Smart stimuli-responsive drug delivery systems based on cyclodextrin-polymers complexes for cancer therapy

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Introduction

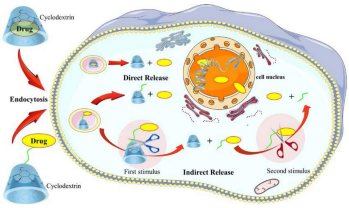

Figure 1. The drug release mechanism of ideal smart stimuli-responsive systems based on Cyclodextrin. Reproduced from the Elsevier[1].

- By virtue of its self-assembly, molecular recognition and dynamic reversibility, cyclodextrin (CD) can be combined with other biocompatible materials to construct smart stimuli-responsive drug delivery.
- This allows feedback regulation on physical and chemical properties of the CD-based carrier, so as to control drug release according to different stimuli including endogenous stimuli and exogenous stimuli.

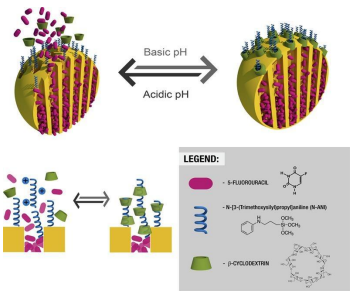

Figure 2. Adsorption and release properties of 5-FU loaded on pH stimuli-responsive drug delivery. Reproduced from the Elsevier[2].

- A system based on mesoporous silica material functionalized with aromatic amines and β-CD that are used as the "gatekeeper", was tested for drug release according to pH changes.
- the drug with more than 80% adsorption capacity was successfully released within 24 h at pH=5.

pH-responsive PDMAEMA/SACD smart nanodrug carriers

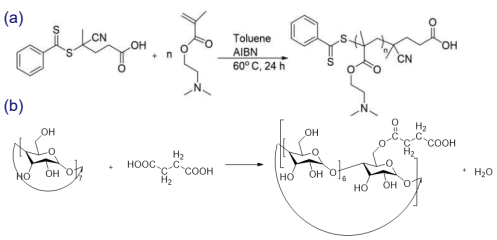

Figure 3. Synthetic scheme for the preparation of poly((N,N-dimethyl amino)ethyl methacrylate) (PDMAEMA) homopolymer (a) and cyclodextrin succinate (b).

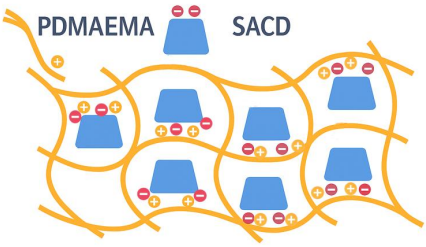

Figure 4. schematic illustration of the intermolecular interactions in PDMAEMA/SACD nanoparticles.

- PDMAEMA/SACD nanoparticles were prepared based on ionic crosslinking combined with anti-precipitation.
- Self-assembly was performed at pH 5.3, 0.1 g/mL (c:c=1, v:v=1).

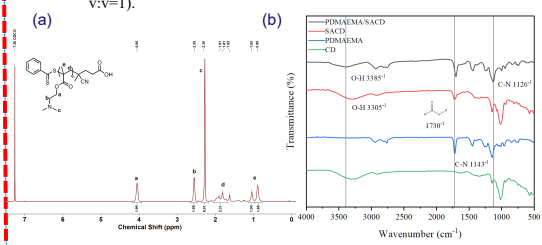

Figure 5. ^{1}H-NMR spectrum of PDMAEMA homopolymer in $CDCl_3$ (a) and PDMAEMA/SACD composites characterized by FTIR spectra (b).

- For **SACD**, the characteristic peak at 1730 cm^{-1} is associated with the stretching vibration of the ester bond, and 3305 cm^{-1}, 2917 cm^{-1}, 1155 cm^{-1}, and 1027 cm^{-1} correspond to the stretching vibrations of O-H, CH_2, C-O-C, and C-OH, respectively.
- For **PDMAEMA/SACD**, The characteristic peak of the C-N of PDMAEMA is red-shifted from 1143 cm^{-1} to 1126 cm^{-1} after electrostatic interactions. On the contrary, the O-H stretching vibrational peak of SACD narrowed and blue shifted from 3305 cm^{-1} to 3385 cm^{-1}.

Temperature-responsive PVIP/CD smart nanodrug carriers

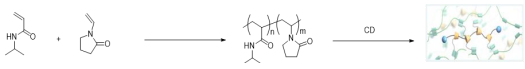

Figure 6. Synthetic scheme for the preparation of PVIP/CD hydrogel.

- Through the design and screening of monomers, a temperature-sensitive hydrogel material possessing a branched chain structure is prepared to form a tight physical cross-link with cyclodextrin to realize drug encapsulation.
- Introduction of hydrophilic monomers to alter Lower Critical Solution Temperature (LCST) will be investigated.
- Increase CD content (≤10%) and change monomer structure to enhance drug loading. Adjustment of drug release rate by adjusting crosslink density.

The materials will be subjected to structural characterization and property characterization, drug release experiments and cytotoxicity tests.

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References:

[1] Tian B, Liu Y, Liu J (2021). Smart stimuli-responsive drug delivery systems based on cyclodextrin: A review. *Carbohydrate polymers*, 251: 116871.

[2] Beňová, E., Bergé-Lefranc, D., Zeleňák, V., Almáši, M., Huntošová, V., & Hornebecq, V. (2020). Adsorption properties, the pH-sensitive release of 5-fluorouracil and cytotoxicity studies of mesoporous silica drug delivery matrix. *Applied Surface Science*, 504, 144028.