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Curcumin-loaded nano-emulsion prepared by high pressure homogenization: impact of emulsifiers on physicochemical stability and in vitro digestion

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Abstract

Curcumin possesses various pharmacological properties such as antioxidation, anticancer, and anti-inflammatory, but performs unexpected physicochemical stability and bioavailability when directly incorporate it into food or medicine. In this work, we fabricated a nano-emulsion system for the delivery and protection of curcumin. A precise and theoretically understandable fabrication procedure of curcumin-loaded nano-emulsion was proposed via systematically evaluating the effect of oil type (medium-chain triglyceride oil (MCT) and canola oil), emulsifier type (Tween-80 and lecithin), and surfactant-to-oil ratios (SOR) on the physiochemical properties and stabilities. In terms of oil phase, nano-emulsion fabricated by using MCT exhibited the highest curcumin loading capacity, smallest particle size and best storage stability. Meanwhile, Tween-80 and higher SOR were suggested to prepare monodisperse uniform, physicochemical stable and high loading nano-emulsion. In *vitro* digestion study indicated that most of curcumin encapsulated within nano-emulsions were released in small intestine, and the increase of particle size of the emulsions could be caused by bile salts displacing some surfactant from lipid surface. This work will finally contribute to the optimization of the curcumin nano-emulsion with better physiochemical characteristics and stability in food and beverage products.

Keywords: curcumin; nano-emulsion; high pressure homogenization; physicochemical stability; in *vitro* digestion.

Practical Application: Optimize the curcumin nano-emulsion physiochemical characteristics and stability.

1 Introduction

Many lipophilic bioactive ingredients, such as carotenoids, polyphenols, fat-soluble vitamins, etc., can help to fight chronic diseases (Kharat & McClements, 2019; Moreira et al., 2019). However, these functional ingredients are always of limited use for their own nature such as low bioavailability, poor solubility, high melting point and so on. In recent years, researchers have found that the emulsion carrier system can effectively enhance the biological activity of these oil-soluble functional components (Santos et al., 2021). Oil in water (O/W) emulsions can increase the dispersibility of hydrophobic functional ingredient and promote its absorption and utilization in the body (El-Ashmawy et al, 2018). In addition, as the carrier of biological active ingredient and oil-soluble pharmaceutical ingredient, the emulsion carrier systems can control the release of the lipophilic functional factors to some extent (mouth, stomach, small intestine or large intestine) (Santos et al., 2021).

In recent years, curcumin has gained more and more attention since an increasing number of studies focused on the extraction and purification of curcumin, its biological activity and pharmacological effects (Shakoor et al., 2021; Sun et al., 2021). Studies have found that curcumin is not only an effective oxygen free radical scavenger, but also a credible bioactive for chronic diseases (Duan et al., 2021; Moon et al., 2021; Siraj et al., 2021). In addition, the study in animal models found that curcumin also has a certain effect in the prevention of Alzheimer's disease (Maiti et al., 2019; Sedighi et al., 2018; Hwang et al., 2019). However, curcumin is insoluble in water and readily biodegradable under the condition of alkaline or light (Shimada et al., 2018; Chen et al., 2021), which greatly limit its utilization in food or bio-related fields. In view of the diverse bioactive activities of curcumin, there are a lot of studies on how to improve the solubility and bioavailability of curcumin, including synthesis of polysaccharide-curcumin, phospholipids-curcumin polymers and curcumin-metal chelate or colloidal emulsion carrier systems approach to achieve the appropriate cite of action (McClements et al., 2007; Tiwary et al., 2017). However, these studies are mainly concentrated in the field of pharmacy. A comprehensive system is not yet available for analyzing the development of curcumin emulsion system and enhancing the curcumin bioavailability. However, emulsion system in food processing also faces many challenges: (1) the cost of completely food-grade raw materials; (2) the physiochemical properties of the emulsion systems should be applied in food; (3) the good stability of emulsion systems in the food production process (McClements et al., 2007). Thus, it is a significant and promising research direction to develop a curcumin emulsion system suitable for food processing.

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As shown in the Supplementary Material, we propose a precise strategy of fabricating nano-emulsion with the aid of high-pressure homogenization for the efficient delivery and protection of curcumin. The effects oil type, emulsifier type, and surfactant-to-oil ratios on emulsion physicochemical characteristics and stability have been discussed in detail to determine the optimal preparation formulation. In particular, we also systematically evaluate the role of nano-emulsion in improving the curcumin digestive properties in vitro. Our work will ultimately contribute to the practical applications in nutraceutical and biomedical-related fields.

2 Materials and methods

2.1 Materials and chemicals

Curcumin (95% purity, Tianxu Biological Technology Co., Ltd, Hebei, China), medium-chain triglyceride oil (MCT, Guangdong Wincom Flavors & Fragrances Co., Ltd, China), canola oil (Canola Harvest, Alberta, Canada), lecithin (food grade, De city food products factory, Henan, China), Tween-80 (Xilong Chemical industry Company Limited, China), 95 wt% elcohol (Beijing Chemical Works, Beijing, China), pepsin from porcine gastric mucosa (P7125, enzymatic activity ≥ 400 units/mg protein), pancreatic lipase from porcine pancreas (L3126, enzymatic activity of 100-500 units/mg protein) and bile salts were purchased from Sigma-Aldrich (St, Louis, Missouri, USA). All other chemicals used were of analytical grade, unless otherwise stated.

