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Research paper

Rheological behaviors of Brij 97 based liquid crystals containing sodium deoxycholate and curcumin

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ABSTRACT

Curcumin encapsulated hexagonal (H_1-Cur) and cubic (I_1-Cur) liquid crystals, which were characterized by small angel X-ray scattering (SAXS), were formed in the mixture of Brij 97 and sodium deoxycholate (NaDC). Rheological experiments showed that at constant surfactants concentration (56.2%), with increasing oil/water ratio, the elastic and viscous moduli of H_1-Cur phases decreased in sequence $M_2Cur_3 \rightarrow M_3Cur_s \rightarrow M_4Cur_s \rightarrow M_6Cur_s \rightarrow M_5Cur_s$, $M_2Cur_3 \rightarrow M_3Cur_3 \approx M_4Cur_3 \rightarrow M_5Cur \rightarrow M_6Cur_3$ at high frequency region. While the moduli of H_1 phase without curcumin increased and then decreased. Moreover, for a H_1-Cur phase (M_3Cur_n), with increasing curcumin content, the elastic modulus decreased from 4.2×10^4 to 2.3×10^4 Pa and then increased to 5.5×10^4 Pa, while the values of a_s increased from 213.4 to 218.4 $Å^2$ and then decreased to 210.4 $Å^2$. For an I_1-Cur phase (M_7Cur_n), with increase in curcumin content, the elastic modulus changed from 1.5×10^5 to 1.2×10^5 Pa, while the values of a_s increased from 214.7 to 217.6 $Å^2$. These results indicated different stability of the liquid crystals containing curcumin. For H_1-Cur phase, the amount of oil, surfactant, curcumin to obtain stable crystal were 6.3%, 56.2%, 0.018 mg/g, while for I_1-Cur phase, these were 4.5%, 40.5%, 0.013 mg/g, which may give guidance for release behavior of curcumin encapsulated liquid crystals.

1. Introduction

Curcumin is a yellow-orange polyphenolic compound derived from the rhizome of the herb Curcuma longa. The chemical structure of curcumin, shown in Fig. 1, has phenolic groups and conjugated double bonds which exhibit keto–enol tautomerism between enol and keto structures, respectively [1]. Besides, curcumin molecule exhibits many significant functions in pharmacologic field including anti-inflammatory [2], antioxidant [3], antimicrobial [4] and anticarcinogenic activities [5]. However, the application of curcumin as a health-promoting agent was hampered by its poor water solubility [6] and its sensitivity to alkaline conditions, light and high temperature.

Generally, two approaches have been applied to improve the disadvantages of curcumin. One is the chemical modification of curcumin [6] and the other is drug carriers. Lyotropic liquid crystals (LLCs), as one of drug carriers, have significant advantages due to their potential ability of sustained [7] and controlled release [8], protecting bioactive molecules from hydrolysis or oxidation, solubilizing various non polar drugs and enhancing the stability of some drugs [8,9]. In our previous work, curcumin encapsulated in LLCs showed sustained release effect [10]. Also, the stability of curcumin against sun-light can be protected by LLCs [11]. Therefore, encapsulation of curcumin in LLCs is an effective mean to improve its shortcomings.

These above investigations showed the positive effects of LLCs on the properties of encapsulated drugs, while the properties of LLCs may be affected after adding drugs. Basic on our previous study [12], rheological properties of LLCs obtained from rheological experiment can reflect the effects of drugs on LLCs properties. A detailed rheological characterization can provide practical guidance for drug delivery [13,14]. For example, the system with higher elastic modulus shows more stable structure, resulting in a slower release of drugs [14]. Moreover, the oscillation experiment of LLC carriers will help us to understand the change of its liquidity after suffering with extrusion and oscillation in vivo. Therefore, the investigation of rheological properties of LLCs is helpful to select the drug carrier.

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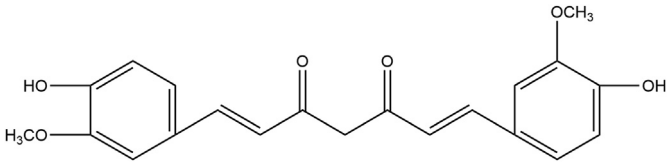

Fig. 1. The chemical structure of curcumin.

To form LLCs encapsulating curcumin, sodium deoxycholate (NaDC), as one of the most important biosurfactants, was introduced to mix with oleyl polyoxyethylene ether surfactant (Brij 97) on the basis of Brij 97/isopropyl myristate (IPM)/H_2O system [15]. In our previous work, it is found that there is strong attractive interaction between NaDC and Brij 97 in mixed micelle. It contains hydrogen bonding between PEO blocks of Brij 97 and hydroxyl of NaDC, Van der Waals force between the molecules of Brij 97 and NaDC, and hydrophobic interaction between the hydrophobic groups of Brij 97 and NaDC [16]. Also, the protection effect of curcumin gets enhancement and the equilibrium time of release was extend by introducing NaDC in the system [11]. The relatively higher concentration of NaDC was chosen to construct liquid crystals, compared to the previous work [12].

