[1]A.N. Frumkin Institute of Physical Chemistry and Electrochemistry, RAS
[2]Department of Chemistry, Moscow State University

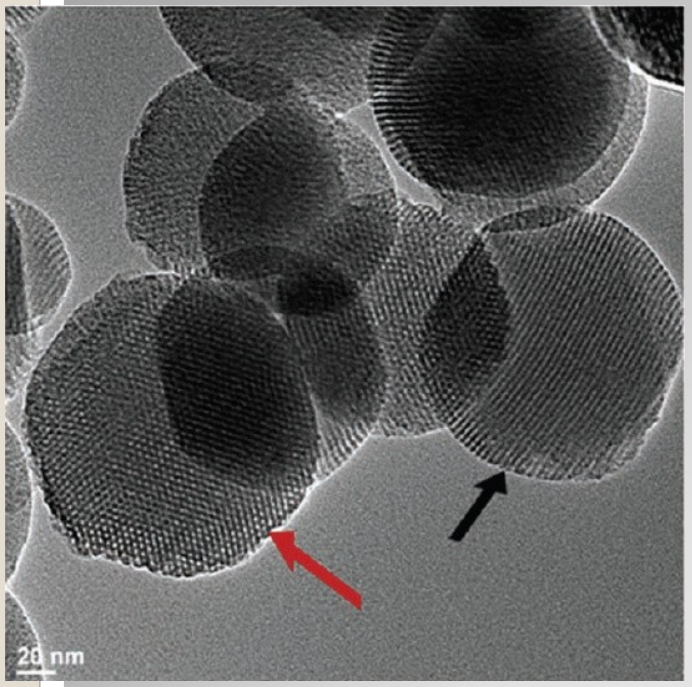
Novel Drug-Templated Mesoporous Silica Nanocontainers and Protocells Based Thereon

O.V. Dement'eva[1], K.A. Naumova[2], M.E. Kartseva[1], V.M. Rudoy[1]

dema_ol@mail.ru

Trends in Nanotechnology International Conference,
June 05–09 2017, Dresden, Germany

What are the benefits of using the mesoporous silica nanoparticles (MNCs) as containers for different substances?



Their specific features:

1) ordered pore system with a narrow size distribution;

2) large specific area;

3) pore size can be finely "tuned" from 2 to 50 nm.

Moreover:

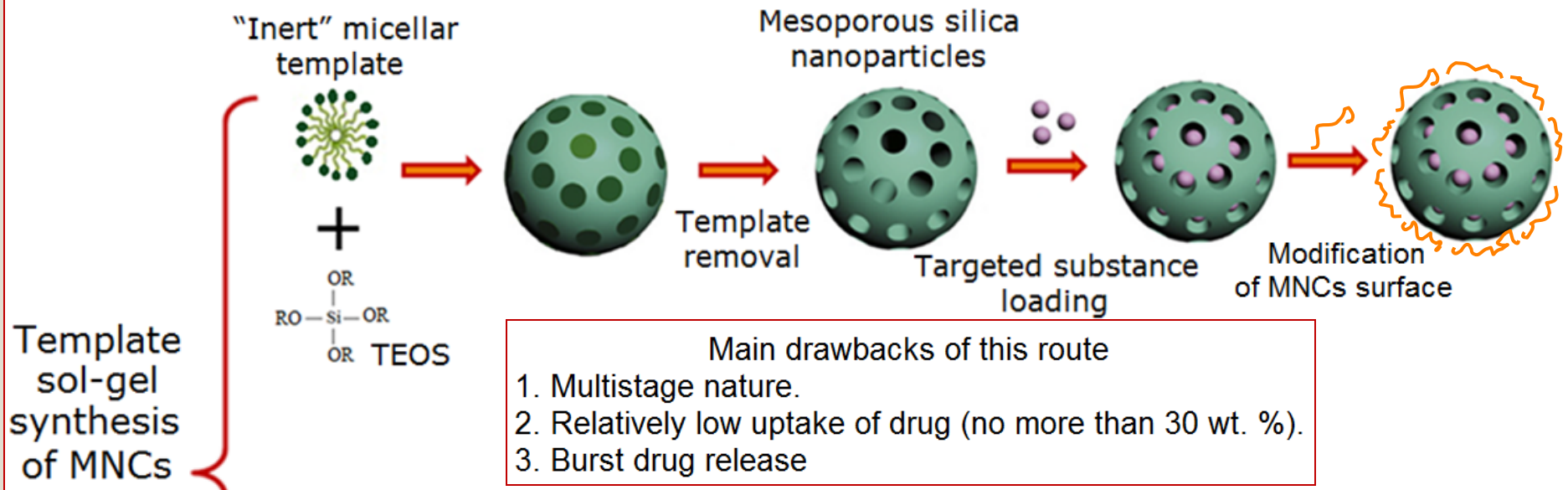
Inner and outer surfaces of such MNCs can be "easily" modified.

