Synthesis and properties of polymer water-soluble films with antitumoral, antiseptic and nitric monoxide (NO) donating activities

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The search for new approaches to the development of effective and non-toxic materials-prodrugs based on metal coordination compounds has been performed intensely in leading laboratories world-wide. Synthetic models of nitrosyl intermediates forming in the cells upon the interaction of endogenous nitric monoxide (NO) with active sites of ferredoxines are of great scientific interest (Fig.1). It is known that nitrosyl iron complexes are intermediates in the decomposition of proteins and formation of S-nitrosothiols, which are catalyzed by the iron, and are reservoirs and transporters of NO in vivo.

The objective of this work is to develop procedures for synthesis of water-soluble polymer composites with iron-sulfur complexes as NO donors with antiseptic and antitumoral activities and to study their properties in order to use them as NO donors materials in the in the treatment of socially significant diseases, viz. in the NO-therapy of oncological and infectious diseases. The high homogeneity with fine distribution of nitrosyl complexes into volume of polymer should be provided.

In present work homogeneous water-soluble composites of polyvinylpyrrolidone and dextran with iron-sulfur nitrosyl complexes with antitumoral activity \([\text{Fe}_2(\text{SR})_2(\text{NO})_4\text{SO}_4\cdot\text{nH}_2\text{O}}\) (\(\text{R}_1\)-cysteamine; penicylamine); and nitrosyl complexes \([\text{Fe}(\text{SR})_2(\text{NO})_2\text{X}\cdot\text{nH}_2\text{O}}\) (\(\text{R}_2\)-thiocarbamid and its derivatives; \(\text{X}=\text{Cl}^-\) and \(\text{SO}_4^{2-}\)); \(\text{Na}_2[\text{Fe}_2(\text{SR})_2(\text{NO})_4\cdot\text{4H}_2\text{O}}\) (\(\text{R}_3\)-thiosulfate) with antiseptic activity were obtained for the first time. Their characteristics in solid state and in the water solutions were studied by X-Ray diffraction, SQUID magnetometry and amperometry.

Based on small-angle diffraction was showed that the samples of the composites lacking aggregates of 10-100 nm, and the nitrosyl iron-sulfur complexes are distributed uniformly in the polymer matrix. According to the analysis of the dependence of the magnetic moment \(\text{M}\) of the magnetic field \(\text{H}\) at \(\text{T} = 2\ \text{K}\) and its approximation were determined average particle spin and temperature characterizing the magnetic interactions of paramagnetic particles.

As follows from electrochemical analysis, polymer composites decomposes to yield NO within seconds after dissolution in aqueous solution without additional thermal and photo activation. The time dependence of NO amount and maximum amounts of NO generated by films at pH 7 were determined.

**Fig. 1.** Nitrosyl iron-sulfur complexes are synthetic analogues of cellular nitrosyl ferredoxine active sites.

**Keywords:** NO donor polymer films, sulfur-nitrosyl iron complexes, powder small-angle X-Ray scattering, SQUID magnetometry, amperometry

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