In this paper, the liquid crystals were constructed by using relatively higher NaDC content in Brij 97-NaDC (BN, $\alpha_{NaDC} = 0.36$)/IPM/H_2O system to loaded curcumin. Small-angle X-ray scattering (SAXS) technique and polarization microscope (POM) were applied to investigate the microstructures and textures of the LLCs. The changes of LLCs containing curcumin after suffering shear stress or oscillation were obtained from rheological measurements.

2. Materials and methods

2.1. Materials

Polyoxyethylene-10-oleyl ether (Brij 97) and sodium deoxycholate (NaDC) were purchased from Sigma–Aldrich China, Shanghai, China. Isopropyl myristate (IPM) and curcumin were obtained from Sinopharm Chemicals Reagent Company (Shanghai, China). All chemicals were used directly without further purification. Deionized water was used after double distilled.

2.2. Phase diagram determination

Ternary phase diagram was measured by the method previously described by Wang et al. [15]. First, surfactant mixture of Brij 97 and NaDC ($\alpha_{NaDC} = 0.36$) has been prepared. Second, different weight ratios varying from 0:10 to 10:0 of surfactants and oil were obtained by adding different amount of oil to surfactant mixture and stirred well at about 60–70 °C in order to make all components mix homogeneous. Third, the water phase was added sequentially and mixed using a vortex mixer following repeated centrifugation. Fourth, the samples were kept in a water bath at 25 °C to achieve phase equilibrium after the homogenization was attained. The phase boundaries were determined by visual observation in normal light and also confirmed by SAXS or rheological technology. Samples were stored at least 6 days to form the complete structures of liquid crystals for further investigation. The elastic and viscous moduli of the samples after 6 days and 14 days have little change, as shown in Fig. A1 (supplementary materials), indicating the properties and the stability of liquid crystals almost invariant after 6 days.

2.3. Preparation of samples

2.3.1. Preparation of saturated IPM for curcumin

Add an excess amount of curcumin to 25 ml IPM in a clean and dry glass vessel. The mixtures were mixed using a vortex stirrer (XW-80A, Shanghai Jingke Industrial Co. Ltd., Shanghai, China) for 10 min to facilitate proper mixing of curcumin and IPM after sealing. Then, the mixtures were stirred using a magnetic stirrer (79-1, Jintan Medical Apparatus Factory, Jintan, China) maintained at room temperature for 24 h to make curcumin fully dissolved in the IPM. Finally, the suspension of curcumin was centrifuged triply at 10,000 rpm for 10 min using a high speed centrifuge (Sigma 1–14, Sigma Laborzentrifugen GmbH, Harz, Germany). The supernatants were saturated IPM of curcumin, stored in glass vials and avoid light. The preparation of saturated curcumin is according to our previous study [12]. The solubility of curcumin in saturated IPM was detected by a UV spectrometer (UV–5500CP, Shanghai Metash Instruments Co., Ltd., Shanghai, China) at a wavelength of 424 nm. The solubility of curcumin in IPM is 0.28 mg/g. Besides, the solubility of curcumin in IPM reported in the previous studies is 0.3 mg/g [17].

2.3.2. Preparation of samples

In this paper, we select several samples from hexagonal and cubic phases, respectively. First, M_3 and M_7 are samples along the water dilution line at the 9/1 mass ratio of BN/IPM. Then, the samples M_1–M_6 are selected with different ratio of oil/water at a constant concentration of surfactant (56.2%). The nomenclature, composition and types of microstructure of these samples are shown in Table 1. Besides, we selected the samples M_2Cur_3, M_3Cur_3, M_4Cur_3, M_5Cur_3, M_6Cur_3, just encapsulating same concentration of curcumin by adding same amount saturated IPM of curcumin with M_2Cur_3. The amount of every composition in these samples is same as M_2–M_6, respectively, except for the concentration curcumin. The samples M_2Cur_s, M_3Cur_s, M_4Cur_s, M_5Cur_s and M_6Cur_s were prepared using saturated IPM of curcumin compared with M_2–M_6. The samples M_3, M_3Cur_1, M_3Cur_2, M_3Cur_3, M_3Cur_4, M_3Cur_5 and M_7, M_7Cur_1, M_7Cur_2, M_7Cur_3, M_7Cur_4 are also selected. The samples were prepared adding different amount saturated IPM of curcumin. Besides, the mass fraction of each component is same with M_3, M_7, respectively, except for the concentration of curcumin. The nomenclature and composition of these samples containing curcumin are shown in Table S1 (supplementary materials).

2.4. Polarization microscopy (POM)

Polarizing optical microscopy was performed with a BK-POL microscopy (Chongqing Aote optician Co). The polarized photos of the liquid crystals were taken with an OPTEC TP DV500 digital camera. The samples were shift to a microscope slide and covered by a cover glass to avoid solvent evaporation [18].

Table 1
Nomenclature and compositions of liquid crystal samples investigated.

Sample	BN (wt %)	IPM (wt %)	H_2O (wt %)	Phase
M_1	56.23	0	43.77	H_1
M_2	56.22	2.77	41.01	H_1
M_3	56.17	6.24	37.59	H_1
M_4	56.23	10.76	33.01	H_1
M_5	56.18	13.70	30.12	H_1
M_6	56.16	15.72	28.12	H_1
M_7	40.46	4.53	55.01	I_1