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Immobilization of therapeutic agents on magnetic iron oxide nanoparticles decreases binding to blood serum proteins and increases resistance to enzymatic cleavage

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Abstract

A drug's affinity for binding blood serum proteins, such as albumin, determines a primary interaction affecting its biological activity. Only the free unbound fraction of a drug can induce a therapeutic effect. A range of effective antimicrobial agents, such as peptides containing N3-(4-methoxyfumaroyl)-L-2,3-diaminopropanoic acid (FMDP), are known to be powerful inhibitors of fungal and bacterial growth in vitro; nevertheless, the use of these compounds in clinics has proven intractable due to their irreversible binding of blood serum proteins, causing complete loss of their biological activity. Nanoparticles are now widely tested as drug carriers. The main purpose of the work was to investigate the differences in physicochemical properties (solubility, penetration capacity, lipophilicity) between acid-soluble drugs in magnetic iron oxide nanoparticles and similar drugs in their unprotected form. The synthesis of Fe3O4 magnetic iron oxide nanoparticles containing (3-aminopropyl) triethoxysilane (APTES) is made with selected adhesive drugs. The detected nanostructures were detected using IR spectroscopy, atomic force microscopy (AFM), vibrating sample magnetometry (VSM) and dynamic light distribution techniques (DLS), as well as the physicochemical properties of untreated drugs were studied. Drug deficiency was measured using a flasksaturation filling method.

The discovery was measured using dialysis membrane, a MWCO 50 kD with pores <10 nm. Lipophilicity was measured separately by octanol. Drugs showed better solubility and low pH values (pH 2.0 and 5.0)and lower solubility and higher pH values (pH 6.5 and 7.5) compared to compatible non-compliant drugs.Another limitation, common to FMDP-agents and a range of other peptide drugs, is low stability in blood serum caused by peptidase cleavage. Our studies have demonstrated that the described caveats of certain drugs can be significantly reduced by immobilization on the surface of magnetic ironoxide, Fe3O4, nanoparticles (MNPs). Ibuprofen, immobilized on MNPs, was found to exhibit high antibacterial activity even at a very low concentration and in the presence of albumin in strong contrast to the unattached form of the drug.Furthermore, immobilizing LysNvaFMDP, one of the most potent antifungal agents among the FMDP-peptides, on MNPs decreased its affinity to albumin and other serum proteins compared to its unbound form and resulted in high antimicrobial activity towards bacteria. Finally, our studies proved that the model peptides immobilized on MNPs were more resistant to enzymatic hydrolysis. Together these findings demonstrate the promising utility of MNPs for enhancing therapeutic drug delivery and efficacy

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