pharmaceutics

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Supplementary Material

Investigation of cytotoxicity and cell uptake of cationic beta-cyclodextrins as valid tools in nasal delivery

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Table 1S. Description of beta-cyclodextrin monomers and polymers studied in this work

Not Fluorescent							Analogue fluorescent cyclodextrin					
Cyclodextrin	Code	DS[1]	MW[2]	CLR[3]	CD[4]	Description	Cyclodextrin	Code	DS[1]	MW[2]	CLR[3]	CD[4]
(2-Hydroxy-3-N,N,N-trimethylamino) propyl-beta-cyclodextrin chloride	QA	3	1589.8	-	3	cationic monomer; purity > 99%	Quaternary ammonium-6-deoxy- 6-[(5/6)-rhodaminyl thioureido]-(2-Hydroxy-3-N,N,N-trimethylamino)-beta-cyclodextrin	**RBITC-QA**	4.5 (QA) 1 (RBITC)	1939.86	-	3.5
Quaternary-ammonium-beta-cyclodextrin soluble polymer crosslinked with epichlorohydrin	QAPS	2.2	40,000	~11	2.2	cationic polymer; CD content: 50-70%	Quaternary-ammonium-rhodamine labeled beta-cyclodextrin soluble polymer crosslinked with epichlorohydrin	**RBITC-QAPS**	2.2 (QA) 0.05 (RBITC)	40,000	~11	2.2
Heptakis (6-deoxy-6-amino)-beta-cyclodextrin heptahydrochloride	HA	-	1383.3	-	7	cationic monomer; purity > 98%						
Soluble amino-beta-cyclodextrin polymer crosslinked with epichlorohydrin	HAPS	1	25,000	~10	1	cationic polymer; CD content: 70%						
(2-Hydroxypropyl)- beta-cyclodextrin	HP	4.5	1400	-	-	control monomer	6-deoxy-6-[(5/6)-rhodaminylthioureido]- hydroxypropyl-beta-cyclodextrin	**RBITC-HP**	4.7 (HP) 0.5 (RBITC)	1675.07		1*
Soluble β-cyclodextrin polymer crosslinked with epichlorohydrin	PS	-	92,000	~11	-	control polymer; CD content: 70%	Rhodamine labeled BCD soluble polymer crosslinked with epichlorohydrin	**RBITC-PS**	0.05 (RBITC)	100,000	~11	-

[1]DS: Average Degree of Substitution; [2]MW: Average Molecular Weight (g/mol); [3]CLR: Cross-Linking Ratio (mol epichlorohydrin/mol CD); [4]CD: Cationic Density (cationic groups per cyclodextrin unit). * anionic group per cyclodextrin unit