It allows:

1) to control the targeted substance loading and release;

2) to "combine" the MNCs with different media (e.g., biological ones).

Conventional route of MNCs synthesis and their loading with targeted substance

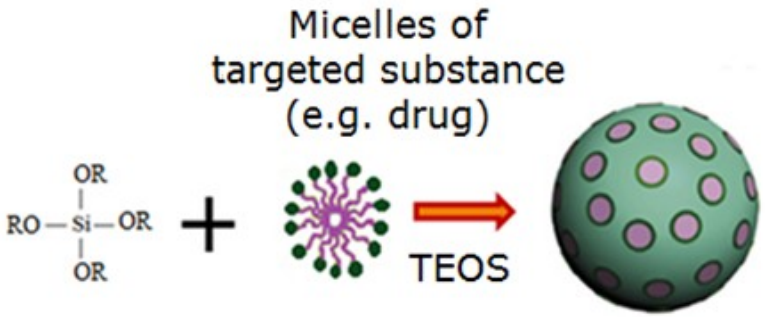


Template sol-gel synthesis of MNCs

Main drawbacks of this route

1. Multistage nature.
2. Relatively low uptake of drug (no more than 30 wt. %).
3. Burst drug release

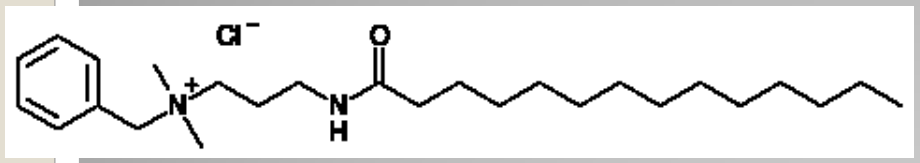
New route



Prospects and benefits

1. One-pot synthesis of silica nanocontainers and their loading with targeted substance.
2. Ultrahigh capacity of MNCs with respect to this substance.
3. High sensitivity of a release to medium pH.

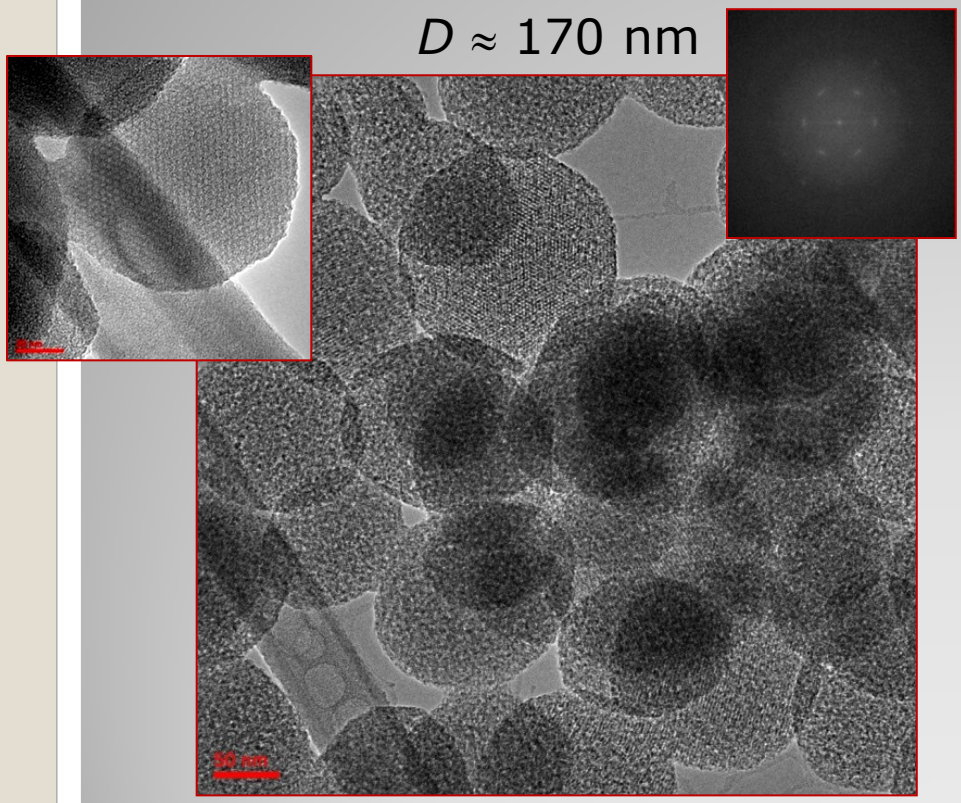
Proof of concept using the micelles of bactericidal drug Miramistin as templates

