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The pH-responsive calix[4]resorcinarene-mPEG conjugates bearing acylhydrazone bonds: Synthesis and study of the potential as supramolecular drug delivery systems

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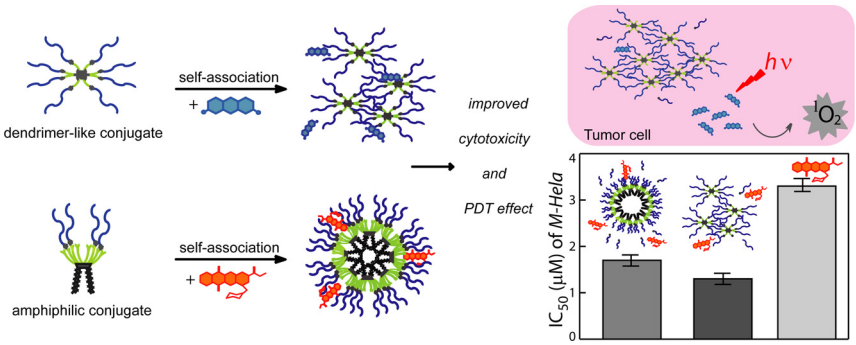
GRAPHICAL ABSTRACT



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ABSTRACT

The synthesis of new conjugates of calix[4]resorcinarenes and methoxy-PEG via acylhydrazone bonds and their study in the formation of pH-sensitive low-toxic supramolecular drug delivery systems have described. The syntheses have been performed on the base of two calix[4]resorcinarenes in chair and boat conformations to obtain the dendrimer-like and amphiphilic conjugates, respectively. The structures of the conjugates have been confirmed by ^{1}H, ^{13}C NMR, and FT-IR spectroscopy, Maldi-TOF mass spectroscopy, and SLS method. The self-association of both amphiphilic and dendrimer-like conjugates has been found (NMR FT-PGSE, fluorimetry, DLS and TEM methods). The hydrolysis of the conjugates at pH 5.5 (proved by ^{1}H NMR and FT-IR spectroscopy, DLS method) lead to the improved release of the conjugate-encapsulated Dox. The low hemolytic activity and low cytotoxicity against Chang liver cells of the conjugates and products of their hydrolysis have been demonstrated. Meanwhile, the improved cytotoxicity and photodynamic activity of conjugates-encapsulated drugs (Dox and Methylene Blue, respectively) has been found in vitro. The results have indicated the potential using of the calix[4]resorcinarene-mPEG conjugates bearing acylhydrazone bonds as supramolecular drug delivery systems.

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