METHODS AND COMPOSITIONS FOR TOPICAL DELIVERY

CROSS REFERENCE

[0001] This application claims priority to U.S. Provisional Application No. 62/571,025, filed on October 11, 2017; U.S. Provisional Application No. 62/571,038, filed on October 11, 2017; U.S. Provisional Application No. 62/598,796, filed on December 14, 2017; U.S. Provisional Application No. 62/571,049, filed on October 11, 2017; U.S. Provisional Application No. 62/598,786, filed on December 14, 2017; and U.S. Provisional Application No. 62/598,828, filed on December 14, 2017, and each of these are incorporated herein by reference in their entirety.

BRIEF SUMMARY

[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. Additionally, higher tissue concentrations can be achieved in the effected areas with a topical verses a systemic administration of an active ingredient if desired. Most transdermal and transmucosal delivery systems achieve penetration by using a penetration-enhancing vehicle or agents. 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, bone, and various other surfaces without the use of standard penetration enhancers known in the art.

[0003] Various examples of the disclosure are directed to compositions comprising one or more active agents and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In one aspect, the present disclosure refers to a topical composition comprising: a mixture comprising ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of at least one extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons~~,~~ and an active agent, wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts.

[0004] Further examples include methods for delivering an active agent comprising the steps of topically applying to a surface tissue of a subject a composition

comprising one or more active agents and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In one aspect, the present disclosure refers to a topical composition for use in a method for delivering an active agent to a subject, ~~comprising: applying to a surface tissue of the subject a composition comprising~~wherein the topical composition comprises ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of an extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons~~,~~ and ~~one or more active agents~~the active agent, wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amount, and wherein the topical composition is to be delivered to a surface tissue of the subject.

[0005] In one example, a composition comprises a plurality of therapeutic cells and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof is provided.

[0006] In another example, a method of delivering therapeutic cells to a tissue surface comprises topically administering a composition comprising a plurality of therapeutic cells and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof is provided. In some examples, a composition comprising therapeutic cells and a composition comprising decoy molecules are administered separately.

[0006a] In one aspect, the present disclosure refers to use of a topical composition in the manufacture of a medicament for treating cancer in a subject, the topical composition comprising a plurality of therapeutic cells expressing a tumor antigen and ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of an extracellular matrix component~~,~~ or a fragment thereof having an average molecular weight of 2,000 daltons to 20,000 daltons, ~~and combinations thereof, in the manufacture of a medicament for treating cancer in a subject~~wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts, and wherein the topical composition is to be administered to a surface tissue of the subject.

[0007] In additional example, a method of eliciting an immune response in a subject comprises topically administering to a tissue surface a composition comprising a plurality of cells expressing an antigen and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof is provided. In some examples, a composition comprising cells expressing an antigen and a composition comprising decoy molecules are administered separately.

[0008] Some examples are directed to a method of treating scars and wrinkles on a skin surface comprising topically administering a composition comprising a plurality of therapeutic cells and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In some examples, a composition comprising therapeutice cells and a composition comprising decoy molecules are administered separately.

[0009] Also disclosed herein are methods and compositions that may be used to deliver an active agent via a transdermal patch. In one example, a transdermal patch comprises a composition comprising one or more active agents and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof.

[0010] In another example, a method of detecting an antigen noninvasively involves applying to a tissue surface a transdermal patch, wherein the transdermal patch comprises a composition comprising one or more active agents and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof is provided. ~~In one aspect, the present disclosure refers to a method of detecting an antigen noninvasively, comprising: applying a transdermal patch to a surface tissue, the transdermal patch comprising a composition comprising an antibody or an antibody fragment, and about 0.001 wt. % to about 10 wt. % of at least one extracellular matrix component or a fragment thereof and having an average molecular weight of about 2,000 daltons to about 20,000 daltons; and detecting the antibody or the antibody fragment by imaging.~~

[0011] In another example, a method of detecting an analyte in a body fluid comprises applying a transdermal patch to a tissue surface to capture the body fluid, wherein the transdermal patch comprises a composition comprising one or more active agents and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof is provided.

[0012] Examples of the disclosure are directed to compositions comprising an effective amount of a neurotoxin agent and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof.

[0013] Examples of the disclosure are directed to methods of topically administering a neurotoxin agent to a subject in need thereof a composition comprising an effective amount of a neurotoxin agent and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In some examples, a composition comprising neurotoxin agent and a composition comprising decoy molecules are administered separately.

[0014] Examples of the disclosure are also directed to methods of treating, reducing or improving the look of frown lines (e.g., glabellar lines), wrinkles or crow's feet lines in a subject in need thereof comprising topically administering to a surface tissue of the subject a composition comprising an effective amount of a neurotoxin agent and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In some examples, a composition comprising neurotoxin agent and a composition comprising decoy molecules are administered separately.

[0015] Examples of the disclosure are directed to methods of treating the symptoms of sweating in a subject in need thereof comprising topically administering to a surface tissue of the subject a composition comprising an effective amount of a neurotoxin agent and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In some examples, a composition comprising neurotoxin agent and a composition comprising decoy molecules are administered separately. In one aspect, the present disclosure refers to use of a topical composition in the manufacture of a medicament for treating the symptoms of excessive sweating in a subject in need thereof, the topical composition comprising a neurotoxin agent and ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of at least one extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons, ~~in the manufacture of a medicament for treating the symptoms of excessive sweating in a subject in need thereof,~~wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts, and wherein the topical composition is to be administered to a surface tissue of the subject, and wherein said neurotoxin agent is selected from the group consisting of botulinum toxin type A, botulinum toxin type B, botulinum toxin type C, botulinum toxin type D, botulinum toxin type E, botulinum toxin type F, abobotulinumtoxinA, BTX-A, daxibotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB, syntaxin, pharmaceutically acceptable salts thereof, and combinations thereof.

