), because the acidic phenolic group of curcumin in alkaline condition provides its H+ ion, forming phenolate ion, which makes its own moiety Dissolution (Tennesen & Greenhill et al., 1992).
- II. Poor stability. The stability of curcumin is also affected by other components in its environment. It can react with proteins (Tapal & Tiku, 2012) or metals (Wanninger et al., 2015) to enhance stability, such as antioxidants presence also enhances its stability (Nimiya et al., 2016). In addition, there are extreme pH levels, moisture and oxygen can also affect its stability, when curcumin is exposed to these conditions, curcumin's three active sites (one diketone moiety and two phenolic groups) undergo oxidation, Especially the phenol-OH functional group is the most reactive, leading to hydrolysis, degradation and enzymatic reactions (Priyadarsini, 2014).



Figure 2. Chemical structure of curcumin; Keto-enol tautomerism of curcumin (Yixuan et al., 2021). A: Keto-enol tautomeric form; B: Beta-diketone tautomeric form.

III. Poor bioavailability. Curcumin has low bioavailability due to factors such as poor chemical stability, low water solubility, and poor absorption and rapid metabolism. Bioactive substances can only be absorbed by gastrointestinal (GIT) epithelial cells and then transported into the systemic circulation to exert their biological activity if they maintain a high bioavailability (Tian et al., 2022).



Figure 3. Color of curcumin at different pH (pH 3-11 from left to right).

2.3 Measures to improve the bioavailability of curcumin

Although curcumin has strong antioxidant properties, its application in food, medicine, active packaging and other fields is hindered due to its poor water solubility, poor stability, and low oral bioavailability. At present, the main ways to improve the bioavailability of curcumin are as follows: (1) Use with appropriate medicinal excipients. For example, curcumin can be used in combination with the liver and intestinal glucuronic acid binding inhibitor piperine (Bishnoi et al., 2011), and curcumin can also be made into a chelate with metal ions, such as copper. (2) Synthetic curcumin analogs. The biological activity of curcumin is largely determined by its chemical structure. Modification of its benzene ring, methylene group and carbonyl group, screening of derivatives and analogs is an important way to improve its bioavailability (Yuan et al., 2012). (3) Colloidal packaging. Compared with several other technologies, the delivery carrier prepared by encapsulation technology has higher entrapment rate and loading capacity, and can carry curcumin for intracellular release, achieving dual effects of targeting and sustained release, making curcumin better stability and bioavailability. In recent years, delivery vehicles such as nano-solid particles, emulsions, and liposomes prepared from natural biological macromolecules such as proteins, polysaccharides, and lipids have not only their own advantages, but also high biocompatibility and digestibility. The advantages of degradability, safety and non-toxicity have very important practical value in the development of functional foods of curcumin.

3 Curcumin encapsulation system

There are various encapsulation systems for curcumin, including emulsions, liposomes, micelles, nanoparticles, microcapsules, and gels. As shown in Figure 4, different types have certain differences in packaging form, stabilization mechanism and application fields.

3.1 Lotion

An emulsion is a liquid form in which one fluid is uniformly dispersed in another fluid in the form of small droplets. Emulsions can not only encapsulate hydrophobic substances to prepare oil-in-water type, but also encapsulate lipophilic substances to prepare water-in-oil type. In recent years, emulsion systems have been continuously used for the encapsulation of active substances, which can improve the stability and bioavailability of the encapsulated substances and reduce the irritation of some substances, such as capsaicin, allicin, curcumin and so on. Common types of emulsions are microemulsion, nanoemulsion, Pickering emulsion, high internal phase emulsion, high internal phase Pickering emulsion, etc.

Microemulsion

Microemulsion is an emulsion in which two or more immiscible liquids are emulsified and mixed, and the droplet diameter is at the nanometer level. Compared with other microscale emulsions, nanoemulsions with small size can be better absorbed by cells, and have great prospects for drug delivery. Studies have shown that the oral encapsulated curcumin microemulsion has a maximum solubility of 14.57 mg/mL, the penetration percentage of the emulsion through the artificial membrane reaches 70%, and the emulsion can be stable for up to 60 days (Bergonzi et al., 2014). Surfactants are often used in the preparation systems of microemulsions, but surfactants are considered unsafe and environmentally friendly, so the research on the preparation of surfactant-free microemulsions (SFMEs) has received more and more attention (Hou & Xu, 2016). In recent years, natural bio-based particles have become a development trend to replace synthetic particle-stabilized emulsions due to their advantages of degradability, safety and environmental protection.

Nanoemulsion

In general, nanoemulsions refer to emulsions with droplet sizes in the nanometer scale (R < 100 nm) (Salvia-Trujillo et al., 2016). Nanoemulsions have small droplet sizes, are kinetically stable, thermodynamically unstable, and overall optically translucent (Christaki et al., 2022; Liu et al., 2019a). Nanoemulsion droplets are small, and the encapsulated active ingredients can be better absorbed by the gastrointestinal tract and improve bioavailability. However, it has been reported that the bioavailability of curcumin in conventional emulsions may be slightly higher than that of nanoemulsions, but nanoemulsions have better physical stability



Figure 4. Various types of curcumin packaging systems (Sun et al., 2012).

(Ahmed et al., 2012). Also, various types of natural bio-based proteins and polysaccharides are used as matrices for stable emulsions. Some studies have used β -lactoglobulin to stabilize curcumin nanoemulsions and conducted in vitro permeation experiments. It was found that curcumin not only has improved stability, but also increased solubility and can permeate through membranes. It is possible to develop local drug delivery in the future (Mekhloufi et al., 2022). Dammak & Sobral (2021) compared two polysaccharides of pectin and gum arabic to prepare curcumin nanoemulsion, and found that the preparation effect of pectin was better, but curcumin in gum arabic nanoemulsion had higher Retention, both polysaccharide-stabilized emulsions resulted in improved curcumin stability. There are also studies using whey protein concentrate-70 and Tween-80 as emulsifiers to prepare curcumin nanoemulsions, with an encapsulation rate of about 90.56%. When simulating digestion, curcumin can be slowly released in the emulsion, which can improve its biological properties utilization (Sari et al., 2015).