2.2 Determination of curcumin content

The solubility of curcumin at room temperature was determined by the following method. Elcohol (EtOH) was used to dissolve curcumin. 6 mg curcumin was dissolved in 100 mL 95% EtOH and 250 μL, 500 μL, 1000 μL, 2000 μL, 3000 μL, and 4000 μL solution was taken from the solution respectively, the alcohol was added to make it 15 mL. The absorbance using the UV spectrophotometer (Shimadzu Corporation, Kyoto, Japan) at a wavelength of 425 nm was determined, Finally the standard curve of curcumin content defining the content of curcumin as X-axis and the absorbance as Y-axis was drawn ($Y=0.0146X+0.0222$, $R^2=0.9993$).

Samples of the solubilizing curcumin and the nano-emulsion were diluted 1000 times in alcohol. Then the absorbance at 425 nm was determined. The content of curcumin was Figured out using the standard curve. All determinations were performed in triplicate.

2.3 Solubility of curcumin in different oil phases

The solubility of curcumin was tested using two different oils, including MCT and canola oil at room temperature. Three different methods, including stirring at 100 °C for 3 min, sonication and microwave treatment were used to treat curcumin as follows (Desai et al., 2020). 1.5 g of curcumin was added into 100 mL oils (MCT and canola oil). Then three methods are used to treat them respectively and the resultant oils were centrifuged to separate the supernatant as the sample solution. Centrifugation time is 2 minutes under 531 g. And samples were then kept at room temperature for 24 hours until analyzed.

2.4 Preparation of emulsion systems

To prepare the oil-in-water emulsions of curcumin, the solubilizing curcumin in two kinds of oils, MCT and canola oil, and two emulsifiers containing lecithin and Tween-80 were applied 3 g of curcumin was added into 250 mL of two different kinds of oils respectively, and then treated with ultrasound under the conditions 390 W and intervals of 1 s for 30 min. Then the supernatant was separated using a centrifuge under 3000 r/min for 2 min and kept at room temperature for 24 hours. To examine the effects of different emulsifiers, 20 g Tween-80 and 50 g lecithin were dissolved in deionized water severally and stirred for 24 hours to be hydrated adequately. Then deionized water was added until the solution reached 1000 mL. Subsequently, the two oils were added into the stock solution correspondingly, and the surfactant-to-oil ratios (SOR) were 19:1, 17:3 and 3:1. these desertions were blended using an Ultra-Turrax T25 high-speed blender (IKA, Staufen, Germany) at 10000 r/min at 25 °C for 6 min to form a coarse emulsion. Then they were homogenized at 60 MPa using a high-pressure homogenizer (Type NS 1001L2K, GEA Niro Soavi S.p.A, Parma, Italy) for three times at ambient temperature to form nano-emulsion finally (Fang et al., 2019).

2.5 Determination of zeta-potential and particle size

Zeta-potential and particle size of the curcumin emulsions were determined using Malvern Zetasizer Nano ZS90 (Malvern Instruments, Worcestershire, UK). Emulsion diluted with deionized water to 1000 times was used for particle size determination and diluted with 95% alcohol to 500 times for zeta-potential determination (Bezerra et al., 2019). All determinations were performed in triplicate.

2.6 Determination of turbidity

Turbidity of the curcumin emulsions was determined using a HACH 2100N laboratory turbidimeter (Loveland, USA). Emulsion diluted with deionized water to 500 times was used for determination. All determinations were performed in triplicate.

2.7 Determination of the heat stability

5 mL nano-emulsion were heated for 5 min or 10 min at temperature of 100 °C in the water bath. And then the absorbance at a wavelength of 425 nm was determined. All determinations were performed in triplicate.

2.8 Determination of the centrifugal stability

5 mL nano-emulsion was centrifuge at 3000 r/min for 3 min. Then the absorbance of the supernatant liquid at 425 nm was determined. All determinations were performed in triplicate.

2.9 Determination of physical stability

The stability of the oil-in-water emulsion were analyzed with LUMiSizer (L.U.M. GmbH, Berlin, Germany), an instrument

employing centrifugal force to accelerate the instability phenomena such as sedimentation, flocculation, or creaming. Emulsion stability was shown as a space- and time-related transmission profile over the sample length. The instrumental parameters used for the measurement were as follows (Aghababaei et al., 2021): volume, 1.8 mL; 4000 r/min; time Experiment, 7650 s; time interval, 30 s; temperature, 25 °C.

Cryo-scanning electron microscopy (Cryo-SEM)

Cryo-SEM (Philips CM12, Philips, Eindhoven, Netherland) was used to qualitatively characterize the droplet size of the prepared emulsions. Emulsions were diluted to 0.5 mg/g of dispersed phase with 10 mmol/L citrate buffer of pH 3.6. One drop of diluted emulsion was placed on a copper grid, which was quickly transferred to a liquid nitrogen bath for solidification. The copper grid was then transferred to the SEM cold stage using a cryo-holder. The stage was kept under -170 °C with liquid nitrogen cooling.

2.10 Determination of storage stability

The samples of the nano-emulsion were deposited for 60 days. During the storage, the content and particle size were determined by UV spectrophotometer and Malvern Zetasizer Nano ZS 90 to represent the change of their characteristics.

