Synthesis and Aggregation Behavior of Pluronic F87/Poly(acrylic acid) Block Copolymer with Doxorubicin

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Abstract **– Poly(acrylic acid) (PAA) was grafted onto both termini of Pluronic F87 (PEO_{67}-PPO_{39}-PEO_{67}) via atom transfer radical polymerization to produce a novel muco-adhesive block copolymer PAA_{80}-*b*-F87-*b*-PAA_{80}. It was observed that PAA_{80}-F87-PAA_{80} forms stable complexes with weakly basic anti-cancer drug, Doxorubicin. Thermodynamic changes due to the drug binding to the copolymer were assessed at different pH by isothermal titration calorimetry (ITC). The formation of the polymer/drug complexes was studied by turbidimetric titration and dynamic light scattering. Doxorubicin and PAA-b-F87-b-PAA block copolymer are found to interact strongly in aqueous solution via non-covalent interactions over a wide pH range. At pH>4.35, drug binding is due to electrostatic interactions. Hydrogen-bond also plays a role in the stabilization of the PAA_{80}-F87-PAA_{80}/DOX complex. At pH 7.4 (α=0.8), the size and stability of polymer/drug complex depend strongly on the doxorubicin concentration. When C_{DOX} <0.13mM, the PAA_{80}-F87-PAA_{80} copolymer forms stable inter-chain complexes with DOX (110 ~ 150 nm). When C_{DOX} >0.13mM, as suggested by the light scattering result, the reorganization of the polymer/drug complex is believed to occur. With further addition of DOX (C_{DOX} >0.34mM), sharp increase in the turbidity indicates the formation of large aggregates, followed by phase separation. The onset of a sharp enthalpy increase corresponds to the formation of a stoichiometric complex.**