High internal phase emulsion

High internal phase emulsions (HIPEs) refer to emulsions whose internal phase volume fraction is greater than 74%. High internal phase emulsions have high loadings and can be used to encapsulate large quantities of active substances. At the same time, the semi-solid nature of the high internal phase emulsion due to its viscosity can hinder the dilution of the digestive juice into the interior of the emulsion, thereby maintaining stability and reducing the loss of active substances (Liu et al., 2019b). For example, the curcumin high internal phase emulsion was prepared by carboxymethylated lignin (Chen et al., 2020a), the curcumin retention rate was 34.6% after UV irradiation for 72 h, and the retention rate was 92.5% after storage for one month. Its stability greatly improves. The use of high internal phase emulsion encapsulation can not only improve the stability of curcumin, but also its encapsulation rate is considerable. For example, Li et al. (2022a) used egg white protein modified by ultrasonic probes to prepare microgel particles, and then used the particles to encapsulate curcumin to prepare a high internal phase emulsion, and the encapsulation rate could be as high as approx. 81%, after 28 days, the retention rate of curcumin is still about 85%, which not only has good stability but also has a large load. There are also studies using two or more composite particles to stabilize high internal phase emulsions to compare the stabilization effect of single particles. For example, some scholars used beet pectin (SPB), tannin (TA) and chitosan (CS) to prepare a complex first, and then prepare a high internal phase emulsion to improve the stability and bioavailability of curcumin. The study found that, The stability of SPB/TA/CS HIPEs was significantly higher than that of pure corn oil and SPB/TA HIPEs. After UV exposure for 60 h, the retention rates were about 60.4%, 46.7%, and 54.8%, respectively. After simulated digestion in vitro, the bioavailability SBP/TA/CS (46.3%) > SBP/ TA (40.4%) > corn oil (33.6%) (Miao et al., 2021). Finally, the emulsion system successfully transported curcumin to epithelial cells for absorption, enhancing the bioavailability of the active substance. In addition to high loadings and reduced curcumin loss, high inward latexes also possess properties such as large interfacial area and tunable viscoelasticity (Jiang et al., 2021). Edible high internal phase emulsions can also serve as possible substitutes for hydrogenated oils (Huang et al., 2019).

Pickering lotion

Pickering emulsions refer to emulsions stabilized with solid particles. In conventional emulsions, surfactants are often used, which are considered unsafe and not environmentally friendly. Particles can also form elastic interfacial films that provide a steric barrier that effectively prevents droplet accumulation and improves emulsion stability (Luo, 2020). Solid particles prepared by extraction of natural biological materials are generally superior to traditional surfactants in terms of stability and food safety (Rayner et al., 2012), and these solid particles are mostly proteins and polysaccharides such as gelatin (pig rind), beet pectin (beet), whey protein isolate (milk), peanut protein (peanut), soy protein isolate (soy), etc., which also provide a strategy for developing edible Pickering emulsions. In general, the stabilization effect of composite particles is better than that of single particles. For example, nanoparticles prepared from glycated whey protein isolate-chitooligosaccharide can effectively prolong the half-life of curcumin (about 156 h) and effectively improve the stability of curcumin (Yu et al., 2021). Nanoparticles were also prepared with chitosan and gum arabic, and the encapsulation rate of curcumin reached 94% and remained stable at different temperatures (Han et al., 2020). However, there are also many studies using a solid particle as a stabilizer. For example, Yuan et al. (Aw et al., 2022) used cellulose nanocrystals to stably encapsulate the curcumin Pickering emulsion, and its half-life was 98.47 days, stable Sexuality improved about 20 times. The curcumin Pickering emulsion is also stabilized with starch base, the encapsulation rate reaches about 80%, and the curcumin is successfully protected from destruction in the oral cavity and stomach, allowing it to reach the intestinal tract for absorption (Marefati et al., 2017).

3.2 Liposomes

Since its discovery in the 20th century (Bangham et al., 1965), liposomes have unique structures that allow them to be used for the delivery of substances. The phospholipid bilayer can encapsulate lipophilic substances, and the inner hollow layer can encapsulate hydrophilic substances (Kolter et al., 2019). One study used a novel cholesterol-free rhamnolipid to prepare liposomeloaded curcumin, which successfully made it have better stability and sustainable release (Cheng et al., 2019). Tai et al. (2020) studied the use of hydrogenated soybean phospholipids added to curcumin liposomes, which not only improved the stability of curcumin, but also increased its encapsulation capacity. slowed the release of curcumin. Curcumin liposomes are also frequently used in drug-targeted therapy. Wang et al. (2021a) used curcumin liposomes in the study of liver cancer treatment and found that it has anti-tumor effect, and curcumin liposomes released 61% after 24 hours with sustained release characteristic. Liposomal curcumin can also be used to treat asthma (Ng et al., 2018), and for multi-targeted skin treatments such as microbial infections and inflammation (Ternullo et al., 2019).

3.3 Micelles

Micelles are molecularly ordered aggregates that start to form in large quantities when the surfactant concentration reaches a certain value, with hydrophilic groups facing outwards and hydrophobic groups facing inwards (Cheng et al., 2002). Nanomicelles can improve the solubility of poorly soluble substances and increase their bioavailability. For example, using polyethylene glycol monomethyl ether-deoxycholic acid as a carrier to prepare curcumin-loaded colloids, the encapsulation rate reaches 88.2%, the stability is good, the hemolysis rate is less than 5%, and its biological safety is also good (Chen et al., 2007). Incorporation of curcumin into micelles helps improve the solubility of curcumin and also prevents its degradation, and in vitro studies have shown that curcumin in micelles increases its bioavailability by 14 times (Chawla et al., 2022). Curcumin micelles are commonly used in drug therapy, and micellar curcumin is more active than natural curcumin in inhibiting adjuvant inoculation-induced edema, with an overall increase in antioxidant activity (Khayyal et al., 2018). Chondroitin sulfatecurcumin micelles have also been prepared by free-radical polymerization, which have good stability and reduction sensitivity, no cytotoxicity, and can be used in anticancer drugs (Zhang et al., 2021). There is also the use of chitosan and lignosulfonate to prepare composite micelles to load curcumin, which increases the stability of curcumin under heat and pH conditions, and also increases the antioxidant activity of curcumin in aqueous solution, which can be added Antioxidant active membranes were prepared in membrane solution (Lin et al., 2022).

3.4 Nanoparticles

Nanoparticles refer to microscopic particles on the nanometer scale. The preparation of curcumin nanoparticles can also improve the shortcomings of curcumin, such as improving its water solubility, stability, and bioavailability. Bio-based proteins and polysaccharides are often used as substrates for the preparation of nanoparticles. Li et al. (2022b) prepared curcumin nanoparticles with fungus polysaccharide as the outer layer and zein as the core, showing stronger stability under UV and heat treatment, simulating in vitro digestion At the same time, the bioavailability can reach about 87%. The water-insoluble rice protein and curcumin were prepared into nanoparticles, and the nanoparticles could be well dissolved in water. Compared with free curcumin, the nanoparticles showed better thermal stability and the antioxidant activity increased by 88.62% (Xu et al., 2022). Some studies have also found that the carrying capacity of casein (Somu & Paul, 2018) for curcumin can reach 285.51 mg/g. After being prepared into loaded curcumin nanoparticles, it has high water dispersibility in water and enhanced biological antioxidant activity. And chemical antioxidant properties are not affected. The preparation of curcumin nanoparticles by whey protein isolate (Solghi et al., 2020) can also achieve a curcumin encapsulation rate of 93.1% and an increase in stability from 10% to 70%.

