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Original Research

Cucurbita pepo oil as a drug microemulsion formulation: study of phase diagram

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Abstract

Objective(s): Investigation of phase diagram of various drug formulations is effective to predict different phase region of drugs to detect final formula. The purpose of this research was to develop the ternary phase diagrams for a drug microemulsion system consisting of *Cucurbita pepo* (pumpkin) oil, surfactant (Tween 80) and deionized water.
Materials and Methods: An electrical conductivity was used to study the properties of system. Particle size analysis of microemulsion system was performed by dynamic light scattering.
Results: The electrical conductivity of the microemulsions increases with increasing of aqueous phase content. Structural transitions from the oil-in-water to a bi-continuous phase then inversion to water-in-oil occured in the system. Diameter of particles was calculated 70 nm (for 75 percent of particles) and 35 nm (for 25 percent of particles). Solubility results showed that microemulsion system of *Cucurbita pepo* oil can increase its solubility in aqueous medium due to droplet size reduction into nanometer size.
Conclusion: Microemulsion technique can be used as a successful method in preparation of *Cucurbita pepo* oil drug formulation.

Keywords: Conductivity, *Cucurbita pepo*, Microemulsion, Nanosized droplet, Phase behaviour

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Introduction

A microemulsion system is composed mainly of water, oil, surfactant and/or co-surfactant. This system is a transparent with low viscosity with an internal droplet size ranging of about 10-100 nm that formed spontaneously (1-5). Due to thermodynamically stability, micro-emulsion is a promising system for designing efficient drug carriers (6). *Cucurbita pepo* from *Cucurbitaceae* family, is a medium sized plant that is popular for its fruits and edible seeds. Hence, it is known to be used as human food in many countries. Other members of this family are also available. It has been used locally in Eritrea to treat tapeworm and has also been used in other regions of the world to treat the early stages of prostate disorders (7). Its use in prostate condition is due to its high zinc content (8). The seed of *C. pepo* contains 30 to 51% of oil; other constituents are fatty acids – linoleic and oleic acids (27 to 38%); proteins (31 to 51%), carbohydrate (6 to 10%); mineral elements (4 to 5%) that includes phosphorous, calcium, potassium, iron, selenium and zinc (9). Selenium is particularly important, as it ranges between 0.08 and 0.40 mg/g. Other substances in the seeds include tocopherols and sterols. The β-sitosterol has been shown to be a strong inhibitor of prostaglandin biosynthesis in prostatic tissue of patients with Benign Prostatic Hyperplasia (BPH) and then to exert a marked anti-inflammatory action. Hence, it seems that use of this plant as an alternative treatment for stages I and II BPH is useful (9). *C. pepo* oil has low solubility and consequently low bioavailability in the body due to oily nature. Use of microemulsion technique can be a useful method to increase its solubility in water media. There are three types of microemulsion: bi-continuous, oil-in-water, and water-in-oil. Oil-in-water (o/w) microemulsions are more important in delivering oil-soluble drugs (10). Conductivity is a useful and very simple method in characterization of type of microemulsion. Microemulsion is also characterized using polarized light microscopy, rheology and dynamic light scattering (DLS). Indeed dynamic light scattering method is used to measure particles in a liquid medium (11, 12).

Materials and Methods

Materials

Tween 80 (polysorbat 80) surfactant (AppliChem, Germany), *Cucurbita pepo* oil (Zardband Co., Iran).

Ternary phase diagrams at constant temperature

The phase behaviour of a system consisting of water, oil and mixed surfactants may be described on a phase diagram whose apexes respectively represent the pure components. However, it is more convenient to describe the phase behaviour on a ternary phase triangles. Mixtures at fixed weight ratios of oil, surfactant and water were prepared in culture tubes sealed with viton-lined screw caps. The phase diagrams were determined at 25± 0.5°C.

Electrical conductivity measurements

Conductivity measurements were performed at 25 ±0.5°C on samples the compositions of which lie along the one phase channel, using conductivity meter, the conductivity cell used is 712 Model, Metrohm, the electrode material is graphite and the cell constant is 0.032 cm^{-1} ± 1.5%. The electrode was dipped in the microemulsion sample until equilibrium was reached and reading becomes stable.

Particle size measurement

Particle size analysis was performed by dynamic light scattering (NANOPHOX PCCS with WINDOX5 software).

Results and Discussion

Phase behaviour

The ternary phase diagrams of the Cucurbita pepo oil + surfactant + water

Table 1. Phase diagram behaviour in ternary phase diagram of microemulsion region of Tween80/ *Cucurbitapepo* oil-water.

