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Research paper

Nano- and microcapsules as drug-delivery systems

M.Y. Koroleva *, T.Y. Nagovitsina, D.A. Bidanov, O.S. Gorbachevski, E.V. Yurtov

Department of Nanomaterials and Nanotechnology, Mendeleev University of Chemical Technology, 125047 Moscow, Russia

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Abstract

Preparation of nano- and micrometer-size capsules with lipid core might have several biomedical applications for delivery of lipophilic drugs. Successful usage of these nano- and microcarriers depends on their colloidal stability. Emulsion based carriers for drug delivery: nanoemulsions, colloidosomes, and solid lipid particles have been investigated in this work. Diameters of oil droplets in nanoemulsions are equal to 15 and 20 nm, however they are not stable to phase separation. In spite of large droplet diameters (several tens of micrometer), colloidosomes stabilized by heteroaggregates of oppositely charged SiO_2 nanoparticles are stable toward creaming. Paraffin emulsions stabilized by Carbopol 940 have particles 190 nm in size and are also stable to creaming during several months. Encapsulation of lipophilic drugs tocopherol, hydrocortisone, nimesulide or curcumin does not cause changing diameters of nanoemulsion based nanocapsules. Incorporation of these drugs in paraffin particles leads to decreased or increased particle sizes, but in all specimens the sizes are equal or less than 700 nm and such particles can be used as microcapsules for lipophilic drug delivery.

Keywords: Nanocapsules; Microcapsules; Nanoemulsions; Colloidosomes; Solid liquid particles; Drug delivery

1. Introduction

The nano- and microcapsules are currently promising systems for drug delivery in the treatment of many types of diseases [1]. Nano- and microcarriers have also been employed as imaging tools that makes possible to increase imaging resolution and highlights small lesions which are undetectable with traditional methods [2,3].

In the case of the administration of drugs using nano- and microcapsules a prolonged drug release with controlled rate may be achieved. Many of pharmacologically active compounds exhibit poor water solubility that requires the creation of new carriers for their administration and delivery. One of the most promising approaches is using appropriate lipid vehicles. Rational design of delivery system can lead to the success of lipid based drug delivery systems [4,5].

A variety of lipid-based systems can be obtained based on the type of excipients and formulation variables [6]. Colloidal systems such as nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, liposomes, niosomes, and colloidosomes have materialized great means toward improved targeted delivery of drug cargoes [7].

Emulsion based carriers: nanoemulsions, solid lipid particles, and colloidosomes were investigated in this paper. Nanoemulsions are emulsions with oil or water droplets that sizes are at most 100 nm. They can encapsulate either lipophilic and hydrophilic drugs or imaging agents in the oil or in the aqueous phase [8,9]. Nanoemulsions can be prepared by high-energy stirring, ultrasonic emulsification, high-pressure homogenization, microfluidics, and membrane emulsification [10] or by low-energy methods, e.g., phase inversion temperature or composition methods [11], spontaneous emulsification [12].

Low-energy methods of nanoemulsion preparation such as phase inversion temperature and phase inversion composition methods are of particular interest recently because they are non-destructive for encapsulated molecules, energy-saving and attractive for large-scale production [11]. Molecules of surfactant, especially nonionic ethoxylated surfactants, show appreciable affinity for aqueous phase at low temperatures due to hydration of polar groups and affinity for oil phase at elevated temperatures because of dehydration of oxyethylene groups. If a W/O emulsion stabilized by ethoxylated surfactant is prepared at elevated temperature and then rapidly cooled, an O/W nanoemulsion is formed through the phase inversion.

* Corresponding author. Department of Nanomaterials and Nanotechnology, Mendeleev University of Chemical Technology, 125047 Moscow, Russia. Fax: +7 495 495 2116.

E-mail address: m.yu.kor@gmail.com (M.Y. Koroleva).

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Solid lipid particles are obtained from nanoemulsions or macroemulsions. Emulsions are prepared at temperatures higher than the melting point of the lipid and cooled to ambient temperature which causes crystallization of the lipid and, as a result, solid lipid particle formation [10].

Colloidosomes are hollow-porous microcapsules which are formed because of self-assembling colloidal particles of different sizes and shapes on the surface of emulsion droplets [13,14]. The self-assembled shell of colloidosomes differs from the shells of other carriers since it consists of the particles and voids between them, and so it is penetrable for drugs encapsulated in the core [15].