2.11 Determination of the digestion property of curcumin

According to the previous study, the in vitro digestion method with some modification was applied to evaluate the digestion property of curcumin emulsions. 10 mL samples were added into the 10 mL simulated gastric fluid (SGF, pepsin 3.2 g, sodium chloride 2 g, sodium azide 200 mg, concentrated hydrochloric acid 7 mL within 1 L distilled water, pH=1.2), then oscillated it at temperature 37 °C for two hours in the water bath oscillator to simulate gastric digestion. 5 mL solution was taken out for determination of the content of curcumin, and then adjusted to pH 7 using NaHCO3 solution (1 M).

15 mL simulated intestinal fluid (SIF, pancreatic lipase 0.4 g, bile salt 5 g, dipotassium phosphate 6.8 g, sodium chloride 8.775 g and sodium azide 200 mg within 1 L phosphate buffer solution (0.01 M), pH=7.4)) was added and the resultant solutions were oscillated for two hours to simulate intestinal digestion.

The absorbance at 425 nm of the digested samples was measured by UV spectrophotometer and the release percent of curcumin content was calculated according to Equation 1.

$$\%\text{Release}_{CCT} = \frac{C_t}{C_0} \times 100 \quad (1)$$

where C_0 is the content of curcumin encapsulated originally in samples, and C_t is the content of curcumin in the released fraction after digestion. All determinations were performed in triplicate.

2.12 Statistical analysis

All data were performed triplicate and were reported as the average±error. Data were analyzed by one-way analysis of variance using the SPSS 16.0 package (SPSS Inc., Chicago, USA).

3 Results and discussion

3.1 Characterization of curcumin nano-emulsion

Figure 1 shows curcumin content and particle size distribution of curcumin emulsion prepared by lecithin and Tween-80 as emulsifier, respectively at different SOR. Compared with curcumin emulsions prepared by Tween-80 as emulsifier, emulsions prepared by lecithin showed a wider range of particle size and curcumin content distribution and a higher mean value (curcumin content in lecithin system: 1.31 g/L, Tween-80 system: 0.96 g/L; particle size in lecithin system: 487.36 nm, Tween-80 system: 234.39 nm). However, after significant analysis, the variation

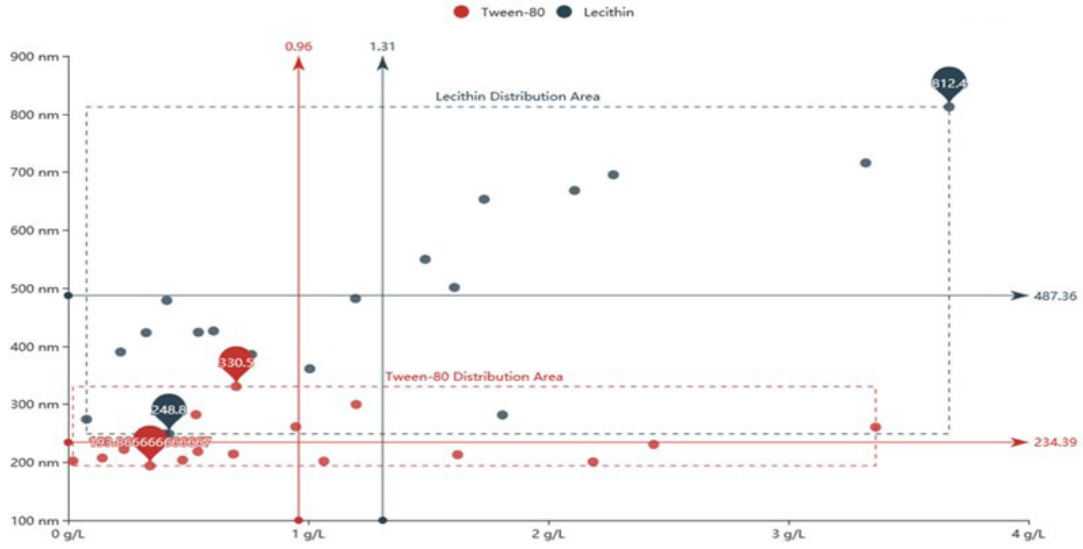

Figure 1. Curcumin content and particle size distribution of emulsion systems prepared by different emulsifiers.

of curcumin content between different emulsifier systems was insignificant (Duncan, $p > 0.05$), but the variation of particle size between different systems was significant. Among them, curcumin emulsion system using Tween-80 as emulsifier exhibited narrower range of particle. Its particle size distribution interval was [193.87, 330.50]. Generally speaking, the aim of preparing curcumin nano-emulsion was to improve the content of loaded curcumin, and smaller particle size is more preferable to increase the physiochemical stability of curcumin (Yan et al., 2022). Therefore, compared with lecithin, Tween-80 was the better choice for preparing curcumin nano-emulsion. At the same time, the value of curcumin content, particle size, turbidity and zeta-potential of different emulsions increased with the decrease of SOR. This result could be attributed to the following reasons: Surfactants would decrease the interfacial tensions of nano-emulsion droplets. With a much more amount of emulsifier, it takes a shorter time for surfactant molecules to adsorb droplet surfaces, providing protection against recoalescence due to steric repulsion (Mundo et al., 2020).