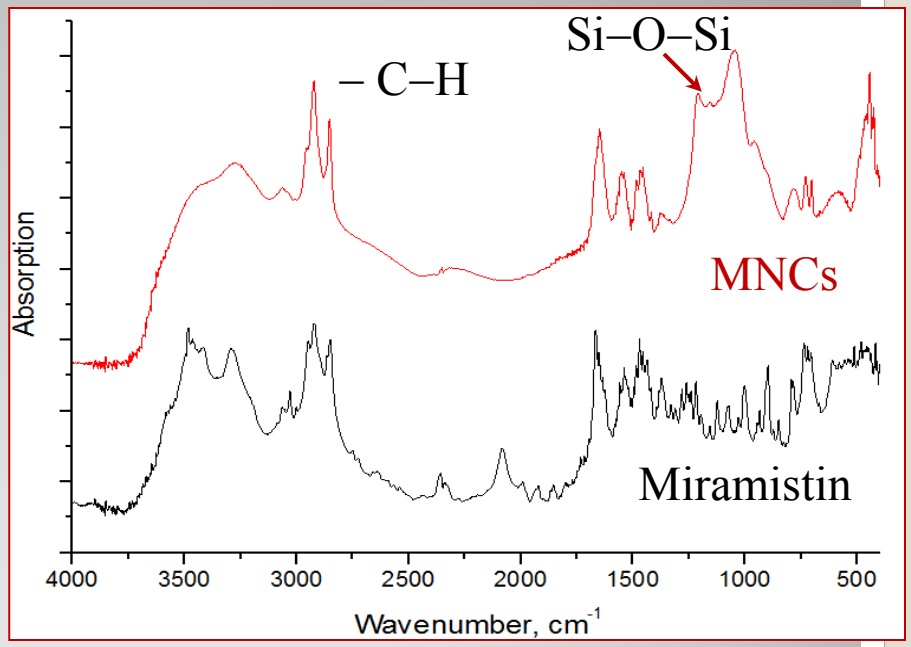


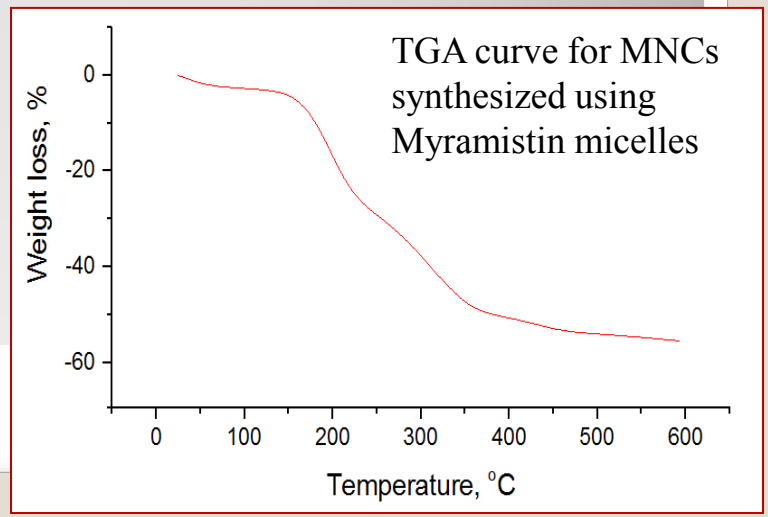
CMC ≈ 1 мМ

Diameter of micelles ≈ 5 nm

D ≈ 170 nm



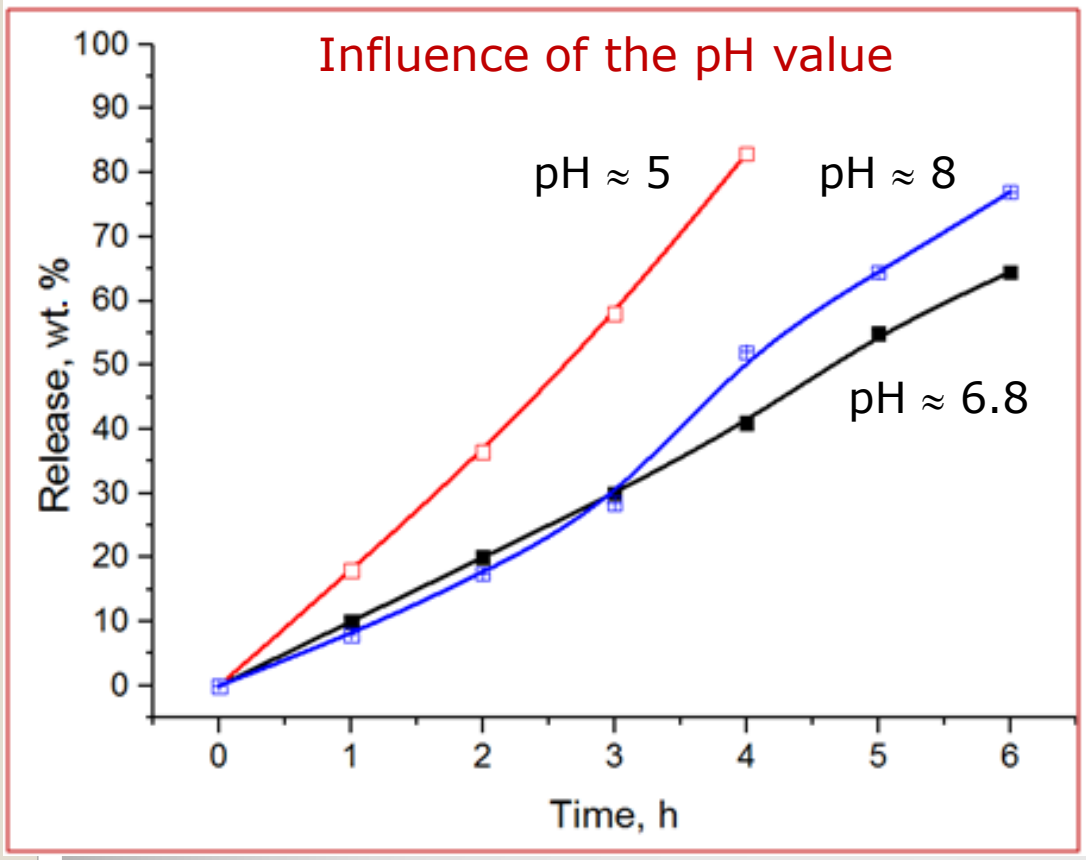




- Almost all Miramistin introduced into the reaction system is incorporated into formed silica particles during their sol-gel synthesis.
- The content of the templating drug in MNCs is equal to about 1 g per 1 g of SiO_2.

O.V. Dement'eva, V.M. Rudoy // RCS Adv. 2016.

