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Investigation Ultrasound Influence On The Size Of Niosomes Vesicles On The Based Of PEG-12 Dimethicone.

EI Diskaeva[1]*, IA Bazikov[2], OV Vecher[1], Elbekyan KS[3], and LS Mecyaceva[1].

[1]Department of Physics and Mathematics, Stavropol State Medical University, Russian Federation, 355017.
[2]Department of Microbiology, Stavropol State Medical University, Russian Federation, 355017.
[3]Department of General and Biological Chemistry, Stavropol State Medical University, Russian Federation, 355017.

ABSTRACT

The purpose of the present investigation is to study and evaluate influence ultrasound on the size of niosomes. Particle size was defined with analysis electronic microscopy images. On the base of electron-microscopy investigation of niosomal dispersion was constructing column charts of the particle size distribution. The numerical analysis has shown that sonication leads to an equalization of the particle size distribution in the range (50-130 nm) i.e. allows obtain a homogenous niosomal dispersion.

Keywords: niosomes dispersion, a homogenous niosomal dispersion, sonication

Corresponding author

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INTRODUCTION

During the last decades, was occurred serious changes in the field of improving the pharmaceutical properties of medicaments [1-3]. Unique approaches have been developed, which let principle change the properties of medicines: make them more effective, give them targetedness, and reduce side effects. For this aim widely use nano- and micro sized carriers of drugs such as liposomes, fullerenes, niosomes, dendrimers and others. In practice liposomes (micro- and nanoscale colloidal spheres, which consist of the lipid layer surrounding the active drug) are most often used for the targent drug delivery system and as an alternative to them – niosomes (single or multichamber vesicles formed by two-layer membrane structures consisting of non-ionic surfactants).

The advantage of application niosomes explained with a several of reasons [4].

- Unlike liposomes, niosomes are not susceptible to oxidation.
- They have delayed clearance thus provides high therapeutic performance.
- They do not require any special storage condition.
- The vesicle suspension is water based thus provides the increased patient compliance over the oily based dosage form.
- Niosomes are osmotically active.
- They are stable and impart stability to the entrapped drug.

Niosome studied in this article are spherical vesicles with the size 20-200 nm, consist of a shell in the form of a water-insoluble double layer of a nonionic emulsifier (surfactant), which are esters of polyethylene glycol and polydimethylsiloxane backbone and encapsulated biologically active substance inside the capsule.In each case of application of the niosomal form of drug delivery, are need vesicles with different parameters, which may depend, for example, on encapsulated preparations, and also have different physicochemical properties [5, 6].

In contemporary literature are described the methods for obtained multilamellar niosomes, large monolamellar niosomes and small monolamellar niosomes with the help of sonication[7-13]. At the same time, the question of the influence of ultrasound on the prepared niosomal dispersion, on the process of its dispergation has not been studied sufficiently.

It is known that the influence of ultrasound on colloidal systems is associated, first of all, with the phenomenon of cavitation.

Cavitation is the formation of voids, or bubbles, in a structure during the rarefaction phase of a sound wave. These bubbles may grow with changes in pressure or collapse during the positive pressure phase, generating strong hydrodynamic perturbation in the liquid.

Thus in liquid take place destruction of the surface of solids bordering with the cavitating liquid.

Additionally, the effect of ultrasound is accompanied by an intensification of mass transfer processes, an increase in the temperature of the colloidal system, and the formation of free radicals.

All these effects depend both on the intensity of the ultrasonic effect, and on the frequency of ultrasound and the time of exposure. It is especially necessary to note the decrease of the particles sizes of the dispersed phase, the increase in the homogeneity of the colloid system upon exposure to it by ultrasound. The size of niosomes is very important in terms of their application.

In some cases, are required a large niosomes, for example, when encapsulated particles included microorganisms, such as bacteria, for produce vaccines.