3.5 Microcapsules

Microcapsules are formed by using a small amount of material as a core material, and then wrapping the core material with a layer of wall material. The encapsulation, controlled release, and stability improvement of active substances can also be achieved through microcapsule technology. Bio-based proteins and polysaccharides are often used as wall materials for the preparation of microcapsules. Solghi et al. (2020) used a mixture of whey protein isolate, maltodextrin and gum arabic to prepare wall-coated curcumin, with a retention rate of about 88% in the stomach, which successfully resisted the digestion of the stomach. The intestinal tract (86.36%) was released, which improved the stability and bioavailability of curcumin in the gastrointestinal tract. Microencapsulation of curcumin results in stronger stability than free curcumin under high temperature and acidic conditions (Guo et al., 2020). Using gelatin and chitosan as composite wall materials, the degradation of curcumin under UV/visible light was successfully protected and its storage stability was improved (Liu et al., 2022). Curcumin microcapsules prepared from gelatin and porous starch have greatly improved solubility in water, and are more heat resistant and more stable than free curcumin at high

temperatures (Wang et al., 2012). There are also studies using coconut milk whey powder (Adsare & Annapure, 2021) and adding gum arabic to microencapsulate curcumin through spray drying, the encapsulation rate reaches 92%, and the stability period of curcumin is as long as 330 days, which proves that curcumin Microencapsulation can improve its stability, water solubility, bioavailability and other characteristics.

3.6 Gel

As a large class of delivery systems, gels are also commonly used to encapsulate and deliver active substances. Among them, emulsion gels have been continuously paid attention by researchers, which have the characteristics of emulsions and can overcome the shortcomings of emulsion thermodynamic instability (Farjami & Madadlou, 2019). Emulsion gels can be used for dissolving delivery of both hydrophobic and lipophilic actives (Torres et al., 2016), increasing material stability. Curcumin emulsion gel prepared as rhamnogalacturonic acid-I and pectin (Zhang et al., 2022) successfully protected curcumin from heatinduced degradation and enhanced thermal stability. There is also research to add curcumin microemulsion to alginate-porous starch to prepare microemulsion gel, which realizes the solubilization of curcumin, prevents curcumin crystallization, enhances stability, and this gel also has good antibacterial properties (Li et al., 2021). Gels can also be used for enteral delivery of substances such as K-carrageenan and whey protein (Alavi et al., 2018) aggregates to prepare curcumin-encapsulating gels that successfully deliver curcumin into the gut for digestion. There is also a type of hydrogel, which can also realize the encapsulation and delivery of curcumin. For example, the whey protein isolate-chitosan composite hydrogel successfully protects curcumin from the degradation of gastric juice and realizes the sustained release of curcumin. Performance (Liu et al., 2020). In addition, there are also nanogels that have also received constant attention. Nanogels can enhance the stability of substances and improve the encapsulation efficiency of substances. Nanogels such as ovalbumin and pullulan (Zeng et al., 2022) were prepared, which enabled curcumin to achieve an encapsulation rate of 88.38%, and the in vitro gastrointestinal digestion retention rate was higher than that of free group, successfully improved pH and storage stability.

4 Stabilization mechanism

4.1 Interaction of curcumin and protein

Combining hydrophobic bioactive substances with proteins can effectively improve the problems of poor water solubility, poor stability and low intestinal bioavailability of active substances. Most proteins are amphiphilic and have good water solubility. Curcumin is very hydrophobic, and binding it to proteins is a great way to do it. (I) Certain residues of proteins can interact with polyphenols (curcumin) through hydrophobic interactions and hydrogen bonds (Patel et al., 2010). Active substances can not only be simply bound to the surface of the protein (Chen et al., 2015), but also embedded inside the protein during unfolding or denaturation (Liu, et al., 2019c). For example, there is a strong hydrophobic interaction between zein and curcumin, and the encapsulation of curcumin is achieved during the process of changing the structure of zein from α to β (Tiwari et al., 2021). Patel et al. (2010) prepared zein-curcumin granules, which enhanced the stability of curcumin under light, and achieved 71.1% ~ 86.8% of curcumin. The encapsulation efficiency of the gastrointestinal tract is high, and more than 60% of the curcumin can be retained in the gastrointestinal tract for 150 minutes during simulated digestion in vitro, which improves its stability in the gastrointestinal tract. (II) Spontaneous combinatorial reactions caused by hydrophobic interactions also occur between soy protein and curcumin. Wang et al. (2021b) studied the interaction between soybean protein-curcumin nanoparticles prepared by a pH-driven method, and found that the structure of soybean protein would open and refold during pH changes, which The process encapsulates curcumin in it, as shown in Figure 5. This improves the water solubility of curcumin, shows higher thermal stability, and retains about 98% of curcumin after 80 minutes of UV irradiation, with a high encapsulation efficiency of 97.43%. Curcumin can also form a stable water-soluble complex with vegetable proteins such as ovalbumin and whey protein, so as to improve the processing and utilization of curcumin, which has great application prospects.

4.2 Interaction of curcumin and polysaccharides

Compared to proteins, which are sensitive to many factors such as pH, temperature and enzymes, polysaccharides are more



Figure 5. Binding mechanism of curcumin and soy protein.

resistant to the environment (Khan et al., 2018). There are also certain interactions (hydrophobic interactions, electrostatic interactions, hydrogen bonds, etc.) between curcumin and polysaccharides. (I) Polysaccharides can encapsulate curcumin through electrostatic interactions or hydrophobic interactions. For example, Ma et al. (2022) prepared curcumin-encapsulated carboxymethylated corn viscose/chitosan nanoparticles through electrostatic interaction, the encapsulation efficiency reached more than 90%, and the bioavailability reached 74.94%. (II) Hydrogen bonding is also involved in the encapsulation of curcumin. Yan et al. (2022) found that curcumin could be properly encapsulated by Cur-48-g-FA/Qcurd (quaternized curdlan) (or Cur-48) through hydrogen bonding and electrostatic interactions./ Qcurd), the stability of the polyelectrolyte nanoparticles was successfully improved, and the controlled release effect was achieved in the intestinal tract. Other polysaccharides such as Tremella polysaccharide, soybean soluble polysaccharide,

pectin, etc. can encapsulate curcumin through interaction and improve its defects.

5 Application

As a major biologically active substance, curcumin has attracted much market attention due to its low source cost and strong functionality. China's GB 2760-2014 "National Food Safety Standard for the Use of Food Additives" stipulates that curcumin can be used in frozen food, chocolate products, candy, carbonated drinks, jelly and other foods. As shown in Figure 6. Total curcumin can be used as a colorant, a nutritional enhancement factor, a preservative, and a pH indicator in the food industry. Curcumin can be used directly as a colorant without modification. As a nutritional enhancement factor, it can be added without modification or after encapsulation; and the preservative and pH indicator can be prepared into a coating or film from curcumin to indicate food preservation and spoilage. As shown in Table 1.