Miramistin release from MNCs into an aqueous medium



❖ The rate of Miramistin release in neutral and weakly acidic media is described by the zero order kinetics:

$$M_t/M_\infty = kt$$

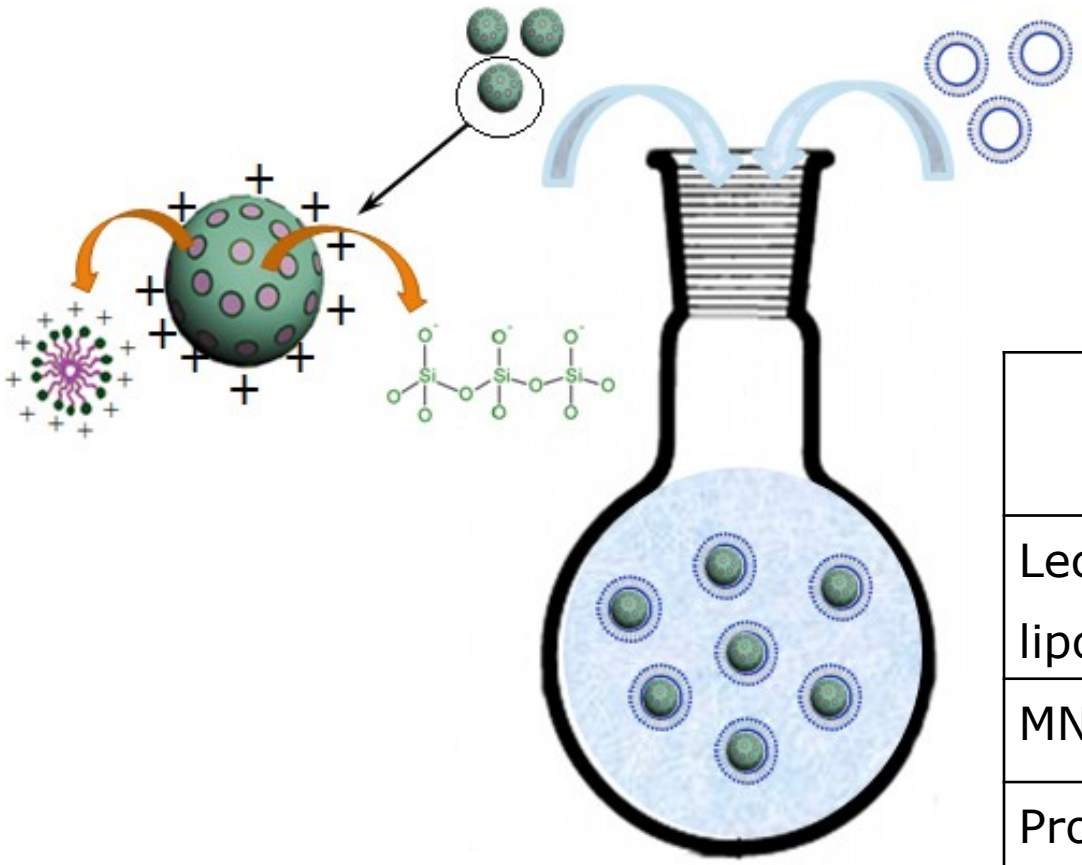
i.e., it is limited by water penetration into MNCs (that is, by their swelling).

❖ The rate of Miramistin release in alkaline media is controlled by diffusion of its molecules from MNCs and erosion (dissolution) of the silica matrix.

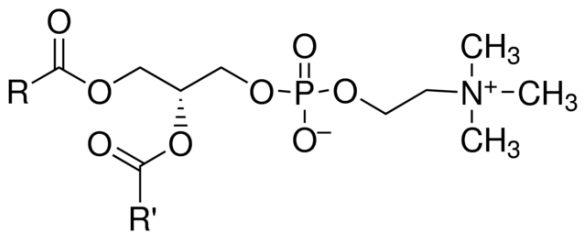
Such MNCs provide the opportunities for the development of new functional materials for medical purposes, e.g., wound dressing or dental materials

O.V. Dement'eva, I.N. Senchikhin, M.E. Kartseva et al. // Colloid J. 2016. V. 78. P. 586.