However, smaller niosomes are more preferable. This is due, firstly, to the fact that they are not so rapidly absorbed by the reticuloendothelial system (RES). The seizure of RES by the nios is increasing with increasing sizes. Secondly, if niosomes are less, then higher their penetration into the deeper layers of the skin

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Monolamellar niosomes (diameter~100 nm) have a thin elastic membrane, which allows one to efficiently move along intercellular spaces, lymphatic and blood capillaries. Dimethicone, which forms a bilayer structure in an aqueous medium, makes it possible to obtain an ultra-thin and elastic membrane niosomes. The particle size distribution, the change in their dispersity with concentration, are also very significant for solving problems of stabilizing niosomes.

MATERIAL AND METHODS OF THE RESEARCH

To study the effectiveness and expediency of using ultrasound to create stable colloidal nanosystems, experimental studies were carried out on the irradiation by ultrasound (880 kHz) of aqueous solutions of niosomes on the basis of PEG-12 Dimethicone. The sonication was performed for 5 to 20 minutes.

The methodology of the work includes two preparatory stages. At the first stage, direct preparation by niosomes is carried out.

To obtain the capsules of silicone nature we used physic-chemical methods for the synthesis of molecules. The shell of the obtained niosomes vesicles generated from PEG-12 Dimethicone. In the hydrophilic part of dimethicone there are functional groups of silicon oxide. The length of the Si-O bond was 1.6 Å, which is much longer than the C-C bond of 1.4 Å. Due to this, the functional groups of the molecules are able to rotate with respect to each other. The use of PEG-12 Dimethicone promoted the formation of vesicles without significant energy effort. The Si-O-Si bond angle was 130 degrees, in contrast to the 109 degrees C-C-C bond, which increased the elasticity and stability [14]. The stage of formation of vesicles occurred with intensive mechanical mixing of the mixture using an automatic reclosure homogenizer.

On the next step samples were diluted with ultrapure water (C=0.01%) and sonicated for 5-20 minutes using a sonicator with frequency 880 kHz and power 1 kWt.

Microscopically images of niosomes, made immediately after preparation and after sonication, are given in Fig. 1.

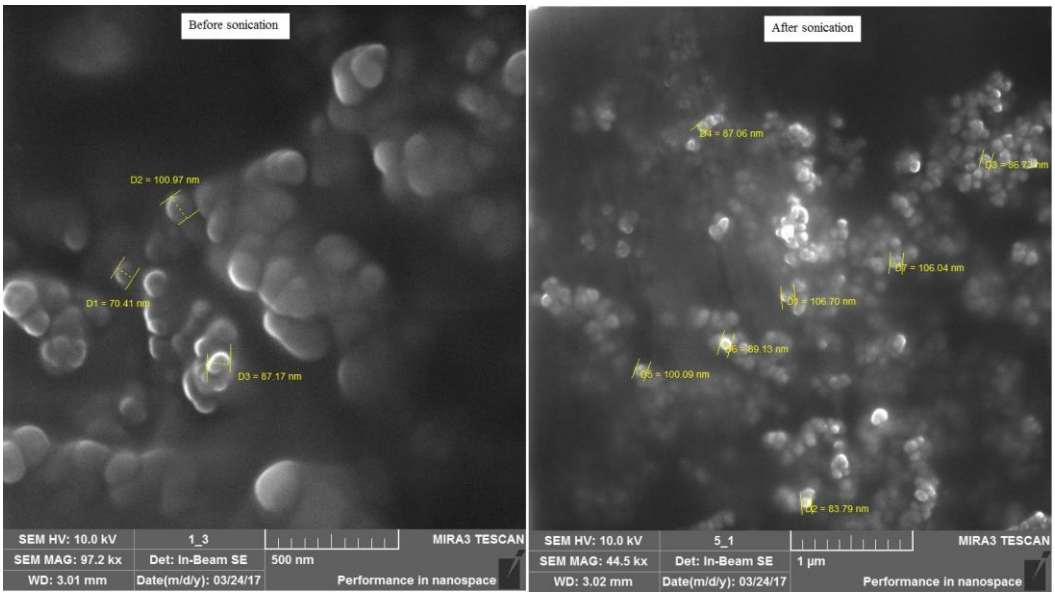

Figure 1: Scanning electron microscopy (SEM) micrographs of niosomes before/after sonication

RESULTS AND DISCUSSIONS

As can be seen from Fig. 1, the original niosomes are polydisperse and multilayered. The determination of the size of the niosomes was carried out by processing micrographs using the ImageJ program [15]. According to the obtained data, histograms of particle size distribution were constructed.

