[0028] In particular, the most common treatment for AMD is intravitreal bevacizumab injection. Injections are administered every three to four weeks and can be a source of procedural risk and inconvenience for the patient.

[0029] Targeted delivery of drugs to other tissues, including but not limited to pancreatic tissue, lung tissue and liver tissue, localizes treatment to these tissues, and has potential benefits for the treatment of diseases specific to these tissues, including pancreatitis, diabetes, brain cancer, lung cancer, and hepatitis.

Summary

[0029a] In one aspect of the disclosure, there is provided a system for delivering a therapeutic treatment to a targeted population of cells of a subject, the system comprising: a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment; a therapeutic composition disposed in the vial, the therapeutic composition is to be provided for administration of the therapeutic treatment and comprising an aqueous solution including a chitosan gel and a plurality of particles embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection; the particles containing a therapeutic agent and having a coating around the therapeutic agent; and the coating including chitosan so as to provide controlled release of the agent from the particles.

[0029b] In another aspect of the disclosure, there is provided a use of the system according to claim 1 in the manufacture of a medical system for treating a targeted population of cells of a subject, wherein the use comprises: loading the aqueous solution into the syringe before the aqueous solution is to be injected into the targeted population of cells by means of the syringe.

[0029c] In another aspect of the disclosure, there is provided a system for delivering a therapeutic treatment to a targeted population of cells of a subject, the system comprising: a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment; a therapeutic composition disposed in the vial, the therapeutic composition is to be provided for administration of the therapeutic treatment and comprising a lyophilized precursor formulated so that upon mixing with water, it dissolves to provide an aqueous solution including chitosan gel and a plurality of particles

embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection; the particles containing a therapeutic agent and having a coating around the therapeutic agent; and the coating including chitosan so as to provide controlled release of the agent from the particles.

[0029d] In another aspect of the disclosure, there is provided a lyophilization method for providing a system for delivering a therapeutic treatment to a targeted population of cells of a subject, the method comprising: forming an aqueous solution including a chitosan gel and a plurality of particles, the particles containing a therapeutic agent and having a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the agent from the particles; freezing the first aqueous solution in a bath containing an aqueous alcoholic solution at a temperature above the freezing temperature of the aqueous alcoholic solution and at most -80°C, to form a frozen layer precursor; drying the frozen layer precursor, to form anhydrous powder embedded with particles; including the anhydrous powder in a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment; and adding water to the container to dissolve the anhydrous powder.

[0030] In one example of the disclosure, there is provided a composition formulated for delivery by injection into a targeted population of cells of subject. In this example, the composition includes an aqueous solution including a chitosan gel and a plurality of particles, the particles containing a therapeutic agent and having a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the agent from the particles.

[0031] One example of the disclosure provides a system for delivering a therapeutic treatment to a targeted population of cells of a subject. In this example, the system includes a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment. In this example, a therapeutic composition is disposed in the vial, the therapeutic composition provided for use in administration of the therapeutic treatment and comprising an aqueous solution including a chitosan gel and a plurality of particles embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection. The particles in this example contain a therapeutic agent and

have a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the agent from the particles.

[0032] In a further related example, the aqueous solution further includes a compound selected from a group consisting of a hydration promotor, a particle adhesion inhibitor, a particle aggregation inhibitor, and combinations thereof.

[0033] The hydration promotor is selected from the group consisting of ethylene glycol, propylene glycol, beta-propylene glycol, glycerol and combinations thereof.

[0034] The particle adhesion inhibitor is selected from the group consisting of HPMC, poloxamer, and combinations thereof.

[0035] The particle aggregation inhibitor is selected from the group consisting of monosaccharides, disaccharides, sugar alcohols, chlorinated monosaccharides, chlorinated disaccharides, and combinations thereof.

[0036] Alternatively or in addition, the composition further includes sodium tripolyphosphate.

[0037] In some examples, the particles are microparticles having an average diameter between 200 nm and 2000 nm. As a further option, the microparticles have an average diameter between 500 nm and 2000 nm.

[0038] Optionally, the aqueous solution further includes a free quantity of the therapeutic agent, not coated with chitosan, wherein the free quantity of therapeutic agent comprises between about 20% to about 80% of a total quantity by weight of therapeutic agent in the aqueous solution.

[0039] Also optionally, the therapeutic agent in the particles is an immunotherapeutic. As a further option, the therapeutic agent is selected from the group consisting of an antibody, a cytokine, a small molecule immunotherapeutic, and combinations thereof.

[0040] In a further related example, the therapeutic agent is a chemotherapeutic.

[0041] Optionally, the particles are in direct physical contact with the chitosan gel.

[0042] In another example, the disclosure provides a method for treatment of a targeted population of cells of a subject. This method includes obtaining a system as described at the beginning of this section, loading the aqueous solution into the syringe, and injecting the aqueous solution into the targeted population of cells by means of the syringe.

