

Anthracyclines gels: chemical structure and functional behaviour

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Anthracyclines are a family of antibiotics often used in cancer chemotherapy. Daunorubicin (DA) was the first isolated from a strain of *Streptomyces peucetius* back in 1960 and still in use for the treatment of several malignancies together with the even more frequently used analogue Doxorubicin (DX, also called Adriamycin) and its semisynthetic derivative Epirubicin (EPI). Despite their extremely close chemical formula (Figure 1), their properties when in solution are enormously different. In fact, whereas the increase of the ionic strength induces the formation of a gel with DX [1-3], in the case of the related EPI and DA molecules what is observed are only the well-known self-association phenomena documented in the literature from decades [4].

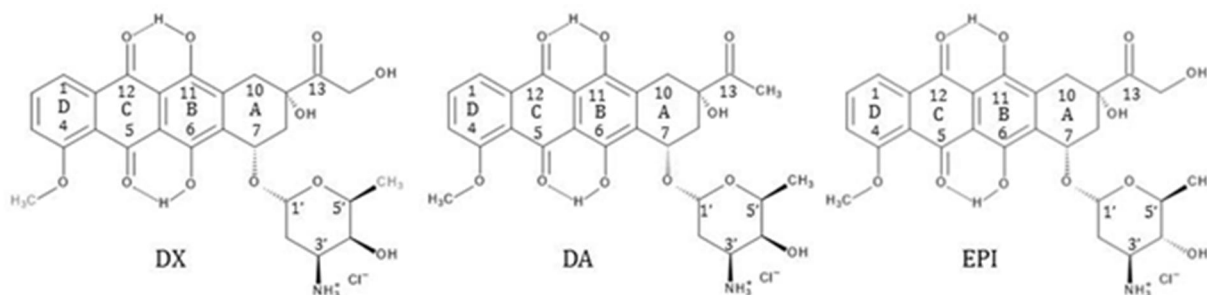


Figure 1 Anthracyclines chemical formula

The present work is aimed to elucidate how and why this happens by the combined use of spectroscopic (UV-Vis, CD, Fluorescence), X-ray scattering, fluorescence imaging and computational methods.

Molecular mechanics simulations performed on the three molecules (250 ns trajectories in any case) revealed that only DX assembles into cylinders close to those revealed by X-ray scattering while the closely related EPI tends to form globular structures. DA shows the tendency to self-aggregate into supramolecular structures recalling those formed by DX, never reaching anyhow the same degree of order. Such a tendency is also revealed by the fluorescence lifetimes of DA since, at high ionic strength (1.0 M NaCl), a fast component in the decay appears with a lifetime close to the one of DX in gel phase (0.2 ns vs. 1.00 ns of the anthracyclines in solution).

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