concentration of the therapeutically effective ophthalmic agent in the fluid. In some cases, the interaction between the ophthalmic agent and a preservative removing device may be tuned by the addition of a support matrix having no affinity for the ophthalmic agent or preservative. Ideally these systems and methods would address at least some of the above drawbacks of prior approaches and reduce patient exposure to preservative while maintaining consistent dosage.

[0006a] In an aspect of the present disclosure, there is provided a preservative removing device, comprising:

a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb a preservative when a solution, emulsion, or suspension comprising an ophthalmic agent and a preservative is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component.

[0006b] In another aspect of the present disclosure, there is provided a method for removing a preservative from an ophthalmic agent, comprising:

providing a solution, emulsion, or suspension comprising the ophthalmic agent and the preservative in a container suitable for drop-wise dispensing;

providing a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb the preservative when the solution, emulsion, or suspension is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component; and

passing at least one drop of the solution, emulsion, or suspension comprising the ophthalmic agent, through the polymeric matrix.

[0007] In an example, a method for administering an ophthalmic agent is provided. The method may comprise: providing a solution, emulsion, or suspension comprising an ophthalmic agent, and a preservative; and providing a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb the preservative when the solution, emulsion, or suspension is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component. The inactive matrix component has substantially no affinity for the ophthalmic agent or the preservative.

[0008] In some examples, the active polymeric matrix component is a polymeric hydrogel. In some examples, the polymeric matrix comprises 2-hydroxyethylmethacrylate. In some examples, the polymeric matrix comprises tert-butyl methacrylate. In some examples, the polymeric matrix comprises a crosslinker. In some examples, the crosslinker is SR-9035.

[0009] In some examples, the inactive polymeric matrix component is a polyolefin. In some examples, the polyolefin is a polyethylene, polypropylene or copolymers thereof.

In some examples, the polyolefin is a low-density polyethylene (LDPE). In some examples, the polyolefin is a high-density polyethylene (HDPE). In some examples, the polyolefin is an ultra-high molecular weight polyethylene (UHMWPE). In some examples, the polyolefin is selected from LDPE, HDPE, or UHMWPE.

[0010] In some examples, the solution, emulsion, or suspension is disposed within a chamber of a compressible bottle. In some examples, the polymeric matrix is disposed between the chamber and an outlet of a compressible bottle. In some examples, compression of the compressible bottle passes the solution, emulsion, or suspension through the polymeric matrix to the outlet. In some examples, compression of the compressible bottle forms a drop at the outlet. In some examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 80%, 85%, 90%, or 95% of a concentration of the ophthalmic agent before passing through the polymeric matrix. In some examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 80% of a concentration of the ophthalmic agent before passing through the polymeric matrix. In some examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 90% of a concentration of the ophthalmic agent before passing through the polymeric matrix. In some

examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 93% of the concentration of the ophthalmic agent before passing through the polymeric matrix. In some examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 95% of the concentration of the ophthalmic agent before passing through the polymeric matrix. In some examples, the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 97% of the concentration of the ophthalmic agent before passing through the polymeric matrix. In some examples, the concentration of the preservative after passing though the polymeric matrix is less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% of the concentration of the preservative before passing through the polymeric matrix. In some examples, the concentration of the preservative after passing though the polymeric matrix is less than 10% of the concentration of the preservative before passing through the polymeric matrix. In some examples, the concentration of the preservative after passing though the polymeric matrix is less than 5% of the concentration of the preservative before passing through the polymeric matrix. In some examples, the concentration of the preservative after passing though the polymeric matrix is less than 1% of the concentration of the preservative before passing through the polymeric matrix. In some examples, a timescale for drop formation is less than 3 seconds.

[0011] In some examples, the active polymeric matrix is polyvinyl alcohol crosslinked with citric acid or other suitable crosslinking agent to render it a hydrogel. In some examples, the active polymeric matrix is selected from crosslinked polyvinylpyrrolidone, crosslinked polyethylene oxide, crosslinked polyacrylamides, crosslinked copolymers of methacrylic acid, polyacrylic acid, or copolymers selected from poly (acrylic acid-co-acrylamide), or poly (methacrylic acid-co-acrylamide). In some examples, the active polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; and the crosslinked polyacrylamide is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP). In some examples, the active polymeric matrix comprises one or more monomers comprising acrylamide, acrylic acid (e.g., a compound having an acrylic acid such as methacrylic acid), or acrylate, which can be crosslinked with one or more crosslinking monomers.