3.2 Physical stability of curcumin nano-emulsion

The integrated transmission-time plots for curcumin loaded nano-emulsion were measured by LUMisizer (Figure 2). The gentle slope means better physical stability. It can be clearly concluded that the nano-emulsion prepared by Tween-80 as emulsifier performed better physical stability in all the concentrations. According to the Stokes' law, large particle size increases viscosity, which leads to slower floating rate of nano-emulsion droplets and better anti-centrifugation stability. On the other hand, reducing emulsifier can improve the physical stability of curcumin nano-emulsion. The main reason for this phenomenon is supposed to be the increase of viscosity of the emulsion (Günal-Köroğlu et al., 2022). When viscosity decreases, the Brownian motion of the microscopic droplets strengthened, resulting in higher aggregation effect. Thus, nano-emulsion prepared by lecithin at low emulsifier concentration led to large droplet size, which can increase the viscosity of the emulsion and perform better physical stability.

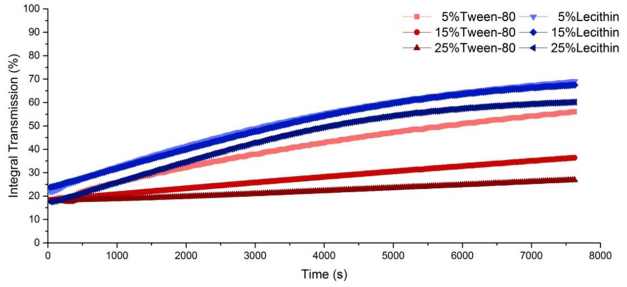

Figure 2. The physical stability of curcumin emulsions formed with Tween-80 and lecithin as emulsifiers.

3.3 Storage stability of curcumin nano-emulsion

The storage stability of the emulsion system is an important factor in determining its suitability in food, especially in the beverage industry (Liu & Tao, 2022). Figure 3a and Figure 3b show the changes in curcumin content during the storage of curcumin emulsion prepared using MCT and linseed oil as the oil phase, respectively. In the early stage of storage, the content of curcumin in emulsion system prepared with lecithin as emulsifier was significantly higher than that in emulsion system prepared with Tween-80 as emulsifier, but the emulsion system prepared with lecithin as emulsifier was more dependent on storage time. With the prolongation of storage time, in the middle and late stages of storage, the embedding amount of curcumin prepared by lecithin as an emulsifier was reduced to a lower level than that of the emulsion system prepared with Tween-80 as an emulsifier. The embedding amount of curcumin in the two systems was basically the same at the end of the 60-day storage.

Figure 4 shows the change in particle size of the curcumin emulsion system prepared in different oil phases during the 60-day storage period. In the system prepared using MCT as the oil phase and Tween-80 as the emulsifier, there was no dependence between the droplet size and storage time. However, when lecithin was used as the emulsifier, the droplet size decreased from

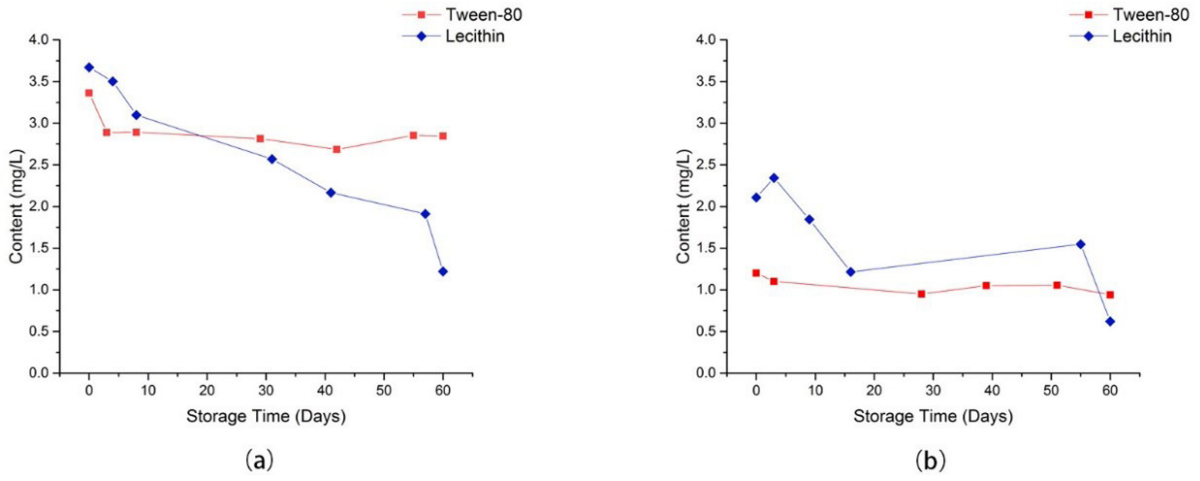

Figure 3. Effect of oil and emulsifier types on curcumin content during storage: (a) MCT as oil phase; (b) linseed oil as oil phase.