Figure 6. Application of curcumin in food industry (Tian et al., 2021)

App types	Apply effects	References
Ice cream coloring	Top sensory scores for curcumin 0.5% added	Manoharan et al., 2012
Yogurt coloring	Curcumin maintains well during yogurt storage without causing changes in nutritional content	Almeida et al., 2018
Curcumin milk	Encapsulation of curcumin in dairy products significantly enhances its in vivo bioactivity (antioxidant, stability) and in vitro bioavailability	Gao et al., 2022
Double layer pH indicator membrane	Curcumin exhibits different colors at different pH, which can be used as an indicator film for monitoring changes in chicken freshness	Zhou et al., 2021
pH smart indicator membrane	The color change can monitor and reflect the deterioration degree of bighead carp meat in real time	Chen et al., 2020b
pH smart indicator membrane	The freshness of shrimp can be detected according to the color of the membrane, and the oxidation of protein can be inhibited to prolong the shelf life	Xiao et al., 2021
Antioxidant film	The anti-oxidation of gelatin-based curcumin film reaches more than 20% in ethanol water medium (pH = 11), and about 10% without curcumin. Curcumin significantly enhances the anti-oxidation of the film.	Musso et al., 2017
Antioxidant film	The scavenging ability of CNPs at a concentration of 20 mg/mL was 64.0%, respectively, and significantly inhibited the weight loss rate, pH changes and lipid oxidation of pork.	Shen et al., 2022
Antibacterial film	The strawberries containing curcumin film did not produce mold for 7 days, and the curcumin film has antibacterial activity	Aydogdu et al., 2020
Photodynamic antibacterial film	Curcumin, β -cyclodextrin, K-carrageenan composite membrane has significant inhibitory effect on Staphylococcus aureus and Escherichia coli, and the membrane can be significantly degraded in soil for 7 days	Lai et al., 2022

Table 1. Some examples of curcumin application.

6 Conclusion and outlook

Curcumin has poor stability due to its poor water solubility and sensitivity to light, heat and other conditions, and its application is hindered by its low oral bioavailability in humans. Curcumin can be encapsulated by colloidal delivery systems to improve its water solubility, stability and bioavailability. Nowadays, with the rise of vegetarianism and the promotion of environmental protection, proteins and polysaccharides, as natural biopolymeric macromolecules, have many advantages such as degradability, safety, and environmental protection. They are attracting more and more attention as solid stable particles in colloidal systems.

The encapsulated curcumin can be used as a nutritional fortifier, nutritional health care product, coloring agent, etc. in food; it can be used as a smart indicator film, antibacterial film, etc. in the food packaging industry; in the field of medicine, it can be used to prevent and inhibit various Inflammation, cancer, can lower blood sugar, and more.

Based on everyone's need for health and immune enhancement, curcumin-based products continue to grow every year, and curcumin has become a botanical supplement that has attracted much attention from consumers and researchers. It is believed that the main application of curcumin in the future is no longer limited to food additives, but more and more diversified.

References

- Adsare, S. R., & Annapure, U. S. (2021). Microencapsulation of curcumin using coconut milk whey and gum arabic. *Journal of Food Engineering*, 298(11), 110502. http://dx.doi.org/10.1016/j.jfoodeng.2021.110502.
- Ahmadabady, S., Beheshti, F., Shahidpour, F., Khordad, E., & Hosseini, M. (2021). A protective effect of curcumin on cardiovascular oxidative stress indicators in systemic inflammation induced by lipopolysaccharide in rats. *Biochemistry and Biophysics Reports*, 25, 100908. http://dx.doi.org/10.1016/j.bbrep.2021.100908. PMid:33506115.
- Ahmed, K., Li, Y., Mcclements, D. J., & Xiao, H. (2012). Nanoemulsionand emulsion-based delivery systems for curcumin: encapsulation and release properties. *Food Chemistry*, 132(2), 799-807. http:// dx.doi.org/10.1016/j.foodchem.2011.11.039. PMid:22868161.
- Alavi, F., Emam-Djomeh, Z., Yarmand, M. S., Salami, M., Momen, S., & Moosavi-Movahedi, A. A. (2018). Cold gelation of curcumin loaded whey protein aggregates mixed with k-carrageenan: impact of gel microstructure on the gastrointestinal fate of curcumin. *Food Hydrocolloids*, 85(DEC), 267-280. http://dx.doi.org/10.1016/j. foodhyd.2018.07.012.
- Almeida, H. H. S., Barros, L., Barreira, J. C. M., Calhelha, R. C., Heleno, S. A., Sayer, C., Miranda, C. G., Leimann, F. V., Barreiro, M. F., & Ferreira, I. C. F. R. (2018). Bioactive evaluation and application of different formulations of the natural colorant curcumin (E100) in a hydrophilic matrix (yogurt). *Food Chemistry*, 261, 224-232. http:// dx.doi.org/10.1016/j.foodchem.2018.04.056. PMid:29739587.
- Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: problems and promises. *Molecular Pharmaceutics*, 4(6), 807-818. http://dx.doi.org/10.1021/ mp700113r. PMid:17999464.
- Aw, Y. Z., Lim, H. P., Low, L. E., Singh, C. K., Chan, E. S., & Tey, B. T. (2022). Cellulose nanocrystal (CNC)-stabilized Pickering emulsion for improved curcumin storage stability. *LWT*, 159, 113249. http:// dx.doi.org/10.1016/j.lwt.2022.113249.

