Methotrexate-Loaded Hydrophilic Gold Nanoparticles for Transdermal Delivery

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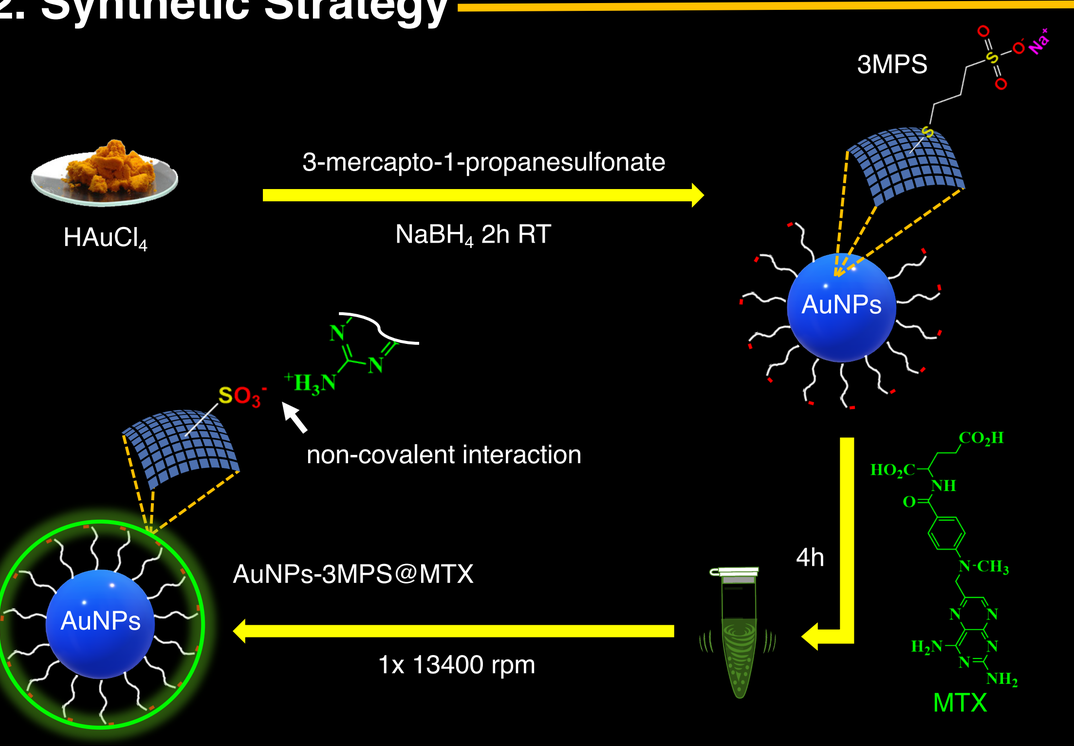
1. Introduction

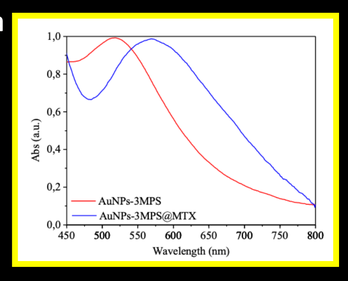
Advances in nanotechnology have enabled the development of multifunctional nanoparticles that can simultaneously perform various functions, including targeting, imaging, and therapy [1]. Recently, gold nanoparticles (AuNPs) have been investigated for potential multifunctional uses in nanomedicine as therapeutic agents and drug carrier, although the mechanisms of interaction with drugs are still little known [2-4].

In the present work, we studied the interaction between functionalized hydrophilic AuNPs and the immune-system suppressant drug Methotrexate (MTX) at molecular level. The aim was to define the overall structure of drug loaded AuNPs and drug location on the colloidal nanoparticles surface, that will improve drug efficacy and knowledge of the pharmacodynamics and pharmacokinetic properties.

2. Synthetic Strategy



3. Results and Discussion [5]



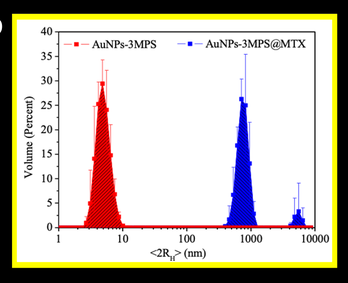


Figure 3.1. a) UV-Vis spectra and b) DLS measurements of AuNPs and AuNPs-3MPS@MTX.

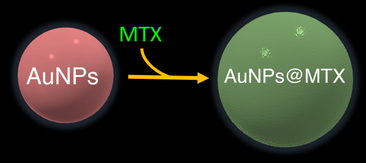
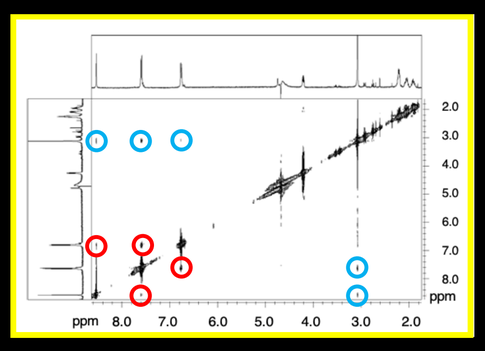
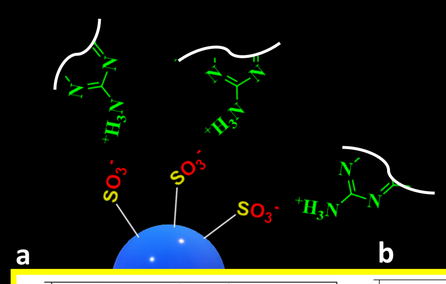


Figure 3.2. Bidimensional ^{1}H-NMR spectra of AuNPs-3MPS@MTX. Red circles highlight spatial correlations among the aromatic protons. Blue circles highlight spatial correlations between aromatic protons and –CH_3 of MTX.





