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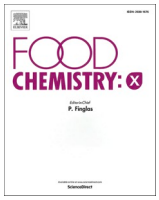

Gum arabic as a sole wall material for constructing nanoparticle to enhance the stability and bioavailability of curcumin

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ABSTRACT

In this study, a kind of nanoparticle prepared using gum arabic as a sole wall material for loading curcumin was obtained. The properties and digestive characteristics of the curcumin-loaded nanoparticle were determined. Results showed that the maximum loading amount of the nanoparticle was 0.51 μg/mg with an approximately 500 nm size. The Fourier transform infrared (FTIR) spectrum showed that the complexation was mainly related to the -C═O, –CH, and -C—O—C- groups. The curcumin-loaded nanoparticle exhibited good stability under highly concentrated salinity stress, and the stability of the curcumin loaded in nanoparticles was significantly higher than that of free curcumin under ultraviolet radiation. The curcumin loaded in nanoparticle was released mainly in the intestinal digestion stage, and the release process was sensitive to the pH changes rather than protease. In conclusion, these nanoparticles can be a potential nanocarrier for enhancing the stability of curcumin which can be applied in the salt-containing food system.

Introduction

Curcumin is a polyphenolic compound generally extracted from the roots and stems of the turmeric plant. Currently, numerous studies have demonstrated that curcumin possesses many bioactivities, including lipid-lowering, anti-tumor, anti-inflammatory, and anti-oxidative functions(Chen et al., 2021; Rafiee, Nejatian, Daeihamed, & Jafari, 2019; Roy, Priyadarshi, Ezati, & Rhim, 2021). However, the characteristics of curcumin, such as being sensitive to pH changes, easily to be degraded under the stresses of oxygen and lights, and low water-solubility, limit its application in the field of food and medical industries (Zhang et al., 2019).

At present, to meet the market demand for functional food, many strategies have been proposed to improve the stability and bioavailability of curcumin (Zheng & McClements, 2020). The most common method is encapsulating curcumin in a carrier system, such as emulsion, liposome, and nanoparticle (Jagtiani, 2022). Among them, the nanoparticle is a simple carrier system and is shaped by the self-assembly effect of polymers. In general, the self-assembly effect of biomacromolecules could be described as the spontaneous formation of cavity structures in biomacromolecules driven by intra- or inter-molecular interactions (such as electrostatic, hydrogen bond, and hydrophobic bond interactions). In this case, the small bioactive molecules would be embedded or wrapped in the cavities to complete the self-assembly process. According to the structural requirement for driving the self-assembly effect of polymers, the biomacromolecules possessing hydrophobic groups, such as polysaccharides and proteins, can be applied as materials for constructing nanocarriers (Akbari-Alavijeh, Shaddel, & Jafari, 2020; Du et al., 2019; Sun, Li, Guo, Wang, Cheng, Yang, Liu, Fan, Guo, & Wang, 2022).

Gum arabic (GA), the “gold standard” food grade emulsifier, is widely used in the food industry, and can be used as one of the carrier base materials for bioactive substances (Rajabi, Jafari, Rajabzadeh, Sarfarazi, & Sedaghati, 2019).As a polymer complex, GA mainly consists of three subfractions, namely arabinogalactan (~90 %of total gum mass), arabinogalactan-protein (~10 %of total gum mass), and glycoprotein (~1%of total gum mass). Among them, arabinogalactan-protein has been identified as the key fraction responsible for the amphiphilic nature of GA and possesses a ‘wattle blossom’ type structure where the hydrophilic blocks of carbohydrate are linked to a common hydrophobic polypeptide chain (Li, Zhang, Jin, & Cai, 2018). In addition, this structure leads to its easy adsorption of hydrophobic substances. The protein

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moiety of GA primarily exists in arabinogalactan-protein (~10%) and glycoprotein (~50%) (Lin, Wang, Meng, & Guo, 2021). Based on the structural characteristics of GA, at least 1.5% protein can be provided to form the hydrophobic cavities in theory. The arabinogalactan provides relatively higher steric hindrance for the carrier system than most of proteins, reducing the degradation of the carrier system in the gastric digestion phase and enhancing the delivery efficiency of bioactives. Besides, the glucuronic acid in GA can be negatively charged in a weakly acidic aqueous solution, which can maintain the stability of the carrier system during the storage process. However, since the carboxyl and hydroxyl groups of GA are almost non-esterified, the protein moiety is the only source of hydrophobicity structure of GA. Therefore, in previous studies, GA was usually used as a supplement or combination material in the nanoparticle system. Hence, the functions of GA were easily neglected, which should be further studied.

Although a few studies about polysaccharides as the sole wall material for constructing nanoparticles have been published, some studies are still needed to further explain their characteristics and mechanisms. In the present work, GA was taken as the sole wall material for preparing a nanoparticle to load curcumin by the self-assembly effect. The changes in GA molecules during the self-assembly process were studied to explain the mechanism of GA for loading curcumin. Next, the stability of the curcumin loaded in nanoparticles under ultraviolet (UV) and sodium chloride (NaCl) stresses was investigated. Moreover, the digestion process of the nanoparticle prepared using GA was simulated *in vitro* to study its digestion characteristics and the fate of the loaded curcumin. The aim of this study was to gain insights into the mechanism of GA as the sole wall material for encapsulating curcumin to shape the nanoparticle, and elucidate the characteristics of this nanoparticle.