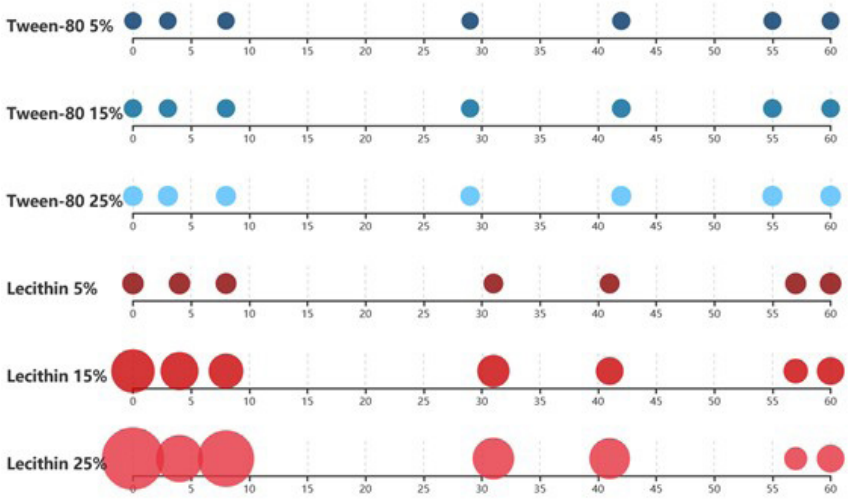

Figure 4. Variation of particle size for emulsions prepared with different emulsifiers during storage.

812.4 nm to 320.9 nm during storage. The results were the same as emulsion systems prepared with linseed oil as the oil phase.

In general, emulsion system is thermodynamically unstable (Liu et al., 2017). As time prolonged, particle aggregation occurred, which weakened the ability of emulsifiers to protect curcumin, and the content of curcumin gradually decreased to a lower level. This result indicated that nano-emulsion prepared by Tween-80 as emulsifier were fairly stable to degradation, which meant better storage ability.

3.4 Centrifugal stability of curcumin emulsion

The effect of the emulsifier on the centrifugation stability of curcumin is shown in Figure 5. As shown in the Figure, the stability of emulsion systems with different emulsifiers showed few differences. The centrifugal stability constants of emulsion systems prepared with Tween-80 as emulsifier were 12.70%, 29.07% and 44.27%, respectively, and the emulsion stability constants of emulsion system prepared with lecithin as emulsifier were 12.20%, 31.85% and 34.53%, respectively. This conclusion was consistent with the above conclusions of physical stability. Firstly, in the short-time centrifugation process, the emulsion system can be basically kept stable, but as the centrifugation time increases, the emulsion system begins to stratify, and the protection capacity is weakened. As the amount of oil phase increases, the viscosity of the emulsion system increases, and the emulsion system is more resistant to centrifugation. Therefore, the protective effect on curcumin is stronger, but as the centrifugation time prolongs, the emulsion begins to stratify to centrifugation. At the end point, the emulsion system loses the protective effect on the emulsifier. The amount of decomposition of curcumin is directly proportional to the initial addition amount of curcumin. That is, the higher the initial addition amount of curcumin, the higher the decomposition rate and the larger the centrifugal stability constant. At the same time, when the light transmission value of the emulsion system is not complete, the degree of decomposition of curcumin has reached a high level,

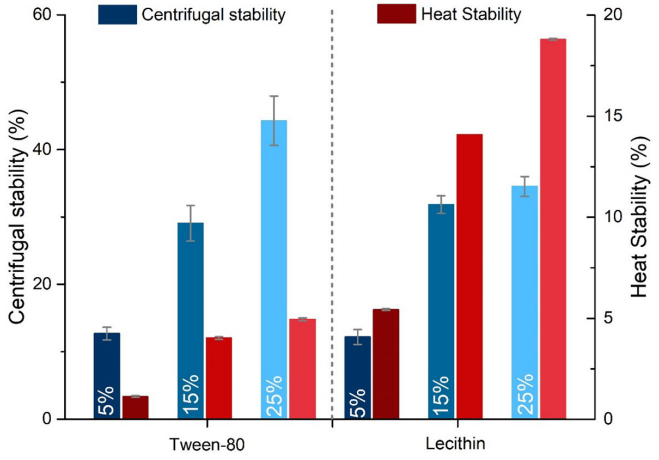

Figure 5. Heat and centrifugal stability of curcumin emulsion prepared with different emulsifiers and SOR.

which further proves that it is necessary to protect the curcumin emulsion system.

3.5 Light stability of curcumin emulsion

In this study, the curcumin emulsion system was placed in a light box for light stability experiments, Figure 6 shows the effect of different illumination on the curcumin emulsion system prepared by different emulsifiers. It was found that curcumin was very sensitive to light. Under the action of light, curcumin had a large amount of decomposition within 10 min, and the degradation rate was significantly higher than the last 5 min. At the same time, the protective effects of different emulsifiers on curcumin also showed significant differences. Under the action of strong light (20*100 lux), the curcumin decomposition rate of different curcumin emulsions systems was about 80%. Other previous studies have also shown that curcumin was very sensitive to light (Mulet-Cabero et al., 2020). The emulsion prepared by Tween-80 as emulsifier had a degradation rate of 24.48%, 47.33%

and 53.10% under strong light for 10 min. The degradation rates of curcumin emulsion prepared by lecithin as emulsifier were 28.27%, 54.95% and 73.89%, respectively. Under the same concentration conditions, the decomposition rate of curcumin emulsion prepared by lecithin was higher than that of emulsion system prepared with Tween-80 as emulsifier. At the same time, the degradation rate of curcumin increased with the increase of oil phase in the emulsion.

