COMPOSITIONS FOR TOPICAL APPLICATION OF COMPOUNDS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/321,626, entitled "Compositions for Topical Application of Compounds," filed April 12, 2016, incorporated herein by reference in its entirety.

BACKGROUND

[0002] A topical route of drug administration is desirable because the risks and inconvenience of parenteral treatment can be avoided; the variable absorption and metabolism associated with oral treatment can be circumvented; drug administration can be continuous, thereby permitting the use of pharmacologically active agents with short biological half-lives; the gastrointestinal irritation associated with many compounds can be avoided; and cutaneous manifestations of diseases can be treated more effectively than by systemic approaches. Most transdermal and transmucosal delivery systems achieve penetration by using a penetration-enhancing vehicle. Such compounds or mixtures of compounds are known in the art as "penetration enhancers" or "skin enhancers." Many of the penetration enhancers in the literature enhance transdermal absorption, yet they also possess certain drawbacks in that some are regarded as toxic; some irritate the skin; some have a thinning effect on the skin on prolonged use; and most are incapable of delivering high molecular weight pharmaceuticals and cosmetic agents. Clearly, there remains a need for safe and effective transdermal delivery compositions and systems that can administer a wide-range of pharmaceuticals and cosmetic agents to and through the skin, mucosa, hair, nails, teeth, and various other surfaces.

SUMMARY

[0003] Various embodiments of the disclosure include compositions containing one or more active agents and about 0.1 wt. % to about 5.0 wt. % of a extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons. In some embodiments, the decoy molecule may be selected from the group consisting of hyaluronic acid, collagen, fibronectin, elastin, lectin, and combinations thereof, and in certain embodiments, the collagen may be selected from the group consisting of collagen type I, collagen type II, collagen type III, collagen type IV, collagen type V, fibrillary collagen, non-fibrillary collagen, and combinations thereof.

[0003a] In a first aspect, there is provided a composition comprising: one or more active agents; and about 0.1 wt. % to about 5.0 wt. % of an extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons.

[0004] In particular embodiments, the compositions may include about 1 mg to about 1000 mg of the extracellular matrix component or a fragment thereof. In some

25 wt. % active agent, and in some embodiments, the compositions of such methods may include about 1 mg to about 1000 mg active agent. In various embodiments, the active agent may be selected from the group consisting of analgesic agents, antibacterial agents, antifungal agents, anesthetics, steroids, retinol, gabapentin, pregabalin, minocycline, salicylate, acetyl salicylic acid, cyclosporine, tacrolimus (FK506), hydrocortisone, lidocaine, bimatoprost, botulinum toxin, tadalafil, an antibody, an antibody fragment, and the like or combinations thereof.

[0008a] In a second aspect, there is provided a method for delivering an active agent, the method comprising: topically applying to a surface tissue of a subject a composition comprising one or more active agents and about 0.25 wt. % to about 10 wt. % of a extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons.

[0008b] In a third aspect, there is provided a method of improving topical delivery of an active agent in a subject, the method comprising: topically administering to the subject a composition comprising the active agent and a composition comprising an extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons, and wherein the extracellular matrix component or a fragment is present at about 0.25 wt. % to about 10 wt. % of the composition.

[0008c] In a fourth aspect, there is provided use of a composition as claimed in the first aspect in the manufacture of a medicament for treating skin condition in a subject.

[0008d] In a fifth aspect, there is provided use of a composition as claimed in claim 1 in the manufacture of a medicament for treating hair loss in a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] For a fuller understanding of the nature and advantages of the present invention, reference should be made to the following detailed description taken in connection with the accompanying drawings, in which:

[0010] **FIGS. 1A-1B** are graphs showing the percent of peptide flux relative to flux of peptide from the composition of peptide alone, for peptide compositions comprising a decoy molecule of hyaluronic acid with a molecular weight of 10,000 Da, 20,000 Da, 40,000 Da, 60,000 Da, or 100,000 Da, where flux was measured in skin with stratum corneum intact (FIG. 1A) and in skin with stratum corneum stripped (FIG. 1B) and each composition was measured in duplicate (solid line, dashed line).