Nanoemulsions, solid lipid particles, and colloidosomes are thermodynamically unstable systems. The main mechanism of nanoemulsion coarsening is Ostwald ripening [16], i.e., the dissolution of smaller oil droplets and the growth of larger ones.

Droplet aggregation takes place if the attractive forces between oil droplets exceed the repulsion ones. If aggregation occurs, the tendency of subsequent coalescence of liquid droplets increases. Solid lipid particles are free from these limitations but these systems are usually unstable toward creaming.

Stability toward creaming can be achieved by steric stabilization of emulsions and the formation of hydrogel in the aqueous phase. For this purpose cross-linked polyacrylate polymers are usually used. Solid lipid nanoparticles in such hydrogel are stable for a period of six months [17].

In colloidosomes templated from Pickering emulsions, the adsorption of particles on the oil–water interface provides steric hindrance to drop–drop coalescence. However Pickering emulsions are much less stable to creaming also.

Solid particles with diameters more than 100 nm can form monolayer on the surface of emulsion droplets. Nanoparticles are adsorbed mainly as aggregates at the water/oil interface [18]. Aggregation of solid stabilizers may be caused by the introduction of electrolytes, surfactants or by change of pH of the aqueous phase in emulsions [19,20]. Colloidosomes can be functionalized with magnetic, semiconductor and other particles [21–23], that increases the fields of these colloidosome applications.

The aim of the present study is to examine the impact of various stabilizers on particle sizes and stability of emulsion based colloid systems such as nanoemulsions, solid lipid particles, and colloidosomes. The effect of lipophilic drugs encapsulation on droplet diameters in nanoemulsion and paraffin particle sizes has been investigated.

2. Materials and methods

2.1. Chemicals

Nonionic surfactants: polyethylene(4)glycol dodecyl ether (Brij 30, HLB 9.7 to 20 °C), polyoxyehylene(20)sorbitan monooleate (Tween 80, HLB 15.0), sorbitan monooleate (Span 80, HLB 4.3) (≥60%), polyoxyethylene sorbitan monostearate (Tween 60, HLB 14.9), sorbitane monostearate (Span 60, HLB 4.7) (45–55%) were purchased from Sigma-Aldrich, cetyl/oleyl acohol ethoxylate EO 10 (Eumulgin O10, HLB 12.5) was purchased from BASF (Germany). **Poly(vinyl alcohol)** Mowiol® 8–88 (PVA, Mw ~ 67 000 was received from Sigma-Aldrich (Steinheim, Germany) and used as polymer stabilizer. Cross-linked polyacrylate Carbopol 940 (Acros organics, USA) was used as gelling agent.

NaCl (extra pure) and NaOH (analytical grade) were provided by Merck (USA).

Liquid paraffin (Britol 20 USP) was obtained from Sonneborn and used as oil phase in nanoemulsions. Paraffin wax was purchased from Lukoil (Russia).

Negatively charged silica particles Ludox HS-30 and positively charged alumina-coated silica particles Ludox CL were purchased from Sigma-Aldrich as 30 wt.% aqueous dispersions at pH 9.8 and 4.5, respectively. The average particle diameter is 10 nm for Ludox HS-30 and 30 nm for Ludox CL as determined by dynamic light scattering. Silica nanoparticles were used as solid stabilizers.

(+)-α-Tocopherol, hydrocortisone (≥98%), nimesulide, curcumin (≥65%) were obtained from Sigma-Aldrich and used as model drugs.

All materials were used as received without further purifications. Bidistilled water was used throughout the study.

2.2. Preparation on nano- and microcapsules

2.2.1. Preparation of nanoemulsions

Oil-in-water nanoemulsions were prepared by the phase inversion temperature method [11]. W/O emulsion was prepared as follows. Liquid paraffin (0.5–4.3 ml), Brij 30 (0.1–0.8 ml) or mixture of Tween 80 and Span 80 (0.5–1.3 ml), and aqueous solution (5.0–8.8 ml) of NaCl (0.15 M) were heated to 80 °C and dispersed for 15 min at 1000 rpm in magnetic stirrer (IKA RCT Basic, Germany). Obtained W/O emulsion was immediately cooled in an ice bath under stirring at 1000 rpm until 5–10 °C temperature was reached. O/W nanoemulsion was formed because of phase inversion.