Materials and methods

Materials

Curcumin (purity > 95%) was purchased from Kermel Chemical Reagent Co., Ltd (Tianjin, China), and bile powder (from pig) was purchased from Sigma Chemical Co., Ltd (St. Louis, MO, USA). GA was purchased from Dingli Gum Industry Co., Ltd (Tai'an, China). Pepsin (1:10000) and trypsin (1:250) were obtained from Solar Bio Science & Technology Co., Ltd. (Beijing, China). Other reagents (NaOH, HCl, $CaCl_2$, $K_2S_2O_8$, absolute alcohol, ethyl acetate, and citric acid) of analytical grade were purchased from Guangzhou chemical reagent factory (Guangzhou, China).

Preparation of curcumin-loaded GA nanoparticles

The curcumin-loaded GA nanoparticle was prepared according to the method reported by (Chen, Ou, Chen, & Tang, 2017) with a slight modification. Briefly, curcumin powder was dispersed in absolute alcohol to prepare its solution (7.5 mg/mL) in a dark place. Next, 1.5 g of GA powder was dissolved in 58.5 g of deionized water to make a 2.5% (w/w) GA stock solution. To prepare the nanoparticles loaded with different concentrations of curcumin, varied volume of the curcumin solutions (1 mL, 2 mL, 6 mL, 10 mL, and 12 mL) was added to the GA stock solution. The absolute alcohol or deionized water was then added to the mixtures to achieve a GA concentration of 1.5% w/w and an ethanol concentration of 40% (v/v). After that, the mixture was stirred for 3 h using a magnetic stirrer in a dark place. Subsequently, the mixture was concentrated using a rotary evaporator equipped with a vacuum pump at 40 °C until the volume of the remaining mixture was 50 mL. The insoluble precipitates in the mixed dispersions were removed by centrifugation at 10,000 *g* for 15 min at ambient temperature. The supernatant was collected and then freeze-dried for 24 h to obtain the curcumin-loaded nanoparticle powder.

Encapsulation efficiency (EE) and loading amount (LA) of curcumin

The curcumin encapsulated in the GA nanoparticle was extracted with an organic solvent composed of ethyl acetate and ethanol at a volume ratio of 10:1. Before measurement, 0.75 g of nanoparticle powder was dissolved in 49.25 g of deionized water to obtain a nanoparticle solution having a concentration of 1.5% w/w. Next, 0.2 mL of nanoparticle solution was taken out and mixed with 3 mL of the organic solvent under vortex shaking. After settling, the supernatant (organic phase) was collected, and the curcumin content was determined at 430 nm using a Cary 60 UV − vis spectrophotometer (Agilent Technologies Inc, China) according to an established standard curve ($R^2 = 0.9995$) of standard curcumin in the same solvent.

The %EE and LA were calculated as follows:

$$\%EE = \frac{\text{curcumin encapsulated in GA}}{\text{total amount of added curcumin}} \times 100\%$$

$$\text{LA } (\mu g/mg) = \frac{\text{curcumin encapsulated in GA}}{\text{GA amount}}$$

Particle size and zeta -potential

The particle size and zeta potential of samples were determined using a Nano-Zetasizer (Malvern Instruments Ltd., UK) as described in a previous study (Lin et al., 2021). The particle size was evaluated using a dynamic light scattering (DLS) technique. Each tested sample was dissolved and diluted to a polysaccharide concentration of about 0.1% (w/v) with deionized water, and the pH value was adjusted to 4.0 using 20 mM NaOH or HCl. Next, about 1.2 mL of particle solution was filled into a particle-sizing cell for measurement using a Zetasizer Nano-ZS instrument (MalvernInstruments, Worcestershire, UK) at 25 °C.

When the zeta potential of samples was measured, each sample solution was dissolved in deionized water at a concentration of 2 mg/mL with stirring, and the pH of the sample solutions was adjusted to 4.0 using 20 M NaOH or HCl. Each sample solution was then filled into a folded capillary cell (DTS1070, Malvern) and measured at ambient temperature.

Fluorescence measurements

The interaction between GA and curcumin was evaluated using an RF-5301PC fluorescence spectrophotometer (Shimadzu Molecular, Japan) according to the method previously described by (Li, Ma, & Ngadi, 2013). The fluorescence determination was performed at a constant curcumin quantity of 1.5 mg with a gradual increase in concentrations (0–20 mg/mL) of GA. The emission spectra of curcumin and GA were recorded from 450 nm to 700 nm and 300 nm to 450 nm with excitation wavelengths of 430 nm and 295 nm, respectively. The excitation and emission slit widths used were 5 nm. Furthermore, the fluorescence of curcumin binding with ethanol-pretreated GA was measured by maintaining the curcumin concentration at 0.1 mM and varying the ethanol-pretreated GA concentration from 0 to 100 mg/mL. Before measurement, GA powder was dissolved in 24 mL of deionized water, and then 16 mL absolute ethanol was added to the solution. Next, 1.5 mg of curcumin powder was added to the resultant dispersions, and the mixture was stirred using a magnetic stirrer for 12 h. Finally, the dispersion was measured at ambient temperature.

