Blood proteins interaction of hybrid Fe_3O_4@Ag NPs engineered for nitric oxide release for the treatment of infections and cancer

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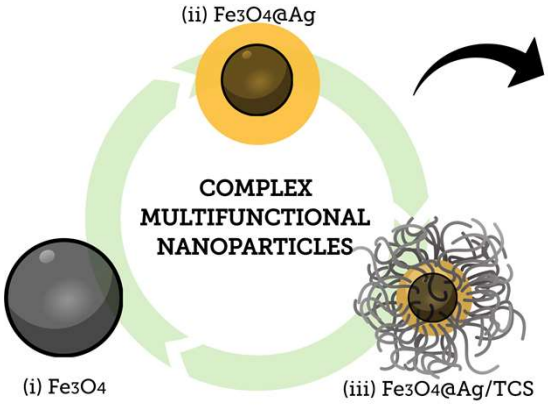
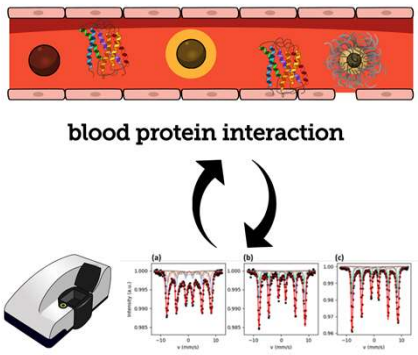
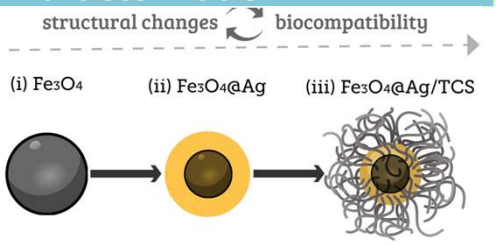
Introduction and Methodology





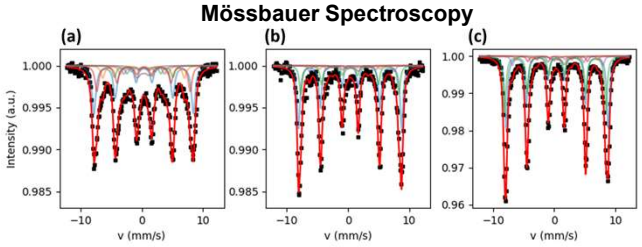
After administration, engineered nanoparticles interact with biological molecules, and the nature of this interaction might directly interfere on the biological fate and action of the nanoparticles. In this work, we synthesized a hybrid magnetic nanostructure, with potential for antibacterial and antitumoral applications, based on magnetite and silver nanoparticles, coated with a modified chitosan polymer (TCS). We investigated the structural properties of the nanoparticles through Mössbauer Spectroscopy after the addition of each layer on their surface. The structural characteristics of the nanoparticles were then correlated to their interaction with blood proteins, evidenced by the influence of the proteins in the nanoparticle properties, proteins retention, and thermodynamic parameters.

Characterization



	(i) Fe_3O_4	(ii) Fe_3O_4@Ag	(iii) Fe_3O_4@Ag/TCS
Hydrodynamic diameter (% number - nm) - PBS	195.1 ± 10.9	106.0 ± 15.7	147.6 ± 14.9
Polydispersity index - PBS	0.398 ± 0.030	0.438 ± 0.030	0.451 ± 0.030
Zeta potential (mV) - PBS	-23.2 ± 2.6	-30.0 ± 1.5	-35.0 ± 0.9
Zeta potential (mV) - water	-8.56 ± 1.00	-32.73 ± 0.31	-19.40 ± 1.00

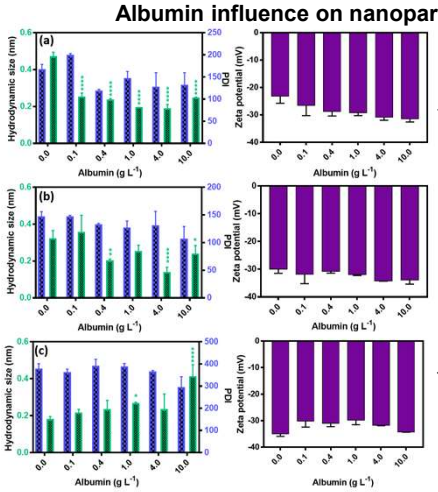
Mössbauer Spectroscopy



❖ Higher stability after adding AgNPs and TCS

❖ Magnetite/maghemite core-shell model

Albumin influence on nanoparticles parameters



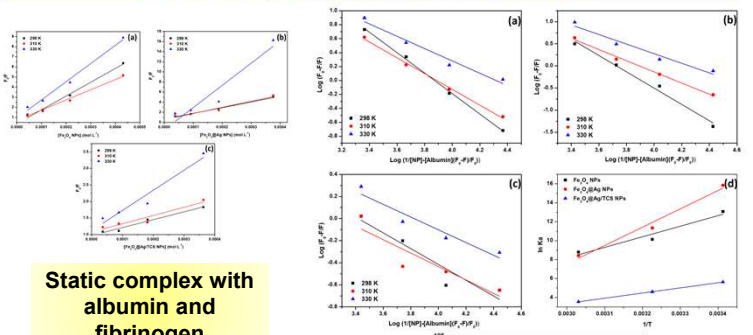
❖ Non-stabilized nanoparticles were stabilized with albumin;

❖ TCS-coated nanoparticles demosntrated a size increasement;

❖ Zeta potential was negative at pH 7.4, as expected due to albumin charge;

❖ Polydispersity index was not significantly modified.

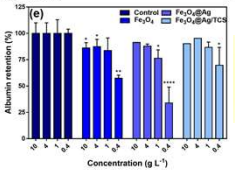
Blood protein interaction



Static complex with albumin and fibrinogen

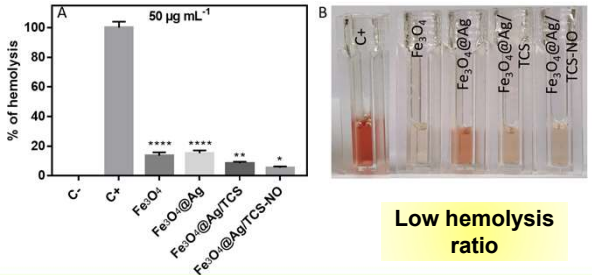
❖ All nanoparticles formed static interactions with albumin and fibrinogen (not shown);

❖ Van der Waals interaction were predominant for all particles.



Low albumin retention

Hemolysis of whole blood



Low hemolysis ratio

Conclusions

In this study, we synthesized multifunctional nanoparticles based on a magnetic core (Fe_3O_4 NPs) coated with AgNPs and TCS. We demonstrated that the addition of metallic nanoparticles and a polymeric layer on the surface of Fe_3O_4 NPs diminished the oxidation (from magnetite to maghemite), and promoted the stabilization, preventing the formation of agglomerates. These properties directly reflected in the mechanisms with proteins, leading to the formation of a static complex with similar interaction mechanism, but presenting higher affinity for the less stabilized nanoparticles

Acknowledgements

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