NOBLE METAL NANOPARTICLES USED AS CARRIERS SYSTEMS FOR NSAIDs DRUGS: SEF, RELEASE AND BINDING

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INTRODUCTION

Targeted drug delivery constitutes, actually, one of the most important research fields. It is necessary to maximize the therapeutic effects jointly with a minimization of the undesired secondary ones. The use of noble metal nanoparticles as drugs nanocarriers presents two principal advantages, firstly they are able to transport several therapeutic molecules adsorbed on their surface and secondly, due to the presence of Localized Surface Plasmon Resonances, an enhancement of the spectroscopic signals of the molecules carried is produced thus permitting to observe them in their traverse through the body to the specific disease tissues. In this work we present part of our research using noble metal nanoparticles as drug delivery systems, based on our previous studies [1, 2]. On one side we show SEF (Surface Enhanced Fluorescence) results of systems formed by several NSAIDs (Non-Steroidal AntiInflamatory DrugS), piroxicam (PX), ketorolac (KT) and indomethacin (IM) and Au nanoparticles. On the other side, and using Ag nanoparticles, we also present results of the binding constant of the albumin-drug system when protein molecules are adsorbed on Ag nanoparticles, and those of the release of the molecules from silver nanostructures.

EXPERIMENTAL METHODS

UV-vis absorption spectra were obtained using a Varian Cary 500 UV-Vis spectrophotometer and quartz cells of 1 cm of path length. Fluorescence: steady-state experiments were recorded on a Perkin Elmer LB50. SEF spectra measurements were carried out on a Renishaw *In via* Raman Microscope, using excitation wavelength of 325 with a spectral resolution of 2 cm^{-1}. The colloid used for SEF experiments was prepared by chemical reduction of metal nitrate with hydroxylamine hydrochloride (Ag) or sodium citrate (Au).

RESULTS AND DISCUSSION

Au: fluorescence experiments of the drugs adsorbed on Au nanoparticles performed at several pH´s indicate that PX shows SEF at pH=2 and quenching for pH=1, 4 or 7, thus indicating simultaneously adsorption and aggregation of the molecules at acidic pH.

IM exhibits SEF at pH=3 and very little SEF at pH=6, what indicates the presence of aggregates at acidic pH, and KT shows quenching at the basic and acidic pH´s studied because of non-aggregation process at any pH used. These results permit a change in the solubility of the drugs with the consequent change in the bioavailability.

Ag: we have studied the binding constants of the drug to serum albumin, the most important drug carrier in the blood, when protein is in solution and when protein is adsorbed on silver nanoparticles. Results for the binding constant in presence and in absence of fatty acids indicate that KT and IM present higher $K_{binding}$ of the drug when protein is adsorbed on the metal surface and the maximum of drug binding increases with metal for IM but decrease for KT.

Finally the dialysis of Ag nanoparticles-drug systems has permitted us to study the release of the drugs from the metal surface. Results indicate that KT establishes stronger bonds than PX.

CONCLUSIONS

We have obtained SEF data from antiinflamatory molecules PX and IM adsorbed on Au nanoparticles, thus increasing their solubility in water solution; on the other hand for KT we have obtained quenching of the fluorescence indicating that there is no aggregation and consequently the big solubility of the drug decreases. Silver nanoparticles are also able to transport the drugs bound to the albumin forming the complex protein-drug. The presence of the nanoparticles changes the binding constants of the systems studied. These data constitute a preliminary study about the knowledge of the physical-chemistry properties of the drugs adsorbed on noble metal nanoparticles surface that will allow us to deep in the design of new drug delivery systems with potential to improve the clinical efficacy of the therapeutic effect of the antiinflamatory molecules used.

REFERENCES

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