PS@PNIPAM core@shell nanoparticles: tuning of LCST

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Problem to be solved

Amphiphilic nanoparticles of the "core-shell" type are intensively used as carriers of small molecules, in particular for intracellular delivery of anticancer drugs [1,2]. Thermo-responsive N-isopropylacrylamide (**NIPAM**)-based NPs used in biomedical field usually are obtained in a form of nanosized gels dispersed in water. The inherent lower critical solution temperature (LCST) of PNIPAM-based "shell" is ~32°C [3] what is a sufficient drawback for NPs intravenous administration due to aggregation of NPs [4].

The problem can be solved by rising the LCST up to ~38-40°C via:

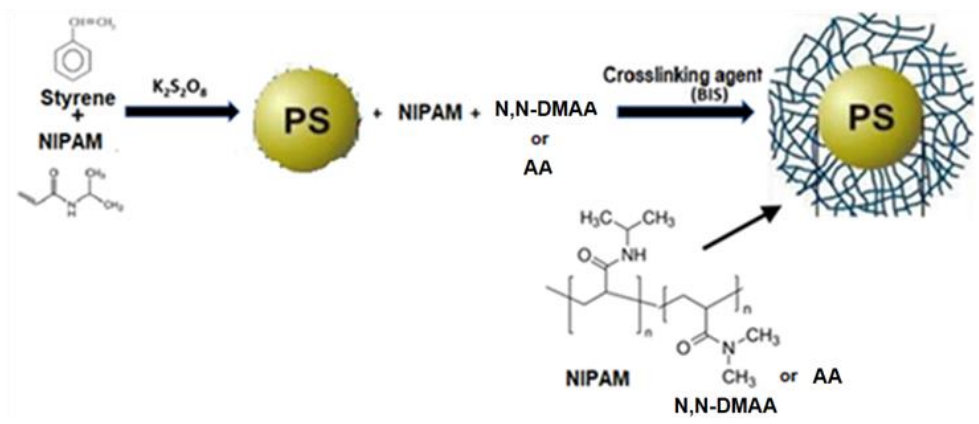
•Copolymerization with such monomers as acrylamide (**AA**) or N,N-dimethylacrylamide (**N,N-DMAA**);

•Incorporation of rigid conjugated polymers, e.g. polyaniline (**PANI**) into the PNIPAM "shell" [5].

NPs synthesis and characterization

Nanoparticles (**NPs**) with polystyrene (**PS**) "core", and the outer "shell" formed by a layer of (NIPAM-co-AA or N,N-DMAA) copolymers with different starting ratio of monomers were synthesized by miniemulsion polymerization (see **Fig. 1, a**).

a.



The synthesis of aqueous dispersions of composite nanoparticles (**NCs**) composed of binary PS@PNIPAM NPs with incorporated into PNIPAM "shell" conjugated polymer PANI is described in [5], see **Fig. 1, b.**

b.

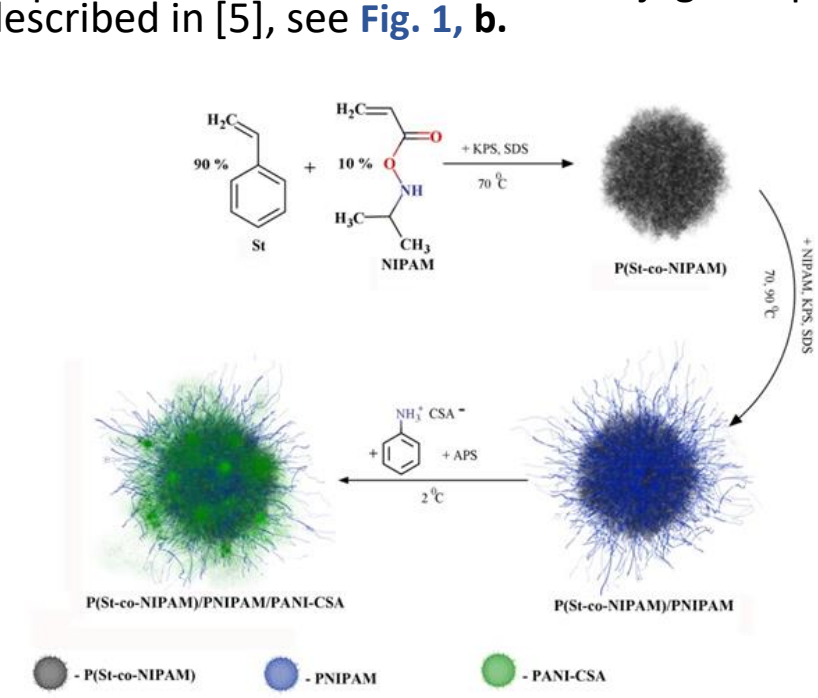


Fig. 1. Schematic representation of (a) PS@poly(NIPAM-co-DMAA or AA) NPs syntheses and (b) the ternary nanocomposite (NCs) PS@PNIPAM/PANI.