Fourier infrared spectroscopy (FTIR)

The FTIR spectra of the samples were recorded using an FTIR spectrometer (Bruker TENSOR 27, Germany) according to the method described by (Ai, Meng, Lin, Tang, & Guo, 2022). Before measurement, each sample powder was mixed uniformly with KBr powder at a molar ratio of 1:100, and extruded into a pellet. Next, the FTIR spectra were

measured in transmission mode with a resolution of 4 cm^{-1} resolution from 400 to 4000 cm^{-1}.

Stability of nanoparticles

The stability of nanoparticles under salinity stress was evaluated by adding varied concentrations of NaCl in the nanoparticle solution system according to the previously reported method by (Liang et al., 2021). Briefly, a series of NaCl solutions (of concentrations from 0 mM to 500 mM) was prepared by stirring at ambient temperature for 6 h. Nanoparticle powder was dissolved into each NaCl solution to obtain a final concentration of 1.5% w/v, and the pH of the sample solution was adjusted to 4.0. After storing at a dark place for 24 h at ambient temperature, the particle size and curcumin content in the nanoparticles were determined as references for evaluating the stability of the nanoparticle under salinity stress.

The photostability study of the nanoparticle was evaluated as described by (Wang et al., 2021) with a few modifications. In brief, the nanoparticle and free curcumin solution (1.5% w/v) were irradiated under UV disinfection lamp (20 W power, Jinweishi Biotechnology Co., Ltd., Dongguan, China) for 5 h at ambient temperature in a hermetic dark box (volume of 50×50×50 cm). After 30 min of standing, the remaining content of curcumin in each sample was determined to evaluate the stability of the nanoparticle under UV radiation.

In vitro digestion

The digestive characteristics of curcumin-loaded nanoparticles were determined using an *in vitro* digestion model consisted of simulated gastric (60 min) and intestinal (120 min) digestion processes, as described in a previous study (Chen et al., 2017) with a few modifications. In brief, 0.3 g of nanoparticle powder was dissolved in 20 mL of deionized water, and the pH of the solution was adjusted to 2.0 with 3 M HCL. Subsequently, 4 mg of pepsin powder was added to the solution and pre-incubated in a water bath shaker at a rate of 100 rpm at 37 °C for 5 min to initiate the simulated gastric digestion process (5–65 min). The pH of the digestive juice was adjusted to 7.0 with 0.5 M NaOH for terminating the gastric digestion process, and 100 mg of bile extract powder and 8 mg of pancreatin powder were added to the digestive juice and pre-incubated in a water bath shaker at a rate of 100 rpm at 37 °C for 10 min to start the simulated intestinal digestion (75–195 min). During these digestion processes, 0.2 mL of the digestive juice was taken out at appropriate intervals to determine the digestive characteristics of the nanoparticle. The tested digestive juice was extracted using 2 mL of ethyl acetate for 5 min under vortex shaking conditions and then centrifuged at 5000 *g* for 5 min. The curcumin content indigestive juice was measured using a Cary 60 UV − vis spectrophotometer by the same method as described in Section 2.3.

Morphological observation using transmission electron microscope (TEM)

The initial morphology of the nanoparticle was measured by dissolving and diluting the nanoparticle powder into deionized water with a concentration of 15 mg/mL. In contrast, the morphology of nanoparticles in the digestion process was measured by collecting the digestive juice after each digestive stage. The morphological characteristics of samples were observed using a TEM (HITACHI H-7650, Japan) at 100 kV.

Statistical analysis

Unless otherwise stated, all experiments were conducted in triplicate. DPS software (version 7.05) was used for statistical evaluation by conducting a one-way analysis of variance with Scheffe's test, and means were considered significantly different at $p < 0.05$.

Results and discussion

EE and LA of curcumin-loaded nanoparticle

As shown in Table 1, with the increasing addition of curcumin, the size of nanoparticles was almost constant and ranged from 457.4 nm to 470.1 nm, indicating that the size of the particles might originate from the aggregation of GA. The polymer dispersity index (PDI) of the nanoparticle solution was lower than 0.3, suggesting that the nanoparticle possessed good dispersibility in water. The LA ranged from 0.32 to 0.51 μg/mg, and the EE% decreased from 6.37% to 0.86% with the increasing curcumin amount. It suggested that the capacity of nanoparticles shaped by GA could not be enhanced by adding of excessive curcumin, and the maximum curcumin loading of GA nanoparticles was 0.51 μg/mg. A Previous study showed that the LA of the nanoparticles prepared using millet protein could reach 17–106 μg/mg (Wang, Gulati, Santra, & Rose, 2017). This disparity of LA could be due to the fact that the protein moiety in GA (less than 3%) (Ai, Guo, Lin, Zhang, & Meng, 2019), which was a vital factor for inducing polymers to shape nanoparticles, was dozens of times lower than that of millet protein (protein content more than 70%).

