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Glycotargeted self-assembled nanocarriers from calixarene-cyclodextrin heterodimers for site-specific delivery of docetaxel

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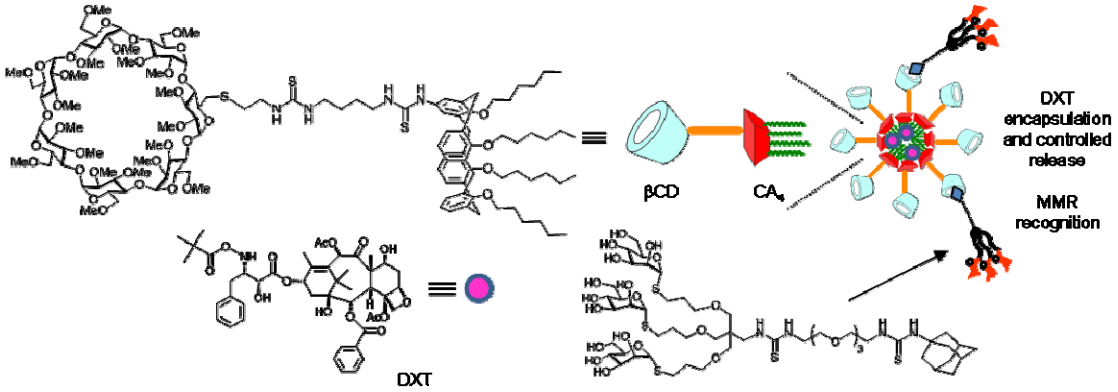
The development of well-ordered functional nanostructures filled with the capacity to assemble under dilute conditions in water or buffer media continues to be one of the more fascinating challenges facing modern chemistry, with relevance in areas like imaging, diagnostics, tissue engineering or drug deliver, among others. Many of those channels require the supramolecular system to be capable of encapsulating a cargo, targeting specific cell surface receptors and allowing the gradual release of the payload. Monodisperse building blocks of the calixarene (CA)[1] and cyclodextrin (CD)[2,3] families are privileged platforms towards this end because of their capacity to form host-guest superstructures and the possibility to be tailored to achieve a predictable and controlled non-covalent organization. In this work we report the successful construction of nanospheres entangling an inner core formed by hydrophobic calix[4]arene (CA_4) units and an external hydrophilic shell exposing β-cyclodextrin (βCD) motifs by the self-assembly in water of amphiphilic CA_4—βCD heterodimers (see Figure). The CA_4 scaffold is very well suited to promote tight packing of fatty chains installed at the narrower ring in its cone conformation, providing a lipid matrix where hydrophobic drugs can be entrapped, whereas the presence of βCD at the nanosphere surface allows host-guest directed decoration. The potential of the new systems in nanomedicine is illustrated by their capacity to encapsulate and provide sustained release of the anticancer drug docetaxel and undergo supramolecular surface post-modification with adamantane-armed glycoligands targeting the macrophage mannose receptor.



[1] Sansone, F.; Casnati, A. *Chem. Soc. Rev*. **2013**, *42*, 4623.
[2] Martínez, A.; Ortiz Mellet, C.; García Fernández, J. M. *Chem. Soc. Rev*. **2013**, *42*, 4746.
[3] Ortiz Mellet, C.; García Fernández, J. M.; Benito, J. M. *Chem. Soc. Rev*. **2011**, *40*, 1586.