[0012] In some examples, the active polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM); and the crosslinked polyacrylamide is modified with 2-sulfoethyl methacrylate (SEM). In some examples, the

active polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP).

[0013] In some examples, the active polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from 2-acrylamido-2-methylpropane sulfonic acid (AMPS), or 2-sulfoethyl methacrylate (SEM). In some examples, the crosslinked polyacrylamide material is isolated in the form of spherical beads.

[0014] In some examples, the active polymeric matrix is an oxidized polyethylene, such as Honeywell A-C 395A, or the like.

[0015] In some examples, the inactive polymeric matrix component is a polyolefin in the form of a ground powder or a spherical bead. In some examples, the shape of the polyolefin particle is regular. In some examples, the shape of the polyolefin particle is irregular. In some examples, the polyolefin particle size is at least 1 micron, 10 microns, 50 microns, or 100 microns. In some examples, the polyolefin particle size is up to 600 microns, 700 microns, 800 microns, 900 microns, or 1000 microns. In some examples, the polyolefin particle size is from about 1 micron to about 1000 microns. In some examples, the polyolefin particle size is from about 10 microns to about 700 microns. In some examples, the polyolefin particle size is from about 50 microns to about 600 microns.

[0016] In some examples, the inactive polymeric matrix component is an inert material selected from metal or glass, wherein the inert material is in bead or powder form. In some examples, the inactive polymeric matrix component is an inert material coated with a surface antimicrobial material which renders the matrix resistant to bacterial or fungal growth during the storage and use.

[0017] In some examples, the inactive polymeric matrix component is a polyolefin having substantially no affinity for the ophthalmic agent, or combination of agents, being administered. In some examples, substantially no affinity means less than 0.1% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 0.5% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 1.0% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than

1.5% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 2.0% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 2.5% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 3.0% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 4.0% of the ophthalmic agent(s) is retained. In some examples, substantially no affinity means less than 5.0% of the ophthalmic agent(s) is retained.

[0018] In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 1% (w/w) to about 99% (w/w). In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 10% (w/w) to about 90% (w/w). In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 20% (w/w) to about 80% (w/w). In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 30% (w/w) to about 70% (w/w). In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 50% (w/w). In some examples, the polymeric matrix comprises an active matrix component and an inactive matrix component in a ratio of about 5% (w/w) to about 95% (w/w), about 10% (w/w) to about 90% (w/w), about 15% (w/w) to about 85% (w/w), about 20% (w/w) to about 80% (w/w), about 25% (w/w) to about 75% (w/w), about 30% to about 70% (w/w), about 35% (w/w) to about 65% (w/w), about 40% to about 60% (w/w), about 45% (w/w) to about 55% (w/w), about 50% (w/w) to about 50% (w/w), about 55% (w/w) to about 45% (w/w), about 60% (w/w) to about 40% (w/w), about 65% (w/w) to about 35% (w/w), about 70% (w/w) to about 30% (w/w), about 85% (w/w) to about 15% (w/w), about 90% (w/w) to about 10% (w/w), or about 95% (w/w) to about 5% (w/w).

[0019] In another example, disclosed herein is a method for administering an ophthalmic agent, comprising: providing a solution, emulsion, or suspension comprising an ophthalmic agent and a preservative in a container suitable for drop-wise dispensing; providing a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb the preservative when the solution, emulsion, or suspension is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component; and dispensing at least one drop of the solution, emulsion, or suspension comprising an ophthalmic agent, said solution, emulsion, or suspension having passed through the polymeric matrix. In some cases, the inactive matrix component has substantially no affinity for the ophthalmic agent or the preservative. The active polymeric matrix component can be a polymeric hydrogel. The inactive polymeric matrix