[0011] **FIG. 2** is a bar graph showing the percent increase of salicylate flux from compositions of salicylate and a decoy molecule of hyaluronic acid with molecular weights designated as small (5,000 Da to 10,000 Da), small to mid (10,000 Da to 20,000 Da), low to mid (20,000 Da to 30,000 Da), and mid (30,000 Da to 40,000 Da) over a composition with no decoy molecule.

[0012] **FIG. 3** is a bar graph showing the percent increase of hydrocortisone flux from compositions of hydrocortisone and a decoy molecule of hyaluronic acid with molecular weights designated as very small (5,000 Da to 10,000 Da), small (10,000 Da to 20,000 Da), mid (30,000 Da to 40,000 Da), and large (40,000 Da to 60,000 Da) over a composition with no decoy molecule.

[0013] **FIG. 4** is a bar graph showing the percent of lidocaine in porcine skin from topically applied compositions of lidocaine and an elastin decoy molecule with a molecular weight designated as very very small (2,000 Da to 5,000 Da), very small (5,000 Da to 10,000 Da), and small (10,000 Da to 20,000 Da) and no decoy molecule.

[0014] **FIG. 5** is a bar graph showing the percent of topically applied minocycline in porcine skin from compositions containing of minocycline and a decoy molecule of

CLAIMS

1. A composition comprising:

one or more active agents; and

about 0.1 wt. % to about 5.0 wt. % of an extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons.

2. The composition of claim 1, wherein the extracellular matrix component or a fragment thereof is selected from the group consisting of hyaluronic acid, collagen, fibronectin, elastin, lectin, and combinations thereof.

3. The composition of claim 1, comprising about 0.1 wt. % to about 25 wt. % active agent.

4. The composition of claim 1, wherein the active agent is selected from the group consisting of analgesic agents, antibacterial agents, antifungal agents, anesthetics, steroids, retinol, gabapentin, pregabalin, minocycline, salicylate, acetyl salicylic acid, cyclosporine, tacrolimus (FK506), hydrocortisone, lidocaine, bimatoprost, botulinum toxin, tadalafil, an antibody, an antibody fragment, and combinations thereof.

5. The composition of claim 1, further comprising one or more pharmaceutical additives selected from the group consisting of diluents, fillers, disintegrants, binders, lubricants, surfactants, hydrophobic vehicles, water soluble vehicles, emulsifiers, buffers, humectants, moisturizers, solubilizers, preservatives, colorants, plastizers, carriers, excipients, and combinations thereof.

6. The composition of claim 1, comprising about 0.1 wt. % to about 2.0 wt. % of the extracellular matrix component or a fragment thereof, and about 0.1 wt. % to about 25 wt. % of the active agent.

7. A method for delivering an active agent, the method comprising:

topically applying to a surface tissue of a subject a composition comprising one or more active agents and about 0.25 wt. % to about 10 wt. % of a extracellular

matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons.

8. The method of claim 7, wherein the extracellular matrix component or a fragment thereof is selected from the group consisting of hyaluronic acid, collagen, fibronectin, elastin, lectin, and combinations thereof.

9. The method of claim 7, wherein the composition comprises about 0.1 wt. % to about 25 wt. % of the active agent.

10. The method of claim 7, wherein the active agent is selected from the group consisting of analgesic agents, antibacterial agents, antifungal agents, anesthetics, steroids, retinol, gabapentin, pregabalin, minocycline, salicylate, acetyl salicylic acid, cyclosporine, tacrolimus (FK506), hydrocortisone, lidocaine, bimatoprost, botulinum toxin, tadalafil, an antibody, an antibody fragment, and combinations thereof.

11. A method of improving topical delivery of an active agent in a subject, the method comprising:

topically administering to the subject a composition comprising the active agent and a composition comprising an extracellular matrix component or a fragment thereof having average molecular weight of about 2,000 daltons to about 60,000 daltons, and wherein the extracellular matrix component or a fragment is present at about 0.25 wt. % to about 10 wt. % of the composition.

12. The method of claim 11, wherein the composition comprising the active agent and the composition comprising the extracellular matrix component or a fragment thereof are to be administered concurrently or sequentially.

13. The method of claim 11, wherein the active agent and the extracellular matrix component or a fragment thereof are present in a single composition.

14. Use of a composition as claimed in claim 1 in the manufacture of a medicament for treating skin condition in a subject.

15. Use of a composition as claimed in claim 1 in the manufacture of a medicament for treating hair loss in a subject.