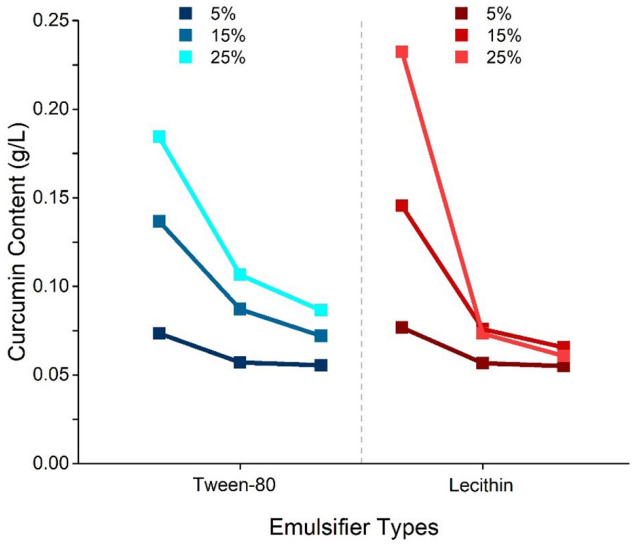

Figure 6. Light stability of curcumin emulsions prepared with different emulsifiers and SOR.

Studies have reported that the emulsion system influences the photostability of curcumin (Bae et al., 2021). Curcumin in solid form was less sensitive to light and more tolerant than emulsion systems. The curative stability of curcumin in the crystalline state was 55% higher than that of curcumin preserved in ethanol solution. The decomposition of curcumin is caused by the instability of the molecular structure of curcumin itself. Under light conditions, light provides energy to accelerate the process of decomposition of curcumin, causing the chemical equilibrium equation of the decomposition reaction to move forward. At the same time, the curcumin content itself also affects the decomposition rate of curcumin. As the content increases, the curcumin molecular groups are more likely to collide, resulting in faster decomposition rate. Compared with the emulsion system prepared by lecithin as an emulsifier, the curcumin emulsion system prepared by Tween-80 as an emulsifier had a smaller particle size, so the dispersibility was higher, and the emulsifier exhibited stronger protection effect on curcumin. The degradation rate of curcumin was lower per unit time.

According to Figure 7, a combination of various properties found that the emulsion system prepared by different emulsifiers showed a large difference in particle size, ζ-potential and turbidity, while the amount of curcumin was relatively less affected. Stability of the emulsion system with better centrifugal stability often means better thermal stability, but with the increase of the oil phase addition and the increase of the viscosity of the system, the light stability of the system deteriorates. Therefore, it is necessary to design the most suitable emulsion system for different use environments.

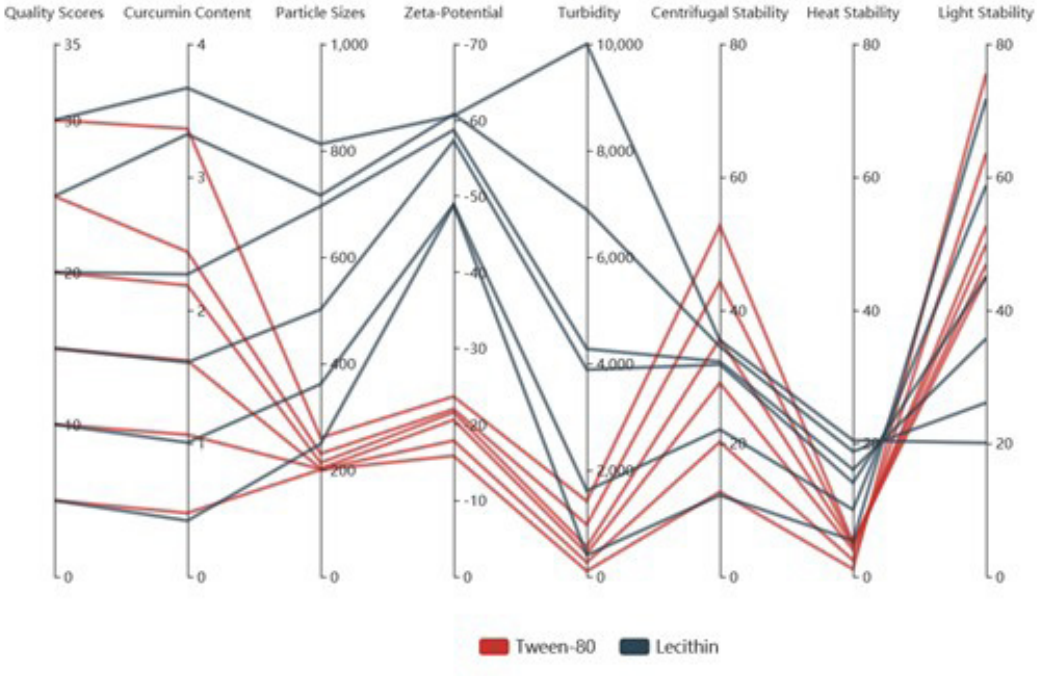

Figure 7. Multi-factor diagram of curcumin emulsions prepared with different emulsifiers.

