Characterization of supramolecular complexes formed between non-steroidal anti-inflammatory drugs and cucurbit[n]urils adsorbed on silver nanoparticles

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Abstract

Design of new drug delivery systems is nowadays one of the most important topics in research fields. It is necessary that medicine molecules arrive to disease tissues like "magic bullets" without interacting with healthy cells thus optimizing their effectiveness and avoiding secondary effects that are to a large extent undesirable. Nanomedicine has revealed a very useful tool to achieve these goals. Silver nanoparticles have very important optical properties due to the excitation of the localized surface plasmon resonances that have enabled the development of high sensitivity molecular spectroscopies like Surface-Enhanced Raman Scattering (SERS) and Surface-Enhanced Fluorescence (SEF) [1]. They can also serve as vehicle to transport drugs, directly or forming complexes with other molecules, which could be included in multi-step drug delivery systems.

Cyclodextrins and calixarenes are synthetic receptors able to form inclusion complexes, but they present several disadvantages associated with their low solubility, except on strongly acid water solutions, ant the difficulty to introduce any functional group. As an alternative in supramolecular chemistry, cucurbiturils constitutes a new family of molecules with important characteristics [2]. They have a highly symmetrical and rigid structure with two identical openings and a hydrophobic defined internal cavity hindered by carbonyl groups which line two rims able to host cationic forms.

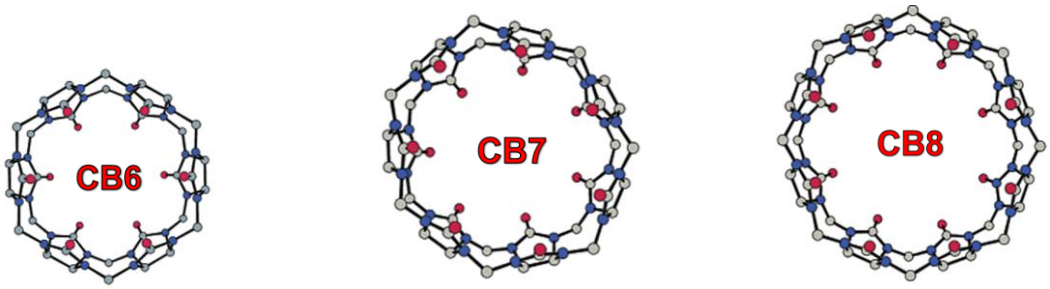

Figure 1. Molecular structure of cuburbit[6]uril, cucurbit[7]uril and cucurbit[8]uril

In this work we present the characterization of several complexes formed by cucurbiturils and non-steroidal anti-inflamatory (NSAIDs) drugs in solution, as well as adsorbed on colloidal silver nanoparticles, based on our previous experience with the spectroscopic characterization of the drugs alone [3]. Guest molecules used are piroxicam (PX), indomethacin (IM) and ketorolac (KT). All the three molecules present and acid-base equilibrium and, while PX and IM are poorly soluble in water, KT exhibits high solubility. None of these extremes are desirable for the release of the drug. In the case of PX and IM, complexation increases the solubility,and in the case of KT, transportation into the host molecule avoids the loss of effectiveness caused by its binding to other molecules found in their way to diseased tissues. Our results show that PX and IM form complexes with cucurbit[8]uril, while KT does with cucurbit[7]uril. We have used the corresponding adequate spectroscopic techniques for every case: i) UV to obtain the Job's plot; ^{1}H NMR, and fluorescence lifetime to detect the presence of complexes and steady-state fluorescence to obtain the binding constant in water solution and ii) SERS and SEF in silver colloids.

These studies provide preliminary results necessary to use these complexes in biotechnology and biomedicine.

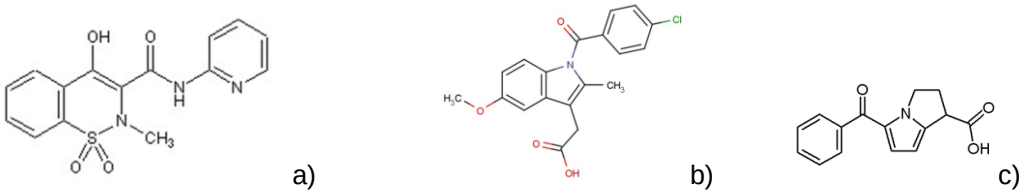

Figure 2. Molecular structures of a) piroxicam, b) indomethacin and c) ketorolac

References

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