

The presently disclosed methods and apparatuses can reduce preservatives in eye drops while substantially retaining the therapeutic agent with very little increase in the amount of bottle pressure to deliver the drops. This can be achieved with a nozzle that fits on the end of a squeeze bottle that allows the drops to be easily delivered. Although reference is made to the treatment of eyes with nozzles coupled to containers, the methods and apparatuses disclosed herein can be configured in many ways to deliver therapeutic agents to many locations of the body, such as with implantable devices, syringes coupled to needles and intravenous drug delivery.

[7] In some embodiments, a porous material is disposed in the squeeze bottle tip and is configured to rapidly and selectively remove the preservative as the fluid comprising a therapeutic agent with preservative flows past. In such embodiments, it may be beneficial to secure the porous material in the tip and to provide a flow path of the drug formulation through the porous material. In some embodiments, a nozzle comprises a flow diverter which directs a flow path from a fluid inlet to a fluid outlet over a length greater than the distance from the inlet to the outlet, which provides an increased interaction of the drug formulation and the porous material in a compact size. The combination of the flow diverter and porous material may enhance the ability to selectively remove the preservative without substantial removal of the therapeutic agent from the drop delivered to the eye, with a nominal increase in pressure as compared with a standard nozzle.

[7a] In an aspect, there is provided a device for removing a preservative from a formulation comprising a therapeutic agent, the device comprising: a nozzle comprising: a fluid outlet, an inlet cap comprising one or more apertures, the one or more apertures in the inlet cap comprising a fluid inlet, a flow diverter, wherein the flow diverter is configured to limit a flow between the fluid inlet and the fluid outlet when the device is not in use, and a matrix disposed within the nozzle, wherein the matrix comprises absorbed particles of the preservative, wherein the preservative is absorbed from the formulation comprising the therapeutic agent and the preservative.

[8] In an aspect, a device for removing a preservative from a formulation comprising a therapeutic agent is provided. The device may comprise: a nozzle comprising: a fluid outlet; an inlet cap comprising one or more apertures, the one or more apertures comprising a fluid inlet, wherein the inlet cap has a hydraulic permeability less than 10 Darcy; and a matrix disposed within the nozzle, wherein the matrix comprises absorbed particles of the preservative and wherein the hydraulic permeability of the inlet cap is less than a hydraulic permeability of the matrix.

[9] In some embodiments, the device further comprises an outlet cap comprising one or more apertures, the one or more apertures comprising the fluid outlet, wherein the outlet cap has a hydraulic permeability less than 10 Darcy. In some embodiments, either of the inlet cap or the outlet cap comprises a screen. In some embodiments, either of the inlet cap or the outlet cap comprises a mesh. In some embodiments, either of the inlet cap or the outlet cap comprises a filter, wherein the filter comprises a pore size of about 0.2 microns. In some embodiments, either of the inlet cap or the outlet cap is prewetted with a preservative. In some embodiments, the nozzle further comprises a flow diverter to divert regions of the fluid flow path in a plurality of different directions, a total distance along the fluid flow path through the matrix from the

## CLAIMS

### WHAT IS CLAIMED IS:

1. A device for removing a preservative from a formulation comprising a therapeutic agent, the device comprising:
  - a nozzle comprising:
    - a fluid outlet;
    - an inlet cap comprising one or more apertures, the one or more apertures in the inlet cap comprising a fluid inlet;
    - a flow diverter, wherein the flow diverter is configured to limit a flow between the fluid inlet and the fluid outlet when the device is not in use; and
    - a matrix disposed within the nozzle, wherein the matrix comprises absorbed particles of the preservative, wherein the preservative is absorbed from the formulation comprising the therapeutic agent and the preservative.
2. The device of claim 1, further comprising an outlet cap comprising one or more apertures, the one or more apertures in the outlet cap comprising the fluid outlet, wherein the outlet cap has a hydraulic permeability less than 10 Darcy.
3. The device of claim 2, wherein either of the inlet cap or the outlet cap comprises a screen or a mesh.
4. The device of claim 2, wherein either of the inlet cap or the outlet cap comprises a filter, wherein the filter comprises a pore size of about 0.2 microns.
5. The device of claim 2, wherein either of the inlet cap or the outlet cap is prewetted with the preservative.
6. The device of claim 1, wherein the flow diverter is configured to divert regions of the fluid flow path in a plurality of different directions, a total distance along the fluid flow path through the matrix from the fluid inlet to the fluid outlet being longer than a distance along an axis from the fluid inlet to the fluid outlet.
7. The device of claim 2, wherein the hydraulic permeability of the inlet cap or the outlet cap is about 0.1 Darcy.
8. The device of claim 2, wherein a pore size of the one or more apertures in the inlet cap or the outlet cap is less than a particle size of the matrix.

9. The device of claim 8, wherein a pore size of the one or more apertures in the inlet cap or the outlet cap is about 0.2 microns.
10. The device of claim 1, wherein a first drop of the formulation from the device and a tenth drop of the formulation from the device comprise equal concentrations of the preservative to within 10%.
11. The device of claim 1, wherein a drop of the formulation from the device dispensed on a first day and a second drop dispensed on a seventh day comprise equal concentrations of the preservative to within 10% at a drop rate of at least one drop per day.
12. The device of claim 1, wherein the formulation is forced through the nozzle from the fluid inlet to the fluid outlet and wherein forcing the fluid through the nozzle removes the preservative from the formulation.
13. The device of claim 12, wherein at least 50 percent of the preservative is removed from the fluid and wherein at least 50 percent of the therapeutic agent is retained.
14. The device of claim 12, wherein the device further comprises a reservoir containing the formulation, and wherein the reservoir is configured to have an internal pressure which increases with increasing squeeze pressure exerted by a user to form a drop.
15. The device of claim 14, wherein the squeeze pressure is within a range from 0.01 Atm to 0.5 Atm.
16. The device of claim 14, wherein the internal pressure comprises a pressure within a range from 1 Atm to 5 Atm.
17. The device of claim 14, wherein the drop is formed within a time defined by a range between 0.1 seconds and 10 seconds.
18. The device of claim 14, wherein the drop comprises a volume defined by a range between 1 $\mu$ L and 100 $\mu$ L.
19. The device of claim 1, wherein the inlet cap has a hydraulic permeability less than 10 Darcy.
20. The device of claim 1, wherein the hydraulic permeability of the inlet cap is less than a hydraulic permeability of the matrix.