3.6 In vitro digestion

When food or beverage enters the human gastrointestinal tract, its structure tends to change due to various physicochemical reactions and physiological and biochemical processes (Mushtaq et al., 2021). In this experiment, the effect of emulsifier type on the digestion characteristics of curcumin emulsion system in the gastrointestinal tract was studied by an improved GIT model. Among them, the overall GIT model consisted of three stages, namely oral stage, gastric digestion stage and small intestine digestion stage. Because the emulsion stays in the oral cavity for a short time, and the factors such as amylase in saliva have little effect on the emulsion system, the simple GIT model of the improved evaluation emulsion system often includes only the gastric digestion stage and the small intestine digestion stage (Bezerra et al., 2019; Yi et al., 2021). Recent studies have shown that even in the standard GIT model, the oral phase is an optional phase rather than a necessary phase (Wang et al., 2020). Based on this, we used a modified GIT model without oral phase to evaluate emulsion systems prepared with different emulsifiers. The changes in particle size and the amount of curcumin released in the GIT model of the emulsion system prepared by different emulsifiers (Tween-80 and lecithin) were determined experimentally.

The change in the amount of curcumin released in the GIT model is shown in Figure 8. Compared with the small intestine digestion stage, the emulsion systems had a large difference in the release amount of curcumin in the gastric digestion stage, especially as the oil phase amount decreased, the release amount of curcumin in the gastric digestion stage decreased. In the small intestine digestion stage, the stability of the curcumin emulsion system was worse, the protective effect of the emulsion system on curcumin was significantly weakened, and the release amount of curcumin was significantly increased. Among them, the release rate of curcumin for the emulsion system using lecithin as an emulsifier in the small intestine was greater than that of the emulsion system prepared by Tween-80 as an emulsifier. At the end of the in vitro simulated digestion process, the difference in fatty acid release rate of the emulsion system prepared by the two emulsifiers was not significant, so the difference in bioavailability was not significant. However, the emulsion systems prepared by the two emulsifiers had a significant difference in the proportion of fatty acid release in different digestive environments, especially as the amount of oil phase decreased. When the oil phase was added at 10%, 52.59% of the fatty acid in the emulsion system prepared with Tween-80 as an emulsifier was released in the stomach. However, in the emulsion system prepared with lecithin as an emulsifier, only 37.08% of the fatty acid was released in the stomach stage in simulated digestion conditions. At the same time, in the emulsion system prepared by lecithin as an emulsifier, 30.42% of the fatty acids were released in the simulated small intestine environment, while only 17.28% of the fatty acid in the emulsion system prepared with Tween-80 as an emulsifier could be released in the small intestine environment. An important reason for this difference was the difference in stability of the emulsion system. As mentioned above, the emulsion system prepared with Tween-80 as an emulsifier had a smaller particle size and was more resistant to external adverse conditions and therefore more stable. In the in vitro simulated digestion conditions, the emulsion system prepared with Tween-80 as

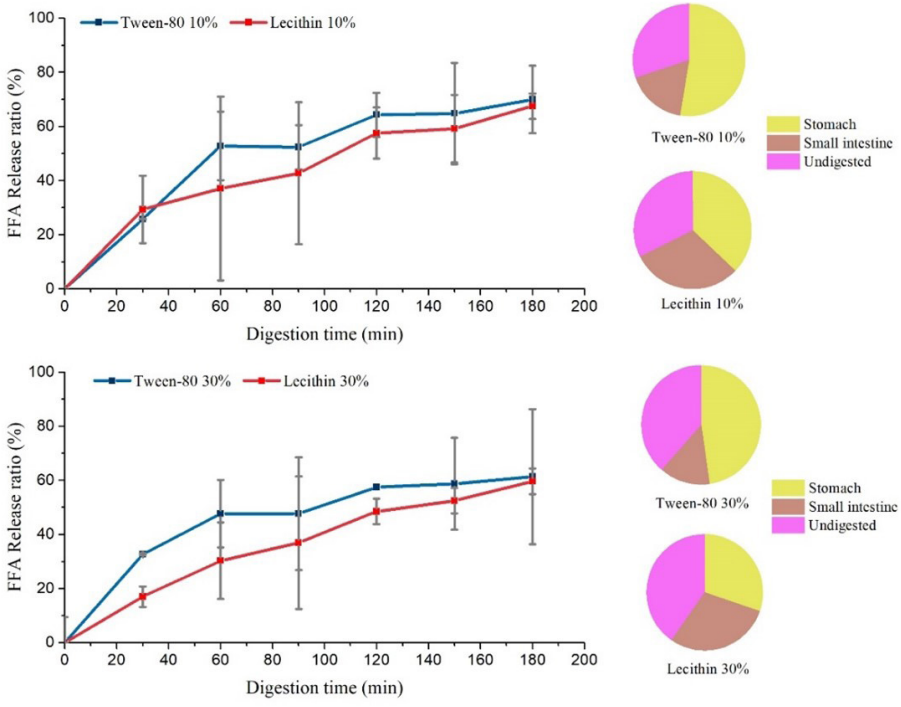

Figure 8. Effect of emulsifier types on FFA release ratio in curcumin emulsions.

emulsifier still showed strong stability and was less affected by digestive tract digestion conditions than emulsion system prepared with lecithin as emulsifier. Therefore, the protective ability of curcumin was stronger, and the release amount in the small intestine was relatively small.

