β-Cyclodextrin Decorated Multicolor Carbon Nanodots as Theranostic Nanosystem for the Deliveryof Sildenafil in Breast Cancer

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Carbon nanodots (CDs) have recently emerged as promising smart agents for drug delivery, imaging and NIR photothermal therapy, due to their distinctive tunable multicolor fluorescence, excellent photothermal conversion capacity and surface characteristics. This combination of features in a unique nanoplatform offers the advantage of concurrent monitoring and treatment of tumors (theranostics), improving early diagnosis, therapeutic outcomes, and avoiding limits of conventional chemotherapy. The structural, surface and optical properties of CDs are highly affected by the precursors and the synthetic route adopted, allowing to design and modulate the physico-chemical and optical profile of CDs in function of the applicative requirements. The focus of the present work is the design of β-cyclodextrins decorated multicolor carbon nanodots as theranostic nanoplatforms for the delivery of sildenafil in breast cancer therapy. The rational idea is to exploit CD as fluorescence contrast agent and cyclodextrins for them well-known capability to form host-guest complexes, in order to maximize the sildenafil loading. To fulfil this goal, in a first step highly homogeneous crystalline N,S-doped CDs were synthetized by an innovative solvothermal synthetic route giving rise to high resolution fluorescence imaging nanotools. Successively, CDs, surface passivated with a short alkyne end-capped PEG by amide coupling, were orthogonally functionalized with modified 6-azido-6-deoxy-β-cyclodextrins by azide-alkyne Huisgen cycloaddition, obtaining a nanoplatform with a well-ordered architecture (CDs-PEG-Cyd). Afterwards, this latter was loaded with sildenafil (CDs-PEG-Cys@SD, DL=20.57 % w/w), chosen as off-label drug for its emerging potential in cancer therapy. Both CDs-PEG- Cyd and CDs-PEG-Cyd@SD were widely characterized in terms of physico-chemical and biological properties. The strategic design of CDs-PEG-Cys allow to obtain an effective theranostic nanocarrier and a high encapsulation efficiency, proving CDs-PEG-Cyd@SD a potential nanoplatform in cancer theranostics.