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The effect of Iopamidol on rheological properties of monoglyceride/water system

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Abstract

Monoglyceride (MO) has the ability to form various liquid crystalline phases spontaneously in the presence of various amount of water at room temperature. The appropriate compositions from binary phase diagram of monoglyceride/water were selected to form the cubic phase. Various systems were studied at different Iopamidol concentrations using rheological method. It was revealed that the viscoelastic properties went through three regions with increasing the concentration of Iopamidol. When the concentration of Iopamidol was higher than 3.97 wt.%, the viscoelastic properties were increased, for the phase structure parameter was decreased which led to the more compact structure. The lipid bilayer would be attenuated or disrupted when the concentration of Iopamidol reached to 9.98 wt.%, for the viscoelastic properties of the system was decreased.

Keywords: Monoglyceride; Rheological property; Viscoelasticity; Cubic phase

1. Introduction

The unique properties of cubic liquid crystals formed from monoglyceride (MO) have been utilized for the preparation of controlled drug release system. The cubic phases formed from MO/water systems were reported to serve as a drug delivery system for drugs with different physico-chemical properties. A lot of studies have been reported recently [1–6].

MO is degradable and innoxious to human body. Cubic liquid crystal is a natural bicontinuous lipid bilayer membrane. It can simulate biomembrane [7,8]. The cubic liquid crystal has a transparent, stiff, gel-like appearance and it is built up of a three-dimensional network of curved lipid bilayers separated by a network of congruent water channels. There are two water channels in the bicontinuous cubic phase (Ia3d). One is open to the outer continuous phase. The other is closed and isolated with outer environment. Drugs can be encapsulated in the bicontinuous cubic phase and are sustained released. It is prone to esterase activity and can be easily cleared from the body. These degradable delivery systems erode or dissolve in the gingival crevice, avoiding removal after treatment [9]. Razumas et al. [10] studied the effects of distearoylphosphatidylglycerol and cytochrome *c* on the molecular organization of the MO–water cubic liquid crystal phase. They found that the protein molecules retained their native secondary structure in the MO–DSPG–Oytc–water phase.

MO is insoluble in water but able to swell, giving rise to different liquid crystal phases described by a complex phase diagram, depending on water content and temperature [11]. When a small amount of water was added to MO (usually less than 5%, w/w), reverse micellar structures were formed with a relatively low viscosity. At this stage a further addition of water leaded to the formation of highly viscous hexagonal or cubic phases. In particular, a tetracycline gel incorporating 10% (w/w) of water which viscosity allowed expression through the 23 – gauge blunt needle used for in vivo administration. After administration, the MO–water system adsorbs the biological fluids, swells and increases its viscosity to a semi-solid form. The unique properties of cubic liquid crystalline phases formed from MO/water systems have been utilized for the preparation of controlled release systems, and

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in topical and mucosal drug delivery systems due to their adhesive properties.

Though, a lot of techniques were used to study such systems of MO/water. The rheological methods were seldom used to study on it [10]. The rheological properties were a function of both the structural arrangement of particles and various interaction forces that operated in the system.

It was discovered that the Iopamidol can enhance the solubility of the paclitaxel, an anticancer drug, in the cubic phase [12]. So in this report, the component of 30 wt.% water was selected for MO/water system. The system was studied at different concentration of Iopamidol. The viscoelastic properties of such systems were different with increasing the Iopamidol concentration and it could be divided into three regions in the whole range of concentration. Between two regions, there was a break, the viscoelastic properties were very low compared with other samples. It was suggested that the structures might be different between the two regions. The other point was that the systems would not be cubic phases when the concentration of Iopamidol was increased to 9.98 wt.%.

2. Materials and methods

2.1. Materials

Monoglyceride (purity 95%) was purchased from Danisco Cultor (Denmark), and was used without further purification. This monoglyceride will be referred to as monoolein or MO in this report. Iopamidol ($C_{17}H_{16}N_3I_3O_8$, purity 99%) was purchased from Bracco S.P.A. (Milano, Italy) and used directly. Water was purified by deionization followed by distillation twice. All other chemicals used were of analytical grade.