FTIR spectroscopy

FTIR spectroscopy is a common method to verify whether the active substance is successfully loaded by the carrier particles and can also use to characterize the main functional group which participated in the interaction between the carrier substance and the active substance (Chen & Zhong, 2014). The FTIR spectra of samples are shown in Fig. 1. The mainly differences among the three samples could be described as the following aspects: Firstly, the absorption peaks around 1423 cm^{-1} (the symmetrical vibrations of $–COO^-$ in GA) (Li et al., 2018), 959 cm^{-1} (–CH vibration in curcumin) (Shah et al., 2018), 825 cm^{-1} (C═C–H stretching in aromatic rings) (de Oliveira et al., 2021), and 713 cm^{-1} (cis CH vibration of aromatic ring) (Mohan, Sreelakshmi, Muraleedharan, & Joseph, 2012) could not be detected in the curcumin-loaded nanoparticle. Secondly, the absorption peak of GA around 1080 cm^{-1}, which corresponded to the sugar glycosidic bond and C—O—C group in GA (Hejazian & Ahmadyari-Sharamin, 2022), became weaker after preparing the nanoparticle. Thirdly, the absorption peaks were shifted, such as the absorption peak of the amide I band (shifting from 1616 cm^{-1} to 1640 cm^{-1}), and the peak shape in the amide I band of GA became shorter and broader. The above three types of FTIR changes suggested that these functional groups were participated in the capture process of curcumin by GA. Although the capture process was caused by hydrophobic interaction, a previous study had demonstrated that the physical mixing of two substances could change the FTIR (Deepika, Prasad, Salar, & Salar, 2022). Therefore, the C—O—C, –CH, and –C═O groups may the main functional groups related to the interactions between GA and curcumin.

Table 1
Particle size, PDI value, zeta potential, EE, and LA of curcumin loaded GA nanoparticle prepared with different curcumin additive amount.

	2.5%	5%	15%	25%	30%
Size(d. nm)	464.2 ±5.3^{ab}	467.7 ±6.0^{ab}	457.4 ±7.1^{b}	469.4 ±4.8^{a}	470.1 ±6.3^{ab}
PDI	0.10 ±0.04^{c}	0.15 ±0.06^{bc}	0.21 ±0.04^{a}	0.19 ±0.05^{bc}	0.23 ±0.05^{ab}
Zeta (mV)	−19.87 ± 0.40^{a}	−19.83 ± 0.46^{a}	−21.83 ± 0.32^{b}	−19.63 ± 0.25^{a}	−19.33 ± 0.21^{a}
EE(%)	6.37 ±0.04^{a}	3.24 ±0.01^{b}	1.42±0.02^{c}	1.02 ±0.01^{d}	0.86 ±0.01^{e}
LA(μg/mg)	0.32 ±0.01^{c}	0.32 ±0.01^{c}	0.43 ±0.01^{b}	0.51 ±0.01^{a}	0.51 ±0.01^{a}

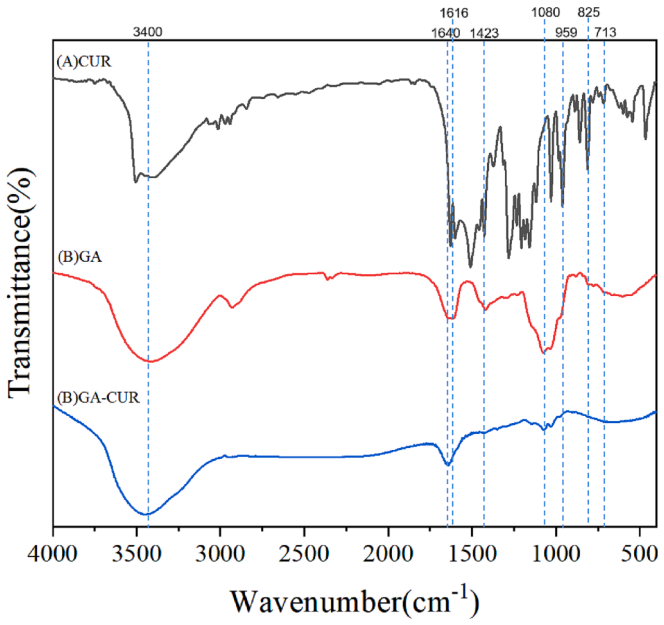

Fig. 1. FTIR spectra of: GA-CUR (A), CUR(B), and GA(C).