Protocells based on the Miramistin loaded MNCs



Lecithin



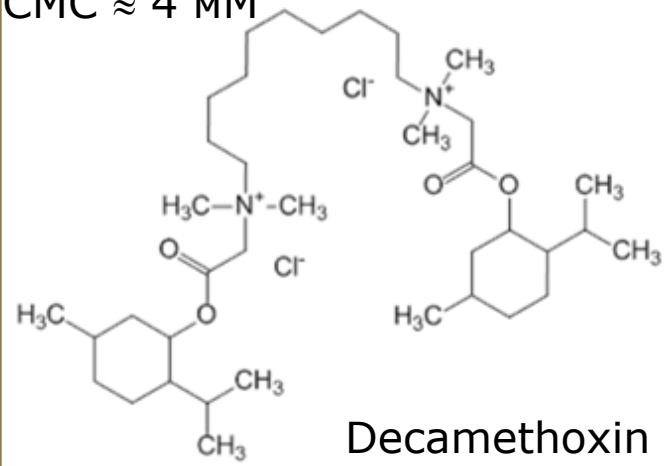
R, R' = fatty acid residues

	Lecithin/MNC ratio	ζ, mV
Lecithin liposomes	–	**–53 ± 3**
MNC	–	**43 ± 3**
Protocells	2	38 ± 4
	5	18 ± 3
	10	**–11 ± 2**

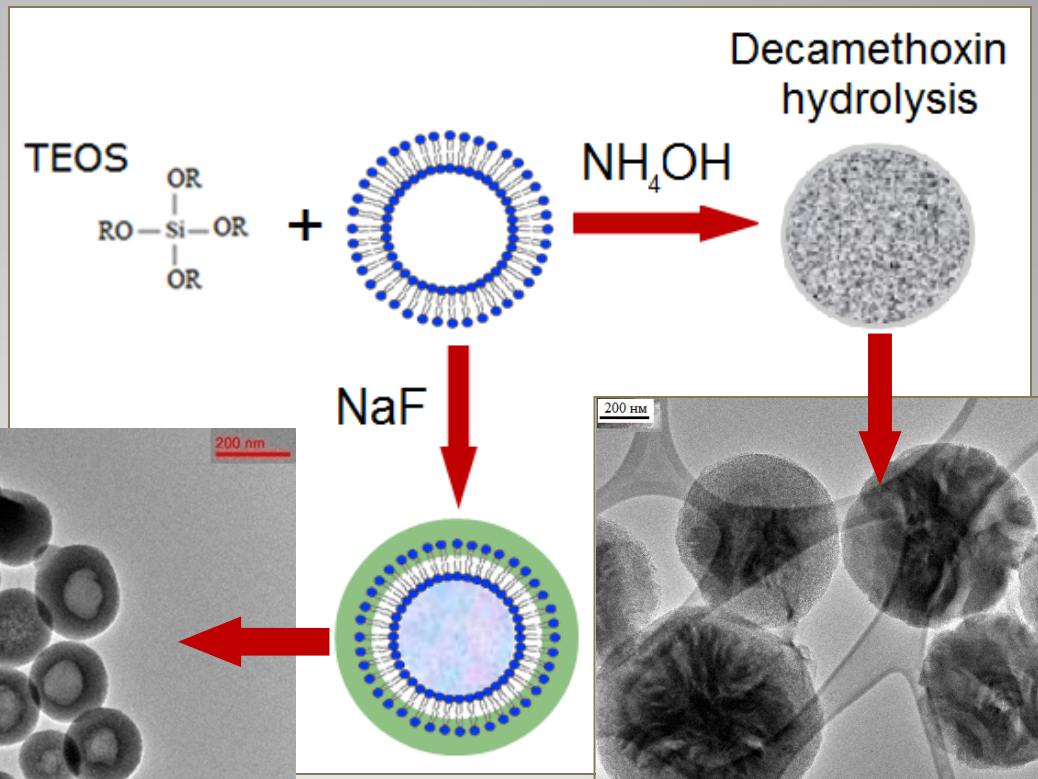
- Formation of lipid bilayers on the MNCs' causes a change in particle surface charge (ζ potential).
- The lipid bilayer supported on the MNC's surface makes it possible to control both the intercellular penetration of such protocells and the release of the encapsulated drug into the surrounding medium.

