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SILVER NANOPARTICLE ADSORPTION ON POLY(LACTIC-CO-GLYCOLIC ACID) FIBER DURING CYCLIC FREEZING THE ARGOGEL WITH GELATIN AND CHITOSAN

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The paper focuses on the sorption activity of silver nanoparticles during cyclic freezing poly(lactide-co-glycolide) fibers up to −37.0°C. Silver nanoparticles are used as a part of the Argogel containing chitosan and polyvinylpyrrolidone-stabilized nanoparticles and as nanoparticles obtained by cavitation-diffusion photochemical reduction. It is found that the content of 15 nm silver nanoparticles significantly grows in the presence of gelatin in the gel composition, whereas the amount of nanoparticle clusters dramatically reduces in the same size range in the presence of chitosan. On the contrary, chitosan in the Argogel leads to the content growth of 40 nm nanoparticles.

Keywords: poly(lactide-co-glycolide), chitosan, gelatin, silver nanoparticles, cyclic freezing.

INTRODUCTION

It is known that poly(lactide-co-glycolide) (PLG) fiber serves as a basis for the creation of different types of resorbable suture materials (Vicryl, Sabfil, PGA, Mepfil) used in ophthalmology and microsurgery. This is explained by biocompatibility of these materials due to the lactic acid formation natural for a human body and their high tensile strength persisting over the time required for wound healing [1]. Moreover, it is possible to flexibly change the destruction and mechanical properties of the fiber by changing the copolymer molecular weight and morphology [2], for example, polymer coatings comprising PLG fiber can be used in abdominal surgery for peptic ulcer closure [3] or regeneration of osteohondrous tissue [4]. Inglin *et al*. [5] use the PLG fiber to prevent intestinal anastomosis dehiscence. The PLG fiber properties can also effectively prevent infectious complications in surgical interference *via* the addition of antibacterial properties to suture materials containing the PLG fiber [6].

In general, the problem of purulent-septic complications in surgical interference or surgical site infections is rather relevant today, and new ways are being searched in the field of prophylactic and treatment of post-surgery complications [7−11], including the addition of antibacterial properties to suture materials by means of silver nanoparticles (AgNPs) [11, 12]. At the same time, the dynamics of the nanoparticle adsorption on the polymeric fiber may differ due to the nanoparticle fabrication technique and external impacts during the adsorption process [13−15]. This can significantly change physical-and-mechanical properties of AgNPs and their antimicrobial activity. Some inventions attest to feasibility of using polymerization product nanoformations of lactide and glycolide as carriers for

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biologically active substances with their successive sustained release [16], that allows assuming an active adsorption of silver nanoparticles on the surface of polymer materials of the given chemical nature.

Several authors [17−20] demonstrated the influence of freezing–thawing cycles on the functional properties and the number of different nanostructures. They noted that the temperature range of –25 to –70°C affected not only the nanoparticle size, but also their higher loading density in submicron- and micron-sized porous structures. That provided the synthesis of multicomponent nanocomposite materials with targeted properties. After freezing–thawing cycles, the nanoparticle aggregation-induced heterogeneity increased as compared to the similar parameter of their adsorption and settling without a negative temperature impact. Moreover, it was shown that in hydrothermal conditions, the Ag^+ reduction reaction caused the molecular interaction in AgNPs accompanied by their coalescence. The latter was induced by the Ag^+ release from AgNPs in gel due to the AgNP oxidation process accelerated by freezing–thawing cycles, when certain chemical groups of nanoparticles modified with the different intensity, depending on their size. The use of the stable ^{107}Ag isotope helped to observe the oxidation-reduction reaction with the involvement of AgNPs, which was accelerated by freezing–thawing cycles unlike the reaction rate after the AgNP incubation in the temperature range of 4 to 25°C.

The aim of this work is to evaluate the sorption activity of silver nanoparticles on the PLG fiber during additional 10 cycles of freezing in the temperature range of 0.0 to −37.0°C.