for drop formation such that the preservative removing device is practical for removing a preservative from a solution, emulsion, or suspension. For example, a timescale for drop formation can be less than 3 seconds. The polymeric matrix can comprise one or more components selected from crosslinked polyvinylpyrrolidone, crosslinked polyethylene oxide, crosslinked polyacrylamides, crosslinked copolymers of methacrylic acid, polyacrylic acid, or copolymers selected from poly (acrylic acid-co-acrylamide), or poly (methacrylic acid-co-The polymeric matrix can be hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; and the crosslinked polyacrylamide is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP). The polymeric matrix can be hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM); and the crosslinked polyacrylamide is modified with 2-sulfoethyl methacrylate (SEM). In some cases, the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP). Sometimes, the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM); the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from 2-acrylamido-2-methylpropane sulfonic acid (AMPS), or 2-sulfoethyl methacrylate (SEM).

[0020] In another example, disclosed herein is a preservative removing device, comprising: a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb a preservative when a solution, emulsion, or suspension comprising an ophthalmic agent and a preservative is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component. In some cases, the inactive matrix component has substantially no affinity for the ophthalmic agent or the preservative. The active polymeric matrix component can be a polymeric hydrogel. The inactive polymeric matrix component can be a polyolefin. The polyolefin can be a polyethylene, polypropylene or copolymers thereof. In some instances, the polyolefin is a low-density polyethylene (LDPE). Sometimes, the solution, emulsion, or suspension comprising an ophthalmic agent and a preservative is contained in a container suitable for drop-

CLAIMS

WHAT IS CLAIMED IS:

1. A preservative removing device, comprising:

a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb a preservative when a solution, emulsion, or suspension comprising an ophthalmic agent and a preservative is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component.

2. The device of claim 1, wherein the inactive matrix component has substantially no affinity for the ophthalmic agent or the preservative.

3. The device of any one of claims 1-2, wherein the active polymeric matrix component is a polymeric hydrogel.

4. The device of any one of claims 1-2, wherein the inactive polymeric matrix component is a polyolefin.

5. The device of claim 4, wherein the polyolefin is a polyethylene, polypropylene or copolymers thereof.

6. The device of claim 5, wherein the polyolefin is a low-density polyethylene (LDPE).

7. The device of any one of claims 1-6, wherein the solution, emulsion, or suspension comprising an ophthalmic agent and a preservative is contained in a container suitable for drop-wise dispensing.

8. The device of claim 7, wherein the container suitable for drop-wise dispensing is a compressible bottle.

9. The device of any one of claims 1-8, wherein the ophthalmic agent comprises latanoprost.

10. The device of any one of claims 1-8, wherein the ophthalmic agent comprises timolol and brimonidine.

11. The device of any one of claims 1-8, wherein the ophthalmic agent comprises brimonidine.

12. The device of any one of claims 1-11, wherein the preservative is benzalkonium chloride.

13. The device of claim 12, where the concentration of the preservative is less than 0.05% by weight.

14. The device of any one of claims 1-13, wherein the polymeric matrix is a hydrogel.

15. The device of any one of claims 1-14, wherein the polymeric matrix is a polymeric hydrogel and the preservative is benzalkonium chloride.

16. The device of any one of claims 1-15, wherein the polymeric matrix comprises 2-hydroxyethylmethacrylate.

17. The device of any one of claims 1-15, wherein the polymeric matrix comprises tert-butyl methacrylate.

18. The device of any one of claims 1-17, wherein the polymeric matrix comprises a crosslinker.

19. The device of claim 18, wherein the crosslinker is SR-9035.

20. The device of any one of claims 1-19, wherein the solution, emulsion, or suspension is disposed within a chamber of a compressible bottle, optionally wherein the polymeric matrix is disposed between the chamber and an outlet of a compressible bottle.

21. The device of claim 20, wherein compression of the compressible bottle passes the solution, emulsion, or suspension through the polymeric matrix to the outlet, optionally wherein compression of the compressible bottle forms a drop at the outlet.

22. The device of any one of claims 1-21, wherein the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 95% of the concentration of the ophthalmic agent before passing through the polymeric matrix, or wherein the concentration of the ophthalmic agent after passing though the polymeric matrix is at least 97% of the concentration of the ophthalmic agent before passing through the polymeric matrix.

