namely, the polymer-polymer, polymer-solution and the solution-solution interactions. Ideally, at a critical gel point, physical cross-linking occurs in which the hydrophilic corona entangles with each other, holding the water molecules together and the hydrophobic segments act as network or crosslink points to hold the gel structure in place, presenting the macroscopic observation of a highly viscous semi-solid hydrogel.

To increase the temperature of the thermogel such that gelation is initiated, heat is applied directly to the thermogel. However, as the heat applied must be in direct contact with the thermogel, this greatly reduces the possible applications of thermogel since direct heating of the thermogel may not be possible in some applications. In addition, the direct application of heat is detrimental to heat sensitive surfaces covering the polymer solution, further limiting the potential applications possible with the thermogelling system. Further, in some cases, the thermogels are unable to revert back to the sol state, that is, the thermogels are irreversible. If the ability to alternate between the sol-gel-sol phases is essential, the irreversibility of the thermogel further limits the application of the thermogel.

There is therefore a need to provide a reversible thermo-initiated system that overcomes, or at least ameliorates, one or more of the disadvantages described above.

Summary

According to ~~a first aspect~~the disclosure, there is provided a reversible thermo-initiated system comprising a heat source comprising particles that act as heat initiators when excited by an electromagnetic source; and a plurality of micellar amphiphilic polymers that are capable of

aggregating when heated by said heat source and which revert back to micellar amphiphilic polymers when cooled.

According to a first aspect, there is provided a hydrogel comprising a reversible thermo-initiated system and an active agent, wherein the reversible thermo-initiated system comprises a heat source comprising particles that act as heat initiators when excited by an electromagnetic source and a plurality of micellar amphiphilic polymers that are capable of aggregating when heated by the heat source and which revert back to micellar amphiphilic polymers when cooled.

The reversible thermo-initiated system may be a reversible thermo-initiated sol-gel system. The reversible thermo-initiated system may be a reversible thermogel.

Advantageously, the particles may be used as absorbers to harvest and convert the energy delivered by the electromagnetic source to heat. This in turn heats up the system *in situ* such that the micellar amphiphilic polymers aggregates to form a gel.

Advantageously, the electromagnetic source can be applied at a distance. Hence, a heat source need not be applied directly to the system since the heat source is provided *in situ* in the form of the heat initiator particles. Accordingly, the gelation of the amphiphilic polymers can be triggered from a distance (that is remote triggered gelation), allowing the system to be applied in hard to reach areas.

Advantageously, an external heat source may not be required. The electromagnetic radiation is typically a light source which does not heat up the amphiphilic polymers on its own. The system generates heat from within based on the interactions between the electromagnetic radiation and the heat initiator particles to cause the gelation to occur.

According to ~~a second aspect~~the disclosure, there is provided a hydrogel comprising the thermo-initiated system as disclosed above and an active agent.

Advantageously, the hydrogel may be used as a drug delivery system to deliver the active agent to a desired site *in vitro* or *in vivo*.

Due to the aqueous nature of the amphiphilic polymer solution (containing the particles therein), the solution may be administered to a target site by injection, without

requiring surgical implantation of a sustained release device. In addition, by passing through a syringe filter, the solution can be sterilized before administration. Further, the high water content of the gel matrix may result in improved biocompatibility with the injection site.

Advantageously, by selecting biodegradable polymers as the amphiphilic polymers, the biodegradable polymers may be removed from a living organism when administered *in vivo* via natural excretion routes.

Where the active agent is a peptide, the peptide/amphiphilic polymer formulations can be prepared under aqueous conditions without using peptide-denaturing organic solvents. This is advantageous for peptides because formulations can be prepared in the sol state at low temperatures which reduces the denaturation rate of the peptides.

According to ~~a third aspect~~the disclosure, there is provided a method for forming a reversible thermo-initiated system comprising the steps of:

a. mixing an aqueous solution of micellar amphiphilic polymers with an aqueous solution of particles that act as heat initiators when excited by an electromagnetic radiation source; and

b. exciting the mixture with the electromagnetic radiation source to cause the particles to absorb electromagnetic radiation and generate heat, thereby causing micellar amphiphilic polymers to crosslink to form a gel.

According to a second aspect, there is provided a method for forming a hydrogel comprising a reversible thermo-initiated system and an active agent comprising the steps of:

a.mixing an aqueous solution of micellar amphiphilic polymers with an aqueous solution of

particles that act as heat initiators when excited by an electromagnetic radiation source; and

b. exciting the mixture with the electromagnetic radiation source to cause the particles to absorb electromagnetic radiation and generate heat, thereby causing micellar amphiphilic polymers to crosslink to form a gel.

Definitions

The following words and terms used herein shall have the meaning indicated:

CLAIMS

1. A hydrogel comprising a reversible thermo-initiated system and an active agent, wherein said reversible thermo-initiated system comprises~~ing~~:

a heat source comprising particles that act as heat initiators when excited by an electromagnetic source; and

a plurality of micellar amphiphilic polymers that are capable of aggregating when heated by said heat source and which revert back to micellar amphiphilic polymers when cooled.