The changes in particle size and ζ-potential of different emulsion systems during in vitro simulated digestion are shown in Figure 9. When the emulsion system prepared by lecithin as an emulsifier was transferred to the simulated stomach condition, the average particle size was significantly increased. This was because when the lipid droplets were dispersed into the simulated gastric juice, the pH, ionic strength, enzyme activity and other factors of the system changed significantly. In particular, the relatively low pH in the gastric digestive system resulted in a relatively high positive charge on all droplet surfaces. Therefore, there may be strong charge attraction between the droplet molecules, resulting in bridging flocculation. An increase in ionic strength also caused a decrease in electrostatic repulsion between the droplets, thereby promoting droplet aggregation. The change in ζ-potential proved the above conclusion. The emulsion droplet size was further increased after treatment in the intestinal digestive conditions. This indicated that a wider concentration of droplets occurred inside the emulsion system, and this result was also caused by factors such as pH and ionic strength. Unlike

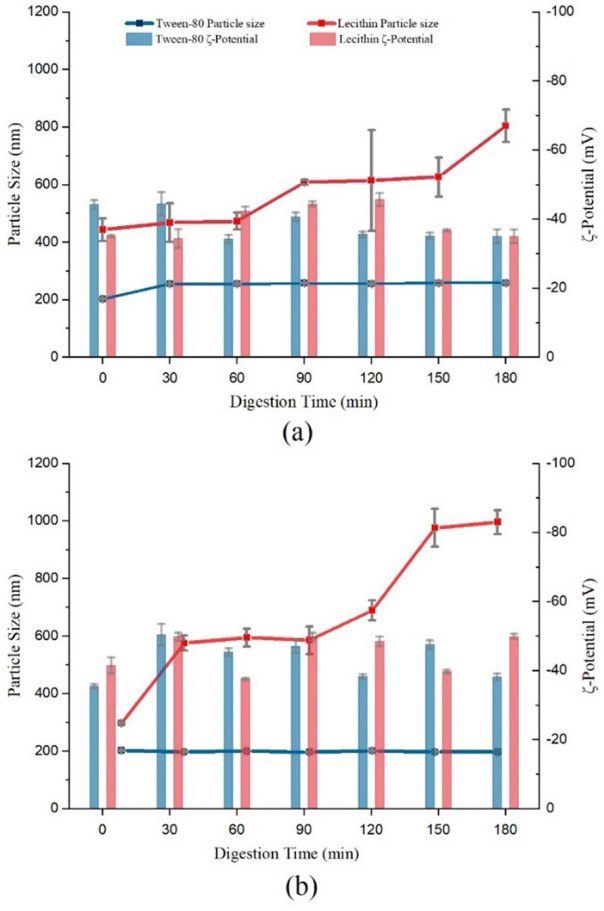

Figure 9. Effect of emulsifier with different contents of 10% (a) and 30% (b) on particle size (a) and zeta-potential in curcumin emulsions (b).

the stomach, the effect of enzyme activity was more pronounced. The presence of lipase under small intestinal conditions will result in hydrolysis of the lipid droplets, causing the lipid droplets to produce colloidal structural units with different characteristics, such as small micelles or large vesicles. At the same time, in the small intestine digestion stage, bile salts could displace the surfactant of the stable emulsion system from the surface of the lipid droplets. This provides a pathway for lipase molecules to enter to hydrolyze to produce free fatty acids (Bae et al., 2021). These results again indicated that the interfacial composition of the modified droplets could alter the gastrointestinal digestive properties of the emulsion system, that is the emulsion systems prepared with different emulsifiers have different gastrointestinal digestive properties.

It is generally believed that the bioavailability of embedding compounds prepared using bioactive ingredients is greater than that of conventional emulsions. It was also found that the fatty acid release rate was negatively correlated with the droplet size of the emulsion system due to the effect of the oil phase on the specific surface area of the aqueous phase (Bae et al., 2021). Therefore, the emulsion system prepared with Tween-80 as an emulsifier exhibited higher stability due to its higher curcumin content and smaller particle size. The emulsion system prepared with lecithin as emulsifier had a significant increase in particle size after transferring to the digestion stage of the small intestine, and the protective effect of emulsifier on curcumin was significantly reduced, so that the release rate of curcumin in the small intestine was significantly increased.

4 Conclusion

In this study, the influence of different oils, emulsifiers and SOR on curcumin nano-emulsions were investigated. Compared with lecithin, Tween-80 as emulsifier achieved smaller particle size, which contributed to load more curcumin and protected curcumin from decomposition during storage. In terms of SOR, curcumin content was negatively correlated with SOR because the oil phase was saturated by curcumin. However, a lower SOR was easier for curcumin nano-emulsion to aggregate, which caused stratification of curcumin, for it lose protection from emulsion. It is no surprise that a higher SOR was good for storage. Compared with the small intestine stage of curcumin's digestion, curcumin had a smaller release in the stomach, especially in high SOR condition. Overall, this study provided valuable information into the impact of emulsifiers and oil on the physicochemical properties of curcumin emulsions, which may be important for the formulation of healthier products.

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Supplementary Material

Supplementary material accompanies this paper.

Figure S1. Graphical abstract.

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