

# ABC micelles for drug delivery – nanoscopic vehicles for potent yet toxic and poorly water-soluble compounds

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Amphiphilic block copolymers (ABCs) assemble into nanoscopic supramolecular core-shell structures called micelles, which are under extensive study for drug delivery. The shell of ABC micelles consists of poly(ethylene glycol) (PEG), a non-toxic water-soluble polymer, which prevents protein adsorption and cellular adhesion, and the core of ABC micelles consists of a smaller hydrophobic block or part, which varies in drug delivery due to the requirements of biocompatibility, compatibility with the poorly water-soluble drug of interest, and stability of ABC micelles in blood. In drug delivery, a goal is to study the potential of ABC micelles as ‘nanocarriers’ for potent yet toxic and poorly water-soluble drugs. Due to low toxicity, PEG-*block*-poly(lactic acid) micelles permit increases in the dose of paclitaxel (anti-tumor drug), relative to its standard formulation, Taxol<sup>®</sup>, without causing changes in paclitaxel’s pharmacokinetics. PEG-*block*-poly(L-amino acid) (p(L-AA)) micelles increase the circulation time of doxorubicin, another anti-tumor drug, reduce its

limiting cardiotoxicity), and increase its accumulation at tumors due to preferential extravasation at leaky vasculature. In our efforts on PEG-*block*-p(L-AA) micelles, we have demonstrated that the side chains of a (L-AA) block can be easily adjusted in order to vary the properties of ABC micelles, enhance drug incorporation, and gain some measure of controlled release. In this study, the length of an acyl side chain attached on PEG-*block*-p(L-AA) was found to govern the extent of interaction, incorporation, and release of an antifungal, amphotericin B (AmB). Hence, the toxicity of AmB (hemolysis) was reduced without a loss of antifungal effects. We hypothesize that PEG-*block*-p(L-AA) micelles increase the therapeutic index of AmB by sustained release or changes in the self-aggregation state of this drug. The latter is due to the membrane activity of AmB, and its preferential interaction with ergosterol versus cholesterol when it exists in a monomeric or deaggregated state.