Lecithin-based microemulsions for medical application

Trofimova Ekaterina Sergeevna

Abstract

The development of targeted drug delivery systems is one of the promising areas of application of nanostructured materials for medicine. Self-organizing nanostructures of phospholipids - lecithin organogels, liquid crystals and microemulsions - can act as carriers for transdermal drug delivery. These structures are lyophilic colloid systems, they are formed spontaneously when the components are mixed and can persist indefinitely provided that the chemical composition and temperature remain unchanged. Nanomaterials for medicine based on lecithin and other phospholipids have such advantages as biocompatibility, the ability to solubilize biologically active substances while maintaining their activity, and the ability to accelerate transport through the skin.

It is known that in the ternary systems lecithin - oil - water, reverse micelles exist, and microemulsions are not formed. To obtain microemulsions based on lecithin, it is necessary to introduce a cosurfactant. To develop a microemulsion for medical application, it is necessary to find non-toxic, biocompatible cosurfactants and organic solvents.

The aim of the research work is to develop a new microemulsion system based on lecithin for medical application, which contains biocompatible components.

To achieve the goal, it is necessary to find a solution to the following **tasks**:

1. To study the effect of a cosurfactant - oleic acid on the physicochemical properties of the lecithin - oleic acid - dodecane - water system, including the width of the region of existence of an organogel or microemulsion, viscosity, hydrodynamic diameter of aggregates, structural transition from a gel formed by cylindrical reverse micelles to a reverse microemulsion.

2. To study the effect of replacing highly purified lecithin with a phospholipid concentrate and dodecane with oils suitable for medical application

on the region of existence and properties of a lecithin-based microemulsion containing oleic acid.

3. To develop a composition and method of obtaining a lecithin-based microemulsion for medical application, to determine the main characteristics of the obtained microemulsion - viscosity, droplet size, temperature stability, solubilization capacity in relation to water and oil-soluble drugs, the rate of release of water-soluble biologically active substances.

Scientific novelty of the work

For the first time, the structural transition from lecithin organogel to microemulsion in the presence of a biocompatible cosurfactant, oleic acid, has been studied. It was shown that the low content of oleic acid ([oleic acid]:[lecithin]<0.1) in the lecithin - oleic acid - dodecane - water system leads to an expansion of the region of existence and a decrease in the viscosity of lecithin organogels. With a high content of oleic acid ([oleic acid]:[lecithin]>0.6) a reverse microemulsion exists in the system, with a viscosity of about 0.01 Pa·s, electrical conductivity less than 0.11 S/m and droplet size less than 10 nm.

On the phase diagram of the lecithin - oleic acid - dodecane - water system the region of existence of a reverse microemulsion was established at the ratio [oleic acid]:[lecithin]=0.8 and, for comparison, lecithin organogels at the ratio [oleic acid]:[lecithin]=0.1, at T=25ºC.

It has been established that the replacement of the organic solvent in the microemulsion in the lecithin - oleic acid - organic solvent - water system from dodecane to a mixture of vaseline oil, avocado oil and tea tree oil leads to a slight decrease in the maximum possible water content in the microemulsion; the maximum solubilization capacity is observed at the ratio [oleic acid]:[lecithin]=0.6-0.8.

It was shown by dialysis that the rate of transfer of a water-soluble dye into a physiological solution at T=37°C from the reverse microemulsion was $14.3 \cdot 10^{-3}$ g/m^2·h), which is higher than from the reverse emulsion ($9.9 \cdot 10^{-3}$ g/(m^2·h)) and from lamellar liquid crystals based on lecithin ($6.0 \cdot 10^{-3}$ g/(m^2·h)).

Practical significance

The composition of lecithin-based microemulsion for transdermal delivery of biologically active substances, containing a phospholipid concentrate – 14.3-23.3 wt.%, vaseline oil – 29.6-34.7 wt.%, oleic acid – 5.0 -7.1 wt.%, fatty vegetable oil – 29.6-34.7 wt.%, essential vegetable oil – 1.4-5.7 wt.% and water has been developed and patented, and a method for obtaining such a microemulsion has been developed.

The developed microemulsion can serve as a basis for medicinal products with prolonged release of drugs, containing water-soluble biologically active substances in concentrations of tenths of a wt.% and oil-soluble ones in concentrations of units of wt.%.

The possibility of creating a wound-healing composition based on the developed microemulsion is shown.

Defense Provisions

1. Structural transition from reverse cylindrical micelles to reverse microemulsion with an increase in the concentration of oleic acid in the system lecithin - oleic acid - dodecane - water; the microemulsion exists at a molar ratio of [oleic acid]: [lecithin]> 0.6.

2. Composition of a lecithin – based microemulsion for medical application, containing oleic acid as a cosurfactant, as well as vaseline oil, fatty vegetable oil, essential vegetable oil and water, and the main properties of the developed microemulsion.