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NANOEMULSION OBTAINMENT BASED ON NAFTALAN OIL

Abstract: The purpose of this work is to study the possibility of forming a nanoemulsion NE as vectors for the transportation of biologically active compounds into the human body. The process was investigated on a high-energy facility. The effect of the stirring rate, temperature, dispersed medium on the size of nanoparticles was investigated. The research of the size allotment of dispersed phase droplets in emulsion was carried out.

Key words: Naftalan oil, nanoemulsion, high-energy method, mechanical dispersing.

Language: English

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Introduction

The interest in nanoemulsions (NE) is constantly rising, since such dispersed systems are perspective in terms of use as a means of targeted delivery of medical and biologically active compounds.

Today, two methods are known to obtain them: high-low energy and combined. Among the high-energy methods, the main attention is paid to mechanical dispersion, dispersion under the effect of ultrasound, homogenization under pressure, as well as microfluidic and membrane methods. Among low-energy ones, phase inversion with the system composition or temperature changes, spontaneous emulsification. The combination of high and low-energy methods makes it possible to obtain reverse nanoemulsions in high-viscosity systems.

We set the target for us: preparation of an emulsion solution in laboratory conditions. In connection with the solution of this issue, the advantages and disadvantages of various methods for getting nanoemulsions at this stage were analysed and discussed and perspective areas of their application were taken into consideration.

Experimental part

The process was carried out in a valve homogenizer and consisted of two stages. At the first stage, the emulsion flow deviated at an angle of 90 ° from the direction of the initial movement. A movable flap-valve allows changing the thickness of the gap varying the flow rate of emulsified liquids and the pressure formed in the apparatus (Pic. 1). The homogenizers of this type operate continuously.

The droplet size in the obtained emulsion depends on the design of the valve and outlet, the viscosity of the emulsified system and the pressure formed in the apparatus. As the thickness of the gap between the piston and the outlet hole is 10-100 microns, very high fluid velocities of the order of hundreds of m / s occur [3].

The indwelling time of the emulsion in the gap is several milliseconds. The issue arose about the rate of surfactant adsorption accordingly. If the rate of adsorption of the surfactant is less than the rate of coalescence of the droplets, then even with the formation of nanosized droplets and the presence of a sufficient amount of surfactant, the droplets will become larger as soon as the emulsion leaves the homogenization zone. Nevertheless, even with the use

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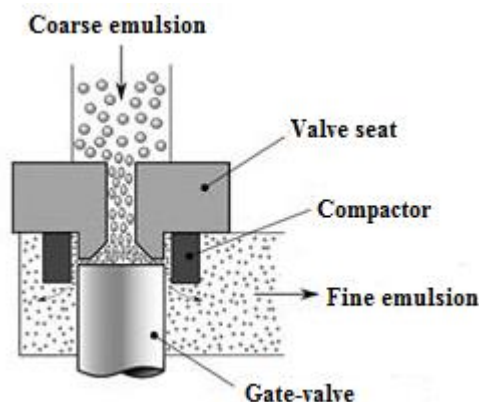
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of rapidly adsorbed surfactants, the effect of coalescence can be significantly reduced, but cannot be eliminated. Therefore, multiple circulation of the emulsion through the homogenizer is often applied. By means of effective stabilization, nanoemulsions can have relatively high kinetic stability. In order to stabilize nanoemulsions, a much lower concentration

of surfactants is required than to get microemulsions. The low content of surfactants in nanoemulsions can significantly reduce the negative effect of surfactants in the practical application of such emulsions in pharmaceutical, cosmetic, food and other industries. We solved this issue by combining surfactant and emulsifier in one Tween 80.



Pic. 1. Schematic image of emulsification in a valve homogenizer

For identifying the type of the obtained nanoemulsion, we used the dilution method. It consists of adding a small amount of liquid to the emulsion, which forms one of the phases of the nanoemulsion. The liquid, which is a dispersion medium, easily dilutes W/O (water-oil) O/W (oil-water), i.e. nanoemulsion, while the dispersed phase cannot dilute it. As in our case, a drop of nanoemulsion was uniformly distributed in water; we designated it as a direct nanoemulsion.

Research methods

The research of dispersed phase droplets in nanoemulsions was carried out by means of such methods like conductometry, dynamic light scattering, differential scanning calorimeter, polarizing optical microscopy, transmission electron microscopy [2, 8].