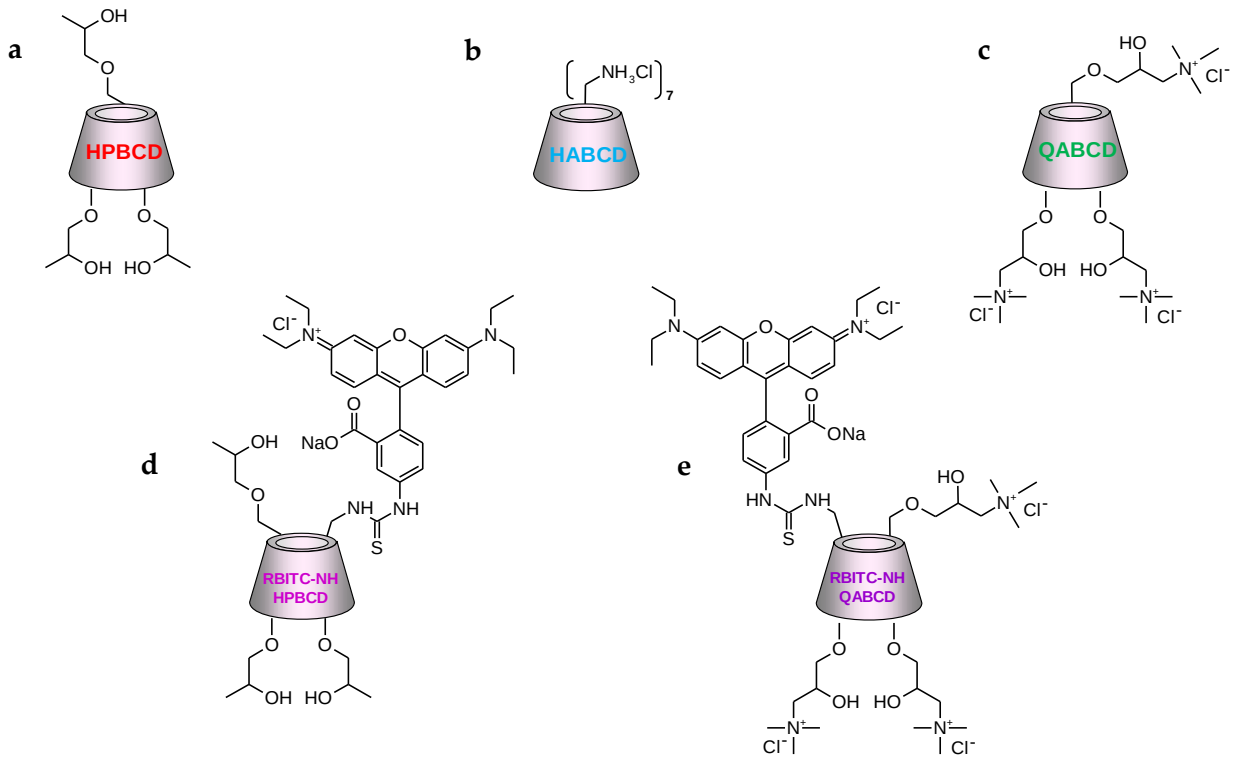

Figure 1S. Cartoon representations for beta-cyclodextrin monomers: a) HP; b) HA; c) QA; d) RBITC-HP; e) RBITC-QA.

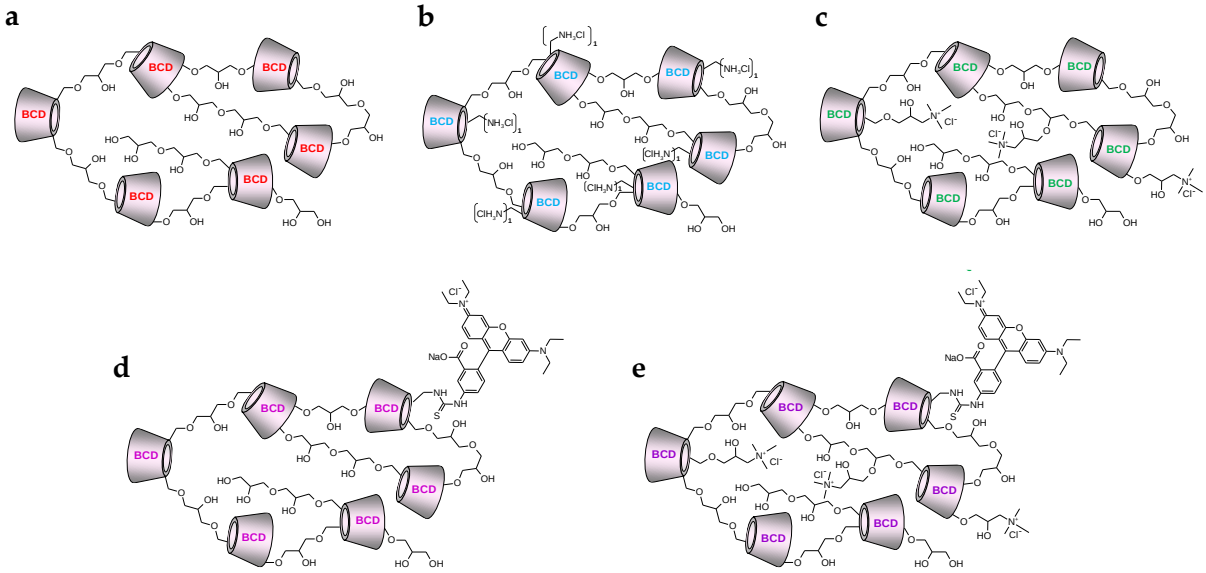

Figure 2S. Cartoon representations for beta-cyclodextrin polymers: : a) PS; b) HAPS; c) QAPS; d) RBITC-PS; e) RBITC-QAPS.