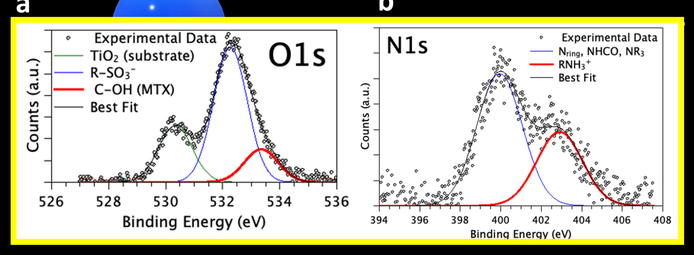
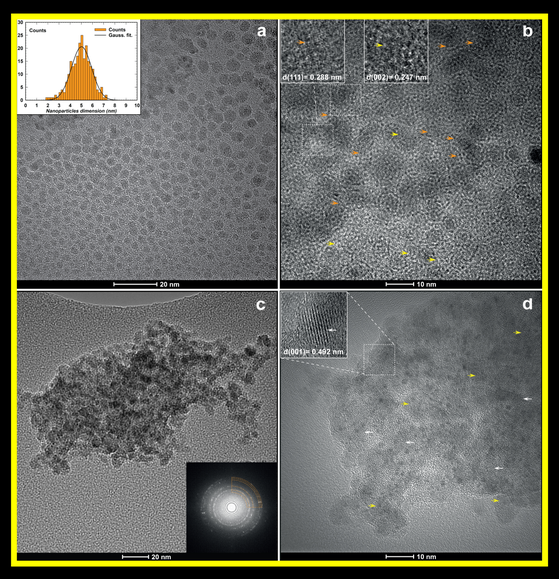


Figure 3.3. a) O1s spectra of AuNPs-3MPS@MTX. Red component evidences the successful loading of MTX. b) N1s XPS spectrum of AuNPs-3MPS@MTX. Red component is related to RNH_3^+, that could interact with negatively charged thiols.

Figure 3.4. a) 2D typical AFM image obtained for pristine AuNPs-3MPS and b) 2D typical AFM image obtained for AuNPs-3MPS@MTX.



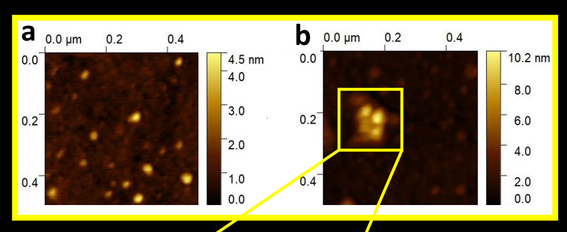


Figure 3.5. (a) BF-TEM image of AuNPs-3MPS. (b) HR-TEM image of gold-sulfide nanocrystals in AuNPs-3MPS, showing lattice fringe images of d-*spacing* 0.288 nm (orange arrows) and 0.247 nm (yellow arrows). (c) BF-TEM image of AuNPs-3MPS@MTX. (d) HR-TEM image showing overlapping lattice fringes of Au_2S nanocrystallites of AuNPs-3MPS@MTX.

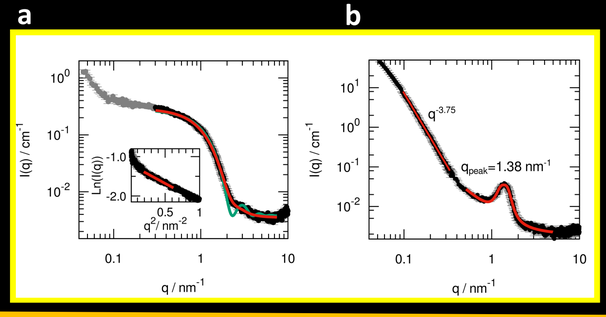


Figure 3.6. a) Model functions: monodisperse homogeneous sphere with radius 1.95 nm (green line), homogeneous sphere with r=1.60 nm and 25% gaussian polydispersity (red line); in the inset the Guinier fit is shown giving a R_g=1.69 nm. b) SAXS data of AuNPs-3MPS@MTX.

4. Conclusions

The nature of AuNPs-3MPS and MTX interaction can be categorized into electrostatic binding between protonated aromatic -NH_2 groups in the ring structure of MTX and negatively charged –SO_3^- of thiols capping agents, as confirmed by NMR and SR-XPS studies. Furthermore, isolated nanoparticles with $<2R_H>$ 5 ± 1 nm showed a tendency to aggregation up to $<2R_H>$ 710 ± 160 nm after addition of MTX as demonstrated by DLS, AFM and HR-TEM measurements. At the same time, electron microscopy and SAXS data revealed that the presence of MTX interacting electrostatically leads to a formation of large clusters with densely packed arrangement of AuNPs-3MPS@MTX.

5. References

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6. Acknowledgements

The authors want to thank the Universidad de Sevilla (Spain) for the use of experimental facilitates at CITIUS, Microscopy (VI PPIT-2019-I.5 Isabel Montealegre Meléndez) and Elettra Sincrotrone Trieste for providing access to its synchrotron radiation facilities and for financial support. IP gratefully acknowledge funding from EUROFEL. This work was supported by the University of Rome "La Sapienza" [grant numbers Sapienza 2019 RM11916B75D8FAF5 and 2017 RM11715C792D1AF3].