EXPERIMENTAL

In our experiment, silver nanoparticles were obtained by cavitation-diffusion photochemical reduction, in which ultrasonic (1.7 MHz) and ultraviolet (280 nm [21]) radiations were combined and applied for 60 min at a continuous mixing with a ligand based on polyvinylpyrrolidone (PVP). The highest effect of such a treatment was achieved *via* the use of gel compositions, in which AgNPs possessed more pronounced biological properties [22]. The concentration of the freshly prepared solution of silver nanoparticles was reduced to 5 μg/mL. Afterwards, gelatin was added under a 60°C thermostat control to obtain the gel composition with a 0.9% concentration. The Argogel containing chitosan and PVP-stabilized silver nanoparticles was used to compare the AgNP concentration with that recommended by manufacturer.

The suture material Sabfil of 2.0 metric size comprising the PLG fiber, was used to study the sorption processes. The polymeric fiber of 1 cm length was immersed in AgNP compositions. After 24 hours, the fiber was extracted and subjected to 10 cycles of freezing and thawing in the temperature range of 0.0 to −37.0°C, both for 24 hours.

A field emission scanning electron microscope JSM-7500F (JEOL, Japan) was used to investigate AgNP sorption/desorption/aggregation activities at 10 kV accelerating voltage, 30,000× magnification, in the back-scattered-electron collection mode. The scanning electron microscopy (SEM) observations were conducted in the Core Facility Center of Diagnostics of Nanomaterial Structure and Properties of Kuban State Medical University, Krasnodar, Russia. The AgNP content was measured within 1−15 nm, 16−40 nm, and over 40 nm size ranges. The effect from thermal treatment on the AgNP adsorption on the copolymer fiber was evaluated through the comparison with the earlier obtained data concerning the suture material Sabfil without cyclic freezing [21].

The obtained data were processed using variation statistics methods. The confidence estimation of the detected differences between the AgNP activity on different fibers and in various size ranges was performed by using the Mann-Whitney *U* test. The level of statistical significance was <0.05.

EXPERIMENTAL RESULTS

According to the experiment, the change in the AgNP content obtained after cavitation-diffusion photochemical reduction, is statistically significant ($p < 0.05$) for two size ranges. If we compare early experimental data on fine (1 to 15 nm) nanoparticles, their content increases by 1.7 times (see Fig. 1), while the content of AgNPs with the size ranging between 16 and 40 nm decreases by 41.6%, and 40 nm AgNPs do not show any statistically significant change as compared to their content before 10 freezing–thawing cycles ($p = 0.275$). We can thus conclude that the additional

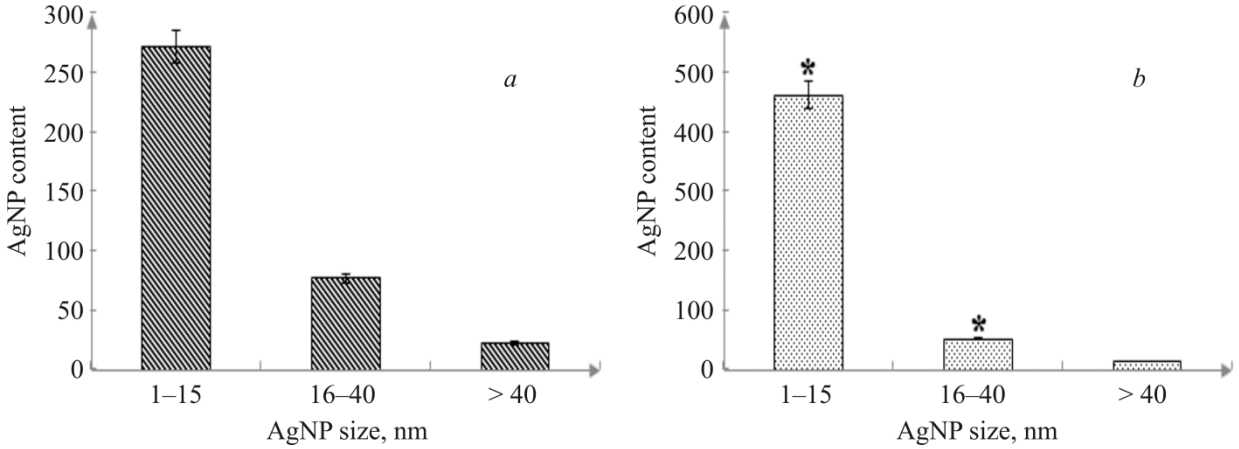

Fig. 1. AgNP distribution over Sabfil suture material after cavitation-diffusion photochemical reduction without thermal exposure below 0.0°C (*a*) and after 10 freezing–thawing cycles (*b*). The sign * indicates $p < 0.05$ compared to the same size range before freezing.