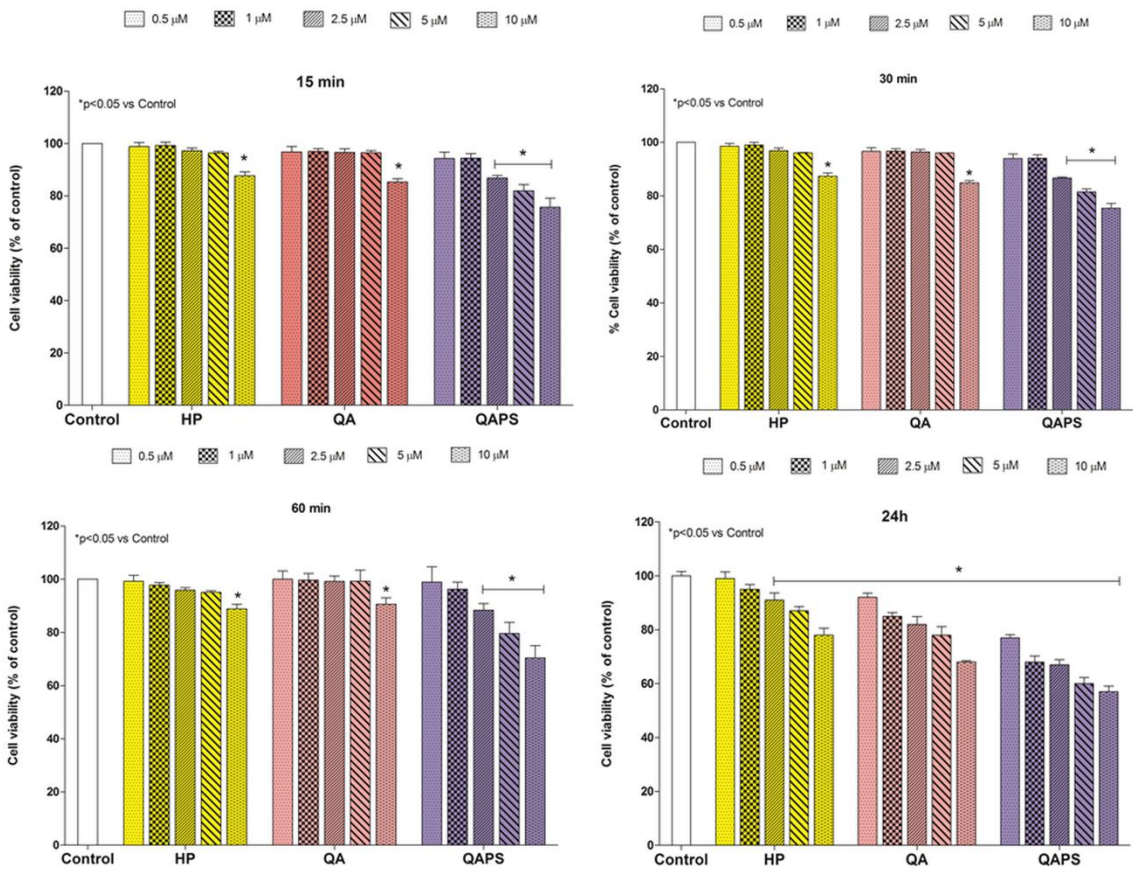

Figure 3S. Effect of different concentrations (0.5 - 1 – 2.5 - 5 - 10 µM) of HP, QA and QAPS on PC12 cell viability at increasing times of exposure (15, 30, 60 min and 24h). *p<0.05 vs Control.

