Advanced Materials Research Vols. 39-40 (2008) pp 347-350
online at http://www.scientific.net

Kinetics of SiO_2 nanofibres dissolution in the simulated lung environment

Lukáš Brázda[1,a], Jarmila Studničková[2,b], Petr Exnar[2,c], Aleš Helebrant[1,d]

[1] Department of Glass and Ceramics, Institute of Chemical Technology, Prague, Technická 5, 16628 Prague 6, Czech Republic

[2] Department of Chemistry, Faculty of Education, Technical University of Liberec, Hálkova 6, 46117 Liberec, Czech Republic

[a] lukas.brazda@vscht.cz, [b] jarmila.studnickova@tul.cz, [c] petr.exnar@tul.cz, [d] ales.helebrant@vscht.cz

Keywords: nanofibres, dissolution, kinetics, simulated lung fluid

Abstract

To avoid the risk of cancer or respiratory diseases, nanofibres have to biodegrade in lung fluid when inhaled. There are two main factors affecting behaviour of the nanofibres in living tissue – geometry of fibres and biopersistence. A dissolution rate of SiO_2 nanofibres in a simulated lung environment was tested in this work. Distilled water buffered with TRIS and HCl to pH 7.6 was used as a simple simulated extracellular lung fluid (SLF). Fibres were tested both under the static and dynamic conditions of the corrosive solution. Dissolution rates were calculated from both SiO_2 concentration changes in solutions and weight changes of fibres during the exposition. The dissolution rate of tested SiO_2 nanofibres was at the rate limit, where fibres could be considered as harmless for health.

Introduction

In general, nanofibres are called fibres with their diameter significantly below 1000 nm. At the Technical University of Liberec a way to mass production of nanofibres has been found [1]. These patented findings enable utilization of specific nanofibre characteristics, such as large specific surface area, high porosity, small pores between fibres in nanofibre web or high strength of nanofibres. Thanks to favourable attributes these materials can be used in medicine or as a filter material. On the other hand, questions about health hazards of nanofibres have to be investigated.

The nanofibres represent a danger to the human body when they are inhaled. Fibres, which were not mechanically captured by cilia in respiratory track, entered in the lungs, where they can cause cancer or other diseases. The WHO considers the fibres potentially dangerous for health, if they are longer than 5 μm, with diameter less than 3 μm and the length/diameter ratio is larger than 3 [2]. To eliminate the risk of health hazards, fibres have to dissolve in environment of pulmonary fluids. The material ability to resist mechanisms of physiological degradation is called biopersistence. The higher biopersistence material has, the longer time for dissolution is needed. Products of fibre dissolution should not cause any other health hazards in surrounding tissue.

Knowledge of material biopersistence is used for estimation of potential health hazards. The *in vivo* tests of biopersistence investigate the time ($t_{0.5}$), in which 50 % of fibres (in general any material) implanted into the laboratory animals are degradated. The *in vitro* tests observe dissolution rate of fibres in simulated lung fluids. Comparison between *in vivo* and *in vitro* test was published by producer of glass and mineral fibres [3]. Resulting from this study, fibres can be considered as harmless, if their dissolution rates vary from tens to hundreds $ng.cm^{-2}.h^{-1}$. The dissolution rate of so-called biosoluble fibres can achieve 1000 $ng.cm^{-2}.h^{-1}$.

The aim of this work was to find out appropriate experimental conditions and to determine the dissolution rate of nanofibres from silica dioxide using static and dynamic *in vitro* tests.

Experimental part

Material. Fibres for dissolution tests were produced in the pilot plant at the Technical University of Liberec. The principle of fibre production is the spinning in high electrostatic field of a polymeric solution prepared by the sol-gel method. The nanofibres web was deposited on non-woven polypropylene support material, removed and then heated at 180°C for 2 hours. The mean value of fibres diameter was approx. 170 nm [4]. The specific surface area measured with BET method using nitrogen was 98.7 $m^2.g^{-1}$. Since SiO_2 nanofibres have high porosity, for comparison their dissolution rates with other non-porous glass and mineral fibres the geometrical surface 11.4 $m^2.g^{-1}$ was used for calculations [4].