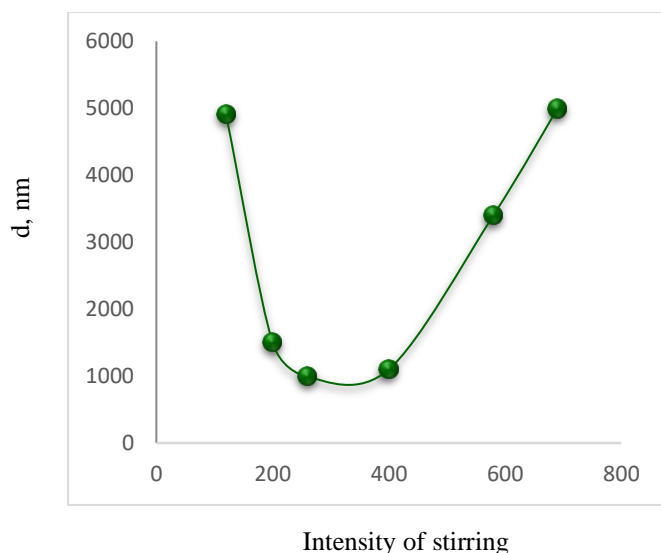
The effect of the intensity of stirring on the droplet size of the dispersed phase was studied. The

size of the dispersed phase droplets in nanoemulsions depends on the intensity of stirring. The effect of stirring on the diameter of the dispersed phase droplets was examined experimentally (Pic. 2). In this work, nanoemulsions containing 20 vol. % of Naftalan oil and 10 vol. % Of Tween 80 were examined.

The components of the nanoemulsion were mixed at a temperature of 25°C on a power mixer with a stirring speed of 100-3000 rpm and simultaneously drop wise using a peristaltic pump ($v = 2.5 \text{ ml / min}$) and distilled water of 0.17 M was added. It can be seen from Pic. 2 that an increase in the mixing intensity led to a decrease in the droplet size only at a low mixing intensity. Thus, with an increase in the stirring speed from 150 to 300 rpm, the diameter of the dispersed phase droplets sharply decreased from 5000 to 1000 nm. In the range of 300-500 rpm, the diameter of the dispersed phase droplets practically did not change and was in the range of 1300-1500 nm [1].

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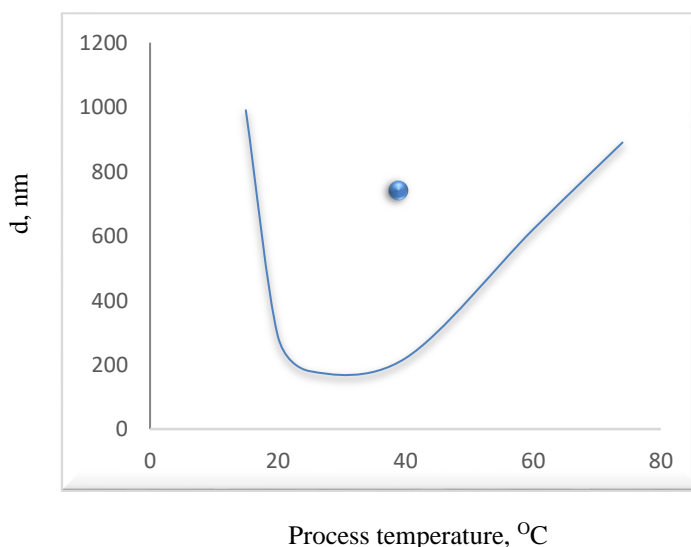


Pic. 2. Droplet size of the dispersed phase dependency on the intensity of stirring.

Thus, at a stirring intensity of 300-500 rpm, droplets of the dispersed phase of the smallest size were obtained. It should be noted that in this case, the formation of emulsions with relatively large droplets also occurred; therefore, the effect of temperature on the dispersion of emulsions was studied.

The effect of the temperature of the process of obtaining nanoemulsions on the droplet size of the

dispersed phase of the emulsion was obtained at temperatures from 25 to 70°C on a driven mixer with a stirring speed of 400 rpm. 0.17 M distilled water was added drop wise using a peristaltic pump ($v = 2.5 \text{ ml / min}$). In fig. 4 the dependence of the droplet size of the dispersed phase on the temperature of the process of obtaining emulsions is given [1].



Pic. 3. Dispersed phase droplet size dependency on the nanoemulsions obtainment temperature.