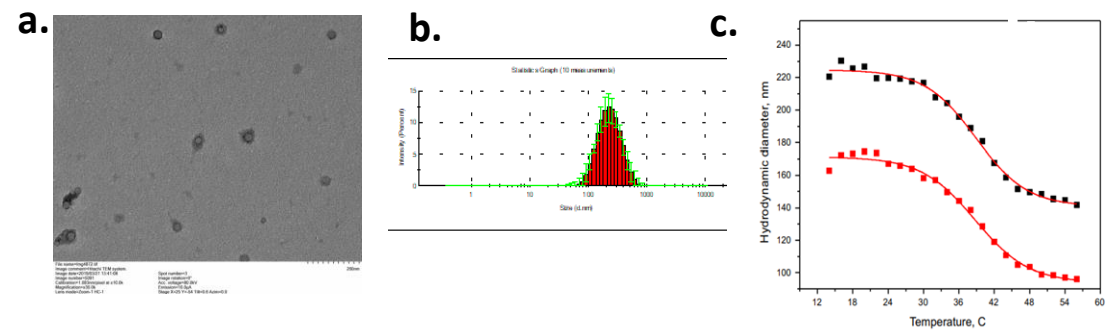


Fig. 2. (a). Transmission electron microscopy (TEM) images of PS@poly(NIPAM-co-AA) core-shell NPs (with contrast agent). (b). NPs size distribution by intensity determined by DLS in water at 20°C. (c) NPs size distribution with temperature from 18 to 55 °C determined by DLS.

Tuning of LCST

- **Copolymerization with 8-14 mol.% of acrylamide (AA) allows to increase LCST up to 40 °C.** Moreover, LCST for "core-shell" NPs PS@poly(NIPAM-co-AA) also depends on the thickness of the PNIPAM-based "shell" (see **Fig.3, a**).

- **Copolymerization with 30 mol.% of acrylamide (AA) leads to disappearance of thermal sensitivity in the region 18-55 C** (LCST could not be detected, see **Fig.3, b**). Instead, for "core-shell" NPs with poly(NIPAM-co-N,N-DMAA) "shell" with 30 mol.% of N,N-dimethylacrylamide LCST is ~38 °C.

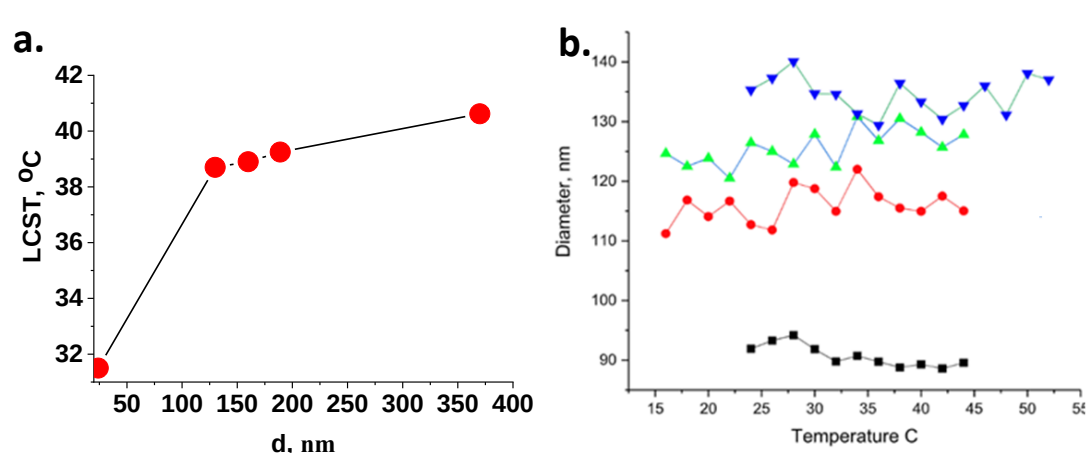


Fig. 3. (a). Dependence of PS@poly(NIPAM-co-AA) NPs LCST values on NPs hydrodynamic diameter (d) determined by DLS in water. Content of AA in thermo-responsive "shell' is 14 mol.%. (b). Dependence of PS@poly(NIPAM-co-AA) hydrodynamic diameter on temperature determined by DLS in water. Content of AA in thermo-responsive "shell' is 30 mol.%.

- Strong physical–chemical interactions in the "shell" between **PNIPAM and PANI affect the shift of LCST from 32 °C (for the binary PS@PNIPAM NPs) to 34 °C for the ternary PS@PNIPAM/PANI (8.7 wt%) latex** [5].

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