Simulated lung fluid. To observe material dissolution fibres were tested in simulated lung fluid (SLF). Demineralized water with pH buffered with TRIS (tris(hydroxymethyl)aminomethane) and HCl to value 7.6 (at room temperature) was used as a simple simulated extracellular lung fluid. Two settlements of *in vitro* test were used for investigating nanofibres dissolution.

***In vitro* static test.** Static environment of SLF was used for the first estimation of fibres behaviour in leaching solution. Fine measured samples of fibres (about 100 mg) were put into the plastic bottle with 200 ml of corrosive solution [5]. The S/V ratio (i.e. ratio between surface area of fibres and volume of SLF) was ~ 510 cm^{-1}. Bottles with samples were placed in shaking apparatus with temperature adjusted to 37°C for 96 hours. The shaking apparatus (160 rpm) was used to accelerate transport of dissolved ions from the solution adjacent to the surface of fibres. 1 ml of the solution was taken from each bottle in certain time periods, diluted and analyzed for SiO_2 concentration. Measurement of pH during the test was not realizable due to fibres floating on the top of solution.

Testing at static conditions has simple adjustment, but there are also some disadvantages. If the S/V ratio is too high, the leaching solution could turn saturated with products of dissolution and this would slow down or stop further dissolution. Back precipitation from the solution could also appear. If the S/V ratio is too low, the changes in ions concentrations in solution caused by material dissolution are very small and difficult to analyze.

***In vitro* dynamic test.** Due to the elimination of static test disadvantages described above, samples were dissolved in dynamic environment of the simulated lung fluid [5]. The test followed EURIMA methodology [6]; however, some parameters had to be changed because of high specific surface of SiO_2 nanofibres. Samples were enclosed in flow cells placed in thermostat set up to 37°C. Capacity of the flow cell was 7 ml, in each cell about 50 mg of fibres were placed. Fresh SLF solution from storage flask flowed round the fibres in the cell. Flow rate of the solution was set up with the peristaltic pump to 120 $ml.day^{-1}$. The F/S ratio (i.e. ratio between flow rate of the solution and surface area of the fibres) was $2.6x10^{-6}$ $\mu m.s^{-1}$. Solutions after interaction with material were taken away in certain time periods to analyze SiO_2 concentrations and to measure pH.

Analytical methods. Weight of each sample was measured before and after exposition in SLF with accuracy of 0.1 mg. Before weighting the undissolved fibres were dried at 60°C for 5 hours. In effluent solutions Si ion concentrations were measured by Atomic Absorption Spectrometry (VARIAN Spectr AA 300, λ = 251.6 nm), lower SiO_2 concentrations from static test were measured by UV-VIS Spectrometry (SHIMADZU UV-1601, λ = 420 nm) and pH values were obtained using glass electrode (inoLab). From these data process of SiO_2 nanofibres dissolution was evaluated.

Results and discussion

Evaluation of dissolution rates. Rates of SiO_2 nanofibres dissolution were calculated both from concentration changes in leaching solution and from sample weight changes. Dissolution rate R_m was calculated (for dynamic test) from weight changes using equation

$$R_m = \frac{\Delta m}{A \cdot t} \quad [\text{ng.cm}^{-2}.\text{h}^{-1}] \qquad (1)$$

where Δm is decrease of sample weight [ng], A surface area of fibres [cm^2] and t time of exposition [h]. Dissolution rates R_c [$ng.cm^{-2}.h^{-1}$] from concentration changes were calculated for static test and dynamic test respectively from equations

$$R_c = \frac{c_{SiO_2}}{x_{SiO_2} \cdot A \cdot t} \cdot V \quad \text{and} \quad R_c = \frac{m_t}{A \cdot t}; \quad m_t = m_{t-\Delta t} + \frac{c_{SiO_2(t)}}{x_{SiO_2}} \cdot F \cdot \Delta t \qquad (2)$$

where c_{SiO2} is SiO_2 concentration in solution [$ng.cm^{-3}$], A surface area of fibres [cm^2], V volume of solution [cm^3], F flow rate of leaching solution [$cm^3.h^{-1}$] and t time of exposition [h]. Value x_{SiO2} represents weight ratio of SiO_2 in fibres, in this case pure SiO_2 fibres ($x_{SiO2} = 1$) were tested. Data shown in graphs are average values from four independent experiments. Error lines define the range of measured values.