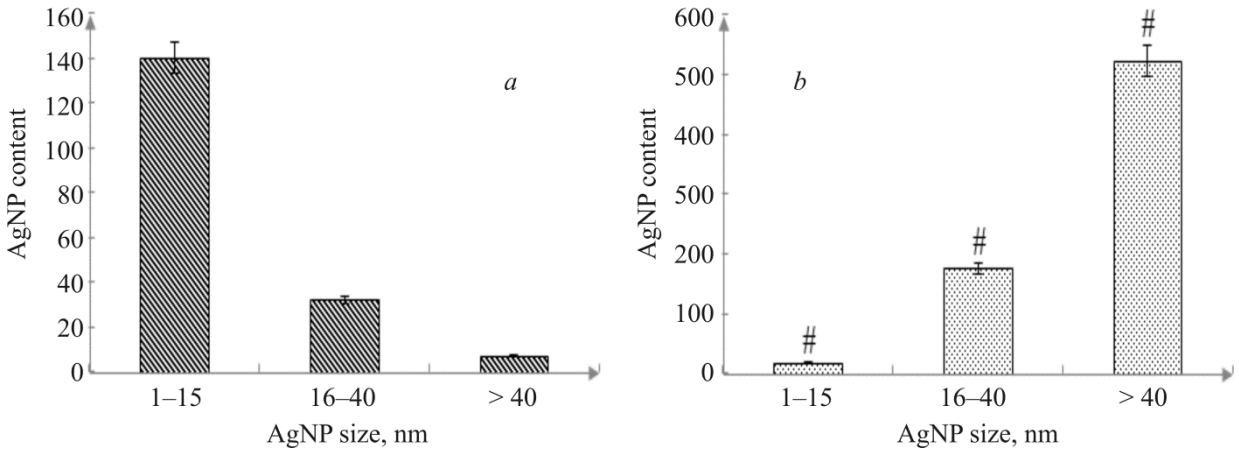

Fig. 2. AgNP distribution over Sabfil suture material without thermal exposure below 0.0°C (*a*) and after 10 freezing–thawing cycles (*b*). The sign # indicates $p < 0.05$ compared to the same size range before freezing. Magnification: 30,000×.

thermal treatment considerably increases the AgNP content on the PLG fiber, especially 1 to 15 nm nanoparticles, i.e., more functionally active relative to microorganisms. This dynamics of the AgNP content probably indicates to the additional adsorption of silver nanoparticles obtained by cavitation-diffusion photochemical reduction on the PLG fiber when using freezing cycles.

According to Fig. 2, the AgNP content in the Argogel is statistically significant after the thermal treatment cycles in all considered size ranges. However, in these size ranges, the fluctuation of the absolute AgNP content quite differs from the described dynamics of the AgNP content in the gel composition. For example, 1 to 15 nm nanoparticle concentration decreases by 87.1% ($p < 0.05$) after the thermal treatment. On the contrary, the SEM image in Fig. 3 demonstrates a 5.4 times growth in the content of 16 to 40 nm nanoparticles ($p < 0.05$). As for 40 nm AgNPs, their content increases by more than 70 times as compared to AgNPs adsorbed on the copolymer fiber before thermal treatment ($p < 0.05$). It cannot be excluded that such changes indicate to highly intensive aggregation of silver nanoparticles and their well-defined desorption from PLG fiber in negative temperature conditions.

