Aqueous dispersions of oxide nanoparticles as a treatment for pyoinflammatory diseases with chronic component

Ph Rutberg¹, V Kolikov¹, A Moshkin², V Snetov¹, A Stogov¹ and M Khalilov²
¹ Institute for Electrophysics and Electric Power Russian Academy of Sciences, 18 Dvortsovaya nab., St.-Petersburg, 191186, Russia
² Oryol State University, Medical Institute, October st. 25, Oryol, 302028, Russia

E-mail: Stogov2007@yandex.ru

Abstract. Promising direction of surgery related to the treatment of acute purulent wounds with chronic component could be utilization of aqueous dispersions of nanostructures (ADN) produced by pulsed electric discharge in water [3, 6]. The investigation is addressed to finding out the opportunity of usage of an ADN for treatment of purulent wounds with a chronic component and comparison of its efficiency with the widespread antiseptics. For realization of investigation was used ADN, which has maximal share of “small” nanostructures (<100 nm) with the greatest surface electric charge. High activity of reparative processes is established at use of ADN and subsequent moderate changes of the further healing. The attributes of cellular atypia and preternatural representations about inflammatory reactions are not revealed at local use of ADN.

1. Introduction
Promising direction of surgery related to the treatment of acute purulent wounds with chronic component could be utilization of aqueous dispersions of nanostructures (ADN) produced by pulsed electric discharge in water [3, 6]. The group of patients with such wounds are of large number and differ on etiology of diseases but their mutual feature is long treatment without marked positive changes [5]. Thus long application of antibiotics leads to abnormality of immune processes and antibacterial resistance of microbial flora [1]. Moreover, local antiseptics are frequently toxic and one can oppress processes of reparation in a wound [2]. The investigation is addressed to finding out the opportunity of usage of an ADN for treatment of purulent wounds with a chronic component and comparison of its efficiency with the widespread antiseptics.

2. Materials and procedure
One of effective ways of oxide metal nanostructures manufacture is processing of water by pulsed electrical discharge. In this case, ADN formed by PED contains both nanostructures of electrode metal or its oxides and metal’s ions [4, 7]. ADN were produced by electrical discharge setup with voltage 60 kV, current 40 A, current pulse duration of 5 - 10 microseconds and pulse repetition rate of 50 Hz.

Distribution of a share of “small” nanostructures subfractions (≤ 100 nm) and a surface electric charge of nanostructures depending on pulse duration had been determined by laser correlation spectrometer “LCS-03” and the device capillary electrophoresis “NANOPHORE 01” (Figure 1).
For the clinical researches, the ADN with maximal share of “small” nanostructures and maximal surface electric charge has been chosen. Such nanostructures at pulse duration of 5 - 10 µs are formed.

Clinical research on 133 rats of both sexes of line “VISTAR” of weight 170 ± 30 g was carried out. For treatment of wounds were used the ADN of silver alloy of 5 mg/l mass concentration in 2 months after its preparation, solution of sodium hypochlorite of 600 mg/l mass concentration and 0.05% solution of chlorhexidine bigluconate. The animals were divided in four groups: one control group of 31 animals and three test groups of 51 animals each.

Purulent wounds were made by means of sewing in inter shoulder-blade areas of a gauze napkin impregnated with a solution of low viral strain of Staphylococcus aureus. Lancing and surgical sanitation of an abscess on 7th day after infecting were carried out. Initial wound surface area was 150 ± 50 mm².

3. Results and discussion
The wound treatment was carried out by daily overlaying of gauze napkin moistened with solutions being compared. Figure 2 presents a graph to reduce the area of wounds for 14 days for the three solutions used.
Figure 2. Reduction of the area of wounds at processing by antiseptics.

The plot shows the expressed tendency to reduction of the area of wounds in all three groups of animals with the common law of waviness of the healing current, caused by as conversion processes, and local inflammatory reactions. It is necessary to note high activity conversion processes at use ADN during the first 5 days from the beginning of treatment with a maximum on 3 - 4 days and subsequent moderate changes of the further healing.

The important factor distinguishing action ADN from two other antiseptics is absence secondary infection, observed on 4 and 9 days (chlorhexidine) and on 7 day (hypochlorite sodium).

