Doxorubicin and alginate interact synergistically to form nanoparticles

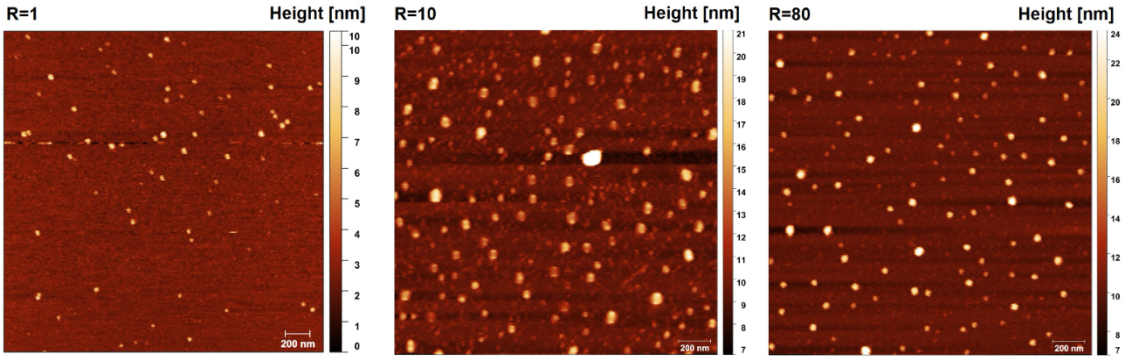
Lucrezia Desiderio[a], Paolo Di Gianvincenzo [b], Desire Di Silvio [b], Sunisa Thongsom [b], Alessio Olivieri [a], Marco D'Abramo [a], Anita Scipioni [a], Sergio E. Moya [a,b], and Mauro Giustini [a,c]

[a] Chemistry Department, Sapienza University, P.le Aldo Moro 5, 00185 Rome (Italy)
[b] CICbiomaGUNE, Paseo Miramón 194, 20014 Donostia/San Sebastián, Gipuzkoa (Spain)
[c] CSGI c/o Chemistry Department, University of Bari "A. Moro", Via Orabona 4, 70126 Bari (Italy).

lucrezia.desiderio@uniroma1.it

Doxorubicin hydrochloride (DX) is a drug widely employed in cancer treatment, although its clinical use is limited by serious side effects, mainly cardiotoxicity and bone marrow suppression. One strategy to control its systemic toxicity is through the encapsulation in polymeric or lipid matrices to achieve targeted delivery into tumour tissues. DX has a distinctive chemical structure, characterized by the presence of a planar anthraquinone moiety, several chiral centres and a unique spatial organization of hydrogen bond donor/acceptor groups, responsible for its ability to intercalate into DNA, for its fluorescent properties and Circular Dichroism (CD) activity. Moreover, DX contains several ionizable groups, and by appropriately adjusting the pH, the molecule can exist in a cationic (pH < 7), neutral (pH ≈ 8) or anionic form (pH > 9). Such a characteristic can be exploited to trigger the DX interactions with other molecules [1].
One of its distinctive features is its ability to self-assemble into dimers and, under certain conditions of drug concentration (≈ 10 mM) and ionic strength (>200 mM NaCl), to further aggregate into self-assembled supramolecular cylindrical polymeric aggregates, the entanglement of which leads to an increase in the macroscopic viscosity, resulting in the formation of a non-covalent gel phase (DX_{gel}) not observed with other anthracyclines [2-4]. However, DX_{gel} easily disrupts upon dilution, necessary to reach the drug therapeutic concentration.
Sodium alginate (ALG) is a natural polymer known to act as a gelator when in the presence of divalent cation, such as calcium. Both DX and ALG alone do not aggregate to form discrete nanoparticles (NP). However, when mixed at the right pH (between 4 and 6) and in the proper molar ratio (R), they do self-assemble into stable and monodisperse NPs (DX@ALG).
Here we present the full spectroscopic and structural characterization of DX@ALG NP for different values of R as well as the first in-vitro tests on selected cell lines.

Keywords:
Doxorubicin, sodium alginate, nanoparticles; biomaterials



AFM images in wet of DX@ALG at different values of R (R= moles ALG/moles DX).

References:

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