because they can potentially form physical gels that do not involve the formation of covalent bonds. In some instances, the self-assembled morphology can change from independent micelles to a network of bridged micelles, and eventually to a hydrogel network at higher polymer concentration.

[0005] Owing to their non-toxicity and biocompatibility, poly(ethylene glycol) (PEG) has been used extensively as the non-ionic hydrophilic B block in hydrogel forming ABA triblock copolymers. Homo- or copolymers of poly(lactides) and poly(caprolactone) have been used for the hydrophobic A blocks. A drawback of the reported triblock copolymers is the high concentration and hydrophobic content needed for hydrogel formation. For example, gelation of an aqueous mixture of poly(L-lactide)-b-poly(ethylene glycol)-b-poly(L-lactide) (PLLA-b-PEG-b-PLLA) triblock copolymer occurs at a polymer concentration of about 16 wt (weight percent) based on total weight of the aqueous mixture. The hydrophobic block content of the triblock copolymer was in a range of about 17 wt to 37 wt based on total weight of the triblock copolymer.

[0006] For many biomedical applications, it would be desirable to have polymeric materials that can form hydrogels at a lower concentration, which can be utilized for the delivery of biologically active substances that include hydrophobic drugs.

SUMMARY

[0007] ~~Accordingly~~In an aspect, there is provided a composite hydrogel ~~is disclosed~~, comprising:

an amphiphilic triblock copolymer (ABA), wherein i) the triblock copolymer comprises two independent peripheral hydrophobic A blocks and a hydrophilic central B block, ii) each of the A blocks comprises a steroidal repeat unit (repeat unit 1) comprising both a backbone carbonate and a side chain comprising a steroid functional group, iii) each of the A blocks has a degree of polymerization of about 0.5 to about 4.0, and iv) the B block comprises a first poly(alkylene oxide) backbone; and

a loaded micelle comprising a biologically active substance and an amphiphilic diblock copolymer (CD), wherein i) the diblock copolymer comprises a hydrophilic C block and a hydrophobic D block, ii) the C block comprises a second poly(alkylene oxide) backbone,

and iii) the D block comprises a steroidal repeat unit (repeat unit 2) comprising both a backbone carbonate group and a side chain comprising a steroid functional group;

wherein the amphiphilic triblock copolymer and the loaded micelle are bound by noncovalent interactions, and the composite hydrogel is capable of controlled release of a biologically active substance.

[0008] ~~Also disclosed~~In another aspect, there is provided a method, comprising:

mixing an amphiphilic triblock copolymer (ABA) with a loaded micelle, the loaded micelle comprising i) a biologically active substance and ii) an amphiphilic diblock copolymer (CD), thereby forming a composite hydrogel capable of controlled release of the biologically active substance;

wherein

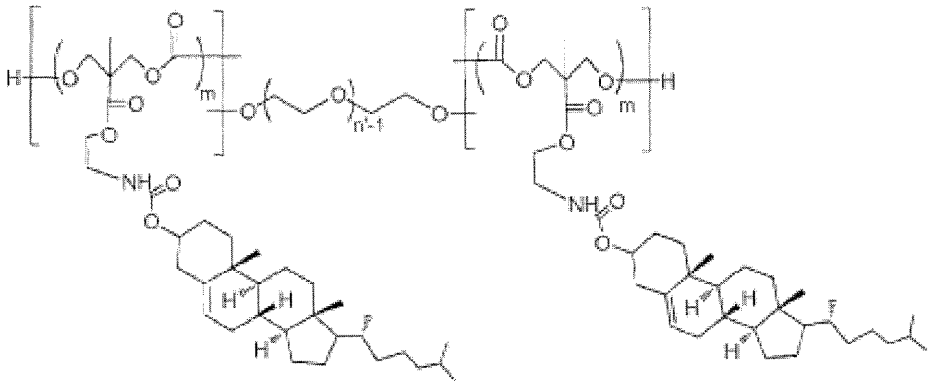
the triblock copolymer (ABA) comprises two independent peripheral hydrophobic A blocks and a hydrophilic central B block, wherein i) each of the A blocks comprises a steroidal repeat unit (repeat unit 1) comprising both a backbone carbonate and a side chain comprising a steroid functional group, ii) each of the A blocks has a degree of polymerization of about 0.5 to about 4.0, and iii) the B block comprises a first poly(alkylene oxide) backbone,

the diblock copolymer (CD) comprises a hydrophilic C block and a hydrophobic D block, wherein i) the C block comprises a second poly(alkylene oxide) backbone, and ii) the D block comprises a steroidal repeat unit (repeat unit 2) comprising both a backbone carbonate and a side chain steroid functional group, and

the triblock copolymer and the loaded micelle are bound by noncovalent interactions.

