Ahmad Malkawi, J Chromatogr Sep Tech 2021, Volume 12

Self-Emulsifying Drug Delivery Systems: Hydrophobic Drug Polymer Complexes Provide a Sustained Release in Vitro

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The aim of this study was to develop hydrophobic ionic drug polymer complexes in order to provide sustained drug release from self-emulsifying drug delivery systems (SEDDS). Captopril (CTL) was used as an anionic model drug to form ionic complexes with the cationic polymers Eudragit RS, RL, and E. Complexes of polymer to CTL charge ratio 1:1, 2:1, and 4:1 were incorporated in two SEDDS, namely FA which was 40% Kolliphor RH 40, 20% Kolliphor EL, and 40% castor oil and FB, which was 40% Kolliphor RH 40, 30% glycerol, 15% Kolliphor EL, and 15% castor oil. Blank and complex loaded SEDDS were characterized regarding their droplet size, polydispersity index (PDI), and zeta potential. Resazurin assay was performed on Caco-2 cells to evaluate the biocompatibility of SEDDS. Release of CTL from SEDDS was determined in release medium containing 0.2 mg/ mL of 5,5'-dithiobis(2-nitrobenzoic acid) (DNTB) allowing quantification of free drug released into solution via a thiol/disulfide exchange reaction between CTL and DNTB forming a yellow dye. The droplet size of SEDDS FA and SEDDS FB were in the range of 100 ± 20 nm and 40 ± 10 nm, respectively, with a PDI < 0.5. The zeta potential of SEDDS FA and SEDDS FB increased after the incorporation of complexes. Cell viability remained above 80% after incubation with SEDDS FA and SEDDS FB in a concentration of 1% and 3% for 4 h. Without any polymer, CTL was entirely released from both SEDDS within seconds. In contrast, the higher the cationic lipophilic polymer to CTL ratio in SEDDS, the more sustained was the release of CTL. Among the polymers which were evaluated, Eudragit RL provided the most sustained release. SEDDS FA containing Eudragit RL and CTL in a ratio of 1:1 released 64.78 ± 8.28% of CTL, whereas SEDDS FB containing the same complex showed a release of 91.85 ± 1.17% within 1 h. Due to the formation of lipophilic ionic polymer complexes a sustained drug release from oily droplets formed by SEDDS can be achieved. Taking into account that drugs are otherwise instantly released from SEDDS, results of this study might open the door for numerous additional applications of SEDDS for which a sustained drug release is essential.