- Aydogdu, A., Radke, C. J., Bezci, S., & Kirtil, E. (2020). Characterization of curcumin incorporated guar gum/orange oil antimicrobial emulsion films. *International Journal of Biological Macromolecules*, 148, 110-120. http://dx.doi.org/10.1016/j.ijbiomac.2019.12.255. PMid:31917216.
- Bangham, A. D., Standish, M. M., & Watkins, J. C. (1965). Diffusion of univalent ions across the lamellae of swollen phospholipids. *Journal* of Molecular Biology, 13(1), 238. http://dx.doi.org/10.1016/S0022-2836(65)80093-6. PMid:5859039.
- Bergonzi, M. C., Hamdouch, R., Mazzacuva, F., Isacchi, B., & Bilia, A. R. (2014). Optimization, characterization and in vitro evaluation of curcumin microemulsions. *Lebensmittel-Wissenschaft + Technologie*, 59(1), 148-155. http://dx.doi.org/10.1016/j.lwt.2014.06.009.
- Bernabé-Pineda, M., Ramírez-Silva, M. T., Romero-Romo, M., González-Vergara, E., & Rojas-Hernández, A. (2004). Determination of acidity constants of curcumin in aqueous solution and apparent rate constant of its decomposition. Spectrochimica Acta. Part A: Molecular and Biomolecular Spectroscopy, 60(5), 1091-1097. http:// dx.doi.org/10.1016/S1386-1425(03)00342-1. PMid:15084328.
- Bishnoi, M., Chopra, K., Rongzhu, L., & Kulkarni, S. K. (2011). Protective effect of curcumin and its combination with piperine (Bioavailability Enhancer) against haloperidol-associated neurotoxicity: cellular and neurochemical evidence. *Neurotoxicity Research*, 20(3), 215-225. http://dx.doi.org/10.1007/s12640-010-9229-4. PMid:21076901.
- Chawla, R., Sahu, B., Mishra, M., Rani, V., & Singh, R. (2022). Intranasal micellar curcumin for the treatment of chronic asthma. *Journal of Drug Delivery Science and Technology*, 67, 102922. http://dx.doi. org/10.1016/j.jddst.2021.102922.
- Chen, F. P., Li, B. S., & Tang, C. H. (2015). Nanocomplexation between curcumin and soy protein isolate: influence on curcumin stability/ bioaccessibility and in vitro protein digestibility. *Journal of Agricultural* and Food Chemistry, 63(13), 3559-3569. http://dx.doi.org/10.1021/ acs.jafc.5b00448. PMid:25779681.
- Chen, H., Zhang, M., Bhandari, B., & Yang, C. (2020a). Novel pHsensitive films containing curcumin and anthocyanins to monitor fish freshness. *Food Hydrocolloids*, 100, 105438. http://dx.doi. org/10.1016/j.foodhyd.2019.105438.
- Chen, J., Qiu, L., & Hu, M. (2007). Studies on preparation and in vitro and in vivo evaluation of docetaxel solid dispersion. *Zhongguo Yao Xue Za Zhi (Zhongguo Yao Xue Hui)*, 42(22), 1717.
- Chen, K., Lei, L., Lou, H., Niu, J., Yang, D., Qiu, X., & Qian, Y. (2020b). High internal phase emulsions stabilized with carboxymethylated lignin for encapsulation and protection of environmental sensitive natural extrac. *International Journal of Biological Macromolecules*, 158, 430-442. http://dx.doi.org/10.1016/j.ijbiomac.2020.04.106. PMid:32320804.
- Cheng, C., Wu, Z., McClements, D. J., Zou, L., Peng, S., Zhou, W., & Liu, W. (2019). Improvement on stability, loading capacity and sustained release of rhamnolipids modified curcumin liposomes. *Colloids and Surfaces. B, Biointerfaces*, 183, 110460. http://dx.doi. org/10.1016/j.colsurfb.2019.110460. PMid:31473408.
- Cheng, S.-X., Gong, F.-Z., Huang, X.-F., & Luo, L. R. (2002). Extraction of the protein and oil from soybean using reverse micelle. *Food Science*, 23(9), 44-46.
- Christaki, S., Moschakis, T., Hatzikamari, M., & Mourtzinos, I. (2022). Nanoemulsions of oregano essential oil and green extracts: characterization and application in whey cheese. *Food Control*, 141, 109190. http://dx.doi.org/10.1016/j.foodcont.2022.109190.
- Dammak, I., & Sobral, P. J. A. (2021). Curcumin nanoemulsions stabilized with natural plant-based emulsifiers. *Food Bioscience*, 43, 101335. http://dx.doi.org/10.1016/j.fbio.2021.101335.

- Farjami, T., & Madadlou, A. (2019). An overview on preparation of emulsion-filled gels and emulsion particulate gels. *Trends in Food Science & Technology*, 86, 85-94. http://dx.doi.org/10.1016/j. tifs.2019.02.043.
- Gao, H., Cheng, C., Fang, S., McClements, D. J., Ma, L., Chen, X., Zou, L., Liang, R., & Liu, W. (2022). Study on curcumin encapsulated in whole nutritional food model milk: effect of fat content, and partitioning situation. *Journal of Functional Foods*, 90, 104990. http://dx.doi.org/10.1016/j.jff.2022.104990.
- Ghosh, S., Banerjee, S., & Sil, P. C. (2015). The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: a recent update. *Food and Chemical Toxicology*, 83, 111-124. http://dx.doi. org/10.1016/j.fct.2015.05.022. PMid:26066364.
- Goel, A., Kunnumakkara, A. B., & Aggarwal, B. B. (2008). Curcumin as "Curecumin": from kitchen to clinic. *Biochemical Pharmacology*, 75(4), 787-809. http://dx.doi.org/10.1016/j.bcp.2007.08.016. PMid:17900536.
- Guo, J., Li, P., Kong, L., & Xu, B. (2020). Microencapsulation of curcumin by spray drying and freeze drying. *LWT*, 132, 109892. http://dx.doi. org/10.1016/j.lwt.2020.109892.
- Han, J., Chen, F., Gao, C., Zhang, Y., & Tang, X. (2020). Environmental stability and curcumin release properties of Pickering emulsion stabilized by chitosan/gum arabic nanoparticles. *International Journal of Biological Macromolecules*, 157, 202-211. http://dx.doi. org/10.1016/j.ijbiomac.2020.04.177. PMid:32344077.
- Hasan, S. T., Zingg, J. M., Kwan, P., Noble, T., Smith, D., & Meydani, M. (2014). Curcumin modulation of high fat diet-induced atherosclerosis and steatohepatosis in LDL receptor deficient mice. *Atherosclerosis*, 232(1), 40-51. http://dx.doi.org/10.1016/j.atherosclerosis.2013.10.016. PMid:24401215.
- Heger, M., Van Golen, R. F., Broekgaarden, M., & Michel, M. C. (2013). The molecular basis for the pharmacokinetics and pharmacodynamics of curcumin and its metabolites in relation to cancer. *Pharmacological Reviews*, 66(1), 222-307. http://dx.doi.org/10.1124/pr.110.004044. PMid:24368738.
- Hou, W., & Xu, J. (2016). Surfactant-free microemulsions. *Current* Opinion in Colloid & Interface Science, 25, 67-74. http://dx.doi. org/10.1016/j.cocis.2016.06.013.
- Huang, X. N., Zhu, J. J., Xi, Y. K., Yin, S. W., Ngai, T., & Yang, X. Q. (2019). Protein-based pickering high internal phase emulsions as nutraceutical vehicles of and the template for advanced materials: a perspective paper. *Journal of Agricultural and Food Chemistry*, 67(35), 9719-9726. http://dx.doi.org/10.1021/acs.jafc.9b03356. PMid:31398015.
- Jamwal, R. (2018). Bioavailable curcumin formulations: a review of pharmacokinetic studies in healthy volunteers. *Journal of Integrative Medicine*, 16(6), 367-374. http://dx.doi.org/10.1016/j.joim.2018.07.001. PMid:30006023.
- Jiang, H., Zhang, T., Smits, J., Huang, X., Maas, M., Yin, S., & Ngai, T. (2021). Edible high internal phase Pickering emulsion with doubleemulsion morphology. *Food Hydrocolloids*, 111, 106405. http:// dx.doi.org/10.1016/j.foodhyd.2020.106405.
- Jovanovic, S. V., Steenken, S., Boone, C. W., & Simic, M. G. (1999). H-atom transfer is a preferred antioxidant mechanism of curcumin. *Chem*, 121(41), 9677-9681.
- Khan, W., Abtew, E., Modani, S., & Domb, A. J. (2018). Polysaccharide based nanoparticles. *Israel Journal of Chemistry*, 58(12), 1315-1329. http://dx.doi.org/10.1002/ijch.201800051.
- Khayyal, M. T., El-Hazek, R. M., El-Sabbagh, W. A., Frank, J., Behnam, D., & Abdel-Tawab, M. (2018). Micellar solubilisation enhances

the antiinflammatory activities of curcumin and boswellic acids in rats with adjuvant-induced arthritis. *Nutrition*, 54, 189-196. http://dx.doi.org/10.1016/j.nut.2018.03.055. PMid:30048884.