[0043] In a related example of the method, the targeted population of cells includes a tumor. In another related example, the targeted population of cells is tissue in an organ. Optionally, the organ is selected from the group consisting of eye, lung, pancreas, liver, kidney, brain, heart, thyroid, and pituitary.

[0044] In another example, a system is provided for delivering a therapeutic treatment to a targeted population of cells of a subject, the system including a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the

therapeutic treatment. In this example, a therapeutic composition is disposed in the vial, the therapeutic composition provided for use in administration of the therapeutic treatment and including a lyophilized precursor formulated so that upon mixing with water, it dissolves to provide an aqueous solution including chitosan gel and a plurality of particles embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection. The particles in this example contain a therapeutic agent and have a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the therapeutic agent from the particles.

[0045] Another example provides a lyophilization method for providing a system for delivering a therapeutic treatment to a targeted population of cells. This method includes: (1) forming an aqueous solution including a chitosan gel and a plurality of particles, the particles containing a therapeutic agent and having a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the agent from the particles, (2) freezing the aqueous solution in a bath containing an aqueous alcoholic solution at a temperature above the freezing temperature of the aqueous alcoholic solution and at most -80°C, to form a frozen layer precursor, (3) drying the frozen layer precursor, to form anhydrous powder embedded with particles, (4) including the anhydrous powder in a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment, and (5) adding water to the vial to dissolve the anhydrous powder.

[0046] Optionally, the aqueous solution in the lyophilization method further includes a hydration promoter, a particle adhesion inhibitor, and a particle aggregation inhibitor.

[0047] In a further related example of the lyophilization method, the hydration promotor is selected from the group consisting of ethylene glycol, propylene glycol, beta-propylene glycol, glycerol and combinations thereof. Also optionally, the particle adhesion inhibitor comprises HPMC, poloxamer, and combinations thereof. In a related example, the particle aggregation inhibitor is selected from the group consisting of monosaccharides, disaccharides, sugar alcohols, chlorinated monosaccharides, chlorinated disaccharides, and combinations thereof. Optionally, the composition further includes sodium tripolyphosphate. Also optionally, the particles are microparticles having an average diameter between 200 nm

and 2000 nm. As a further option, the particles are microparticles having an average diameter between 500 nm and 2000 nm.

[0048] Some examples of the disclosure, a particle-based composition is formulated for delivery by intravitreal injection for treating an ocular condition.

[0049] Optionally, the ocular disease is age-related macular degeneration (AMD).

[0050] According to some examples, the therapeutic agent for intravitreal injection is selected from the group consisting of an antibody, a cytokine, a small molecule immunotherapeutic, a chemotherapeutic, an aptamer, and combinations thereof. In some examples the therapeutic agent for intravitreal injection is bevacizumab.

Brief Description of the Drawings

[0051] The foregoing features of embodiments will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

[0052] Fig. 1A provides an injectable chitosan formulation according to the instant invention (PRV311), frozen at -80 °C and stored properly. Notably, the formulation provides a clear aqueous solution. (Left) versus PRV311 at room temperature (Middle), and PRV111 (Right). PRV111 is a similar product to PRV311 but is frozen more quickly in liquid nitrogen (-196 °C) rather than in a freezer at -80 °C when it is made.

[0053] Fig. 1B shows for comparison an injectable chitosan formulation according to the instant invention (PRV311), frozen at -80 °C and stored at room temperature for five days.

[0054] Fig. 1C shows for comparison an injectable chitosan formulation according to the instant invention (PRV311), frozen in liquid nitrogen at -196 °C and stored at room temperature for five days.

[0055] Fig. 2 is an FTIR Spectrum of injectable chitosan powder comprising cisplatin internal standard, with peaks at 1400 and 1560 cm^{-1}.

[0056] Fig. 3 is a photograph of the matrix (2x zoom) when frozen in liquid nitrogen (-196 °C) and subsequently lyophilized. Note the multi-layered, dense, fabric-like structure.

What is claimed is:

1. A system for delivering a therapeutic treatment to a targeted population of cells of a subject, the system comprising:

a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment;

a therapeutic composition disposed in the vial, the therapeutic composition is to be provided for administration of the therapeutic treatment and comprising an aqueous solution including a chitosan gel and a plurality of particles embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection;

the particles containing a therapeutic agent and having a coating around the therapeutic agent; and

the coating including chitosan so as to provide controlled release of the agent from the particles.