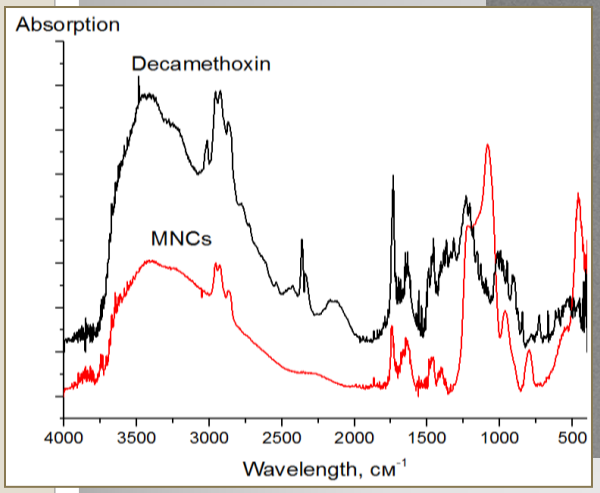
Proof of concept using the vesicles of cleavable gemini surfactant with bactericidal properties as templates

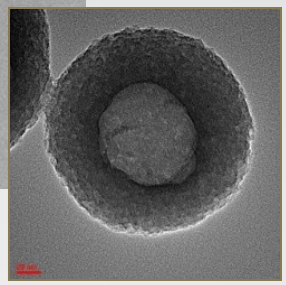
CMC ≈ 4 мМ



Decamethoxin



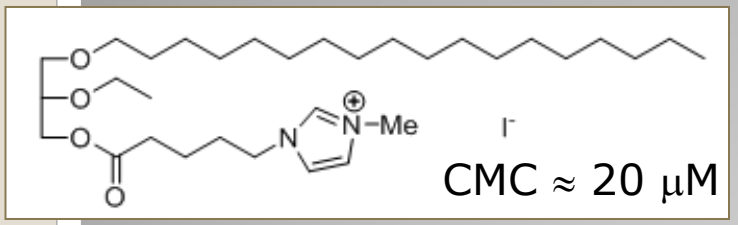




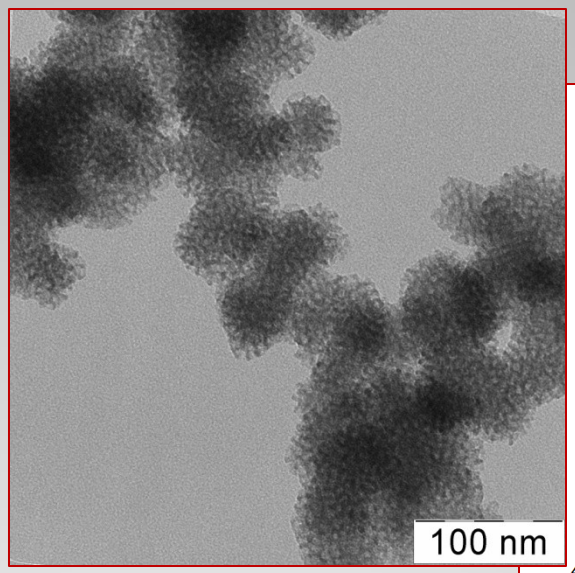
- In neutral media the decamethoxin hydrolysis does not take place.
- The content of templating surfactant in MNCs is equal to about 0.35 g per 1 g of SiO_2.

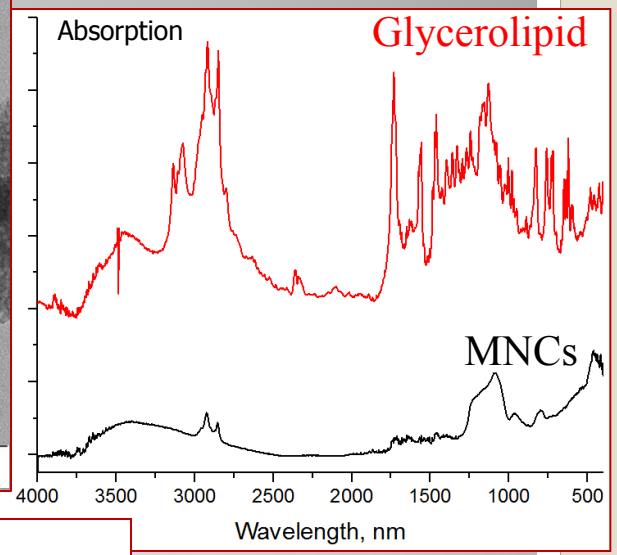
O.V. Dement'eva, K.A. Naumova, I.N. Senchikhin et al. // Colloid J. 2017. V. 79. in press.