- Kolter, M., Wittmann, M., Köll-Weber, M., & Süss, R. (2019). The suitability of liposomes for the delivery of hydrophobic drugs – A case study with curcumin. *European Journal of Pharmaceutics* and Biopharmaceutics, 140, 20-28. http://dx.doi.org/10.1016/j. ejpb.2019.04.013. PMid:31015019.
- Lai, D., Zhou, F., Zhou, A., Hamzah, S. S., Zhang, Y., Hu, J., & Lin, S. (2022). Comprehensive properties of photodynamic antibacterial film based on κ-Carrageenan and curcumin-β-cyclodextrin complex. *Carbohydrate Polymers*, 282, 119112. http://dx.doi.org/10.1016/j. carbpol.2022.119112. PMid:35123747.
- Li, D., Wei, Z., Sun, J., & Xue, C. (2022a). Tremella polysaccharidescoated zein nanoparticles for enhancing stability and bioaccessibility of curcumin. *Current Research in Food Science*, 5, 611-618. http:// dx.doi.org/10.1016/j.crfs.2022.03.008. PMid:35373147.
- Li, Y. H., Wang, Y. S., Zhao, J. S., Li, Z. Y., & Chen, H. H. (2021). A pHsensitive curcumin loaded microemulsion-filled alginate and porous starch composite gels: characterization, in vitro release kinetics and biological activity. *International Journal of Biological Macromolecules*, 182, 1863-1873. http://dx.doi.org/10.1016/j.ijbiomac.2021.05.174. PMid:34058207.
- Li, Z., Wang, Y., & Luo, Y. (2022b). High internal phase Pickering emulsions stabilized by eggyolk low density lipoprotein for delivery of curcumin. *Colloids and Surfaces. B, Biointerfaces*, 211, 112334. http://dx.doi.org/10.1016/j.colsurfb.2022.112334. PMid:35051889.
- Lin, D., Xiao, L., Qin, W., Loy, D. A., Wu, Z., Chen, H., & Zhang, Q. (2022). Preparation, characterization and antioxidant properties of curcumin encapsulated chitosan/lignosulfonate micelles. *Carbohydrate Polymers*, 281, 119080. http://dx.doi.org/10.1016/j. carbpol.2021.119080. PMid:35074131.
- Liu, H., & Ho, Y. (2018). Anticancer effect of curcumin on breast cancer and stem cells. *Food Science and Human Wellness*, 7(2), 134-137. http://dx.doi.org/10.1016/j.fshw.2018.06.001.
- Liu, L.-L., Li, X.-T., Zhang, N., & Tang, C.-H. (2019a). Novel soy β -conglycinin nanoparticles by ethanol-assisted disassembly and reassembly: outstanding nanocarriers for hydrophobic nutraceuticals. *Food Hydrocolloids*, 91, 246-255. http://dx.doi.org/10.1016/j. foodhyd.2019.01.042.
- Liu, Q., Huang, H., Chen, H., Lin, J., & Wang, Q. (2019b). Food-grade nanoemulsions: preparation, stability and application in encapsulation of bioactive compounds. *Molecules.*, 24(23), 4242. http://dx.doi. org/10.3390/molecules24234242. PMid:31766473.
- Liu, W., Gao, H., McClements, D., Zhou, L., Wu, J., & Zou, L. (2019c). Stability, rheology, and β -carotene bioaccessibility of high internal phase emulsion gels. *Food Hydrocolloids.*, 88, 210-217. http://dx.doi. org/10.1016/j.foodhyd.2018.10.012.
- Liu, Y., Ma, Y., Liu, Y., Zhang, J., Hossen, M. A., Sameen, D. E., Dai, J., Li, S., & Qin, W. (2022). Fabrication and characterization of pH-responsive intelligent films based on carboxymethyl cellulose and gelatin/curcumin/chitosan hybrid microcapsules for pork quality monitoring. *Food Hydrocolloids*, 124, 107224. http://dx.doi. org/10.1016/j.foodhyd.2021.107224.
- Liu, Z., Liu, C., Sun, X., Zhang, S., Yuan, Y., Wang, D., & Xu, Y. (2020). Fabrication and characterization of cold-gelation whey proteinchitosan complex hydrogels for the controlled release of curcumin. *Food Hydrocolloids*, 103(4), 105619. http://dx.doi.org/10.1016/j. foodhyd.2019.105619.
- Luo, Y. (2020). Food colloids binary and ternary nanocomplexes: innovations and discoveries. *Colloids and Surfaces*. *B, Biointerfaces*,

196, 111309. http://dx.doi.org/10.1016/j.colsurfb.2020.111309. PMid:32798989.

Ma, Z., Yao, J., Wang, Y., Jia, J., Liu, F., & Liu, X. (2022). Polysaccharidebased delivery system for curcumin: fabrication and characterization of carboxymethylated corn fiber gum/chitosan biopolymer particles. *Food Hydrocolloids*, 125, 107367. http://dx.doi.org/10.1016/j. foodhyd.2021.107367.

Mahesh, K. (2019). Recent advances in colloidal delivery systems for nutraceuticals: a case study – delivery by design of curcumin - sciencedirect. *Journal of Colloid and Interface Science*, 557, 506-518. http://dx.doi.org/10.1016/j.jcis.2019.09.045. PMid:31542691.

Manoharan, A., Ramasamy, D., Dhanalashmi, B., Gnanalashmi, K. S., & Thyagarajan, D. (2012). Studies on sensory evaluation of Curcumin powder as natural color for butterscotch flavor ice cream. *Indian Journal of Drugs and Diseases*, 1(1), 2278-2958.

Marefati, A., Bertrand, M., Sjöö, M., Dejmek, P., & Rayner, M. (2017). Storage and digestion stability of encapsulated curcumin in emulsions based on starch granule Pickering stabilization *Food Hydrocolloids.*, 63, 309-320. http://dx.doi.org/10.1016/j.foodhyd.2016.08.043.

Mekhloufi, G., Vilamosa, N., & Agnely, F. (2022). Nanoemulsion stabilized by β -lactoglobulin: a promising strategy to encapsulate curcumin for topical delivery. *Materials Today: Proceedings*, 53, 168-173.