Fluorescence

Fluorescence analysis is a common approach for studying the interactions between polyphenols and polysaccharides (Liu, Jing, Han, Zhang, & Tian, 2019). As shown in Fig. 2A, curcumin floated or settled in the aqueous solution, while it was equally dispersed in the GA solution. Additionally, with the increasing concentration of GA (from 0 to 20 mg/mL) in the solutions, the fluorescence intensity around 350 nm increased considerably (Fig. 2B), which was attributed to the increase in protein moiety content in the aqueous solution. When the GA content in the curcumin-GA solution increased, the fluorescence intensity around 500 nm increased gradually (Fig. 2C), indicating that the GA could enhance the solubility of curcumin in a water system without alcohol. The solubilization of nanoparticles was attributed to its protein moiety, which could combine with curcumin by hydrophobic interaction (Liu et al., 2018; Weng, Cai, Zhang, & Wang, 2019). A similar phenomenon was observed in the complex consisting of curcumin and soy soluble polysaccharides (Chen et al., 2017). The result suggested that curcumin could combine with the protein moiety in polysaccharide chains even in the aqueous solution. As shown in Fig. 2D, when curcumin was dissolved in pretreated GA solution (containing 40% v/v ethanol), with the increase in GA concentration, the fluorescence intensity presented a gradually increasing tendency at the excitation wavelength of 425 nm. Notably, this increasing tendency did not only rely on the existence of the ethanol, but also related to the interactions between GA and curcumin. Otherwise, the blue-shift in the fluorescence spectrum (the maximum absorption wavelength shifted from 542 nm to 524 nm) would not be occurred.

In order to explain the function of the ethanol pretreatment, the fluorescence spectrum of GA was measured after pretreatment with different concentration of ethanol. As shown in Fig. 2E, the fluorescence intensity of GA increased with the concentration of ethanol, indicating the ethanol pretreatment could unfold the molecular structure of GA, thereby increasing the exposure of hydrophobic groups. Based on the above, the formation mechanism of the self-assembled nanoparticle induced by the ethanol pretreatment could be described as Fig. 2F. The exposure degree of the hydrophobic group of GA was relatively lower in aqueous solution, and could not load the hydrophobic small molecular substances well (accompanied with turbidity or sedimentation in usual, shown as Fig. 2A-b). When GA was pretreated with ethanol, the exposure degree of the hydrophobic structural elements would be enhanced, thereby increasing the opportunity of the interaction between GA and curcumin. In the ethanol removing stage, the hydrophobic structural elements gradually refolded with the decrease ethanol concentration, and formed as hydrophobic cavity together with the curcumin driven by the hydrophobic force.

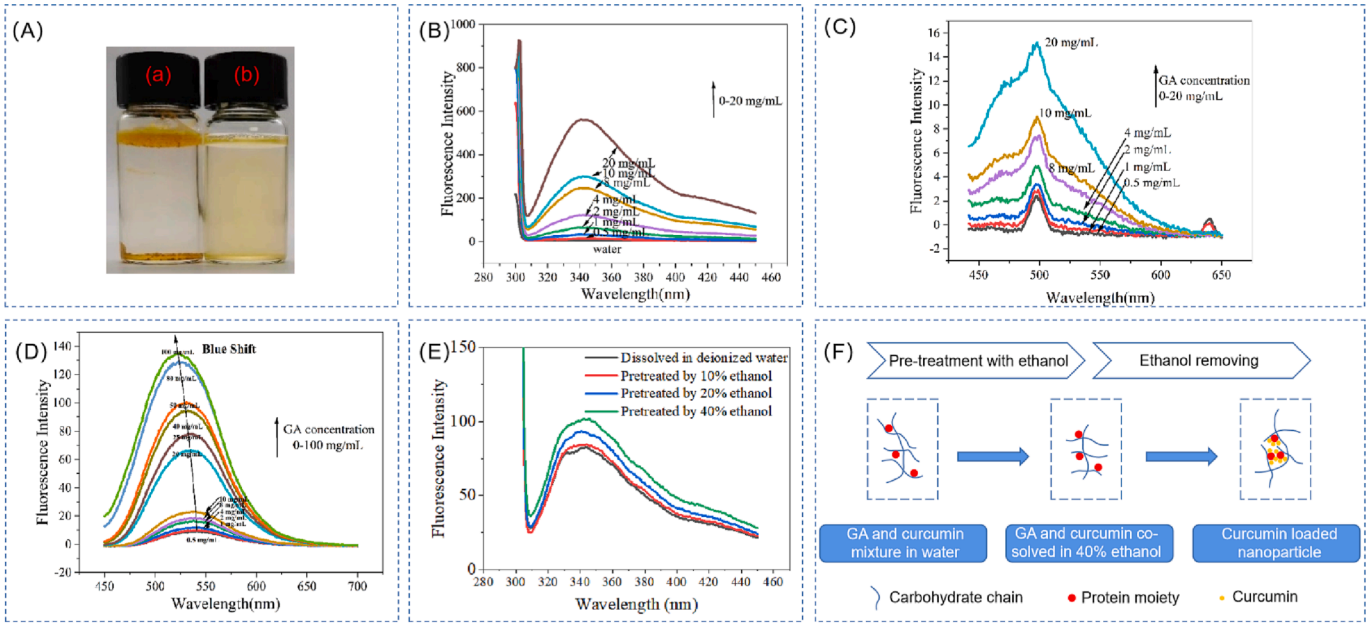

Fig. 2. Visual images (A) of the aqueous solution of free curcumin (a) and curcumin loaded nanoparticle (b), and the fluorescence spectra of the GA aqueous solution with excitation wavelength of 295 nm (B); the fluorescence spectra of the curcumin-GA complex aqueous solution with excitation wavelength of 425 nm (C); the fluorescence spectra of the curcumin mixed in ethanol-pretreated GA with excitation wavelength of 425 nm (D); the fluorescence spectra of the GA pretreated with different ethanol concentration; Mechanism diagram of the formation of the curcumin loaded GA nanoparticles (F).

