Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2015, **25**, 389–390

Mendeleev Communications

Properties of nanocapsules obtained from oil-in-water nanoemulsions

Marina Yu. Koroleva,* Tatyana Yu. Nagovitsina and Evgeny V. Yurtov

Department of Nanomaterials and Nanotechnology, D. I. Mendeleev University of Chemical Technology of Russia, 125047 Moscow, Russian Federation. Fax: +7 495 495 2116; e-mail: m.yu.kor@gmail.com

DOI: 10.1016/j.mencom.2015.09.026

Nanocapsules that are highly stable towards Ostwald ripening were obtained from oil-in-water nanoemulsions stabilized by the mixtures of Tween and Span surfactants. The structure adsorption layer in these nanoemulsions is discrete and, apparently, consists of domains with different surfactant ratios, and consequently, different melting points.

Nanoemulsions are promising drug delivery systems, and they can be used in cosmetics, food industry, *etc*.[1,2] The maximum size of the dispersed phase droplets in nanoemulsions is less than 100 nm. Therefore, they penetrate easily through epidermal stratum corneum when used as transdermal carriers loaded with therapeutic drugs and bioactive substances.

The main problem restricting widespread applications of oil-in-water (O/W) nanoemulsions is their low stability to Ostwald ripening. The solubility of oil droplets in the aqueous phase rises with decreasing their size. Smaller droplets are dissolved and the larger ones increase in size. As a result, nanoemulsions coarsen with time and ultimately breakdown.

The stability of O/W emulsion can be increased if the liquid crystal interfacial membrane retards the diffusion of oil molecules from oil droplets.[3] An analogous result can be obtained if droplets are coated with a solid shell. The latter in nanoemulsions should be sufficiently thin due to the small sizes of oil pools. Such a shell can be created by surfactant molecules, which form a solid-like surface layer at ambient temperature. In this case, nanoemulsion resistance towards coalescence would be achieved and Ostwald ripening would be inhibited.

Other difficulties are associated with nanoemulsion preparations. Usually low-energy emulsification methods are applied, *i.e.*, phase inversion temperature and phase inversion composition methods.[4] In these methods, the curvature of the surfactant adsorption layer at the interface in emulsions is changed with temperature or emulsion composition. As a result, phase inversion occurs, and a nanoemulsion is formed.

There is a limited range of optimal conditions for the preparation of nanoemulsions with unimodal distributions of droplets. Emulsions with bimodal (and even trimodal) droplet distributions are formed when low-energy emulsification methods are used. Therefore, the preparation of nanoemulsions with nanodroplets smaller than 50 nm is not always possible.

Such surfactants as Tween and Span are employed in pharmaceuticals and food compositions. Their mixtures can be applied to nanoemulsion stabilization. For example, emulsions with unimodal droplet distributions (mean diameter, 133 nm) were obtained with a Tween 20/Span 20 mixture.[5] Nanoemulsions with 40 nm diameters were stabilized by Tween-80 and Span-20.[6] The average diameter ranged between 76.02 and 94.20 nm in nanoemulsions with Tween 20 and Span 80.[7] Tween 80/Span 80 were used as emulsifiers in nanoemulsions with mean diameters of 85,[8] 90[9,10] and 137–215 nm.[11]

In this study, the O/W nanoemulsions were prepared by a phase inversion temperature method. The presence of a low HLB surfactant (HLB = 4–5) is necessary at this point for the stabilization of the W/O emulsion. As a result, an O/W nanoemulsion is formed; for this reason, the presence of a high HLB surfactant (HLB ≈ 15) is also necessary for the stabilization of this nanoemulsion. The mixtures of nonionic surfactants of polyoxyethylene sorbitan and sorbitan fatty acid ester types (Tween 60, Tween 80, Span 60 or Span 80) were used as emulsifiers. The fraction of oil phase in nanoemulsions was 25 vol%. The total surfactant concentration was 12.5 vol%. Phase inversion occurred in a temperature range from 70–72 to ~95 °C in investigated nanoemulsions.