2.2.2. Preparation of colloidosomes

O/W Pickering emulsions stabilized by heteroaggregates of oppositely charged SiO_2 nanoparticles were prepared as follows. Aqueous dispersions of silica particles Ludox HS-30 or Ludox CL were diluted to the required concentrations by bidistilled water and mixed. The pH value was adjusted to 6 with 0.1 M HCl or NaOH aqueous solution. Aqueous dispersion of heteroaggregates (15 ml) was added to liquid paraffin (15 ml) and pre-homogenized in a magnetic stirrer at 1000 rpm for 2 min. The primary emulsion was then further homogenized using in a high shear mixer (Ultra-Turrax T 25, IKA, Germany) at 11 000 rpm for 2 min.

2.2.3. Preparation of paraffin emulsions

Paraffin emulsions were prepared by the high-share homogenization method. Three grams of paraffin was melted and heated at 75 °C. Aqueous solution (27 ml) of Eumulgin O10 (0.3 g), and PVA (0.03–0.15 g) or Carbopol 940 (0.01–0.10 g) was previously heated to 75 °C and added to melted paraffin. Concentration of paraffin and Eumulgin O10 in next prepared emulsions was fixed and equal to 10 and 1 wt.%, respectively. This mixture was homogenized in Ultra-Turrax T 25 for 10 min.

Obtained emulsions were cooled to ambient temperature in a magnetic stirrer at 200 rpm. In the case of stabilization by Carbopol 940 aqueous phase of paraffin emulsions was neutralized by 0.1 M NaOH aqueous solution before cooling for gelation of Carbopol 940 hydrogel.

2.3. Characterization of nanocapsules and microcapsules

2.3.1. Particle size analysis

The particle size distribution and mean diameter were analyzed by dynamic light scattering using laser analyzer (Zetasizer Nano ZS, Malvern Instruments, UK) at scattering angle of 173° using He–Ne laser with $\lambda = 633$ nm. Each measurement was the average of 14 runs. Measurements were carried out at 20 °C.

Nanoemulsions were not diluted before measurements. Paraffin emulsions were diluted 100-fold with bidistilled water.

2.3.2. Transmission electron microscopy

A transmission electron microscope (TEM) (JEOL JEM-1011, Japan) operating at 80 kV was used to evaluate sizes and morphology of nanoemulsions, Pickering emulsions, and paraffin particles. Negative staining by uranyl acetate was applied for visualization in TEM analysis.

2.3.3. Optical microscopy

The droplet size and morphology of Pickering emulsions were investigated by optical microscopy using a microscope (Carl Zeiss Axiostar Plus light microscope, Germany), equipped with a digital camera Canon. Emulsions were diluted 10-fold with HCl aqueous solution with pH value equal to 6. The samples were prepared by direct deposition of aliquots on glass slides. Average sizes for the samples have been estimated directly from about 50 images.

3. Results and discussion

3.1. Nanoemulsions stabilized by nonionic surfactants

Different parameters may influence on droplet sizes in emulsions. It is known that increasing surfactant concentration to a certain value leads to decrease in the sizes of nanoemulsion droplets [24]. On the other hand, an increase of the dispersed phase fraction in emulsion at fixed surfactant concentration results in an increase of droplet diameters [11].

Nanoemulsions prepared by phase inversion temperature method and stabilized by Brij 30 were investigated in the present work. The relationship between the droplet sizes of the obtained nanoemulsions and the volume fractions of the oil phase at different Brij 30 concentrations is shown in Fig. 1.

The droplet diameters are reduced to 15–30 nm and then almost plateaued as the volume fraction of liquid paraffin in nanoemulsion increases. The further enhancement in oil phase fraction leads to sharp increase in droplet sizes.

At low concentrations of liquid paraffin, the amount of Brij 30 is insufficient to stabilize W/O emulsions and these emulsions produce larger droplets during phase inversion. At high concentrations of liquid paraffin, the amount of Brij 30 is not enough to stabilize oil droplets in O/W nanoemulsions. Coalescence of nanodroplets takes place after phase inversion and as a result coarse emulsions are formed.

