Porous silicon nanoparticles for drug delivery

E N Abramova, A M Khort, A G Yakovenko, A I Lvovsky, E A Slipchenko, D I Prokhorov, V I Shvets

Department of material science and technology of functional materials and structures, Moscow technological university, Institute of fine chemical technologies, prospect Vernadskogo, 86, Russia

anavenko@yandex.ru

Abstract: Based on main principles of porous silicon (por-Si) formation the research of producing containers for drug delivery systems was launched. Nanoparticles for loading medicine were obtained.

1. Introduction
Targeted drug delivery to pathologic focuses of a human body is a way to increase the effectiveness of medicines. An advanced approach for directional drug delivery is using nanostructured containers that should be biocompatible, bioavailable, biodegradable and nontoxic.

Porous silicon (por-Si) is a very promising material for such containers, as long as it corresponds to the conditions mentioned above [1-3]. To use porous silicon as nanocontainers one should take into account its characteristics, including radial and axial pore dimensions, pore partition width, porosity, surface extension measure, chemical composition of por-Si surface, electronic state of por-Si surface. The chemical composition and electronic state of por-Si surface are important for researching the mechanisms of adsorption of a medicine, possible chemical interactions, and peculiarities of drug loading.

These parameters depend on the silicon wafer properties (the conductivity type, dopant concentration, structure imperfections, etc.) as well as the porous etching conditions (the electrolyte solutions composition, current density, etching time, etc.). Simultaneous taking into consideration all the factors is extremely difficult. In this regard, it is more reasonable to determine general principles of por-Si formation and dependences of por-Si parameters on the etching conditions to get por-Si with required characteristics.

2. Experimental
We used n- and p-type silicon wafers with the resistivity in the range $\rho = (0.01 – 100)$ ohm-cm, oriented long the (100) and (111) crystallographic planes. The wafers were etched with hydrofluoric acid solutions (45% HF) in H$_2$O or C$_2$H$_5$OH (96%) in a galvanostatic mode. The etching cell, made of Teflon, allowed for one-sided horizontal etching. The anode used was a polished massive copper plate, and the cathode had the form of a thin platinum plate. The electric field applied during etching was varied by diaphragms of various sizes and changing the electrode separation. The current density were 1-50 mA/cm$^2$.

The nanopore size, shape, and orientation and the thickness of nanoporous layers were determined using a JEOL electron microscope and a POLARM R optical microscope.
The chemical composition of por-Si surface was investigated with infrared spectroscopy on the spectrophotometer Equinox 55 (Bruker).

Por-Si nanoparticles were made with ultrasonic treatment of por-Si layers after their preparation. It lasted 4 h. The ultrasonic frequency was 35 kHz (capacity was 80 W).

Por-Si nanoparticles sizes were investigated with photon correlation spectroscopy and electrophoretic light scattering on the particle-size analyser Delsa™Nano and with polarization intensity differential scattering (PIDS) on the device LS13320.

3. Experimental results and discussion

Based on experimental data, some of which are described in our previous articles [4-6], it is necessary to focus on the most important principles of por-Si formation that crucially influence on the por-Si characteristics:

1. The pore frequency function increases while the electric-field intensity decreases.
2. Pores, generated on (100) wafers, are perpendicular to the substrate. As to pores on (111) wafers they are at some angle the substance surface, that results in branched structures and a larger internal surface.
3. Under other conditions being equal, the thickness of n-type porous layers significantly overtops the thickness of p-type porous layers. The thickness of por-Si layers, obtained on silicon wafers with P dopant (n-type) 8·10¹⁴ cm⁻³ (ρ= 5 ohm·cm), 4·10¹⁴ cm⁻³ (ρ= 10 ohm·cm), j=25 mA/cm², t=30 minutes, was 180-220 micron. The thickness of por-Si layers, obtained on silicon wafers with B dopant (p-type) 1.2·10¹⁵ cm⁻³ (ρ= 10 ohm·cm) with other conditions being equal, did not exceed 50-60 micron.
4. Porous layers on p-type of Si are more fragile than on n-type.
5. The correlation between radial pore dimensions and Si resistivity (ρ) (dopant concentration in Si substrate) is near-linear in the range from 0.01 to 10 ohm·cm. According to SEM data, the radial pore dimensions varies from 12 to 600 nm on n-Si and from 10 to 30 nm on p-Si.
6. The dopant type does not reveal any significant influence.
7. Figure 1 shows the results of infrared spectroscopy. There are mainly Si-H, Si-OH and Si-O-Si bonds on por-Si surface.

![Figure 1](image-url)

**Figure 1.** The dependence of por-Si layers thickness on the etching time
Table 1. Assignment of the infrared observed in anodically oxidized por-Si

| \( \omega_{IR} [\text{cm}^{-1}] \) | mode                      |
|----------------------------------|---------------------------|
| 460                              | Si-O-Si bending           |
| 640                              | Si-H bending              |
| 835                              | Si-H\(_2\) wagging        |
| 870                              | Si-H\(_2\) scissors       |
| 1040-1160                        | Si-O-Si stretching        |
| 2100                             | Si-H stretching           |
| 2250                             | O-Si-H stretching         |
| 3420-3580                        | O-H stretching            |

We have revealed [4-6] that porous etching of Si is stipulated not F\(^-\) ion, but (HF\(_2\))\(^-\) ion, which is contained in HF solutions > 1mol/l.

Preferable parameters of por-Si containers for the drug delivery of psychoneurological medicine include the pore size about 20 nm, porosity near 50\%, and the container size around 50 nm to avoid embolism. Based on the proposed mechanism of por-Si formation in our previous articles [4-6] electrochemical etching conditions of Si were determined. The conditions stipulate the formation of por-Si with the parameters required to solve the task of the principle possibility of producing nanocontainers to load carbamazepine. We chose basic silicon wafers of p-type with \( \rho = (10 – 50) \) ohm-cm. Etching time was 30 minutes, current density was 5-50 mA/cm\(^2\). It led to por-Si layers with the depth about 50 \( \mu \)m and the radial pore size around 20 nm.

Immediately after por-Si forming porous layers were processed with ultrasonic treatment (frequency is 35 khz) in H\(_2\)O or C\(_2\)H\(_5\)OH. It is observed, that the ultrasonic treatment of por-Si immediately after its preparation results in nanoparticles of various sizes, including the required ones less than 100 nm.

The results of por-Si nanoparticles sizes measurements with photon correlation spectroscopy, electrophoretic light scattering, polarization intensity differential scattering (PIDS) and scanning electron microscopy are on figures 2.

Figure 2. The measurements of por-Si nanoparticles size on Delsa\textsuperscript{T M}Nano

The nanoparticles of preferable sizes to make nanocontainers were separated with centrifugation and filtration.

To prevent coagulation and sedimentation por-Si layers were processed with organic substances. After such a treatment, and taking into account peculiarities of the material and the specifics of the research method, sizes of nanoparticles were also measured with PIDS on LS13320 to confirm pervious results.
It was determined that the ultrasonic treatment of porous layers let obtain nanoparticles with sizes in the required range (figure 3).

Figure 3. The measurements of por-Si nanoparticles size with PIDS on LS13320: a) average distribution, b) distribution during discrete measurements
When solving the problems of loading medicine in por-Si, one should take into consideration drugs electronic state and por-Si surface electronic state, which was covered in our articles about the mechanism of pores formation.

4. Conclusions
Based on key regularities of por-Si formation the porous etching conditions were chosen to obtain por-Si with the required characteristics. The nanoparticles for loading psychoneurotical medicine were produced. The research of the possibility of loading drugs were started.

References
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