Miao, J., Xu, N., Cheng, C., Zou, L., Chen, J., Wang, Y., Liang, R., McClements, D. J., & Liu, W. (2021). Fabrication of polysaccharidebased high internal phase emulsion gels: enhancement of curcumin stability and bioaccessibility. *Food Hydrocolloids*, 117(3), 106679. http://dx.doi.org/10.1016/j.foodhyd.2021.106679.

Morsy, M. A., & El-Moselhy, M. A. (2013). Mechanisms of the protective effects of curcumin against indomethacin-induced gastric ulcer in rats. *Pharmacology*, 91(5-6), 267-274. PMid:23689497.

Musso, Y. S., Salgado, P. R., & Mauri, A. N. (2017). Smart edible films based on gelatin and curcumin. *Food Hydrocolloids*, 66, 8-15. http://dx.doi.org/10.1016/j.foodhyd.2016.11.007.

Ng, Z. Y., Wong, J. Y., Panneerselvam, J., Madheswaran, T., Kumar, P., Pillay, V., Hsu, A., Hansbro, N., Bebawy, M., Wark, P., Hansbro, P., Dua, K., & Chellappan, D. K. (2018). Assessing the potential of liposomes loaded with curcumin as a therapeutic intervention in asthma. *Colloids and Surfaces. B, Biointerfaces*, 172, 51-59. http:// dx.doi.org/10.1016/j.colsurfb.2018.08.027. PMid:30134219.

Nimiya, Y., Wang, W., Du, Z., Sukamtoh, E., Zhu, J., Decker, E., & Zhang, G. (2016). Redox modulation of curcumin stability: redox active antioxidants increase chemical stability of curcumin. *Molecular Nutrition & Food Research*, 60(3), 487-494. http://dx.doi.org/10.1002/ mnfr.201500681. PMid:26608515.

Patel, A., Hu, Y. C., Tiwari, J. K., & Velikov, K. P. (2010). Synthesis and characterisation of zein-curcumin colloidal particles. *Soft Matter*, 6(24), 6192-6199. http://dx.doi.org/10.1039/c0sm00800a.

Priyadarsini, K. I. (2014). The chemistry of curcumin: from extraction to therapeutic agent. *Molecules (Basel, Switzerland)*, 19(12), 20091-20112. http://dx.doi.org/10.3390/molecules191220091. PMid:25470276.

Rauf, A., Imran, M., Orhan, I. E., & Bawazeer, S. (2018). Health perspectives of a bioactive compound curcumin: a review. *Trends in Food Science & Technology*, 74, 33-45. http://dx.doi.org/10.1016/j. tifs.2018.01.016.

Rayner, M., Sjoo, M., Timgren, A., & Dejmek, P. (2012). Quinoa starch granules as stabilizing particles for production of Pickering emulsions. *Faraday Discussions*, 158, 139-155, discussion 239-266. http://dx.doi.org/10.1039/c2fd20038d. PMid:23234165.

Sabet, S., Rashidinejad, A., Melton, L. D., & McGillivray, D. J. (2021). Recent advances to improve curcumin oral bioavailability. *Trends* *in Food Science & Technology*, 110(6), 253-266. http://dx.doi. org/10.1016/j.tifs.2021.02.006.

Sahne, F., Mohammadi, M., Najafpour, G. D., & Moghadamnia, A. A. (2016). Enzyme-assisted ionic liquid extraction of bioactive compound from turmeric (Curcuma longa L.): isolation, purification and analysis of curcumin. *Industrial Crops and Products*, 95, 686-694. http://dx.doi.org/10.1016/j.indcrop.2016.11.037.

Salvia-Trujillo, L., Martín-Belloso, O., & McClements, D. (2016). Excipient nanoemulsions for improving oral bioavailability of bioactives. *Nanomaterials (Basel, Switzerland)*, 6(1), 17. http:// dx.doi.org/10.3390/nano6010017. PMid:28344274.

Sari, T. P., Mann, B., Kumar, R., Singh, R. R. B., Sharma, R., Bhardwaj, M., & Athira, S. (2015). Preparation and characterization of nanoemulsion encapsulating curcumin. *Food Hydrocolloids*, 43, 540-546. http:// dx.doi.org/10.1016/j.foodhyd.2014.07.011.

Shakoor, S., Ismail, A., Sabran, M. R., Mohtarrudin, N., Kaka, U., & Nadeem, M. (2022). In-vivo study of synthetic and natural food colors effect on biochemical and immunity parameters. *Food Science and Technology*, 42, e41420. http://dx.doi.org/10.1590/fst.41420.

Shen, W., Yan, M., Wu, S., Ge, X., Liu, S., Du, Y., Zheng, Y., Wu, L., Zhang, Y., & Mao, Y. (2022). Chitosan nanoparticles embedded with curcumin and its application in pork antioxidant edible coating. *International Journal of Biological Macromolecules*, 204, 410-418. http://dx.doi.org/10.1016/j.ijbiomac.2022.02.025. PMid:35150779.

Singh, M., Pandey, A., Karikari, C. A., Singh, G., & Rakheja, D. (2010). Cell cycle inhibition and apoptosis induced by curcumin in Ewing sarcoma cell line SK-NEP-1. *Medical Oncology (Northwood, London, England)*, 27(4), 1096-1101. http://dx.doi.org/10.1007/s12032-009-9341-6. PMid:19859844.

Solghi, S., Emam-Djomeh, Z., Fathi, M., & Farahani, F. (2020). The encapsulation of curcumin by whey protein: assessment of the stability and bioactivity. *Journal of Food Process Engineering.*, 43(6), 1-10. http://dx.doi.org/10.1111/jfpe.13403.

Somu, P., & Paul, S. (2018). Bio-conjugation of curcumin with selfassembled casein nanostructure via surface loading enhances its bioactivity: An efficient therapeutic system. *Applied Surface Science*, 462, 316-329. http://dx.doi.org/10.1016/j.apsusc.2018.08.094.

Sun, M., Su, X., Ding, B., He, X., Liu, X., Yu, A., Lou, H., & Zhai, G. (2012). Advances in nanotechnology-based delivery systems for curcumin. *Nanomedicine*, 7(7), 1085-1100. http://dx.doi.org/10.2217/ nnm.12.80. PMid:22846093.

Tai, K., Rappolt, M., Mao, L., Gao, Y., & Yuan, F. (2020). Stability and release performance of curcumin-loaded liposomes with varying content of hydrogenated phospholipids. *Food Chemistry*, 326, 126973. http://dx.doi.org/10.1016/j.foodchem.2020.126973. PMid:32413757.

Tapal, A., & Tiku, P. K. (2012). Complexation of curcumin with soy protein isolate and its implications on solubility and stability of curcumin. *Food Chemistry*, 130(4), 960-965. http://dx.doi.org/10.1016/j. foodchem.2011.08.025.