Static test. The static test provided first point of view on dissolution of SiO_2 nanofibres. As it is shown on the Fig. 1, rapid increase in SiO_2 concentration occurred during first hours of exposition. The solution had turned slightly supersaturated before the concentration stabilized at ~ 100 $mg.l^{-1}$. Results from static test were not suitable for evaluation of dissolution rate due to rapid saturation of solution – the S/V ratio proved to be too high.

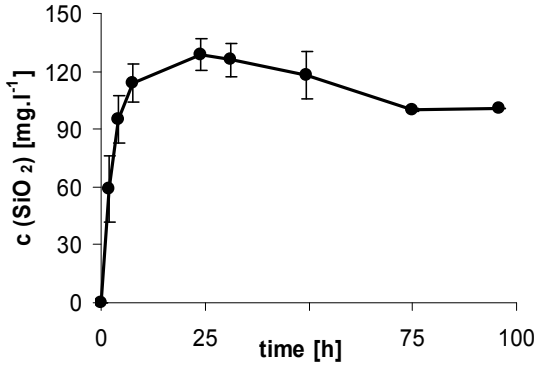

Fig. 1: Development of SiO_2 concentration - static test

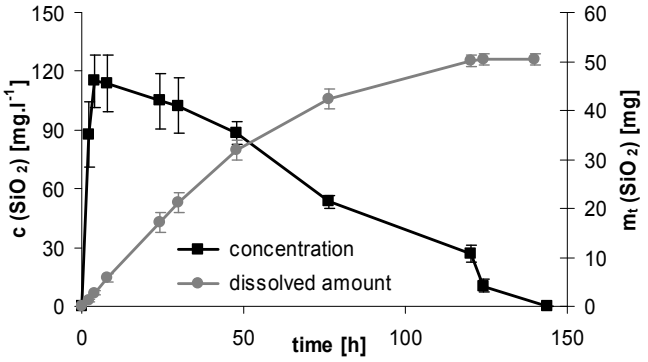

Fig. 2: Development of SiO_2 concentration and amount of dissolved fibres - dynamic test

Dynamic test. Time development of SiO_2 concentrations in solution and total amount of dissolved SiO_2 during the dynamic test are shown in Fig. 2. Since the dissolved mass of fibres calculated from SiO_2 concentrations was lower than weighted amount, the concentrations were corrected. The pH value change during the test was only ± 0.1. An increase of SiO_2 concentration appeared in first hours of experiment following with nearly steady decrease of concentration in effluents till the end of experiment. Also accumulation of dissolved SiO_2 calculated per originate fibre surface slowed down. From this data it could seem, that the dissolution of fibres decelerated with time. Average dissolution rate calculated from concentration changes (t = 4-77 h) was R_c = 10.3 $ng.cm^{-2}.h^{-1}$ and from sample weight changes R_m = 7.5 $ng.cm^{-2}.h^{-1}$. The situation changed if the decreasing surface area caused by fibre dissolution was taken into account (see Fig. 3). Two models of fibre dissolution were used. In "one-dimensional" (1D) model fibres have only one dimension (length). Decrease of fibre length during dissolution is proportional to fibre weight changes. Second model approximates fibre as a cylinder with decreasing diameter during dissolution. At the beginning of exposition, SiO_2 dissolution ran slower probably because the SiO_2 gel-like layer, more soluble than the original surface, was just forming on surface [7]. After approx. 8 hours the accumulation of dissolved SiO_2 was nearly linear except the last values - at the end of experiment almost all fibres were dissolved. Dissolution rate was calculated from the linear part of time dependence of normalized dissolved mass to be 15.3 $ng.cm^{-2}.h^{-1}$, using "cylinder" model. For comparison intermediate dissolution rates for each time period between solution sampling were calculated (Fig. 4). The nearly constant dissolution rate from 4-77 hour was 15.7 $ng.cm^{-2}.h^{-1}$. These

results allow us to use simpler linear regression for evaluation of dissolution rates. Since the SiO_2 nanofibres are highly porous, the dissolution rates had to be calculated per geometric surface in order to compare biopersistence of these fibres with non-porous glass or mineral fibres. Theoretical fibre surface without pores was 11.4 $m^2.g^{-1}$. The dissolution rate was calculated with respect to the decreasing fibre surface during exposition to be 137 ± 14 $ng.cm^{-2}.h^{-1}$. From the point of view of biopersistence the SiO_2 nanofibres could be considered as harmless.