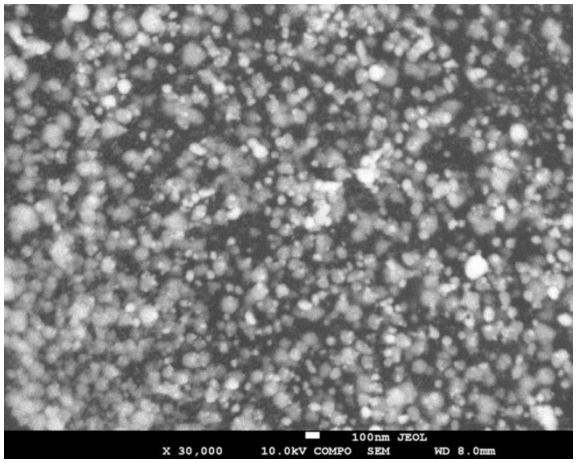

Fig. 3. SEM image of Sabfil suture material with AgNPs in the Argogel after 10 freezing–thawing cycles.

In comparing the AgNP content on the Sabfil surface after freezing–thawing cycles appearing in the presence of gelatin (gel composition) and chitosan (Argogel), the statistically significant difference is observed for all size ranges. This is explained by the above indicated dynamics of the AgNP content in each gel. As far as the gel composition is concerned, the content of 16 to 40 nm nanoparticles notably lowers, whereas a significant growth in large (>40 nm) nanoclusters occurs in the Argogel. All this is observed at a considerable increase in the fine nanoparticle content and a constant amount of 40 nm nanoparticles, as presented in Fig. 4. After freezing–thawing cycles, the content of large nanoclusters in the Argogel is 37.2 times higher than that in the gel composition ($p < 0.05$), although the situation is quite different before freezing–thawing cycles, and 16 to 40 nm nanoparticles manifest the 3.1 times higher content in the gel composition ($p < 0.05$).

It is worth noting that before and after freezing–thawing cycles, the content of 1 to 15 nm nanoparticles in the gel composition is respectively 1.9 and 25.7 times higher ($p < 0.05$) than in the Argogel. It is therefore advisable to use gelatin, rather than chitosan in order to obtain 1 to 15 nm nanoparticles on the PLG fiber. The statistically significant difference in the content of 16 to 40 nm nanoparticles is less important than in other size ranges and does not exceed 3.9 times after 10 freezing–thawing cycles with the domination of their absolute content in the chitosan Argogel.

CONCLUSIONS

According to our experiments, changes in the AgNP content could be caused by the following factors. Firstly, the content growth of 1 to 15 nm nanoparticles (see Figs. 1 and 4*b*) was probably associated with the porosity modification of the PLG fiber after its cyclic freezing, that was indirectly confirmed by Reis *et al*. [23]. They demonstrated the higher AgNP content for a potential acne treatment after the increased porosity of structures consisting of lactide and glycolide provided by lyophilization and centrifugation. At the same time, other parameters of nanostructures also changed, including their size, zeta-potential, kinetics of *in vitro* release, while toxicity profiles did not change. Secondly, in the case with the Argogel, the content fluctuation of different-size AgNPs could be determined by the interaction between the PLG fiber and chitosan [24]. Although the latter inhibited the initial (explosive) recovery rate of hydrophil components in AgNPs, it prolonged their cumulative effect, that could intensify hydrothermal Ag^+ reduction after, for example, 10 cycles of freezing and thawing. That intensified the molecular interaction between AgNPs and functionally active chemical groups both of ligand (PVP) and sorbent polymer. These phenomena expectedly occurred under the multiple treatment at −37.0°C on the fiber with adsorbed nanoparticles, and the described