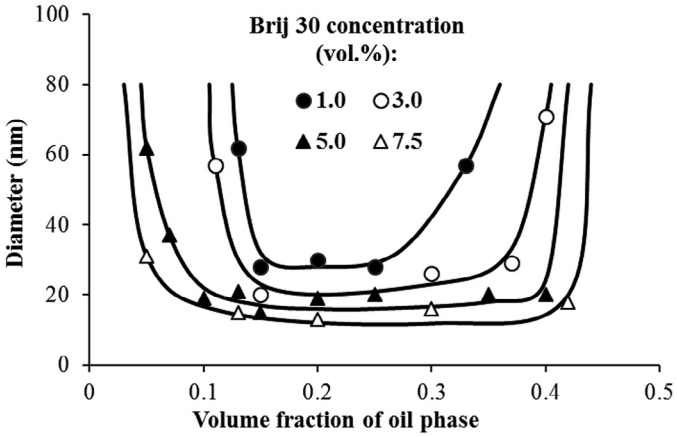

Fig. 1. Droplet diameters as functions of volume fraction of liquid paraffin in nanoemulsions stabilized by Brij 30.

Increasing surfactant concentration from 1.0 to 7.5 vol.% leads to decrease in droplet sizes from 30 to 15 nm on the plateaus of plots (Fig. 1).

If hydrophilic–lipophilic balance of surfactant is not sensitive to temperature variations, mixtures of low HLB and high HLB surfactants are used for nanoemulsion preparation. Nonionic surfactants Tween 80 (HLB 15) and Span 80 (HLB 4.3) can be used for these purposes [25].

The effect of molar ratio of Tween 80 to Span 80 on droplet sizes in nanoemulsion was studied. Volume fraction of liquid paraffin in nanoemulsions was 0.25. Droplet diameters as functions of molar ratio of Tween 80 to Span 80 are presented in Fig. 2.

Diameters of oil droplets steeply decrease with increasing the molar ratio of Tween 80 to Span 80. The minimum size observed at Tween 80/Span 80 ratio equals to 0.76. Further enlargement of Tween 80 fraction in surfactant mixture is followed by an increase in the droplet diameters.

If Span 80 prevails in emulsions, the amount of high HLB surfactant is insufficient to stabilize O/W nanoemulsions. After

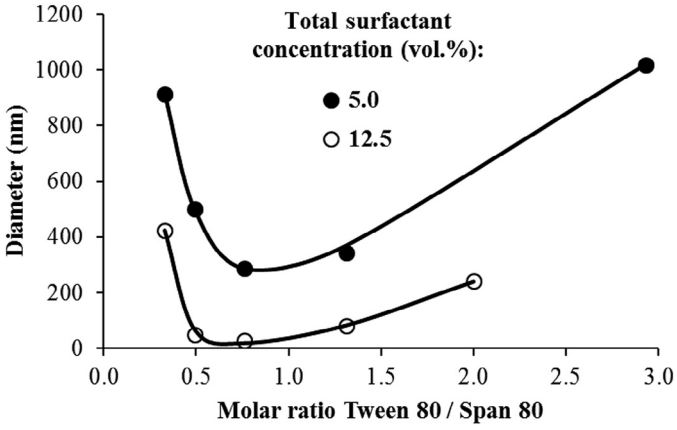

Fig. 2. Droplet diameters as functions of molar ratio of Tween 80 and Span 80. Volume fraction of oil phase is 0.25.

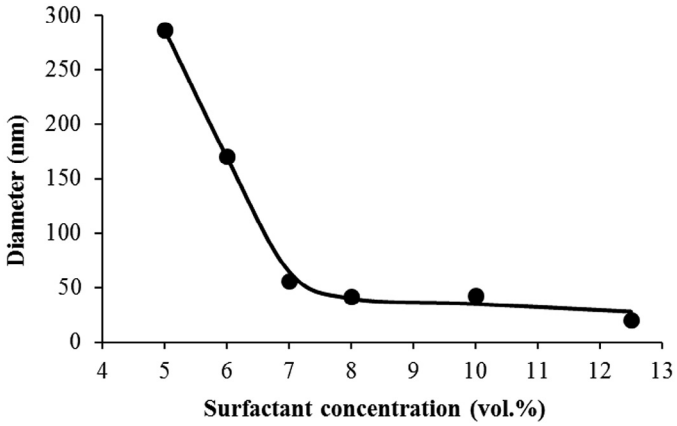

Fig. 3. Droplet diameter as a function of the total concentration of Tween 80 and Span 80. Volume fraction of liquid paraffin in nanoemulsions is 0.25, molar ratio of Tween 80 to Span 80 is 0.76.

