

Conference Proceedings Paper

Synthetic Strategies for the Preparation of Multifunctional Cyclodextrin Derivatives

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Abstract: Cyclodextrins (CDs) are cyclic oligosaccharides able to modify the solubility, stability and the aggregation behaviour of a large variety of molecules via complexation. Thanks to their water solubility and biocompatibility, CDs are particularly well-considered as building-blocks for the construction of nanodevices within the nanomedicine field, such as biomolecular sensors and gene/drug delivery systems. CDs have been widely utilized as pharmaceutical excipients and have been recently rediscovered as API in form of (2-hydroxypropyl)- β -cyclodextrin and Sugammadex. In order to achieve specific purposes, these versatile sugars can be ad-hoc chemically modified with additional functionalities such as fluorescent moieties, photosensitive groups and units targeting biological systems. However, the controlled and regioselective functionalization is quite often challenging due to the large number of hydroxyl groups present on the macrocycles and the substantial differences in their reactivities according to their position on the ring. Thus, well-defined synthetic pathways must be thoroughly planned for each target derivative and the development of versatile synthetic procedures is highly desirable in this field. In this contribution, the syntheses and the possible uses of CD-based fluorescent systems in imaging processes will be presented through several examples. In particular, the synthetic approaches towards rhodaminy, fluoresceiny, nitrobenzofuranyl and anthracenyl CD-based systems will be described and their applications in the visualization and/or targeting of biological process will be discussed. The preparation of CD-based architectures combining molecules able to release singlet oxygen (1O_2) and nitric oxide (NO) will be disclosed together with their utility in photodynamic therapy (PDT). In particular, the synergistic effect of modified CDs and photosensitizers such as porphyrins, xanthene dyes and trifluoromethyl-nitroanilines will be shown. Green synthetic methods for the production of active-targeting delivery systems such as folate-appended CDs will be discussed and the manufacture of amphiphilic CDs for the effective stabilization and complexation of DNA and RNA will be elucidated. Finally, the syntheses of the two CD-based APIs, (2-hydroxypropyl)- β -cyclodextrin and Sugammadex will be analysed and examined with particular attention to the industrial scale-up.

Keywords: Synthetic building-blocks - Fluorophores - Photosensitizers - Folate - Amphiphilic systems

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