Claims

1. A sustained release composition comprising:

an active agent having a positive or negative charge when placed in an aqueous environment;

a crosslinked hydrogel tuned to have an overall charge that facilitates electrostatic interaction between the crosslinked hydrogel and the active agent, wherein:

the crosslinked hydrogel is formed from:

a gelatin comprising a first set of functional groups that are positively charged and a second set of functional groups that are negatively charged in an aqueous environment; and

a heterobifunctional crosslinking agent selected from phenolic molecules with carboxylic acid groups and phenolic molecules with amine groups, where the heterobifunctional crosslinking agent comprises:

at least one functional group capable of forming a bond to a further molecule of said heterobifunctional crosslinking agent; and

at least one functional group suitable to form a bond with the first or second set of functional groups of the gelatin, so as to reduce the number of the first or second functional groups in the first or second sets of functional groups, thereby modifying the overall charge of the crosslinked hydrogel and facilitating the electrostatic interaction between the crosslinked hydrogel and the active agent,

and where the active agent is a small molecule active agent and/or a charged biomolecule selected from one or more of CRiSPR components, a nucleic acid, a microRNA and a siRNA.

2. The sustained release composition according to Claim 1, wherein the small molecule active agent is selected from the group consisting of cisplatin and paclitaxel.

3. The sustained release composition according to Claim 1, wherein:

the microRNA is selected from one or more of 5’-UUGUGCUUGAUCUAACCAUGU-3’ (miR-218), 5’-UAGCACCAUUUGAAAUCAGUGUU-3’ (miR-29b duplex), 5’-AUCACAUUGCCAGGGAUUACC-3’ (miR-23b), and 5’-UGAAAUGUUUAGGACCACUAG-3’ (miR-203); and

the siRNA is selected from one or more of 5’-AACAAGACCUUCGACUCUUCC-3’ (SPARC), 5’-AACCTGAAGATCTTCAACAACCCTGTCTC-3’ (Smad3), 5’-AACCUGCUGAAGGAUGGUGAC-3’ (p53), 5’-CCAAGAACCGGAACCUGCUTT-3’ (MC1R),

5’-GCAGUACCUUUCUACCACUTT-3’ (MITF), and 5’-UCACUUACAGGAUCUAUAAUU-3’ (Elastase).

4. The sustained release composition according to any one of the preceding claims, wherein

the phenolic molecules with carboxylic acid groups are selected from one or more of 3-(4-hydroxyphenyl)propionic acid and 3,4-dihydroxyphenylacetic acid; and

the phenolic molecules with amine groups are selected from one or more of 4-hydroxybenzylamine, dopamine, and tyramine.

5. The sustained release composition according to any one of the preceding claims, wherein the overall charge of the crosslinked hydrogel also facilitates the sustained release effect of the composition, optionally wherein the sustained release effect is from 1 to 30 days, such as from 2 to 25 days, such as 5 to 20 days.

6. The sustained release composition according to Claim 1, wherein the active agent is a siRNA and the crosslinked hydrogel is formed from gelatin and tyramine, where the zeta potential of the crosslinked hydrogel is from -1 mV to +10 mV, such as from 0 mV to +9 mV, such as from +0.4 mV to +8.5 mV, such as from +0.6 mV to +1 mV.

7. The sustained release composition according to Claim 1, wherein the active agent is cisplatin and the crosslinked hydrogel is formed from gelatin and 3-(4-hydroxyphenyl)propionic acid, where the zeta potential of the crosslinked hydrogel is from -4 mV to -10 mV.

8. A sustained release composition as described in any one of Claims 1 to 7 for use as a medicament.

9. Use of a sustained release composition as described in Claims 1, 3 or 6 in the preparation of a medicament for the treatment and/or prevention of scarring, wherein the active agent of the sustained release composition is a siRNA (e.g. the siRNA is 5’-AACAAGACCUUCGACUCUUCC-3’), optionally wherein the use relates to the treatment and/or prevention of scarring in a subject who has undergone surgery (e.g. eye surgery for glaucoma).

10. Use of a sustained release composition as described in any one of Claims 1, 2 or 7 in the preparation of a medicament for the treatment and/or prevention of cancer, wherein the

active agent of the sustained release composition is a small molecule active agent (e.g. the small molecule active agent is an anti-cancer agent such as cisplatin).

11. A pharmaceutical composition comprising the sustained release composition as described in any one of Claims 1 to 7 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

12. A kit of parts, comprising:

(Aa) a first composition comprising:

a complex of an active agent having a positive or negative charge when placed in an aqueous environment and an un-crosslinked hydrogel tuned to have an overall charge that facilitates electrostatic interaction between the un-crosslinked hydrogel and the active agent; and

an enzyme suitable to crosslink the un-crosslinked hydrogel; and

(Bb) a second composition comprising an oxidation source (e.g. H_2O_2), wherein:

the un-crosslinked hydrogel comprises a gelatin that has a first set of functional groups that are positively charged and a second set of functional groups that are negatively charged in an aqueous environment, where a portion of the first or second set of functional groups are capped by a heterobifunctional crosslinking agent selected from phenolic molecules with carboxylic acid groups and phenolic molecules with amine groups, such that the overall charge of the un-crosslinked hydrogel is modified to facilitate the formation of the complex between the un-crosslinked hydrogel and the active agent, where:

the heterobifunctional crosslinking agent that is selected from phenolic molecules with carboxylic acid groups and phenolic molecules with amine groups comprises at least one functional group capable of forming a bond to a further molecule of said heterobifunctional crosslinking agent when the first and second compositions are combined, and at least one functional group that has formed a bond to a portion of the first or second set of functional groups of the gelatin, so as to reduce the number of the first or second functional groups, thereby modifying the overall charge of the un-crosslinked hydrogel and facilitating the electrostatic interaction between the un-crosslinked hydrogel and the active agent,

and where the active agent is a small molecule active agent and/or a charged biomolecule selected from one or more of CRiSPR components, a nucleic acid, a microRNA and a siRNA.