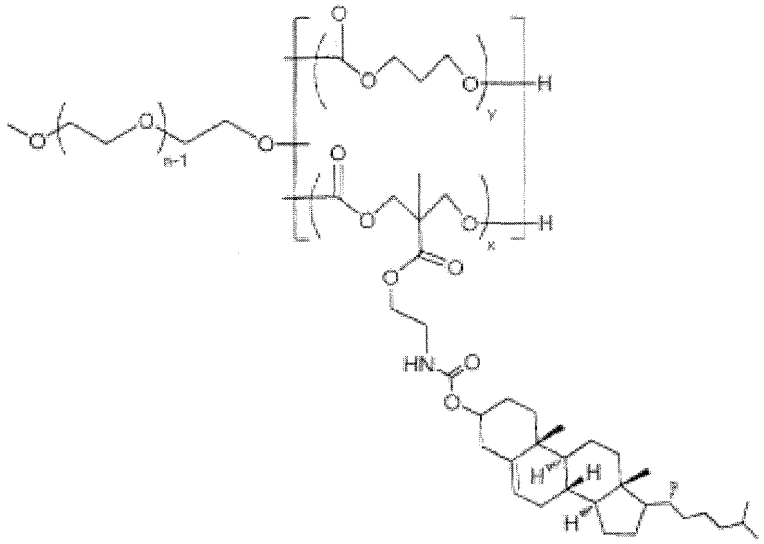
[0009] ~~Further disclosed~~In another aspect, there is provided a composite hydrogel for controlled release of a biologically active substance, comprising:

an amphiphilic triblock copolymer (ABA) having the structure:



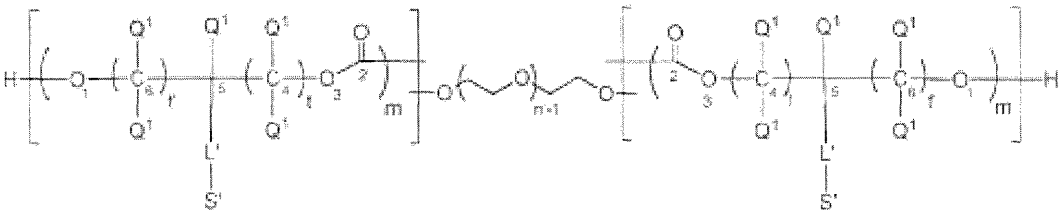
wherein each m is an independent number having a value of about 0.8 to about 2.5, and n' has a value of about 200 to about 800; and

a loaded micelle comprising i) the biologically active substance and ii) an amphiphilic diblock copolymer (CD) having the structure:



wherein n has a value of about 100 to about 120, x has a value of about 11, and y has a value of about 30, and wherein the amphiphilic triblock copolymer and the loaded micelle are bound by noncovalent interactions

[0010] ~~Also disclosed~~In another aspect, there is provided a triblock copolymer having the formula (19)



(19)

wherein

each m is an independent number having a value of about 0.8 to about 4,

n' has a value of about 200 to about 800,

each t is an independent integer having a value of 0 to 6,

each t' is an independent integer having a value of 0 to 6,

t' and t cannot both be zero in any repeat unit,

each Q1 is an independent monovalent radical selected from the group consisting of hydrogen, halides, alkyl groups comprising 1 to 30 carbons, and aryl groups comprising 6 to 30 carbon atoms,

each L" is an independent linking group selected from the group consisting of a single bond and divalent radicals comprising 1 to 30 carbons, and

each S' is an independent steroid group.

[0011] The above-described and other features and advantages of the present ~~invention~~ disclosure will be appreciated and understood by those skilled in the art from the following detailed description, drawings, and appended claims.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

[0012] Figure 1 is a graph showing the intensity ratio (1339/1334) versus logarithm of concentration (mg/L) of block copolymers (Examples 4, and 6 to 9), respectively, in deionized (DI) water. These data were used to determine critical micelle concentrations (CMC) values of Examples 4, and 6 to 9 of 2.1 mg/L, 2.1 mg/L, 1.5 mg/L, 1.5 mg/L and 2.1 mg/L, respectively (Table 8).

[0013] Figures 2A to 2F are transmission electron micrograph (TEM) images of aqueous micelles formed by the block copolymers of Examples 4 to 9, respectively. The