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Carbon Dot-DNA Hybrid Hydrogel for Controlled Release of Drugs

Seema M. Singh, Sonam Kumari and Prolay Das*

Department of Chemistry, Indian Institute of Technology Patna, Patna 801103, Bihar, India

* Presenting author

The biocompatibility and sustained release of the drugs from polymer based hydrogel often pose challenges and limitations for efficient drug delivery. Herein, we report the creation of non-toxic and biocompatibleCarbon dot (CD)-DNA hybrid hydrogel in aqueous phase for sustained and targeteddelivery of two drug molecules. Cytosine (C) rich ssDNA were covalently conjugated to amine functionalized CDs by phosphoramidate linkage. Under slightly acidic conditions, C-rich region of DNA sequence forms i-motif structure that facilitates the formation of CD-DNA hydrogel.As a proof of principle, Doxorubicin (Dox),an anticancer chemotherapeutic drug was loaded in the hybrid hydrogel to study sustained release of the drug. To show the general applicability of the hydrogel, the Protoporphyrin IX (PpIX) as a Photosensitizer (PS) drug was also loaded in the hydrogel and generation of ROS was studied, for potential applications in photodynamic therapy. In the hybrid hydrogel, CDs act as a cross linker for gel formation and also play a key role in encapsulating the drug by electrostatic interaction in conjunction with DNA. The photophysical properties of CD were utilized for tracking of hydrogel dissolution and drug cargo loading. The transition of CD-DNA conjugate from sol to gel was visually detectable by changing pH of the solution from alkaline toneutral. *In vitro* time dependent release profile of drug from hydrogel was studied in acidic and neutral pH. While stability of hydrogel was maintained for about a month at normal physiological pH, sustained release of drug with complete dissolution of hydrogel were achieved over 10-11 days in acidic pH, relevant to tumourmicroenvironment. Cytotoxicity assay on HeLa cells shows slow killing of the cells either by Dox or through ROS generation from PpIX loaded in the hydrogel due to favourable acidic pH for disruption of hydrogel.