2.2. Sample preparation

For the rheological measurements, cubic gels of MO/water/Iopamidol with water concentration of 30 wt.% were used. MO was melted at 40 °C and Iopamidol was solubilized in water. Subsequently, Iopamidol solutions were added into MO in small glass ampoules. The ampoules were sealed at once to avoid water evaporation. And then these ampoules were centrifuged with centrifugal machine (Shanghai Medical Apparatus Company, China) at 2000 × g for about 1 h at room temperature. The mixtures were then placed in an oven at 40 °C for 24 h. Then the sample was placed at room temperature for about 1 month. Transparent and viscoelastic cubic gel was formed.

2.3. Rheology measurement

All rheological properties were measured with the Rheostress RS 75 apparatus (HAAKE, German). A cone-plate sensor was used with a diameter of 20 mm and cone angle of 1°. The temperature was maintained at 37 ± 0.1 °C during measurements. Because the rheological properties of such systems may be dependent on the shear deformation history, the sample was gently inserted onto the top of the plate with constant velocity. The sample squeezed out from the sensor system was gently removed. Measurements were carried out after a period of 10 min to allow for some stress relaxation to be reached and temperature to be stabilized. All the measurements were done after 1 month in order for the samples were balanced and stable. Initially, steady-shear measurement was performed in which the stress amplitude σ was varied while the frequency was kept 1.0 Hz. Once the linear viscoelastic region was established, measurements were carried out as a function of frequency at constant stress (choosing an amplitude within this region).

3. Results and discussion

3.1. Steady flow properties

The stresses as a function of the shear rate were shown in Fig. 1. It was seen clearly that there were three regions in the figure. First, the concentration of Iopamidol was 1.09–3.97 wt.%, the range of stresses were 50–300 Pa. Second, the concentration of Iopamidol was 4.98–7.97 wt.%, the stresses were higher than 300 Pa. Third, the last curve was that the concentration of Iopamidol was 9.98 wt.%. The stress of it was decreased at the beginning and then leveled off at the value of about 10 Pa. It can be concluded that there were three types of structures among these systems. Viewed by eyes, the samples were more and more opaque with increasing Iopamidol concentration when the concentration increased to 5.96 wt.%. The assured structures were needed to be confirmed further.

Fig. 2 was the viscosity of samples as a function of the shear rate. All the samples showed weak shear – thin

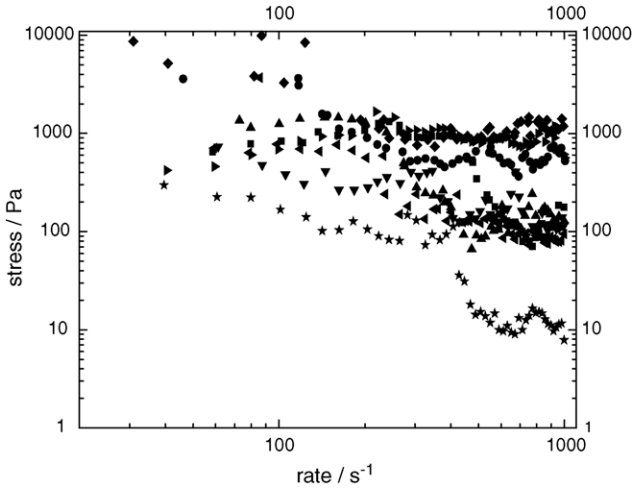

Fig. 1. The stress of samples as a function of the shear rate at 37 ± 0.1 °C, the concentration of Iopamidol: (■) 1.09 wt.%, (◄) 1.99 wt.%, (▲) 2.98 wt.%, (▼) 3.97 wt.%, (♦) 4.98 wt.%, (●) 5.96 wt.%, (►) 7.97 wt.%, (⋆) 9.98 wt.%.