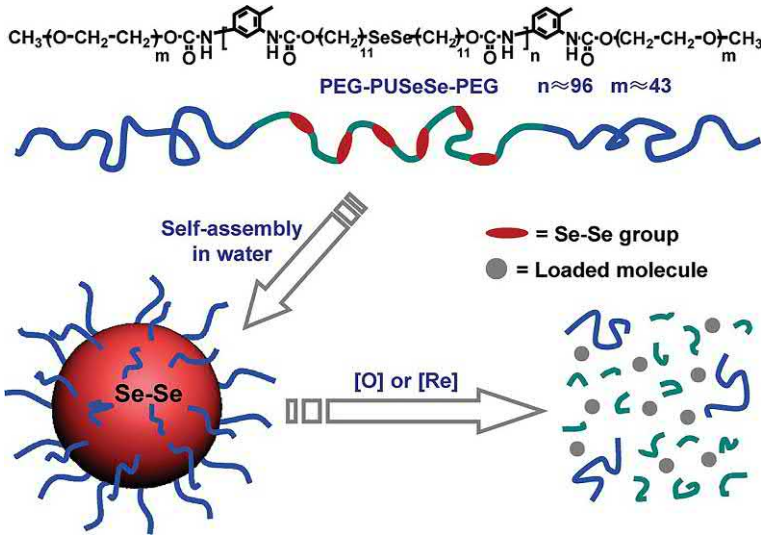

FIG. 3 Structure of PEG-PUSeSe-PEG copolymers and redox-responsive disassembly of PEG-PUSeSe-PEG micelles [5].

relative to that of COS-7 normal cells. DOX@HSD can be a promising redox-responsive DDS besides good biocompatibility in the clinical treatment of laryngopharyngeal carcinoma given that the GSH level is two to three orders higher in the cytosol of cancer cells compared with that in the extracellular environment. The high GSH level will trigger a fast micellar disassembly, which leads to the release of DOX into the cytosol of cancer cells.

Selenium compounds have been extensively applied in the pharmacochemistry as an antioxidant in the glutathione peroxidase (GPx) activity, among which diselenide is a proper dual redox response because it has good activity in the presence of oxidants and reductants. Commonly, Se—Se bonds oxidize to seleninic acid in the presence of oxidants and reduce to selenol in a reducing condition. In a study [5], PEG-PUSeSe-PEG amphiphilic triblock copolymer was synthesized with one hydrophobic diselenide-containing block and two hydrophilic PEG blocks and its self-assembly behavior in water and in the oxidants or reductants presence was investigated. In this work, the diselenide groups were first imported into a diol composition, which obtains the desirable solubility. Then the diselenide containing polyurethane (PUSeSe) blocks were synthesized via polymerization of toluene diisocyanate (TDI) in light excess with diselenide-containing diols and finally terminated by PEG monomethyl ether. PEG-PUSeSe-PEG self-assemble in an aqueous environment and create micelles. It was predictable that the Se—Se bonds would cleavage in the presence of oxidants (H_2O_2) or reductants and the consequent disassembly of the PEG-PUSeSe-PEG micelles occur. After adding H_2O_2, the micellar structure was turned into irregular aggregates and then decomposed into small aggregates of various nanometers in size during 3 hours of oxidation. This group has shown that the micelles of PEG-PUSeSe-PEG are also responsive to the reduced environment because the Se-Se bonds are completely sensitive and prone to cleavage in the presence of reductants such as reduced glutathione (GSH). Hence when GSH was added to PEG-PUSeSe-PEG micelle, they became broken and, then, tiny aggregates formed during the reduction process. Therefore it is confirmed that the diselenide groups in the polymer backbone can form micelles with dual redox responsiveness (Fig. 3).

4. THERMORESPONSIVE DRUG DELIVERY SYSTEMS

The cancer cells are more sensitive to heat-induced damage than the normal cells because of their rapidly dividing nature [38]. This fact causes to use hyperthermia as a supplement treatment besides chemotherapy and radiation for the destruction of cancer cells. Incorporation of temperature-sensitive components in the nanocarriers such as liposomes, micelles, and dendrimers along with other NPs such as gold NPs or superparamagnetic iron oxide particles (SPIONs) that can produce heat in external stimuli presence including alternating magnetic field (AMF) or near-infrared (NIR) light. These structures have developed hyperthermia as an adjunct to radiotherapy and chemotherapy for the treatment of