Porous-silicon-based nanocontainers for intranasal administration of drugs

© D.A. Shishkina, M.A. Zhuravleva, N.A. Poluektova, A.N. Zakolpina, S.Yu. Kulagina

Samara National Research University, Samara, Russia
E-mail: tkachevara@mail.ru

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A system of targeted delivery of drugs encapsulated in nanosilicon containers by intranasal administration is described. This type of drug delivery will significantly reduce side effects and improve treatment and diagnosis of diseases. Up-to-date literary sources are considered.

Keywords: targeted drug delivery, intranasal administration, nanocontainers, porous silicon.

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Targeted delivery of therapeutic drugs to target cells and tissues is the most important issue of modern medicine. Improving the quality of this process will have an effect on the efficacy of drugs being under development now. This method has good potential for realizing this line, but is being mainly used for systemic drug administration. In this regard, we have considered such a promising tool for delivering various substances to certain organs and tissues as nanosilicon containers which are nothing but porous silicon obtained by an appropriate technique. Those containers are convenient to be used in the system for intranasal targeted delivery of medicines directly to the brain; this technique allows regulating the time of substance release and degradation of the containers themselves inside the body. It has been shown that a special technique of anodic etching of monocrystalline silicon in fluoride electrolytes allows obtaining nanosilicon containers with different-size porous formations. As a result, the containers obtained may have high technological and biomedical potential [1].

State-of-the-art medical concepts imply creating therapeutic drugs of high selectivity and low toxicity. However, such drugs can realize their potential only through selective delivery to certain target organs, tissues and cells. Significant progress in the field of targeted drug delivery has been achieved by using nanoparticles. Silicon nanoparticles used as carriers of substances necessary for therapy possess a number of advantages, e.g. natural biocompatibility, timely degradation, and formation of a safe final product of decomposition in the form of orthosilicic acid [2]. This approach will make possible the transition to personalized medicine and improvement of life quality. Currently, an extremely hot issue in implementing therapeutic practice in medicine is the targeted delivery of drugs. Targeting presents a wide range of structures and approaches to be used for this purpose.

There are many approaches to the targeted drug delivery for the oral and intramuscular administrations, as well as for direct covering of wound surfaces. However, the intranasal delivery method deserves special attention; this method enables delivering various substances directly to the brain, which is especially important for neuropeptides that can be destroyed by gastrointestinal enzymes [3].

Targeted intranasal drug delivery is characterized by that, upon getting on the nasal mucosa, the substances pass through the synapse into the olfactory bulb mitral cell, after which they are transported through the lateral olfactory tract to the brain and/or spinal cord. Substances may also get on the synapse receptors and transmit information through signals. In addition, substances can pass chemically through the trigeminal nerve via synapses and signally through trigeminal nerve receptors, since this nerve also directly contacts the mucosa. Substances then penetrate into the brain and/or spinal cord, thus bypassing the blood-brain barrier (BBB). This method of administering medical substances ensures achieving the desired effect within 15 min. Therefore, for instance, encapsulation of immunotherapeutic agents for the neurological and functional recovery of patients with viral infections of the brain is a particularly hot topic today.

Nanoparticles for targeted drug delivery

1. Polymers. One of the polymers of interest is biopolymer Chitosan. It gets obtained by a semi-synthetic method in processing chitin and consists of p-(1-4)-B-glucosamine units and M-acetyl-B-glucosamine. The polymer is biocompatible with body tissues. However, exposure to large doses can result in an increase in activity of the pro-inflammatory factors [4].

2. Dendrimers. Medicines may be delivered with dendrimers. These are nanosized particles of a spherical 3D shape, which possess unique characteristics. Such nanoparticles may have multiple end-functionalized groups. Their disadvantage is toxicity of the peripheral end groups to normal cells [5].

3. Extracellular vesicles. Delivery directly to the desired organ or tissue can be performed with the aid of

extracellular vesicles. They have a number of undeniable advantages, such as natural biocompatibility with cell membranes. Nevertheless, the problem of the long-term effect of extracellular-vesicles natural content getting into cells has not yet been solved [1].

4. Multifunctional systems. Currently, the most widely used drug-delivery systems are multifunctional systems that are multicomponent composite capsules fabricated by layer-by-layer adsorption. As a result, polymeric polyelectrolyte capsules get obtained, which consist of polyarginine and dextran sulfate. Polyarginine, in its turn, retains mitoxantrone in the capsule. The most noticeable manifestation of this property is formation of numerous medium and strong bonds in the arginine-mitoxantrone complex. The latter is a buffer substance, which ensures a uniform portion-wise release of the substance during the propagation and gradual dissolution of the carrying capsule [6].