2. The hydrogel ~~system~~ of claim 1, wherein said particles is selected from the group consisting of metal particles and carbon particles.

3. The hydrogel ~~system~~ of claim 2, wherein the metal of said metal particles is selected from the group consisting of ruthenium, rhodium, palladium, silver, osmium, iridium, platinum, gold, mercury, rhenium, copper and alloys thereof.

4. The hydrogel ~~system~~ of claim 2, wherein said carbon particles are selected from the group consisting of carbon tubes, graphene particles and graphene oxide particles.

5. The hydrogel ~~system~~ of any one of the preceding claims, wherein said particles have an absorption peak in the range selected from the group consisting of 100 nm to 1,000 nm, 200 nm to 1,000 nm, 300 nm to 900, 400 nm to 900 nm and 400 nm to 800 nm.

6. The hydrogel ~~system~~ of any one of the preceding claims, wherein ~~the concentration of~~ said particles have a concentration ~~is~~ in the range selected from the group consisting of 0.1 ppm to

100 ppm, 0.5 ppm to 100 ppm, 1 ppm to 100 ppm, 5 ppm to 100 ppm, 10 ppm to 100 ppm, 20 ppm to 100 ppm, 30 ppm to 100 ppm, 1 ppm to 50 ppm and 15 ppm to 60 ppm.

7. The hydrogel ~~system~~ of any one of the preceding claims, wherein ~~the size of the~~said particles have a size ~~is~~ in the micron-sized range or in the nano-sized range.

8. The hydrogel ~~system~~ of claim 7, wherein said particles are nanoparticles and the size of said nanoparticles is in the range selected from the group consisting of 1 nm to 100 nm, 10 nm to 100 nm, 20 nm to 100 nm, 30 nm to 100 nm, 40 nm to 100 nm, 50 nm to 100 nm, 10 nm to 90 nm, 10 nm to 80 nm, 20 nm to 80 nm and 30 nm to 80 nm.

9. The hydrogel ~~system~~ of any one of the preceding claims, wherein said amphiphilic polymer is selected from the group consisting of block copolymers, graft copolymers and homopolymers.

10. The hydrogel ~~system~~ of any one of the preceding claims, wherein said amphilphilic polymers comprise monomers selected from the group consisting of diols, urethanes, esters, hydroxyesters, carboxylic acids, lactones, carbonates, siloxanes, alkylenes, amides, oxazolines, imines, alcohols, lactams, aminos and combinations thereof.

11. The hydrogel ~~system~~ of any one of the preceding claims, wherein the concentration of said amphiphilic polymer is in the range selected from the group consisting of 0.5 wt% to 30 wt%, 1 wt% to 30 wt%, 5 wt% to 30 wt%, 10 wt% to 30 wt% and 0.5 wt% to 20 wt%.

12. The hydrogel ~~system~~ of any one of the preceding claims, wherein the electromagnetic source has a wavelength that matches an absorption peak of said nanoparticles.

~~13. A hydrogel comprising a thermo-initiated system of any one of the preceding claims and an active agent.~~

~~14.~~13. The hydrogel of claim 1~~3~~, wherein ~~an~~ said active agent is selected from the group consisting of DNA, protein, antibody, peptide, small-molecule drug, nucleic acid-based drug, enzyme inhibitor, antibiotic, chemotherapeutic agent, anti-inflammatory agent, analgesic and mixtures thereof.

~~15.~~14. A method for forming a hydrogel comprising a reversible thermo-initiated system and an active agent comprising the steps of:

a. mixing an aqueous solution of micellar amphiphilic polymers with an aqueous solution of particles that act as heat initiators when excited by an electromagnetic radiation source; and

b. exciting said mixture with said electromagnetic radiation source to cause said particles to absorb electromagnetic radiation and generate heat, thereby causing micellar amphiphilic polymers to crosslink to form ~~a gel~~the hydrogel.

~~16.~~15. The method of claim ~~15~~14, comprising the step of using a laser source to excite said mixture.

~~17.~~16. The method of claim ~~16~~15, comprising the step of selecting the power of said laser source to thereby control the aggregating rate.

~~18.~~17. The method of claim ~~15~~14 or ~~16~~15, comprising the step of selecting the wavelength of said laser source to match an absorption peak of said particles.

~~19.~~18. The method of any one of claims ~~15~~14 to ~~18~~17, comprising the step of selecting the concentration of said particles to thereby control the aggregating rate.

~~20.~~19. The method of any one of claims ~~15~~14 to ~~19~~18, wherein said exciting step (b) is carried out for 1 to 60 minutes.

~~21.~~20. The method of any one of claims ~~15~~14 to ~~19~~18, comprising the step of cooling said hydrogel to reverse said aggregating and thereby obtain said aqueous mixture.