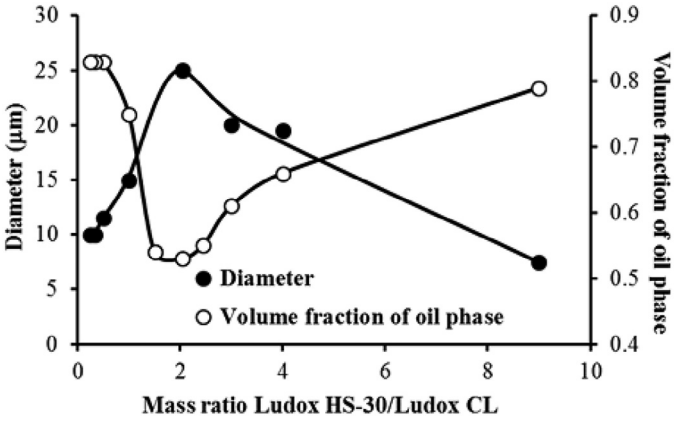

Fig. 4. Droplet diameter and volume fraction of oil phase as a function of mass ratio of Ludox HS-30 to Ludox CL nanoparticles in Pickering emulsions. Initial fraction of oil phase is 0.5.

phase inversion, the coalescence of oil droplets is rapid and large drops are formed. At high Tween 80 concentrations, the amount of low HLB surfactant is insufficient for the stabilization of W/O emulsion from which O/W nanoemulsion is produced upon cooling the system. This also results in an increase in droplet sizes [26].

Droplet diameter as a function of total concentration of Tween 80 and Span 80 is presented in Fig. 3. Volume fraction of liquid paraffin in nanoemulsions is 0.25, the molar ratio of Tween 80 to Span 80 is equal to 0.76.

Diameters of liquid paraffin droplets decrease sharply from 290 to 55 nm with increasing surfactant concentration from 5 to 7 vol.%. At higher surfactant concentrations, decreasing sizes is less significant – from 55 to 20 nm.

Thus, nanoemulsions stabilized by nonionic surfactants Brij 30 or mixtures of Tween 80 and Span 80 with droplet sizes of 15–20 nm can be prepared by the phase inversion temperature method. However these nanoemulsions are not stable and the phase separation occurs during 7–11 days.

3.2. *Colloidosomes formed by SiO_2 nanoparticles*

As it is known, nanoparticles are adsorbed mainly as aggregates at the water/oil interface [18], since they undergo intensive Brownian motion. If the electrostatic repulsion between nanoparticles is lowered, their kinetic energy is sufficient to overcome the potential barrier and particle aggregation takes place.

In the case of oppositely charged nanoparticles, heterocoagulation occurs and heteroaggregates adsorb onto the surface of droplets in emulsions.

The effect of oppositely charged silica nanoparticles on the formation and stability of colloidosomes was investigated. Hydrophilic negatively charged nanoparticles Ludox HS-30 and positively charged nanoparticles Ludox CL were used. The total concentration of oppositely charged nanoparticles in aqueous phase of emulsions was 3 wt.%. Volume fraction of liquid paraffin in O/W Pickering emulsion was 0.5.

Average droplet diameters in freshly prepared O/W emulsions increase from 7.5 to 25.0 μm with increasing mass ratio of Ludox HS-30 to Ludox CL in the mixture up to 2 (Fig. 4). At higher Ludox HS-30/Ludox CL ratios droplet sizes decrease.

Obtained Pickering emulsions were incubated at room temperature and time-dependent creaming profiles were determined. Experiments have shown that emulsions underwent visible phase separation of water. This process was more intensive during the first two weeks of emulsion aging. During a longer period of time, emulsion creaming almost stopped.

As the aqueous phase was partly segregated, the oil fraction in unseparated part of emulsions increased. Fig. 4 presents the effect of mass ratio of Ludox HS-30 to Ludox CL nanoparticles on the oil phase fraction in emulsions after 2 weeks.

Increasing the ratio of negatively charged nanoparticles Ludox HS-30 to positively charged nanoparticles Ludox CL in the mixture from 0.25 to 2.00 leads to enhancement of the emulsion stability. If mass ratio Ludox HS-30/Ludox CL is equal to 0.25, emulsion creaming leads to increasing oil phase fraction up to 0.83, i.e., the major part of water is segregated from emulsions.