2. The system according to claim 1, wherein the aqueous solution further includes a compound selected from the group consisting of a hydration promotor, a particle adhesion inhibitor, a particle aggregation inhibitor, and combinations thereof, wherein:

(a) the hydration promotor is selected from the group consisting of ethylene glycol, propylene glycol, beta-propylene glycol, glycerol and combinations thereof,

(b) the particle adhesion inhibitor is selected from the group consisting of HPMC, poloxamer, and combinations thereof, and

(c) the particle aggregation inhibitor is selected from the group consisting of monosaccharides, disaccharides, sugar alcohols, chlorinated monosaccharides, chlorinated disaccharides, and combinations thereof.

3. The system according to any of claims 1 and 2, wherein the aqueous solution further includes sodium tripolyphosphate.

4. The system according to any of claims 1 and 2, wherein the particles are microparticles having an average diameter between 200 nm and 2000 nm.

5. The system according to any of claims 1 and 2, wherein the particles are microparticles having an average diameter between 500 nm and 2000 nm.

6. The system according to any of claims 1 to 5, the aqueous solution further including a free quantity of the therapeutic agent, not coated with chitosan, wherein the free quantity of therapeutic agent comprises between about 20% to about 80% of a total quantity by weight of therapeutic agent in the aqueous solution.

7. The system according to any of claims 1 to 6, wherein the therapeutic agent is an immunotherapeutic.

8. The system according to claim 7, wherein the immunotherapeutic is selected from the group consisting of an antibody, a cytokine, a small molecule immunotherapeutic, and combinations thereof.

9. The system according to any of claims 1 to 6, wherein the therapeutic agent is a chemotherapeutic.

10. The system according to claim 1, wherein the particles are in direct physical contact with the chitosan gel.

11. Use of the system according to claim 1 in the manufacture of a medical system for treating a targeted population of cells of a subject, wherein the use comprises:

loading the aqueous solution into the syringe before

the aqueous solution is to be injected into the targeted population of cells by means of the syringe.

12. The use according to claim 11, wherein the targeted population of cells includes a tumor.

13. The use according to claim 11, wherein the targeted population of cells is tissue in an organ.

14. The use according to claim 13, wherein the organ is selected from the group consisting of eye, lung, pancreas, liver, kidney, brain, heart, thyroid, and pituitary.

15. A system for delivering a therapeutic treatment to a targeted population of cells of a subject, the system comprising:

a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment;

a therapeutic composition disposed in the vial, the therapeutic composition is to be provided for administration of the therapeutic treatment and comprising a lyophilized precursor formulated so that upon mixing with water, it dissolves to provide an aqueous solution including chitosan gel and a plurality of particles embedded in the gel, the gel having a viscosity rendering it suitable for administration by injection;

the particles containing a therapeutic agent and having a coating around the therapeutic agent; and

the coating including chitosan so as to provide controlled release of the agent from the particles.

16. A lyophilization method for providing a system for delivering a therapeutic treatment to a targeted population of cells of a subject, the method comprising:

forming an aqueous solution including a chitosan gel and a plurality of particles, the particles containing a therapeutic agent and having a coating around the therapeutic agent, the coating including chitosan so as to provide controlled release of the agent from the particles;

freezing the first aqueous solution in a bath containing an aqueous alcoholic solution at a temperature above the freezing temperature of the aqueous alcoholic solution and at most -80°C, to form a frozen layer precursor;

drying the frozen layer precursor, to form anhydrous powder embedded with particles;

including the anhydrous powder in a vial enclosed with a septum that is penetrable by a needle of a syringe to be used for administration of the therapeutic treatment; and

adding water to the container to dissolve the anhydrous powder.

17. The lyophilization method according to claim 16, wherein the anhydrous powder further includes a compound selected from the group consisting of a hydration promoter, a particle adhesion inhibitor, and a particle aggregation inhibitor, and combinations thereof,

wherein the hydration promoter is selected from the group consisting of ethylene glycol, propylene glycol, beta-propylene glycol, glycerol and combinations thereof,

wherein the particle adhesion inhibitor is selected from the group consisting of hydroxypropylmethylcellulose, poloxamer, and combinations thereof, and

wherein the particle aggregation inhibitor is selected from the group consisting of monosaccharides, disaccharides, sugar alcohols, chlorinated monosaccharides, chlorinated disaccharides, and combinations thereof.

18. The method according to claim 16, wherein the anhydrous powder further includes sodium tripolyphosphate.

19. The method according to claim 16, wherein the particles are microparticles having an average diameter between 200 nm and 2000 nm.

20. The method according to claim 16, wherein the particles are microparticles having an average diameter between 500 nm and 2000 nm.

21. The system according to claim 1, configured for delivering a therapeutic treatment for an ocular condition by intravitreal injection.

22. The system according to claim 21, wherein the therapeutic agent is selected from the group consisting of an antibody, a cytokine, a small molecule immunotherapeutic, a chemotherapeutic, an aptamer, and combinations thereof.

23. The system according to claim 21 wherein the ocular condition is age-related macular degeneration.

24. The system according to claim 23, wherein the therapeutic agent is bevacizumab.