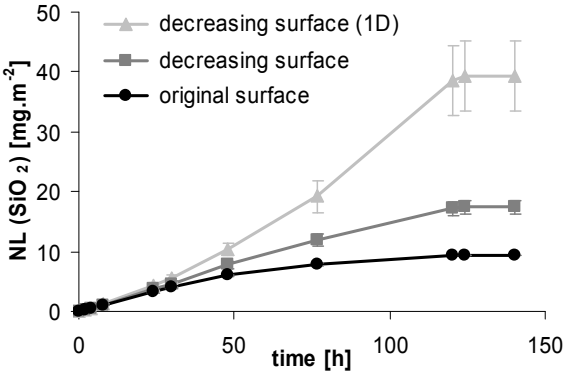

Fig. 3: Normalized amount of dissolved SiO_2 fibres ($NL = m_t / A$)

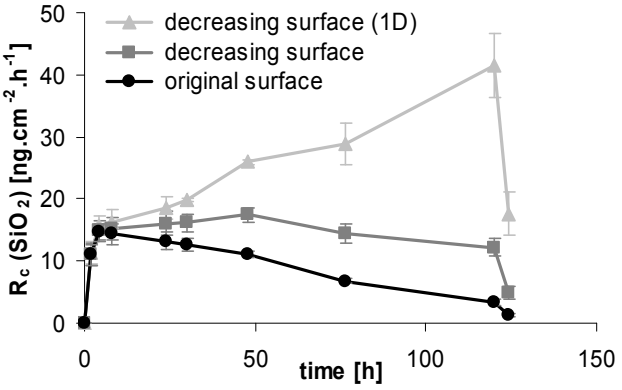

Fig. 4: Intermediate SiO_2 dissolution rates calculated for each time period

Conclusions

Appropriate experimental conditions for SiO_2 nanofibres dissolution test were found as well as methodology for evaluation of results. Because the nanofibres are dissolving rapidly, it is more accurate to calculate with decreasing fibre surface during the exposition. Dissolution rate R_c of SiO_2 nanofibres was calculated to be 15.3 $ng.cm^{-2}.h^{-1}$. For comparison of SiO_2 fibres dissolution with other glass and mineral fibres the dissolution rate was calculated per geometrical surface of fibres. The value 137 ± 14 $ng.cm^{-2}.h^{-1}$ allow us to consider these fibres as harmless from the point of view of biopersistence. In next work the impact of experimental parameters (number of fibres in cell, flow rate, pH...) on dissolution rate evaluation will be observed.

Acknowledgements

This work was supported by the research programme MSM 6046137302 “Preparation and research of functional materials and material technologies using micro- and nanoscopic methods”.

References

[1] Jirsák O., Sanetrník F., Lukáš D., Kotek V., Martinová L., Chaloupek J.: Patent CZ 20032421, 10.11.2004.

[2] World Health Organization: Reference methods for measuring man-made mineral fibers. Prepared by WHO/EURO Technical Committee for evaluating MMVF, Copenhagen, 1985.

[3] Hesterberg T.W. et al.: Toxicology and Applied Pharmacology 151, pp. 262-275, 1998.

[4] Studničková J. et al.: In: Proc. of 14th Int. Conf. STRUTEX, Liberec, November 2007, pp. 263-268, Technical University of Liberec, 2007.

[5] Brázda L. et al.: .: In: Proc. of VIIth Conf. of Preparation of Ceramic Materials, Herľany, pp. 139-143, Technical University of Košice, 2007.

[6] Sebastian K. et al.: Glass Science Technology 75, pp. 263-270, 2002.

[7] Helebrant et al.: Glass Science Technology 75 C2, pp. 197-202, 2002.