The most stable emulsions occur under conditions where mass ratio Ludox HS-30/Ludox CL is in the range 1.5 to 2.5. Very small amounts of water separate from these emulsions and the fraction of oil phase increases only from 0.50 to 0.53–0.55 after 2 weeks. At higher fraction of Ludox HS-30 in the mixture of SiO_2 nanoparticles, emulsion stability toward creaming decreases.

These phenomena can be explained by competitive processes: heterocoagulation of oppositely charged SiO_2 nanoparticles and their adsorption on the surface of oil droplets. At low and high fractions of Ludox HS-30, the growth of aggregates is terminated at an early stage because they acquire the same sign of charge [27]. Nevertheless nanoparticle adsorption on the surface of oil droplets occurs. Emulsions with nanoparticle-adsorbed layer on the surface of oil droplets are more stable toward coalescence hence droplet sizes in these emulsions are lower. However such emulsions are unstable toward creaming because small nanoparticle aggregates are not able to reduce significantly the rate of droplet approaching.

For mass ratios between 1.5 and 2.5, extensive aggregate growth occurs with the formation of heteroaggregates with net

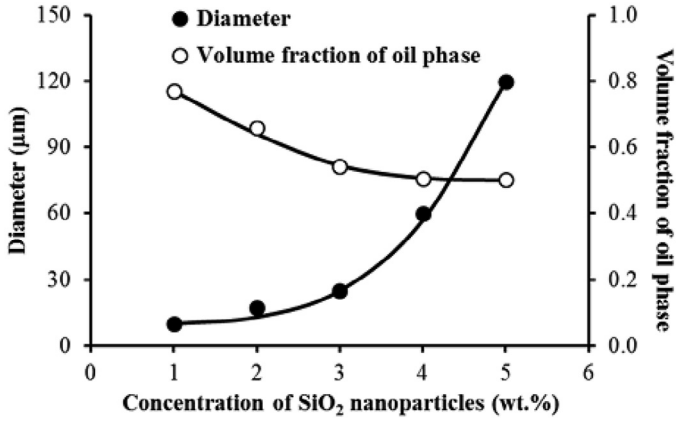

Fig. 5. Droplet diameter and volume fraction of oil phase as a function of the total concentration of Ludox HS-30 and Ludox CL. Mass ratio Ludox HS-30/Ludox CL is 2, initial volume fraction of oil phase is 0.5.

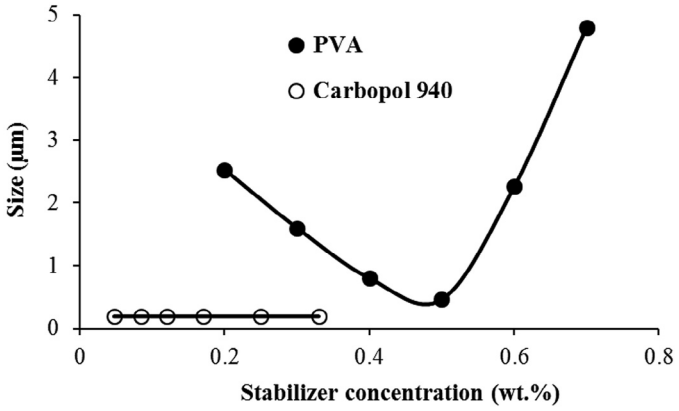

Fig. 6. Size of paraffin particles as a function of PVA or Carbopol 940 concentration.

charge close to zero. The rate of aggregate adsorption on the surface of oil droplets is lower than single nanoparticles. So droplet coalescence takes place at the initial periods of time and droplet sizes increase. During the time heteroaggregates form a percolating network in the aqueous phase of O/W Pickering emulsions that prevent droplet motion. As a result, emulsion stability toward creaming and separation of the aqueous phase increases greatly.

The effect of the total concentration of nanoparticles on the droplet sizes and emulsion stability is shown in Fig. 5. Mass ratio of Ludox HS-30 to Ludox CL nanoparticles is equal to 2. Initial volume fraction of the oil phase is 0.5.

Emulsion stability to creaming enhances with the growth of nanoparticle concentrations due to increasing the strength of particle network in the aqueous phase. At the same time, droplet sizes in emulsions increase greatly – up to 120 μm. This unexpected result correlates with data reported in [27], where a dodecane-in-water emulsion prepared from an aqueous dispersion of 24 wt.% fumed silica hydrophilic nanoparticles was very unstable to coalescence in comparison with emulsions with 1–2 wt.% silica nanoparticles. More probably that this is attributed to lower adhering large heteroaggregates to drop interfaces.