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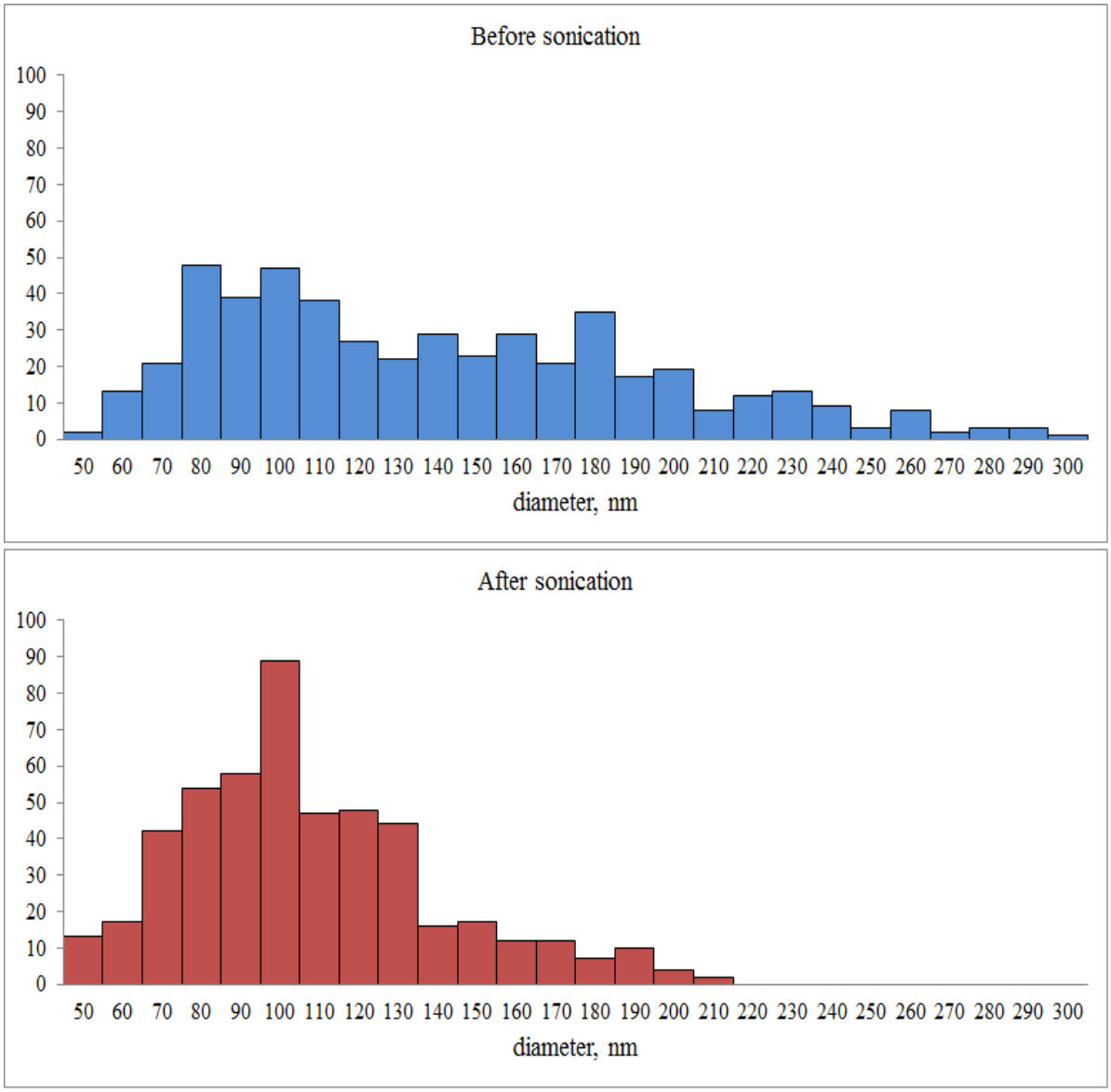

Figure 2: Column charts of particle size distribution in niosomal dispersions before/after sonication

Sonication leads to equalization of the distribution of niosomes in size and destruction of multilayer structures. For given conditions (temperature, surfactant concentration), spherical single-layer niosomes of a fixed size possess the maximum thermodynamic stability, and ultrasound irradiation facilitates the transition by niosome to the average equilibrium form.