Electrical conductivity status	Fraction of water content in two phase system(surfactant and water)	Fraction of surfactant content in two phase system(surfactant and water)	Type of formed phase with increasing of water content in presence of oil
Increases with increasing of aqueous phase content	0-21	79-100	oil-in-water
Maximum amount of electric conductivity	21-42	58-79	bi-continuous
Decreases with increasing of aqueous phase content	42-100	0-58	water-in-oil

system was studied at 25 °C. Figure 1 and Table 1 presents the phase behaviour of this ternary system. In figure (1) you can see an isotropic and low-viscosity one phase microemulsion region.

Electrical conductivity

Electric conductivity was measured as a function of water content Φ (wt%) for the oil, surfactant mixture along the dilution red line (Figure 1).

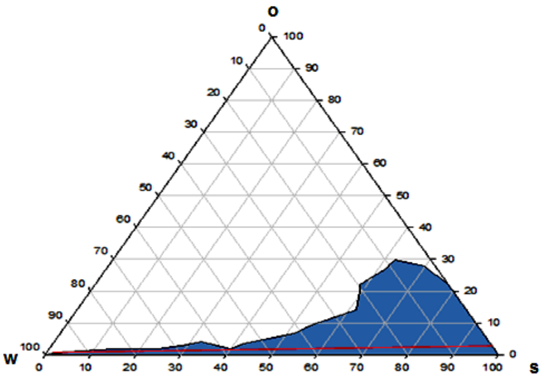

Figure 1. Ternary phase diagram showing micro-emulsion region of Tween80/ *Cucurbita pepo* oil /water (O: oil, S: surfactant, W: water).

The results of variation of σ as a function of water content Φ (wt%) are shown in Figure 2. The conductivity is initially low in oil/surfactant mixture but increases with increase in aqueous phase. The low conductivity below Φc suggests that the

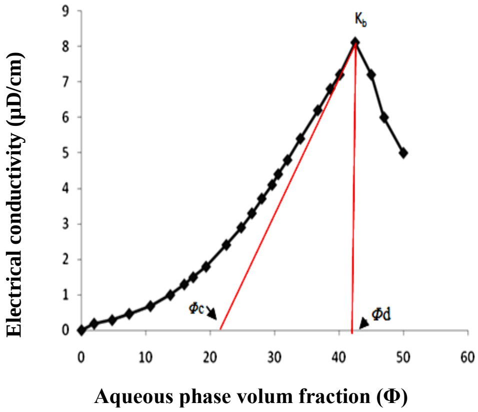

Figure 2. Electrical conductivity (σ) as function of aqueous phase volume fraction along the red line of the system where the phase diagram is presented in Figure (1).

reverse droplets are discrete (isolated droplets in a non-conducting oleic medium forming w/o microemulsion) and have little interaction. When the water content is raised above Φc, the value of σ increases linearly and steeply up to Kb. The interaction between the aqueous domains becomes increasingly important and forms a network of conductive channel (bi-continuous microemulsion). With further increase in water content above Φd, the σ shows a sharp decrease.

Particle size measurement

Figure 3 shows the particle size distributions of our microemulsion. Results showed bimodal distribution that diameter of particles were calculated 70 nm (for 75 percent of particles) and 35 nm (for 25 percent of particles).

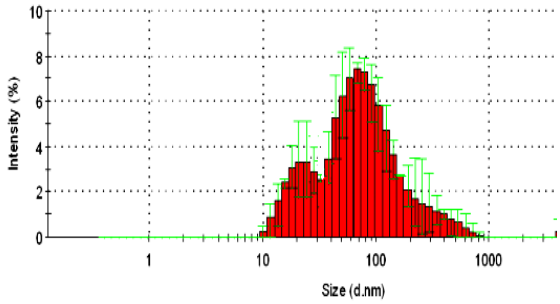

Figure 3. Particle size distribution of *Cucurbita pepo* microemulsion by DLS.

Conclusion

We develop the microemulsion areas of ternary phase diagrams for a drug delivery system consisting of Tween80, *Cucurbita pepo* oil and water. Electrical conductivity of the microemulsions increases with increasing of aqueous phase content. Results show that structural transitions from the water-in-oil to a bi-continuous phase then inversion to oil-in-water occured in the system. Particle size of microemulsion system was measured by dynamic light scattering. The microemulsion phase of surfactant systems can be used for delivery of water-insoluble drugs in oral delivery. Results showed that microemulsion system of *Cucurbita pepo* oil can increase its solubility in water medium. Therefore, the microemulsion technique will be successful method in preparation of drug formulation of *Cucurbita pepo* oil.

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