Thus, O/W Pickering emulsions stabilized by the mixture of oppositely charged hydrophilic SiO_2 nanoparticles can be obtained. However, droplet sizes in these emulsions are high enough, of the order of tens of micrometers. Besides, such emulsions are stable toward creaming only in the case of formation of particle network in the aqueous phase of emulsions.

3.3. Paraffin particles stabilized by nonionic surfactant and polymer

Nanoemulsions and colloidosomes with liquid paraffin as an oil phase are generally unstable and undergo degradation. To avoid quick phase separation, liquid paraffin can be substituted by paraffin wax that is solid at room temperature.

In this work, paraffin particles were stabilized by nonionic surfactant Eumulgin O10 and polymer PVA or Carbopol 940. The main emphasis was placed on effective stabilization of paraffin droplets before solidification for preparing stable emulsions with the smallest particles.

In the case of PVA stabilization, average particle sizes exhibit an initial decrease, pass through a minimum, and then steeply increase (Fig. 6). The decrease with concentrations in the range of 0.2–0.5 wt.% is attributed to steric stabilization by adsorbed PVA molecules. PVA loops and tails protrude the aqueous phase and prevent approaching liquid paraffin droplets and their coalescence before solidification. As a result, particle average sizes decrease from 2.5 μm to 460 nm.

Increasing PVA concentration above 0.5 wt.% causes emulsion destabilization by bridging flocculation accompanied by coalescence, that gives rise to the steep increase in particle sizes.

In the case of using Carbopol 940, stabilization is more efficient and more effective. The size of paraffin particles remains almost unchanged ~190 nm with increasing Carbopol 940 concentration from 0.05 to 0.33 wt.% (Fig. 6).

Stability of paraffin emulsions to creaming is significantly improved in comparison with nanoemulsions and colloidosomes. Emulsions stabilized by PVA do not undergo visible creaming during 20 days.

Gel-like structure is formed in the aqueous phase of emulsions with Carbopol 940. Polymer network provides more effective stabilization. Paraffin emulsions with Carbopol 940 are stable at least 4 months.

In order to compare sizes in investigated nano- and microcapsules, the obtained data are shown in Table 1. Fig. 7 illustrates microphotographs of nanoemulsion, colloidosome, and paraffin nanoparticles.

Nanoemulsions, stabilized by nonionic surfactants such as Brij 30 or mixture of Tween 80 and Span 80, with droplet diameters as low as 15–20 nm have been obtained. The smallest sizes of paraffin particles are ~460 nm in the case of PVA stabilization and ~190 nm in emulsions with gel-like aqueous phase formed by Carbopol 940.

O/W Pickering emulsions stabilized by oppositely charges SiO_2 nanoparticles are presented in Fig. 7b. The structure of nanoparticle-adsorbed layer is more compact near the surface of oil droplets. Heteroaggregates are coupled to the interface

Table 1
Sizes of nano- and microcarriers.

Carrier type	Stabilizer type	Stabilizer	Minimum size
Nanoemulsions	Nonionic surfactants	Brij 30	15 ± 3 nm
		Tween 80 and Span 80	20 ± 5 nm
Colloidosomes	Solid lipid nanoparticles	Ludox HS-30 and Ludox CL	10 ± 1 μm
Paraffin particles	Nonionic surfactant and polymers	Eumulgin O10 and PVA	460 ± 40 nm
		Eumulgin O10 and Carbopol 940	190 ± 20 nm

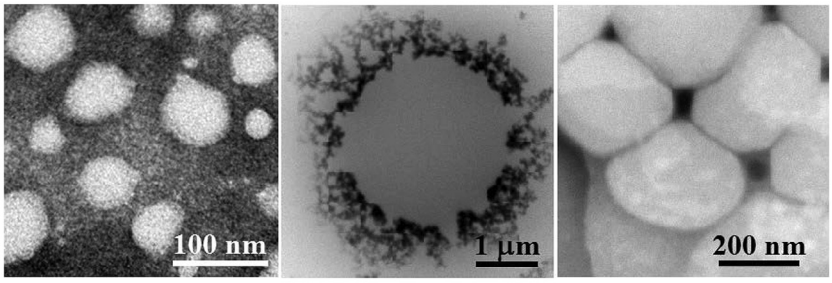

Fig. 7. TEM micrographs of nanoemulsion stabilized by Tween 80 and Span 80 (a), colloidosome formed by SiO_2 nanoparticles (b) and paraffin particles stabilized by Eumulgin O10 and PVA (c).