«Proof of concept» using the antitumoral cationic glycerolipid as a templating agent

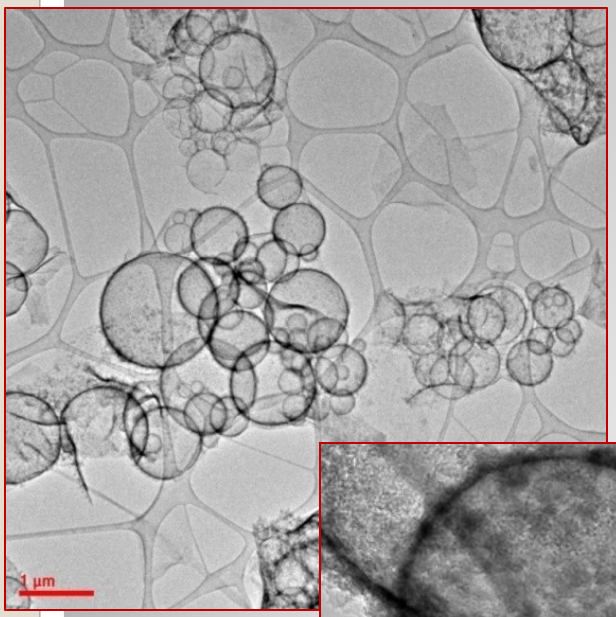


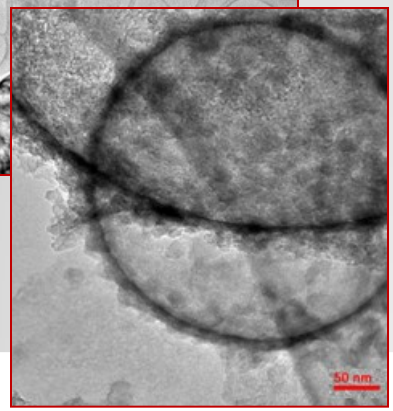
Neutral media

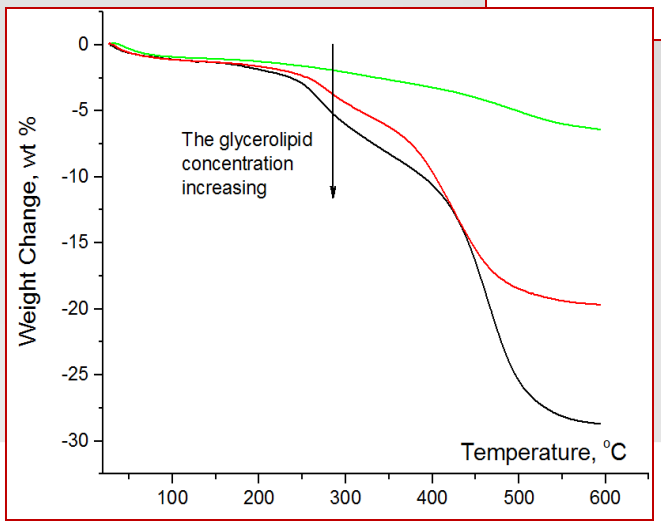




Basic media







❖ Imidazolium group can catalyze the hydrolysis and condensation of TEOS.

❖ Glycerolipid could be partly hydrolyzed.

❖ The content of templating glycerolipid in MNCs is equal to 0.03–0.4 g per 1 g of SiO_2.

O.V. Dement'eva, T.B. Roumyantseva, V.M., Rudoy // Colloid J. 2016. V. 78. P. 281.

IPCE RAS

I.N. Senchikhin

Yu.I. Kuznetsov

A.M. Semiletov

K.A. Naumova

L.V. Frolova

A.I. Zvyagina

GEOKHI RAS

E.M. Sedykh

I.N. Gromyak

L.N. Bannikh

Center for Collective Use "Microanalysis"

P.R. Kazanskii

We are sincerely grateful to

V.N. Barvinchenko (Institute of Surface Chemistry, National Academy of Sciences of Ukraine, Kyiv, Ukraine) and A.A. Shtil' (Blokhin Russian Cancer Research Center) for supplying the samples of functional surfactants

Thank you for your attention