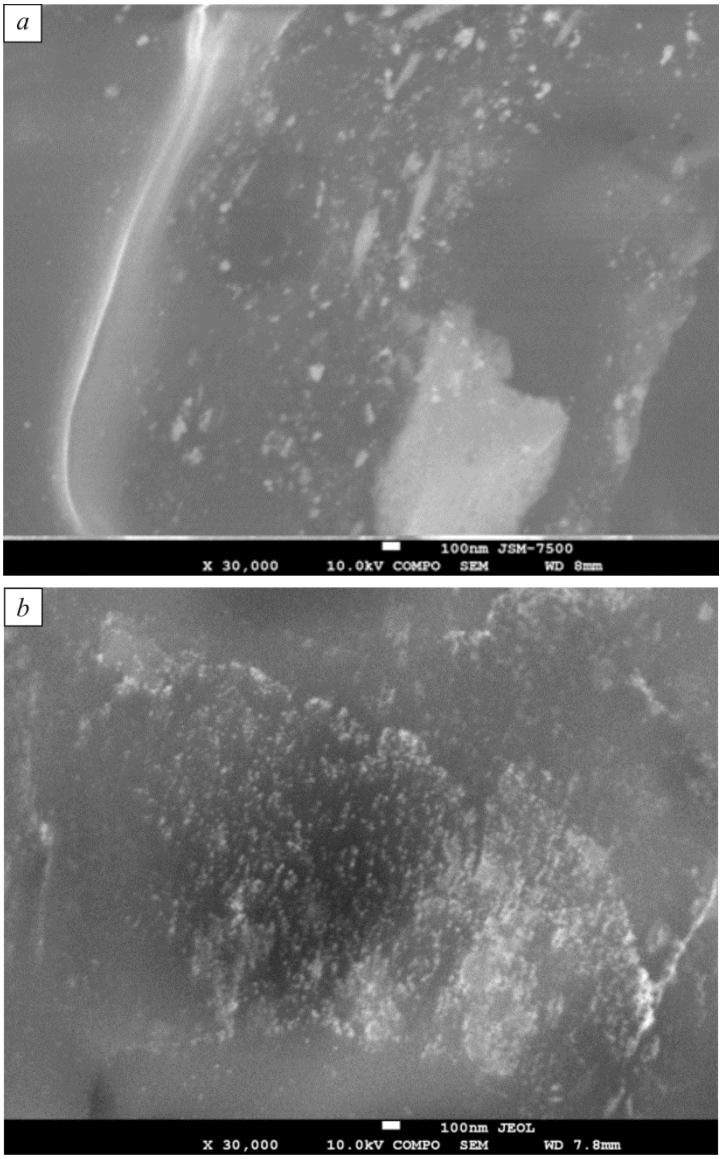

Fig. 4. SEM images of Sabfil suture material with AgNPs obtained by cavitation-diffusion photochemical reduction without thermal exposure below 0.0°C (*a*) and after 10 freezing–thawing cycles (*b*).

process was characterized by the dynamic transformation in the AgNPs–Ag^{+}–fiber system. Along with the reparative regeneration, that transformation provided the conversion of fine nanoparticles into large nanostructures (see Fig. 2).

Moreover, the stability change in chitosan-containing AgNPs was obvious at pH-value fluctuations during their interaction with the PLG fiber [25]. Positively charged chitosan (cationic polysaccharide) could modify the resistance of lactide and glycolide components. We thus assumed that the interaction between the chitosan Argogel and polymeric fiber affected the AgNP stability, thereby increasing their sensitivity to pH-value fluctuations in the region of neutral and base values, first of all, due to the drop of AgNP zeta-potential resulted from neutralization of positively charged aminogroups of *N*-acetyl *D*-glucosamine residues and, indirectly providing their aggregation on the suture material surface during freezing–thawing cycles. Another mechanism of the AgNP coarsening during 10 freezing–thawing cycles applied to the Argogel-treated Sabfil, was folding of chitosan molecules with a successive AgNP encapsulation

at neutral pH values [26], which was consistent with SEM observations (see Figs 2 and 3). During freezing–thawing cycles, AgNP modifications on the PLG fiber could significantly improve the effectiveness of their practical use, thus providing both a steady effect and longer-term *in situ* microbicidal effect without increasing their cytotoxicity for intact cell structures [16, 27].

Based on the results in can be concluded that before and after 10 freezing–thawing cycles, the use of gelatin in the gel composition provided the adsorption of mostly 1 to 15 nm nanoparticles on the PLG fiber, which were obtained by cavitation-diffusion photochemical reduction, potentially creating conditions for the microbicidal effect of the fiber. The proposed thermal treatment significantly increased the AgNP content on the PLG fiber and their general content, first of all, the content of fine nanoparticles. 10 freezing–thawing cycles modified AgNPs on the Sabfil fiber in the presence of chitosan and resulted in the statistically significant increase in their size with the dominant content of 40 nm nanoparticles, that could prolong their interaction on the tissue, albeit with lower antibacterial activity.

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