The emulsions were stabilized by mixtures of Tween 60/Span 60, Tween 80/Span 60, Tween 60/Span 80. The nanoemulsion with Tween 80 and Span 80 was used for comparison.†

If Span prevailed in emulsions, the amount of high HLB surfactant is insufficient to stabilize O/W nanoemulsions. After phase inversion, the coalescence of oil droplets is rapid and large drops are formed. At high Tween 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.†

The largest fraction of nanodroplets was obtained at a Tween/Span molar ratio of ~0.76 in all emulsions (Figure 1). The first maximum corresponds to individual droplets, and the second one is related to large drops (or flocs of small droplets). The predominant formation of nanodroplets proceeds in nanoemulsions

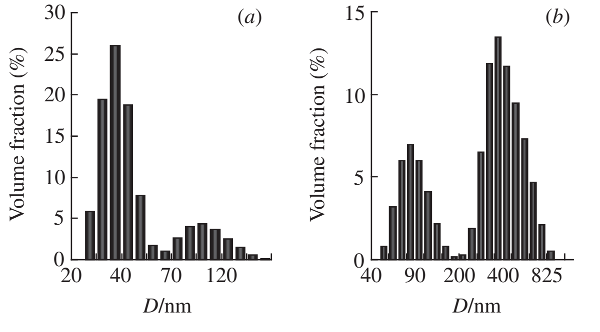

Figure 1 Size distributions of droplets in emulsions stabilized by (*a*) Tween 60/Span 60 and (*b*) Tween 80/Span 80. Tween/Span molar ratio, 0.76.

† Tween 80 and Span 80 are liquid substances at 20 °C. The melting points of solid surfactants were determined by differential scanning calorimetry (DSC) using a TA Instruments model SDT Q600 TG/DSC Thermal Analyzer. The melting points of Tween 60 and Span 60 are ~23 and 51.5 °C, respectively. Droplet sizes were measured by Zetasizer Nano ZS (Malvern).

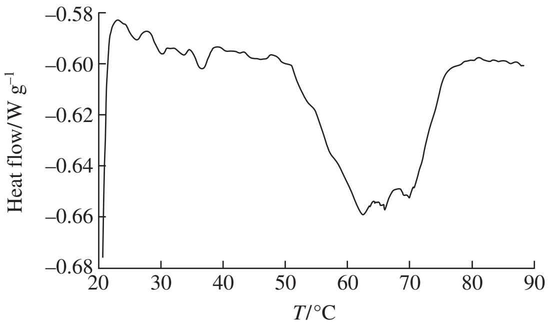

Figure 2 DSC curve for nanoemulsion with Tween 60/Span 60 in flowing air. The specimen was heated up to 90 °C at a rate of 1 K min^{-1}.

with Span 60 at this surfactant ratio. In nanoemulsions stabilized by Tween 60/Span 60 [Figure 1(*a*)] and Tween 80/Span 60, the first maxima correspond to 33 and 37 nm, respectively. The second peak at diameters of less than 90 nm is observed, and the portion of such droplets in nanoemulsion is less than 4 vol%.

Droplets of a larger size are formed in emulsions with Tween 80 and Span 80 liquid surfactants. The first peak in size distribution is located at about 80 nm, but these nanodroplets do not predominate in emulsions. The fraction of coarse drops of ~340 nm is almost twice as large [Figure 1(*b*)].

The DSC thermogram in air for the nanoemulsion stabilized by Tween 60/Span 60 (Figure 2) shows peaks at 26, 30, 34 and 37 °C due to the melting of a mixed adsorption layer. More probably, the structure of a solid adsorption layer is discrete. Tween 60 and Span 60 molecules form domains with different component ratios and, consequently, different melting points.

The endothermic peak at above 50 °C corresponds to phase inversion in nanoemulsion.