The plot of changes of bacterial seeding (number of bacteria per gramme of weight of a wound tissue) shows oppression of tissue flora in all groups of animals. Approach of wound sterility occurred on 5 - 7 days, that is related to the activity of antiseptics and the factors of local immunity (Figure 3).
Figure 3. Changes of bacterial seeding.

The average weight of animals in test groups decreased due to long proceeding inflammatory reaction (Figure 4).

Figure 4. Change of average weight of animals during experiment.
At use of ADN average absolute rate of healing (mm$^2$/day) is a little bit lower, than in percentage expression that is related, apparently, with intensive wounds healing in the initial days and with the subsequent decrease of healing rate in conditions when the wound is disinfected and has the smaller area (Figure 5).

It is important to note that at use of ADN the number of animals with full wound healing by the end of 14 day appeared a little bit more than in two other groups.

Conformity of a microscopic picture to a visual estimation of wound process has been established at research of histologic cuts. At local use of ADN there were no revealed attributes of cellular atypia which are beyond of preternatural representations about inflammatory reactions.

![Figure 5](image_url)

**Figure 5.** Average for 14 day parameters of reduction of the wound areas concerning its initial size.

Current practice of treatment of chronic purulent wounds on the background of the damaged tissue metabolism and local pathomorphism shows that there is no reason to rely on their quick healing, and therefore, the aim of treatment is to prevent complications.

In addition, the reactivation of an existing microflora when adapting it to antibiotics and the accession of additional associations of pathogens in the nutrient medium of wounds result to considerable adverse effects. Antibiotic resistance is becoming every year more and more pressing problem. Traditionally used antiseptics can inhibit regeneration in the wound and sometimes they lead to total intoxication patient with their long-term use in large-affected areas.

The investigation showed that the ADN have not of systemic toxicity, which may open new possibilities to cure a broad category of patients.

Another significant positive quality of ADN is the relative ease and cheapness of their manufacturing, as well as the fact that their storage does not require special conditions and they retain their antibacterial properties for a long time.

**4. Conclusion**

For realization of investigation was used ADN, which has maximal share of “small” nanostructures (<100 nm) with the greatest surface electric charge.

High activity of reparative processes is established at use of ADN during the first 5 days from the beginning of treatment with a maximum on 3 - 4 days and subsequent moderate changes of the further healing.

At use of ADN the number of animals with full wound healing by the end of 14 day appeared a little bit more than in groups where were used chlorhexidine and hypochlorite sodium.

The attributes of cellular atypia and preternatural representations about inflammatory reactions are not revealed at local use of ADN.

It is possible to assume that use of ADN will allow to correct a little in the long term practice of out-patient therapy of chronic and slow pyoinflammatory diseases.
Acknowledgements

Work was supported in part by the Russian Foundation for basic research, projects №№ 08-08-00477-a, 10-08-00239-a.

References

[1] Volenko A V, Menshikov A A, Titova G P and Kuprikov S V 2004 Surgery Preventive maintenance wound infections by immobilised antibacterial preparations 10 54-58.

[2] Ljapunov A N, Datsenko B M and Mohert N A 1995 The problem of medicinal therapy Theory and practice of local treatment of purulent wounds Kiev 132-196

[3] Kolikov V A, Kurochkin V E, Panina L K and Rutberg F G 2005 Doklady Biological Sciences, Pulse electric discharges and prolonged microbial resistance of water 403 279-281

[4] Kolikov V A, Kurochkin V E, Panina L K, Rutberg A F, Rutberg F G, Snetov V N and Stogov A J 2007 Technical Physics Prolonged microbial resistance of water treated by a pulsed electric discharges 52, no.2 263-70

[5] Fedorov D N, Ivashkin A N, Shinin V V, Vasiljev A V and Ivanov A A 2002 Archive of a pathology Morphological and immunological characteristic conversion processes in long not healing wounds 64 № 1 8-11

[6] Rutberg Ph G, Kolikov V A, Kurochkin V E, Panina L K and Rutberg A Ph 2007 IEEE Transactions on Plasma Science Electric Discharges and the Prolonged Microbial Resistance of Water 35 no.4 1111-18

[7] Rutberg Ph, Kolikov V, Snetov V, Stogov A, Noskin L, Landa S and Arutunjan A 2007 IEEE Pulsed Power and Plasma Science Conf. (PAPS-2007) Pulsed electric discharges in water and oxide nanostructures 1244-47