Environmental stability of nanoparticles

Ionic strength stability of nanoparticles

Salt is the most common component in the food system. It is important to investigate the stability of nanoparticles in the salt-containing food system for its application in the food industry. As shown in the Fig. 3A, the zeta potential of the nanoparticle solution decreased with increasing NaCl concentration. This phenomenon was caused by the electrostatic shielding effect, which was in agreement with the previous studies (Wang et al., 2022). The particle size of the nanoparticle was decreased when NaCl was added to the solution, but when the concentration of NaCl was higher than 25 mM, the changes became less obvious. Previous studies have shown that the addition of salts in an aqueous solution can increase the mean size of nanoparticles, even precipitation of the nanoparticles (Chuacharoen & Sabliov, 2019; Liang et al., 2021). This inconsistency in results could be due to the fact that the Na^+ screened the negative charge of GA, decreasing the solubility of nanoparticles, and tended to aggregate due to hydrogen bond and Van Der Waals force. When the solution was centrifuged at high-speed, the aggregates could separate from the nanoparticle solution, and thus, the particle size became smaller. In the case of the curcumin content of the nanoparticle, it decreased with the increase in the amount of NaCl. However, the curcumin content of the solutions remained more than 80% even when the concentration of NaCl reached 500 mM, implying that the curcumin-loaded nanoparticle could be used in a high-salt food system (Fig. 3B).

Photostability

A major problem with curcumin is sensitivity to light. As shown in Fig. 4, the retention of free curcumin sharply decreased to 27.4% after 5 h of lighting. However, the curcumin content of the nanoparticles was remained at 82.0%. It indicated that curcumin loaded with in the nanoparticle was resistant to UV irradiation. The protection of the loaded bioactivity by the nanoparticle system has been reported. Liu et al. (2018) demonstrated that the carrier system consisted of ovalbumin could enhance the remaining amount of curcumin by ~30% under visible light irradiated by a 30 W fluorescent lamp after storing for 5 h, and the protective effect was corresponded to the ratio of macromolecules in the system. Therefore, in this study, the protection of GA for curcumin could be attributed to the following two aspects: first, the curcumin loaded in the nanoparticles was embedded in the hydrophobic cavity shaped by the protein in GA. The protein in GA could block and absorb most of the light energy (Wang et al., 2021). Second, GA is a macromolecular polysaccharide existing on the outer layer of the nanoparticle. Due to the light scattering effect of this polysaccharide, a stronger physical barrier was provided against UV irradiation. As a result, the integrity of the chemical groups of curcumin was obviously enhanced.

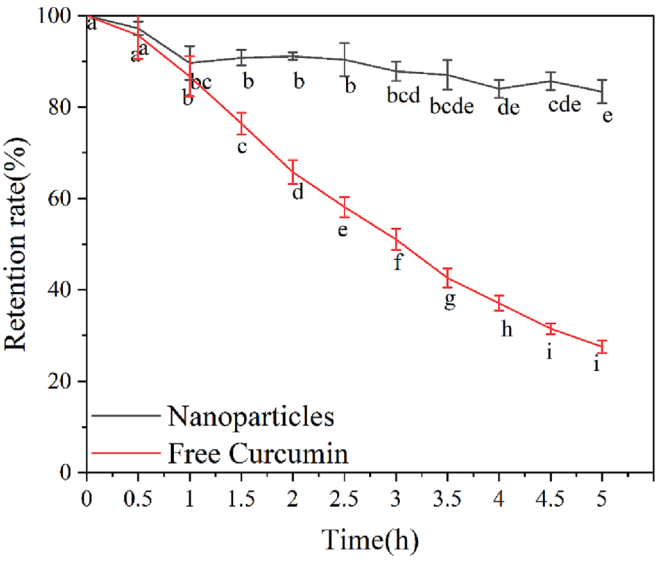

Fig. 4. The curcumin stability under UV lamp irradiation.

In vitro digestibility

The bioavailability of free curcumin and the curcumin loaded in GA nanoparticles during the digestion process was determined *in vitro*, as shown in Fig. 5. The free curcumin content in the aqueous solution ranged from 0.02 μg/mL to 0.11 μg/mL in the whole simulated digestive process, respectively, indicating that free curcumin exhibited low solubility in the digestive juice and possessed an extremely low bioavailability. In the case of the curcumin loaded in nanoparticles, the initial curcumin content in the aqueous solution of the nanoparticle group was 3.39 μg/mL, indicating a higher bioavailability of these nanoparticles. After adding pepsin, adjusting the pH value, and pre-incubating for 5 min, the curcumin content in the aqueous solution was decreased to 2.82 μg/mL, suggesting the pH changes may affect the bioavailability of the curcumin loaded in GA nanoparticle. A powerful piece of evidence is that digestive enzymes can not instantly cause nanoparticle degradation within 5 min. Furthermore, the curcumin content in the whole gastric digestion process (within 60 min) was only reduced from 2.82 μg/mL to