Due to differences in the interfacial curvatures, Ostwald ripening can occur in such emulsions. Study of long-term stability showed that all emulsions exhibited no obvious visual changes over time. Phase separation was not observed in ~45 days. Nevertheless, droplet sizes do not remain unchanged in all emulsions. Figure 3 illustrates the time evolution of oil droplet diameters, which correspond to the first maxima on the size distributions.

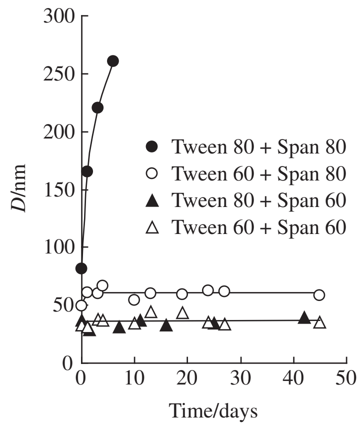

Figure 3 Time evolution of droplet diameters in nanoemulsions stabilized by surfactant mixtures.

The stability of nanoemulsions without a solid-like layer with Tween 80/Span 80 is very low. Coalescence of oil droplets and Ostwald ripening take place in these nanoemulsions; as a result, oil droplets grow rapidly from 80 to 260 nm for six days.

Droplet diameters in nanoemulsions stabilized by Tween 60/Span 60 and Tween 80/Span 60 mixtures do not alter markedly after ~45 days. The ratio of small droplets and larger ones remained constant.

Emulsions with Tween 60/Span 80 are slightly less stable at the initial period. Droplet diameter increases from 50 to 60 nm.

Thus, the most stable nanoemulsions are obtained in the case of stabilization by Span 60 and Tween 60 or Tween 80. A solid layer of Span 60 or Tween 60/Span 60 mixtures is formed on the surface of the droplets after phase inversion, thus hindering their coalescence. In nanoemulsions with Tween 60 and Span 80, a solid shell is formed at lower temperatures, so the initial diameter of oil droplets is higher.

A solid shell on droplet surfaces retards oil molecules penetrating through it. Therefore, Ostwald ripening is significantly reduced in these nanoemulsions, as indicates by the droplet diameters remaining unchanged after ~45 days of storage.

These results suggest that nanoemulsions stabilized by Span 60 and Tween 60 or Tween 80 can be loaded by active ingredients and investigated as nanocapsules for the development of nanoemulsion-based drug delivery systems.

This work was supported by the Ministry of Education and Science of the Russian Federation under government assignment and grant no. 16.962.2014.

References

1 D. J. McClements, *Nanoparticle- and Microparticle-based Delivery Systems: Encapsulation, Protection and Release of Active Compounds*, CRC Press, 2014.
2 M. Yu. Koroleva and E. V. Yurtov, *Russ. Chem. Rev.*, 2012, **81**, 21.
3 S. Mun and D. J. McClements, *Langmuir*, 2006, **22**, 1551.
4 C. Solans and I. Solé, *Curr. Opin. Colloid Interface Sci.*, 2012, **17**, 246.
5 X. Xin, H. Zhang, G. Xu, Y. Tan, J. Zhang and X. Lv, *Colloids Surf., A*, 2013, **418**, 60.
6 M. Kong, X. Chen and H. Park, *Carbohydr. Polym.*, 2011, **83**, 462.
7 T. Dey, S. Ghosh, M. Ghosh, H. Koley and P. Dhar, *Food Res. Int.*, 2012, **49**, 72.
8 S. Rebolleda, M. T. Sanz, J. M. Benito, S. Beltrán, I. Escudero and M. L. G. San-José, *Food Chem.*, 2015, **167**, 16.
9 Z. Mei, J. Xu and D. Sun, *Colloids Surf., A*, 2011, **375**, 102.
10 W. Liu, D. Sun, C. Li, Q. Liu and J. Xu, *J. Colloid Interface Sci.*, 2006, **303**, 557.
11 Y. Li, Z. Teng, P. Chen, Y. Song, Y. Luo and Q. Wang, *J. Colloid Interface Sci.*, 2015, **438**, 130.

Received: 10th March 2015; Com. 15/4582