Fig. 3 shows the dependence of the average effective diameter by the irradiation time. It is important to note that further ultrasonic treatment (including at increased power) does not alter the average diameter of the niosomes (after 15 minute of sonication), which is connected with their attaining thermodynamic equilibrium and stability.

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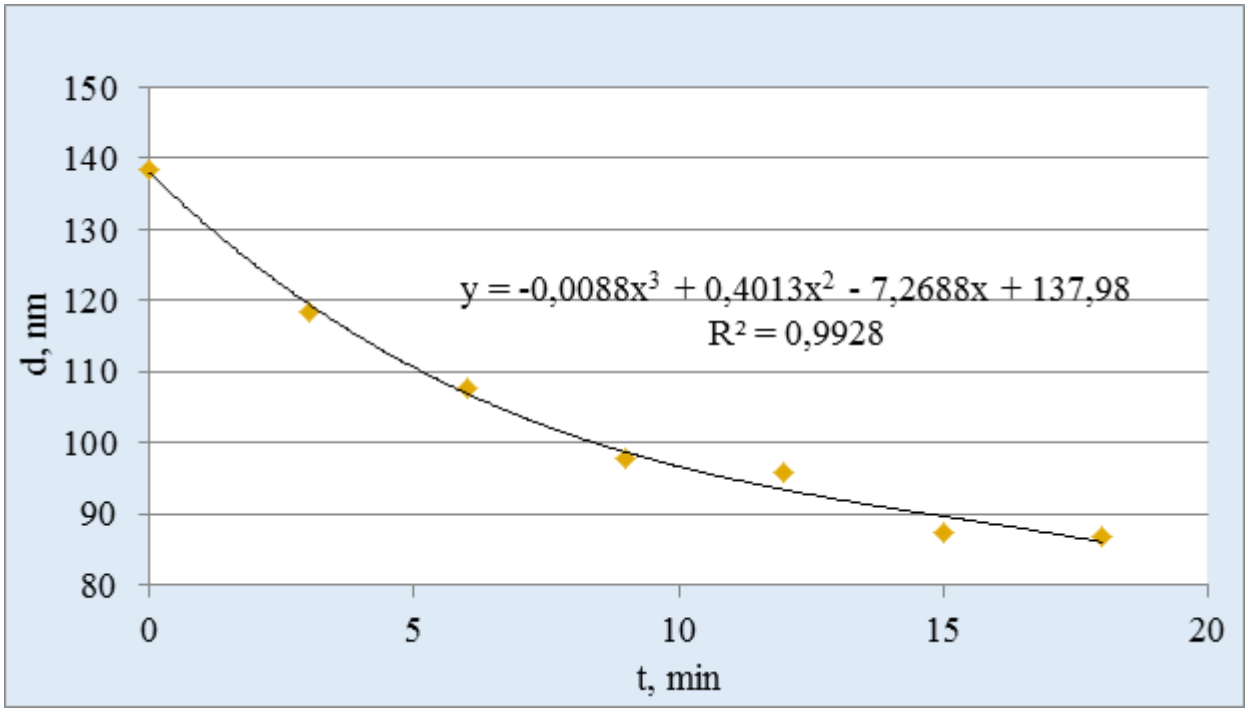

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Figure 3: The average effective diameter as a function of irradiation time

Described method allows to obtain single-layer niosomes with controlled average diameter and narrow size distribution in a relatively simple and easily accessible way, without use of additional processing methods.

CONCLUSIONS

As a result of the research, the use of sonication makes it possible to obtain homogeneous niosomal preparations that have a deeper level of penetration and enhanced selectivity of accumulation. The decrease in the proportion of large particles in the composition of the niosomal dispersion also prevents the rapid removal of drugs.

Additionally, cavitation processing of niosomal dispersion with the help of ultrasound contributes to its stabilization and makes possible long-term storage without violating the integrity of the vesicles.

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