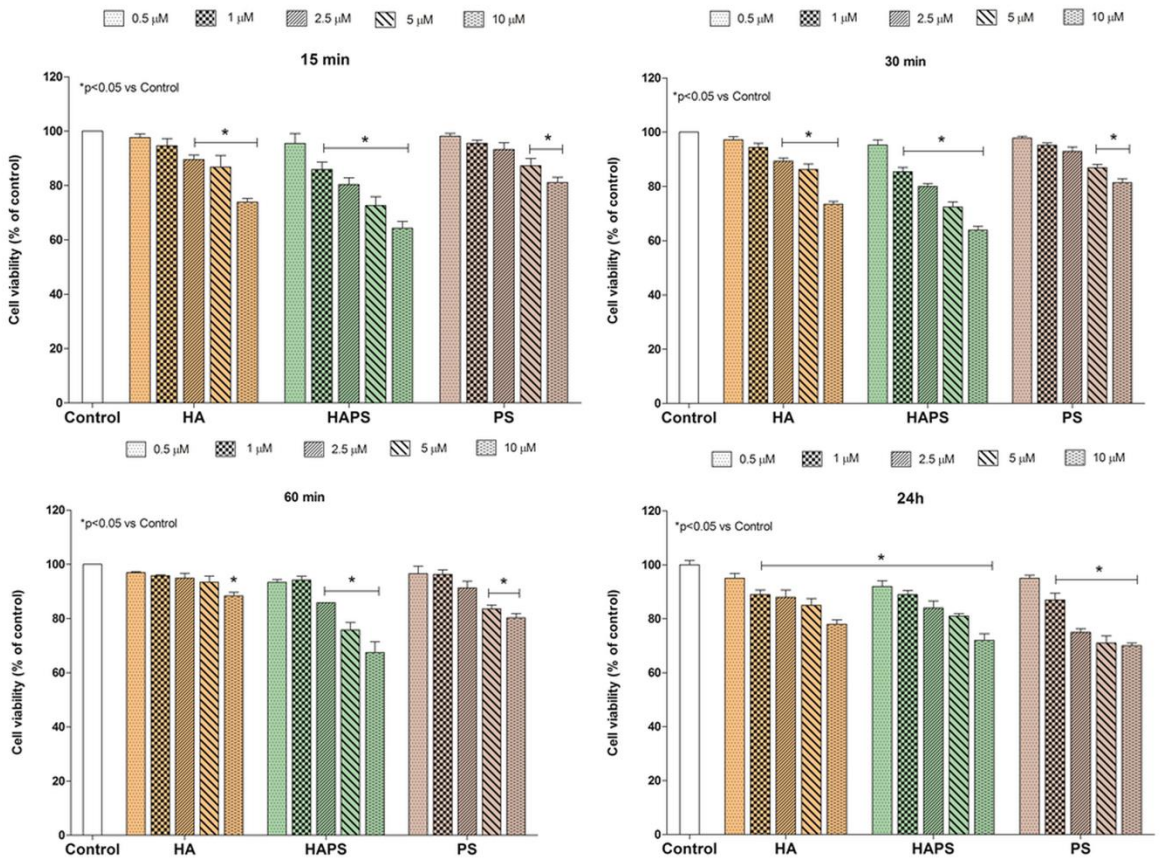

Figure 4S. Effect of different concentrations (0.5 - 1 – 2.5 - 5 - 10 μM) of HA, HAPS and PS on PC12 cell viability at increasing times of exposure (15, 30, 60 min and 24h). *p<0.05 vs Control.