23. The device of any one of claims 1-22, wherein the concentration of the preservative after passing though the polymeric matrix is less than 10% of the concentration of the preservative before passing through the polymeric matrix, wherein the concentration of the preservative after passing though the polymeric matrix is less than 5% of the concentration of the preservative before passing through the polymeric matrix, or wherein the concentration of the preservative after passing though the polymeric matrix is less than 1% of the concentration of the preservative before passing through the polymeric matrix.

24. The device of any one of claims 1-23, wherein a timescale for drop formation is less than 3 seconds.

25. The device of any one of claims 1-24, wherein the polymeric matrix is polyvinyl alcohol crosslinked with citric acid or other suitable crosslinking agent to render it a hydrogel.

26. The device of any one of claims 1-24, wherein the polymeric matrix is selected from crosslinked polyvinylpyrrolidone, crosslinked polyethylene oxide, crosslinked polyacrylamides, crosslinked copolymers of methacrylic acid, polyacrylic acid, or copolymers selected from poly (acrylic acid-co-acrylamide), or poly (methacrylic acid-co-acrylamide).

27. The device of any one of claims 1-24, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; and the crosslinked polyacrylamide is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP).

28. The device of any one of claims 1-24, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM); and the crosslinked polyacrylamide is modified with 2-sulfoethyl methacrylate (SEM).

29. The device of any one of claims 1-24, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP).

30. The device of any one of claims 1-24, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from 2-acrylamido-2-methylpropane sulfonic acid (AMPS), or 2-sulfoethyl methacrylate (SEM).

31. A method for removing a preservative from an ophthalmic agent, comprising:

providing a solution, emulsion, or suspension comprising the ophthalmic agent and the preservative in a container suitable for drop-wise dispensing;

providing a polymeric matrix, wherein the polymeric matrix is configured to selectively absorb the preservative when the solution, emulsion, or suspension is passed therethrough, and wherein the polymeric matrix comprises an active matrix component and an inactive matrix component; and

passing at least one drop of the solution, emulsion, or suspension comprising the ophthalmic agent, through the polymeric matrix.

32. The method of claim 31, wherein the active polymeric matrix component is a polymeric hydrogel, optionally wherein the inactive polymeric matrix component is a polyolefin.

33. The method of claim 32, wherein the polyolefin is a polyethylene, polypropylene or copolymers thereof, optionally wherein the polyolefin is a low-density polyethylene (LDPE).

34. The method of claim 31, wherein the ophthalmic agent comprises latanoprost, brimonidine, or timolol and brimonidine.

35. The method of claim 31, wherein the preservative is benzalkonium chloride.

36. The method of any one of claims 31-35, wherein the polymeric matrix is selected from crosslinked polyvinylpyrrolidone, crosslinked polyethylene oxide, crosslinked polyacrylamides, crosslinked copolymers of methacrylic acid, polyacrylic acid, or copolymers selected from poly (acrylic acid-co-acrylamide), or poly (methacrylic acid-co-acrylamide).

37. The method of any one of claims 31-35, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; and the crosslinked polyacrylamide is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP).

38. The method of any one of claims 31-35, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM); and the crosslinked polyacrylamide is modified with 2-sulfoethyl methacrylate (SEM).

39. The method of any one of claims 31-35, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with at least one crosslinking monomer selected from N,N'-methylenebis(acrylamide) (MBAM), triacrylamido triazine (TATZ), SR 351, or SR9035; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from methyl methacrylate (MAA), 2-acrylamido-2-methylpropane sulfonic acid (AMPS), 2-sulfoethyl methacrylate (SEM), acrylic acid (AA), or vinylphosphonic acid (VP).

40. The method of any one of claims 31-35, wherein the polymeric matrix is hydrogel prepared from polyacrylamide crosslinked with N,N'-methylenebis(acrylamide) (MBAM; the crosslinked polyacrylamide material is isolated; and the crosslinked polyacrylamide material is modified with at least one modifying monomer selected from 2-acrylamido-2-methylpropane sulfonic acid (AMPS), or 2-sulfoethyl methacrylate (SEM).