Cryochemical Production of Hybrid Nanoforms of Antibiotics with Bioactive Metals/Metal Oxides: Approach to Drug Delivery and Controlled Drug Release

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Cryochemical synthesis is a powerful method of reducing the size of drug substances particles, changing their form and crystal structure and to improve their pharmaceutical properties. The use of antibiotics and other antimicrobial agents in medicine has led to the emergence of many resistant strains of microorganisms. This problem can be solved by the synthesis of new drug substances and by the creation of hybrid nanoforms of antibiotics with metal/metal oxides nanoparticles. The application of cryochemical method allowed us to obtain antibiotics nanocrystals and hybrid nanocomposites of drug substances with metal/metal oxide nanoparticles¹⁻³. Antibacterial compositions were produced by low temperature freeze drying technique of water solutions containing metal/metal oxide nanoparticles and antibacterial components dioxidin or gentamicin.

The thorough studies by transmission electron microscopy (TEM), electron microdiffraction, Fourier transformation infrared spectroscopy (FTIR), UV absorption spectroscopy, X-ray powder diffraction, differential thermal analysis (DTA) have been made, It was shown that the hybrid compositions were including Ag and/or Cu nanoparticles of 5-50 nm in size and nanoparticles of antibiotic drugs of 50-300 nm in diameter. Drug cryoforms possessed modified crystal structures and lower melting temperatures. New cryoformed hybrid compositions of nanosized metal/metal oxides and antibiotic particles demonstrates higher antibacterial activity against *E. coli 52, S.aureus 144, M. cyaneum 98, B. cereus 9* compared to the original drug substance and individual metal nanoparticles ⁴.

The samples have been included in cryostructured polymer matrices of chitosan, Ca-alginate and gelatine. It was shown the possibility of directed deliver and controlled release of antimicrobial compositions.¹

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¹. Shabatina, T.I., Vernaya, O.I, Shabatin, V.P., Melnikov, M.Y, Semenov A M., Lozinsky, V.I., Metal Nanoparticle Containing Nanocomposites of Drug Substances and Their Potential Biomedical Applications. *Applied Sciences*, (*MDPI*), **2020**, *10*, 170, 1-11.

². Shabatina, T.I., Vernaya O.I, Shabatin, V.P., Melnikov, M.Y Magnetic Nanoparticles for Biomedical Purposes: Modern Trends and Prospects. *Magnetochemistry (MDPI)* **2020**, *6*, 3, 1-18.

³. Shabatina, T.I., Vernaya, O.I, Shabatin, V.P., Semenov A M., Melnikov, M.Y Low-Temperature Synthesis of Hybrid Nanoforms Based on the Antibacterial Drug Dioxidine and Nanoparticles of Bioactive Metals (Silver, Copper) Incorporated into Biopolymer Cryogels. *Russian Journal of Physical Chemistry A*, (Pleiades Publishing, Ltd), **2019**, *93*, 10, 1970-1975.

⁴. Shabatina, T.I., Vernaya, O.I, Shumilkin A.S., Semenov A M., Melnikov, M.Y.Nanoparticles of Bioactive Metals/Metal Oxides and Their Nanocomposites with Antibacterial Drugs for Biomedical Applications. *Materials(MDPI)* **2022**, *15*, 3602.