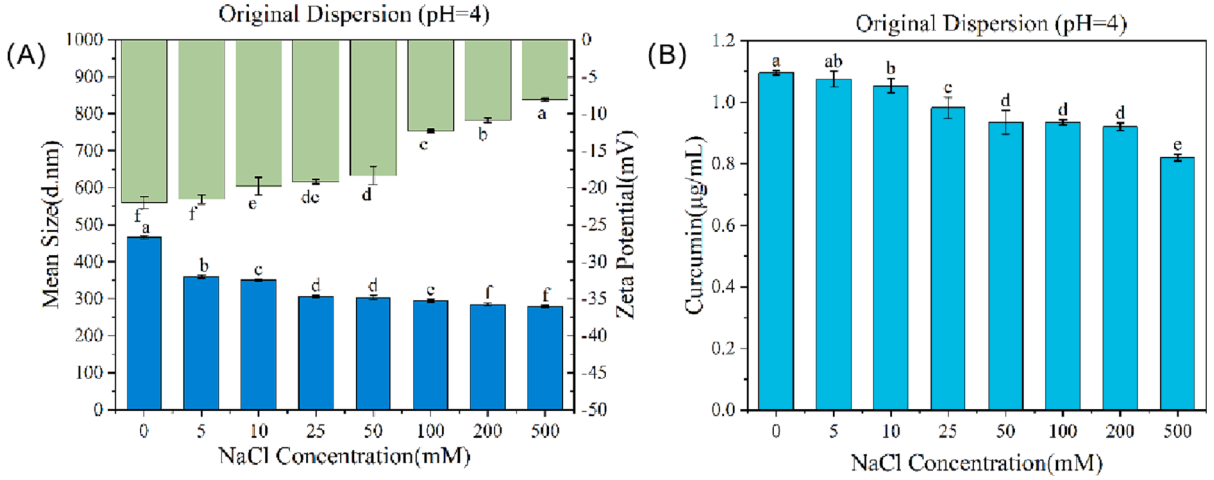

Fig. 3. The changes of the particle size, zeta potential (A) and the curcumin content of curcumin loaded GA nanoparticlesunder the Na + stress within different concentration (B).