5. Gold nanoparticles. Functionalized gold nanoparticles with controllable geometric and optical properties may be optionally applied in biomedicine, e.g. in genomics, biosensing, immunoassays, clinical chemistry, laser phototherapy of cancer cells and tumors, DNA and antigens, optical bioimaging and monitoring of cells and tissues by means of up-to-date detection systems. However, further research into the properties of such containers is necessary [7].

6. Porous silicon. One of the materials promising for biomedicine and targeted drug delivery is porous silicon. It has a number of advantages, such as the ease of manufacturing, biocompatibility, and biodegradability. Comparing to other variants, the nanosilicon containers for encapsulation of neuropeptides are most acceptable and easy-to-use in intranasal administration. A significant disadvantage of intranasal administration of substances may be their direct rapid leaching from the nasal cavity.

However, the use of nanosilicon containers significantly simplifies the task due to increasing the mucoadhesive properties of such a delivery system. The reasonability of using nanosilicon containers lies in their good biodegradability and biosafety. The biosafety of such containers is due to the fact that their final decomposition product is orthosilicic acid. It easily gets absorbed in the gastrointestinal tract and excreted by the urinary system [8].

Chitosan polymers and gold nanoparticles are incapable to penetrate BBB and are not detected in the brain. In contrast, dendrimers and multicomponent composite capsules can penetrate the barrier, presumably through absorption-mediated endocytosis. Extracellular vesicles also penetrate BBB, probably through an extracellular route. Porous silicon is assumed to pass through the highly-selective semipermeable endothelial cell boundaries via adsorption transcytosis and receptor-mediated endocytosis [9].

The paper demonstrates the benefits of intranasal delivery of drugs encapsulated in nanosilicon containers in fighting diseases, mainly brain ones. The capabilities considered may be aimed at correcting brain diseases in patients with viral, neurodegenerative and oncological diseases.

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] L.A. Ovchinnikova, I.N. Filimonova, M.Yu. Zakharova, D.S. Balabashin, T.K. Aliev, Ya.A. Lomakin, A.G. Gabitov, Acta Naturae, **13** (3), 114 (2021). DOI: 10.32607/actanaturae.11478 (in Russian)
[2] O.I. Ksenofontova, A.V. Vasin, V.V. Egorov, A.V. Bobyl', F.Yu. Soldatenkov, E.I. Terukov, V.P. Ulin, N.V. Ulin, O.I. Kiselev, Tech. Phys., **59** (1), 66 (2014). DOI: 10.1134/S1063784214010083.
[3] A.N. Inyushkin, A.A. Petrova, M.A. Tkacheva, E.M. Inyushkina, Neurosci. Behav. Physiol., **47** (3), 337 (2017). DOI: 10.1007/s11055-017-0402-6.
[4] D.S. Gorshenin, Yu.V. Zhernov, G.G. Krivtsov, M.R. Khaitov, Immunologiya, **41** (5), 470 (2020). DOI: 10.33029/0206-4952-2020-41-5-470-478 (in Russian)
[5] M.V. Amdzhad, Farmatsiya i farmakologiya, **9** (1), 4 (2021). DOI: 10.19163/2307-9266-2021-9-1-4-16 (in Russian)
[6] I.L. Plastun, A.A. Naumov, A.A. Zakharov, Izv. Saratov. un-ta. Novaya seriya. Fizika, **21** (4), 329 (2021). DOI: 10.18500/1817-3020-2021-21-4-329-342 (in Russian)
[7] L.A. Dykman, N.G. Khlebtsov, Acta Naturae, **3** (2), 34 (2011). DOI: 10.32607/20758251-2011-3-2-34-55.
[8] T. Yoshida, Y. Yoshioka, S. Tochigi, T. Hirai, M. Uji, K. Ichihashi, K. Nagano, Y. Abe, H. Kamada, S. Tsunoda, H. Nabeshi, K. Higashisaka, T. Yoshikawa, Y. Tsutsumi, Part. Fibre Toxicol., **10**, 41 (2013). DOI: 10.1186/1743-8977-10-41
[9] M.I. Yakhnind, K.R. Tarantseva, Izv. Penz. gos. ped. un-ta im. V.G. Belinskogo, № 29, 293 (2012). (in Russian)

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