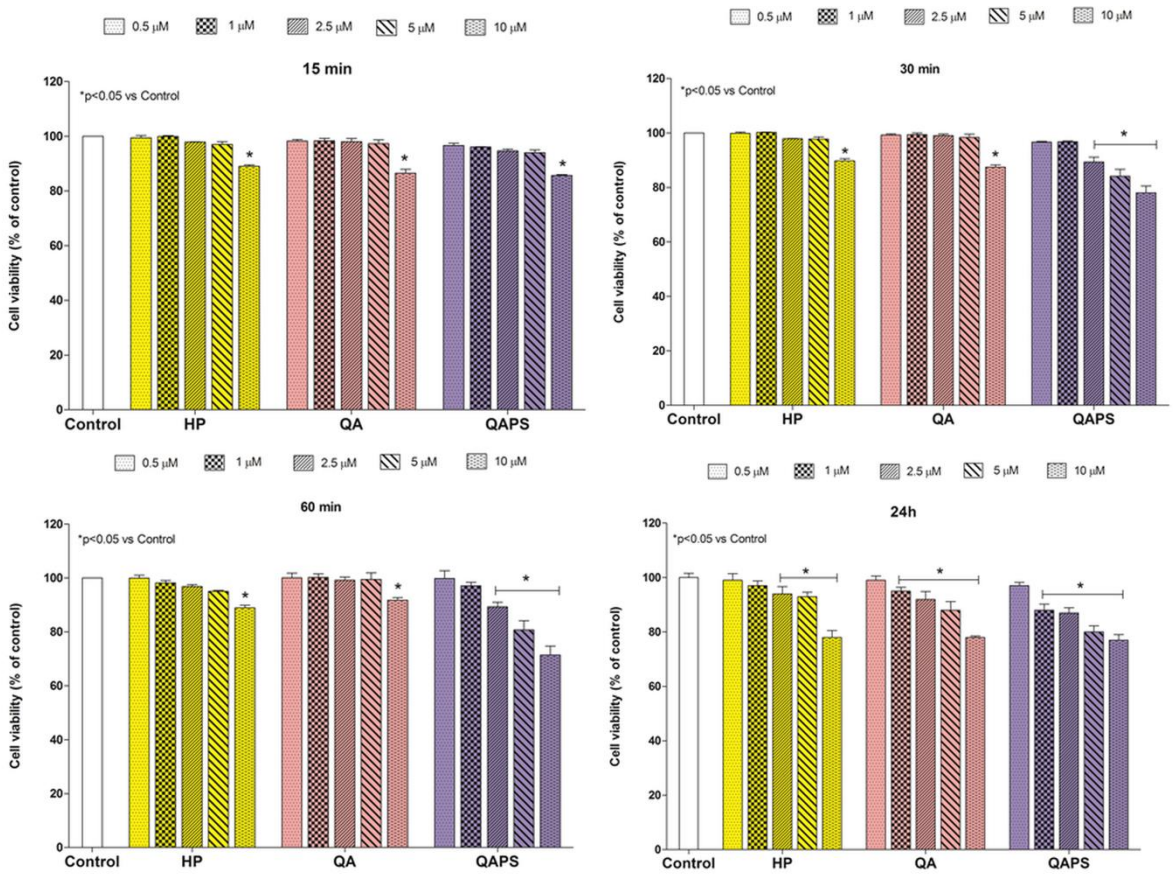

Figure 5S. Effect of different concentrations (0.5 - 1 – 2.5 - 5 - 10 µM) of HP, QA and QAPS on CACO-2 cell viability at increasing times of exposure (15, 30, 60 min and 24h). *p<0.05 vs Control.

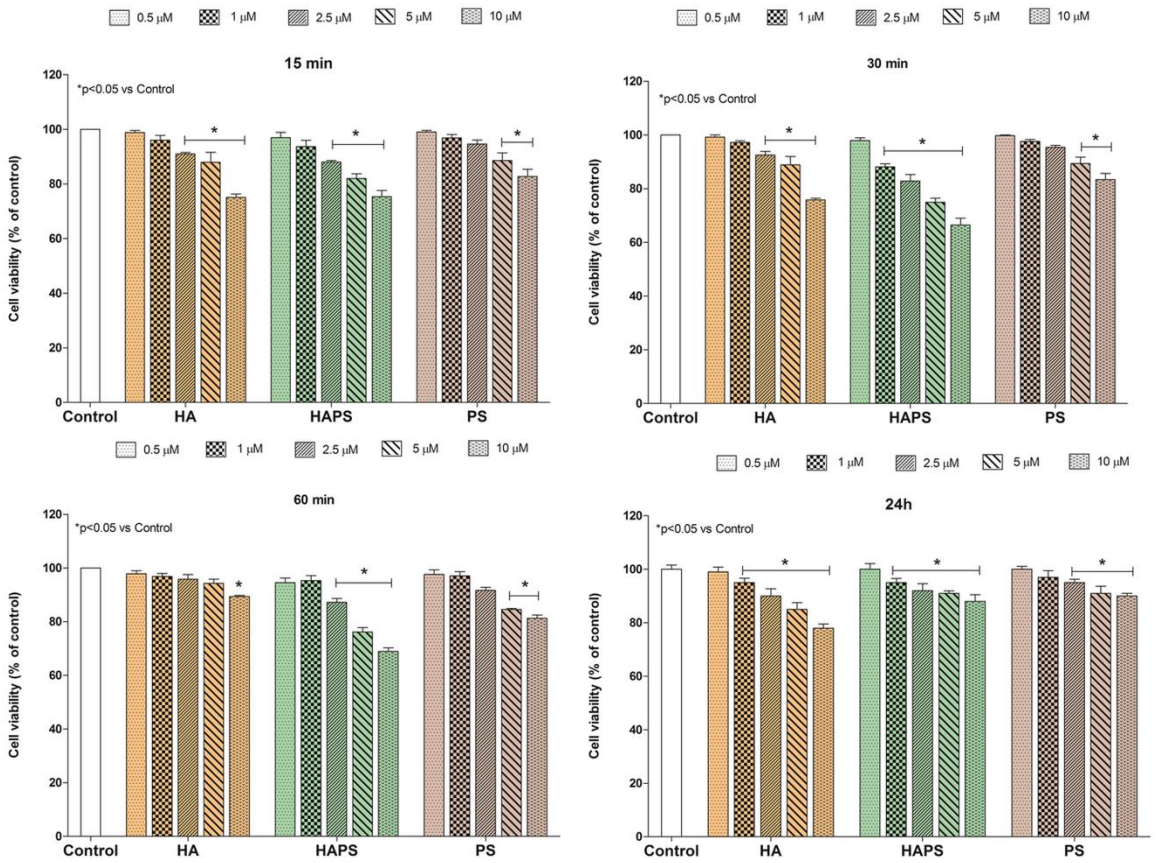

Figure 6S. Effect of different concentrations (0.5 - 1 – 2.5 - 5 - 10 µM) of HA, HAPS and PS on CACO-2 cell viability at increasing times of exposure (15, 30, 60 min and 24h). *p<0.05 vs Control.