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ARTICLES

Wound-Healing Properties of Copper Nanoparticles as a Function of Physicochemical Parameters

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Abstract—Results of a study on the wound-healing potential and physicochemical characteristics of copper nanoparticles prepared by high-temperature condensation and modified with a variety of agents (including oxygen, water vapors, and air) are reported. The modification of copper nanoparticles under monitored conditions guarantees the synthesis of particle species differing in size, phase composition, thickness, and composition of the oxide layer. Modified copper nanoparticles in the form of an ointment showed wound-healing behavior that differs in effectiveness depending on their physicochemical parameters. Nanoparticles of copper oxide (sample 7) (modified with air), with a particle size of 119 nm and crystalline copper content of ~0.5%, and copper nanoparticles (sample 2) (modified with oxygen), with a particle size of 103 nm and crystalline copper content of 96%, demonstrated the maximum specific rate of wound adhesion.

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Technical progress in the second half of the 20th century provided methods to obtain metals and nonmetals in the form of highly dispersed powders, as well as a basis for studies on the physicochemical properties and structure of nanoparticles [1]. Nanosized particles, due to their highly specific surface area, proved highly reactive. The particular properties of nanoparticles have already been employed in processes of catalysis and combustion along with other fields of physics and engineering. Due to their high reactivity, small size, and the presence of a metal crystalline phase in the particles, upon being introduced into a live organism, nanoparticles trigger biological responses different from those produced by the traditional ionic form of elements. Our 30 years of experience (1977–2009) in studying how nanoparticle affect living systems of various levels of organization (as well as the whole body); the activity of enzymes; the structure and function of biomembranes; and biochemical processes, including metabolism of elements, have created a foundation for the experimental development of metallotherapy of various pathologies with nanoparticles [2].

The studies performed on the effect of nanoparticles on biosystems made it possible to reveal their unique properties:

(1) metal nanoparticles are 7–50 times less toxic than their corresponding ionic forms;

(2) nanoparticles produce a prolonged effect, serving as a depot for elements in an organism;

(3) nanoparticles introduced in biotic doses stimulate the metabolic processes of an organism;

(4) the nanoparticles' effect is multifunctional [3].

To summarize, the data obtained so far have preconditioned the development of a new type of drugs for metallotherapy in order to improve the quality of life with the highly efficient, prolonged, polyfunctional, and nontoxic effect of nanoparticulate metal drug formulations [4, 5].

One-tenth of the Russian population suffers injuries each year, and this number is increased by military activities, terrorist attacks, and natural disasters. For this reason, the search for new wound-healing preparations remains a topical issue. Wound healing is a complex process which requires balanced concentrations of microelements, antioxidants, matrix metalloproteinases, and other factors. Copper deficiency is among the factors inhibiting wound healing [6]. Today, it is understood that the physicochemical properties of nanosized objects differ from those of bulk metal objects and individual atoms. However, biological activity in the function of physicochemical characteristics of metal nanoparticles has not been studied yet. In a study of copper nanoparticle toxicity, we have demonstrated that a decrease in the particle size to 33.8 ± 0.3 nm results in an increased toxicity in comparison to larger particles of 103 ± 2.0 nm; however, according to the maximum tolerated dose (MTD), LD_{50}, and LD_{100} values, copper nanoparticles are 2.5–6 times less toxic than copper salts [7].

In connection with this, the aim of this work was to establish a relation between the physicochemical characteristics and biological activity of copper nano-