Iron (III) complexes with humic and polysaccharide macroligands for correction of iron deficiency anemia

Zhirkova A.M.¹, Volikov A.B.¹, Volkov D.S.¹, Buyko E.E.², Zykova M.V.², Perminova I.V.¹

¹Moscow State University MV Lomonosov, Moscow, Russia, Zhirkova_am@mail.ru

²Siberian State Medical University, Tomsk, Russia

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More than 2 billion people worldwide suffer from iron deficiency anemia (IDA) [1]. Despite the variety of drugs produced, the incidence rate is not decreasing. The most promising are Fe(III) preparations stabilized by polysaccharides, but the bioavailability of these preparations is 5 times lower than that of Fe(II) preparations [2]. We considered natural humic substances (HS) as new ligands capable of increasing bioavailability of Fe(III) and of reducing the number of side reactions. Humic macroligands contain phenolic and carboxyl groups, possess complexing and redox properties, which determines the prospects of their use for obtaining bioavailable complexes with Fe(III).

The following precursors were used: humic acids of coal (HA), fulvic acids of peat (FA), polymaltose (PM). We have synthesized 5 preparations: mixed-ligand (HS:PM = 1:1) and monoligand (HS=100%) preparations of iron (III) hydroxide humates with an iron content of 12-13%; mixed-ligand and monoligand fulvates of iron (III) hydroxide with an iron content of 7-8% and a monoligand reference preparation of iron (III) hydroxide polymaltose - 6% by weight of the dry preparation.

These preparations were characterized by X-ray phase analysis (XPA) and transmission electron microscopy (TEM). Diffraction patterns confirmed that all samples are characterized by low crystallinity of the iron-containing phase, presented in the form of ferrihydrite. The phases are NaCl in fulvate and KCl in humic samples. According to the TEM data for the preparations, discrete nanoparticles with a size of 2-5 nanometers are observed.

To assess the bioavailability of iron in the composition of the preparations obtained, the ferrozine method was used.

According to the results of the ferrozine study, it was shown that the highest percentage of the content of bioavailable iron in the sample was shown by mixed-ligand preparations, about 6%. In monoligand preparations, the percentage of bioavailable iron was found to be lower within the range of 1-4%.

Cytotoxicity was assessed on two cell lines, 3T3-L1 and HepG2, by the MTT test.

The results of cytotoxicity assessment showed the absence of pronounced cytotoxicity in the entire line of drugs, IC50 was not achieved.

The conclusions are that the largest percentage of iron and bioavailable iron is contained in the preparation of iron (III) hydroxide. In view of its non-cytotoxicity and bioavailability of iron, we can talk about the prospects for further study of mixed-ligand preparations as a potential active pharmaceutical substance (APS).

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