The concentration of Tween 80 is 5 vol.% from the data presented, it can be concluded that with an increase in temperature from 13 to 20°C, the diameter of the dispersed phase droplets sharply decreased, in the temperature range 20-40°C the diameter of the droplets was 225-285 nm, at temperatures above 40°C the droplet size increased. Consequently, at room

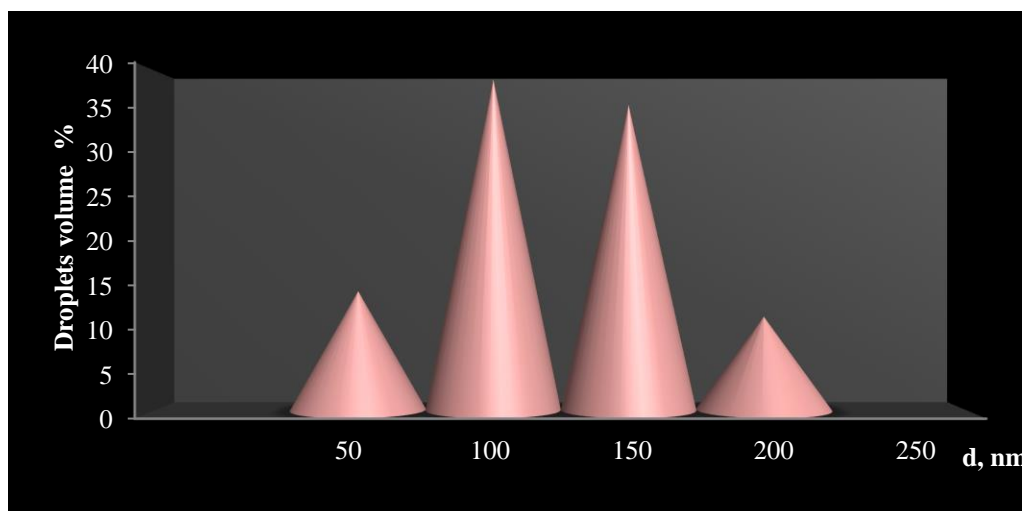
temperature 20-25°C, the average diameter of the dispersed phase droplets was the smallest.

Afterwards, we investigated the size distribution of dispersed phase droplets in an emulsion stabilized with Tween 80 at a stirring speed of 3000 rpm for 15 min. The emulsions with the smallest droplet size were obtained by dispersing at a temperature of 25°C

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with a mixture consisting of 25% Naftalan oil, 13.5% surfactant (Tween 80) and 61.5% distilled water (Pic.4).



Pic.4. Size distribution of dispersed phase droplets in an emulsion stabilized with Tween 80 obtained by high-energy dispersion.

The features of Ostwald ripening are analysed. Methods for reducing the rate of this process are considered because it is especially relevant for nanoemulsions, in which it is often the main one and leads to the destruction of these dispersed systems limiting their practical application [3, 6, 7].

According to the literature [4, 5, 10, 14], if the fraction of the dispersed phase is in the range of up to 5 vol.%, then the rate of Ostwald ripening is practically independent of the concentration of the dispersed phase. In order to determine the values of the rates of Ostwald ripening in nanoemulsions stabilized with Tween 80, nanoemulsions with a dispersed phase fraction of 25-vol. % were diluted with 0.17 M distilled water to dispersed phase concentrations from 1 to 5 vol. %. Then, we studied the change in the size of the dispersed phase droplets from time to time.

The research has shown that the droplet size distributions in nanoemulsions stabilized with Tween 80 has only one maximum, which indirectly indicates the absence of coagulation. From time to time, the position of the maximum shifted to the area of large values. This once again proved the correct choice of the emulsifier [11-13].

Conclusions and discussions

A nanoemulsion based on naphthalene oil was obtained by the method of high-energy dispersion.

The process was carried out in a valve homogenizer and consisted of two stages. The effect of stirring speed, temperature was investigated. We chose Tween 80 as an emulsifier. It was also a surfactant to stabilize the resulting emulsion. The dependence of the droplet size of the dispersed phase on the intensity of stirring, the dependence of the droplet size of the dispersed phase on the temperature of obtaining nanoemulsions was studied, and the character of the size distribution of the dispersed phase droplets in the emulsion stabilized with Tween 80 was investigated.

NEs are thermodynamically unstable systems; they undergo the same processes leading to delamination as in conventional emulsions. There is practically no sedimentation in the NE, since the droplet size is very low and the speed of the Brownian motion is high. The coalescence, as in traditional emulsions, can be significantly slowed down, with the right choice of emulsifier.

As a rule, direct NEs are not resistant to Ostwald ripening (isothermal distillation), during which smaller droplets dissolve and larger ones increase in size. Even if an NE with a very narrow droplet size distribution is obtained, due to the difference in droplet size, there is a difference in the chemical potential of the substance inside the droplets. In result, Ostwald ripening occurs, the coarsening of the droplets of the internal phase, which inevitably leads to the subsequent stratification of emulsions.

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