Tennesen, H. H., & Greenhill, J. V. (1992). Studies on curcumin and curcuminoids. XXII: curcumin as a reducing agent and as a radical scavenger. *International Journal of Pharmaceutics*, 87(1-3), 79-87. http://dx.doi.org/10.1016/0378-5173(92)90230-Y.

Ternullo, S., Gagnat, E., Julin, K., Johannessen, M., Basnet, P., Vanić, Ž., & Škalko-Basnet, N. (2019). Liposomes augment biological benefits of curcumin for multitargeted skin therapy. *European Journal of Pharmaceutics and Biopharmaceutics*, 144, 154. http:// dx.doi.org/10.1016/j.ejpb.2019.09.016. PMid:31542438.

- Tian, J., Ghosh, R., & Charcosset, C. (2021). Extraction, purification and applications of curcumin from plant materials: a comprehensive review. *Trends in Food Science & Technology*, 112(1)
- Tian, Y., Pang, X., & Wang, F. (2022). Isolation of curcumol from zedoary turmeric oil and its inhibitory effect on growth of human hepatocellular carcinoma xenografts in nude mice. *Food Science* and Technology, 42, e46621. http://dx.doi.org/10.1590/fst.46621.
- Tiwari, P., Ali, R., Ishrat, R., & Arfin, N. (2021). Study of interaction between zein and curcumin using spectroscopic and in silico techniques. *Journal of Molecular Structure*, 1230, 129637. http:// dx.doi.org/10.1016/j.molstruc.2020.129637.
- Torres, O., Murray, B., & Sarkar, A. (2016). Emulsion microgel particles: novel encapsulation strategy for lipophilic molecules. *Trends in Food Science* & *Technology*, 55, 98-108. http://dx.doi.org/10.1016/j.tifs.2016.07.006.
- Uğur, H., Çatak, J., Özgür, B., Efe, E., Görünmek, M., Belli, I., & Yaman, M. (2022). Effects of different polyphenol-rich herbal teas on reducing predicted glycemic index. *Food Science and Technology*, 42, e03022. http://dx.doi.org/10.1590/fst.03022.
- Wang, Y., Ding, R., Zhang, Z., Zhong, C., Wang, J., & Wang, M. (2021a). Curcumin-loaded liposomes with the hepatic and lysosomal dualtargeted effects for therapy of hepatocellular carcinoma. *International Journal of Pharmaceutics*, 602, 120628. http://dx.doi.org/10.1016/j. ijpharm.2021.120628. PMid:33892061.
- Wang, Y., Sun, R., Xu, X., Du, M., Zhu, B., & Wu, C. (2021b). Structural interplay between curcumin and soy protein to improve the watersolubility and stability of curcumin. *International Journal of Biological Macromolecules*, 193(Pt B), 1471-1480. http://dx.doi.org/10.1016/j. ijbiomac.2021.10.210. PMid:34742837.
- Wang, Y.-F., Shao, J.-J., Zhou, C.-H., Zhang, D.-L., Bie, X.-M., Lv, F.-X., Zhang, C., & Lu, Z.-X. (2012). Food preservation effects of curcumin microcapsules. *Food Control*, 27(1), 113-117. http://dx.doi. org/10.1016/j.foodcont.2012.03.008.
- Wanninger, S., Lorenz, V., Subhan, A., & Edelmann, F. T. (2015). Metal complexes of curcumin – synthetic strategies, structures and medicinal applications. *Chemical Society Reviews*, 44(15), 4986-5002. http:// dx.doi.org/10.1039/C5CS00088B. PMid:25964104.
- Xiao, Y., Liu, Y., Kang, S., Cui, M., & Xu, H. (2021). Development of pH-responsive antioxidant soy protein isolate films incorporated with cellulose nanocrystals and curcumin nanocapsules to monitor shrimp freshness. *Food Hydrocolloids*, 120, 106893. http://dx.doi. org/10.1016/j.foodhyd.2021.106893.

- Xu, P., Qian, Y., Wang, R., Chen, Z., & Wang, T. (2022). Entrapping curcumin in the hydrophobic reservoir of rice proteins toward stable antioxidant nanoparticles. *Food Chemistry*, 387, 132906. http://dx.doi.org/10.1016/j.foodchem.2022.132906. PMid:35413554.
- Yan, J.-K., Wang, Z.-W., Zhu, J., Liu, Y., Chen, X., & Li, L. (2022). Polysaccharide-based nanoparticles fabricated from oppositely charged curdlan derivatives for curcumin encapsulation. *International Journal of Biological Macromolecules*, 213, 923-933. http://dx.doi. org/10.1016/j.ijbiomac.2022.05.179. PMid:35654222.
- Yixuan, L., Qaria, M. A., Sivasamy, S., Jianzhong, S., & Daochen, Z. (2021). Curcumin production and bioavailability: a comprehensive review of curcumin extraction, synthesis, biotransformation and delivery systems. *Industrial Crops and Products*, 172, 114050. http:// dx.doi.org/10.1016/j.indcrop.2021.114050.
- Yu, J., Wang, Q., Zhang, H., Qin, X., Chen, H., Corke, H., Hu, Z., & Liu, G. (2021). Increased stability of curcumin-loaded pickering emulsions based on glycated proteins and chitooligosaccharides for functional food application. *LWT*, 148, 111742. http://dx.doi. org/10.1016/j.lwt.2021.111742.
- Yuan, P., Chen, Y., Xiao, F., & Shen, L. R. (2012). The bioactivities of curcumin and its application in foods. *Science and Technology of Food Industry*, 14, 371-375.
- Zeng, Q., Zeng, W., Jin, Y., & Sheng, L. (2022). Construction and evaluation of ovalbumin-pullulan nanogels as a potential delivery carrier for curcumin. *Food Chemistry*, 367, 130716. http://dx.doi. org/10.1016/j.foodchem.2021.130716. PMid:34384981.
- Zhang, L., Zheng, J., Wang, Y., Ye, X., Chen, S., Pan, H., & Chen, J. (2022). Fabrication of rhamnogalacturonan-I enriched pectin-based emulsion gels for protection and sustained release of curcumin. *Food Hydrocolloids*, 128, 107592. http://dx.doi.org/10.1016/j. foodhyd.2022.107592.
- Zhang, S.-F., Hu, W., Yan, X., Wang, D., Yang, W., Zhang, J., & Liu, Z. (2021). Chondroitin sulfate-curcumin micelle with good stability and reduction sensitivity for anti-cancer drug carrier. *Materials Letters*, 304, 130667. http://dx.doi.org/10.1016/j. matlet.2021.130667.
- Zhou, X., Yu, X., Xie, F., Fan, Y., Xu, X., Qi, J., Xiong, G., Gao, X., & Zhang, F. (2021). pH-responsive double-layer indicator films based on konjac glucomannan/camellia oil and carrageenan/anthocyanin/ curcumin for monitoring meat freshness. *Food Hydrocolloids*, 118, 106695. http://dx.doi.org/10.1016/j.foodhyd.2021.106695.