Table 2
Sizes of drug-free and drug-loaded carriers.

Carrier type	Sizes of drug-free carriers, nm	Sizes of drug-loaded carriers, nm			
		Tocopherol	Hydro-cortisone	Nimesulide	Curcumin
Nano-emulsion	30 ± 5	29 ± 5	29 ± 5	31 ± 5	33 ± 5
Paraffin particles	460 ± 40	400 ± 40	700 ± 60	360 ± 30	670 ± 60

Nanoemulsions are stabilized by 10 vol.% Tween 80 and Span 80.
Paraffin particles are stabilized by 1 wt.% Eumulgin O10 and 0.5 wt.% PVA.

and provide the high surface coverage. Ramified branches of heteroaggregates stretch into the aqueous phase. Diameters of colloidosomes prepared on the base of O/W Pickering emulsions are about 10 μm and higher.

3.4. Drug-encapsulated nanoemulsions and paraffin particles

The effect of drug encapsulation on carrier sizes was studied. (+)-α-Tocopherol, hydrocortisone, nimesulide, and curcumin were used as model lipophilic drugs in this work.

Nanoemulsions were stabilized by mixture of Tween 80 and Span 80 with molar ratio 0.76. Paraffin emulsions were stabilized by 1 wt.% Eumulgin O10 and 0.5 wt.% PVA. Nanoemulsion droplets and lipid particles contained liquid paraffin or paraffin wax, respectively, with drug concentration 1 wt.%.

Average sizes of nanoemulsion droplets and paraffin particles are presented in Table 2.

Drug-free nanoemulsion has droplet diameters equal to 30 nm. Encapsulation of lipophilic drugs does not cause any significant changing diameters of nanoemulsion based nanocapsules.

Variations in sizes of paraffin particles loaded by tocopherol in comparison with drug-free particles are within the measurement accuracy. Encapsulation of nimesulide leads to decrease in particle sizes; encapsulation of hydrocortisone and curcumin enhances particle sizes. The difference in sizes of drug-loaded paraffin particles is apparently caused by the different polarities of pharmaceutical components and their influence on adsorption properties of Eumulgin O10 and PVA that should stabilize emulsion, especially before paraffin solidification. In all specimens the sizes are equal or less than 700 nm and such particles can be used as microcapsules for lipophilic drugs.

4. Conclusions

Many of therapeutic compounds exhibit low polarity and low water solubility that requires the development of new kinds of carriers for their administration and delivery. Recent publications have shown that the promising approach is using appropriate lipid-based systems [6,7]. Emulsion based carriers: nanoemulsions, solid lipid particles, and colloidosomes have been investigated in this paper.

Droplet diameters in nanoemulsions, stabilized by nonionic surfactants Brij 30 or Tween 80 and Span 80 mixture, exhibit a minimum of 15–20 nm. However these colloid systems are unstable to droplet growth due to the predominant influence of Ostwald ripening [11,16].

Droplet sizes ranged from 7.5 to 20 μm in diameter in colloidosomes composed of oppositely charged SiO_2

nanoparticles Ludox HS-30 and Ludox CL. At mass ratio Ludox HS-30/Ludox CL of 2, colloidosomes are stable toward coalescence and creaming probably due to the adsorption of nanoparticle heteroaggregates around oil droplets and the enhanced viscosity of the aqueous phase reducing droplet motion [27].

Paraffin emulsions stabilized by Carbopol 940 have particles 190 nm in size and are stable to phase separation at least 4 months. The long-term stability of paraffin particles is achieved by the formation of gel-like structure by polyacrylate molecules in the aqueous phase of emulsions that prevent droplet coalescence before solidification and particle aggregation after solidification.

Encapsulation of lipophilic drugs tocopherol, hydrocortisone, nimesulide or curcumin does not cause changing diameters of nanoemulsion based nanocapsules. Incorporation of these drugs in paraffin particles leads to decreased or increased particle sizes, but in all specimens the sizes are equal or less than 700 nm.

This study provides information and additional approach for further understanding the preparation of nano- and microcapsules based on emulsions. The advantages of these carriers qualify them as promising candidates in the development of targeted delivery systems.

Acknowledgments

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