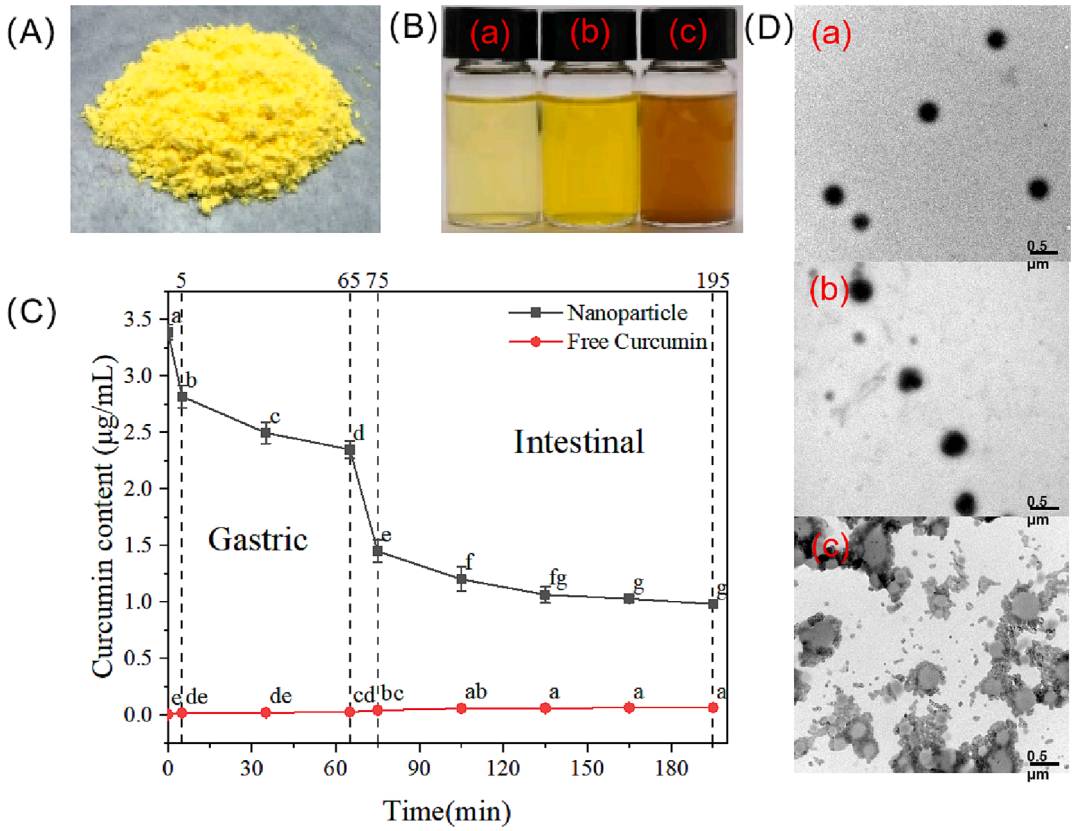

Fig. 5. The appearance of the dried curcumin loaded GA nanoparticle (A); the appearance of the aqueous solution of curcumin loaded GA nanoparticle (B-a), the curcumin loaded GA nanoparticle after simulated gastric digestion (B-b), and the curcumin loaded GA nanoparticle after simulated intestinal digestion (B-c); The curcumin content in aqueous phase during digestion process (C); The TEM images of curcumin loaded GA nanoparticle aqueous solution (D-a), curcumin loaded GA nanoparticle after gastric digestion (D-b), and curcumin loaded GA nanoparticle after intestinal digestion (D-c).

2.35 μg/mL. Similarly, this sudden decreasing tendency also occurred in the pre-incubation stage before intestinal digestion (from 2.35 μg/mL to 1.45 μg/mL). This phenomenon suggested that pH value played a vital role in releasing curcumin from the nanoparticles. In fact, the polysaccharide is a pH-sensitive macromolecule and the changes in pH value can result in the inter/intra molecular interaction changes, thereby altering the molecular configuration of polysaccharides. However, the hydrophobic groups, charged groups, and molecular configuration are the key points determining the drug-carrying capacity of the nanoparticles made using polysaccharides. Therefore, when the pH value was changed, the curcumin might have been released from the nanoparticles and converted into free form, decreasing the bioavailability of curcumin. Besides, the degradation of the protein moiety of GA by digestive enzymes could cause the release of curcumin from the nanoparticle because when the pH value was constant at 7.0, the curcumin content in the aqueous solution still gradually decreased (from 75 to 195 min), and finally, the curcumin content was at 0.98 μg/mL after the whole simulated digestion. Previous work showed that ~25% of β-carotene loaded in the nanoparticle prepared using soy protein isolate transferred into the aqueous phase in the gastric digestion stage, and almost all the β-carotene transferred after the intestinal digestion phase, which was accompanied by the degradation of the protein (Deng, Zhang, & Tang, 2017). After comparison with this study, the curcumin release rate of the nanoparticle prepared using GA was obviously lower in the gastric digestion phase. It could be attributed to the fact that the protein content of GA was less than 2%, which is far less than that of soy protein isolate, resulting in a low dependency on protease. Another evidence to support this supposition was that the β-carotene loaded in a starch-based system possessed a relatively lower release rate (<60%) (Mun, Kim, & McClements, 2015).

To understand the digestion process of nanoparticles, TEM was used to analyze the micromorphological changes of the nanoparticle. As shown in Fig. 5, the initial nanoparticle was shaped as a regular sphere of different sizes (Fig. 5D-a), which was in agreement with the shapes of the nanoparticles formed by polysaccharides in previous studies (Zhang et al., 2022). After gastric digestion, the micromorphology of nanoparticles showed no significant changes (Fig. 5D-b). However, many aggregates emerged in the digestive juice after the intestinal digestion stage (Fig. 5D-c). These aggregates were shaped as spherical chains, and might be caused by the existence of salts in the bile powder. The cations in salts of bile powder could be captured by the ionized free carboxyl group of GA, resulting in a weaker electrostatic repulsion in the nanoparticle system. As reported in previous work, the chain aggregates were observed when there was insufficient electrostatic repulsion among curcumin nanoparticles (Li et al., 2021). Therefore, according to the above morphological changes in the curcumin-loaded nanoparticle, its structure was stable during the simulated gastric digestion. However, its structure was significantly affected by the environmental factors in the digestive juice (e.g., enzyme, bile salt, and pH changes), thereby generating the aggregates (Fig. 5D-c), which is hardly observed by the naked eye (Fig. 5B-c), thereby significantly decreasing the curcumin content in the aqueous solution.

Conclusion

To improve the stability and bioavailability of curcumin, we prepared a curcumin-loaded nanoparticle using GA as wall material and curcumin as core material. After loading curcumin in the GA nanoparticle, the curcumin content in the aqueous solution was efficiently enhanced. Moreover, the light-sensitive nature of curcumin was

improved. Since the main force for constructing this nanoparticle is the hydrophobic interaction between the protein moiety and curcumin rather than the electrostatic force, it possessed high stability under NaCl stress, suggesting its application in the high salt-containing food system. The preparation process of the GA nanoparticle is facile, and the preparation condition is mild. Based on TEM analyses, the nanoparticle was presented as a sphere in the aqueous solution. The drug loading capacity of the GA nanoparticle is lower than that of the nanoparticle prepared using mainly proteins. Due to the low protein content nature of GA, the tested curcumin-loaded GA nanoparticle showed low protease dependence, but the release of curcumin was sensitive to pH changes. Overall, this study demonstrates that using GA as the sole material in preparing curcumin-loaded nanoparticles is an efficient way to improve the light sensitivity and solubility of curcumin, which has potential applications in the field of functional foods and food beverages.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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