[0016] Examples of the disclosure are directed to methods of treating migraines in a subject in need thereof comprising topically administering to a surface tissue of the subject a composition comprising an effective amount of a neurotoxin agent and a decoy molecule selected from an extracellular matrix component, fragments thereof and combinations thereof. In some examples, a composition comprising neurotoxin agent and a composition comprising decoy molecules are administered separately.

CLAIMS

1. A topical composition comprising:

a mixture comprising ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of at least one extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons~~,~~ and

~~———~~an active agent, wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts.

~~2. The composition of claim 1, wherein the composition does not contain any extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts.~~

~~3~~2. The topical composition of claim 1, further comprising ~~about~~ 0.1 wt. % to ~~about~~ 10 wt. % of an enzyme selected from the group consisting of hyaluronidase, elastase, or a combination thereof.

~~4~~3. The topical composition of claim 1 or 2, wherein the extracellular matrix component is selected from the group consisting of hyaluronic acid, collagen, fibronectin, elastin, lectin, and fragments thereof and combinations thereof.

~~5~~4. The topical composition of any one of claims 1-3, wherein the ~~composition~~mixture comprises ~~about~~ 0.1 wt. % to ~~about~~ 25 wt. % of the active agent.

~~6~~5. The composition of any one of claims 1-4, wherein the active agent is selected from the group consisting of small molecule drugs, macromolecular drugs, biologics, antibodies, chimeric antibodies, antibody fragments, diagnostic antibodies, antigens, peptides, adjuvants, antioxidants, cosmetic ingredients, therapeutic cells, diagnostic agents, radioactive tracers, contrast agents, neurotoxins, sensation modifying agents, and combinations thereof.

~~7~~6. A topical composition for use in a method for delivering an active agent to a subject~~,~~ ~~comprising:~~

~~applying to a surface tissue of the subject a composition comprising~~wherein the

topical composition comprises ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of an extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons~~,~~ and ~~one or more active agents~~the active agent, wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amount, and wherein the topical composition is to be delivered to a surface tissue of the subject.

~~8. The method of claim 7, wherein the composition does not contain any extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts.~~

~~9~~7. The ~~method of~~topical composition for use according to claim ~~7~~6, wherein the extracellular matrix component is selected from the group consisting of hyaluronic acid, collagen, fibronectin, elastin, lectin, and combinations thereof.

~~10~~8. The ~~method of~~topical composition for use according to claim 6 or 7, wherein the composition comprises ~~about~~ 0.1 wt. % to ~~about~~ 25 wt. % of the active agent.

~~11~~9. The ~~method of claim 7~~topical composition for use according to any one of claims 6-8, wherein the active agent is selected from the group consisting of small molecule drugs, macromolecular drugs, biologics, antibodies, chimeric antibodies, antibody fragments, diagnostic antibodies, antigens, peptides, adjuvants, antioxidants, cosmetic ingredients, therapeutic cells, diagnostic agents, radioactive tracers, contrast agents, neurotoxins, sensation modifying agents, and combinations thereof.

~~12~~10. The ~~method of~~topical composition for use according to claim ~~11~~9, wherein the therapeutic cells are selected from the group consisting of stem cells, genetically engineered mammalian cells, antigen presenting cells, and combinations thereof.

~~13~~11. Use of a topical composition in the manufacture of a medicament for treating cancer in a subject, the topical composition comprising a plurality of therapeutic cells expressing a tumor antigen and ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of an extracellular matrix component~~,~~ or a fragment thereof having an average molecular weight of 2,000 daltons to 20,000 daltons, ~~and combinations thereof, in the manufacture of a medicament for treating cancer in a~~

~~subject~~wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts, and wherein the topical composition is to be administered to a surface tissue of the subject.

~~14~~12. The use of claim ~~13~~11, wherein the tumor antigen is selected from stomach tumor, colon tumor, prostate tumor, cervical tumor, skin tumor, uterine tumor, ovarian tumor, pancreatic tumor, kidney tumor, liver tumor, head and neck tumor, squamous cell tumor, gastrointestinal tumor, breast tumor, lung tumor, and brain tumor.

~~15~~13. Use of a topical composition in the manufacture of a medicament for treating the symptoms of excessive sweating in a subject in need thereof, the topical composition comprising a neurotoxin agent and ~~about~~ 0.001 wt. % to ~~about~~ 10 wt. % of at least one extracellular matrix component or a fragment thereof having an average molecular weight of ~~about~~ 2,000 daltons to ~~about~~ 20,000 daltons, ~~in the manufacture of a medicament for treating the symptoms of excessive sweating in a subject in need thereof,~~wherein the topical composition does not contain an extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts, and wherein the topical composition is to be administered to a surface tissue of the subject, and

wherein said neurotoxin agent is selected from the group consisting of botulinum toxin type A, botulinum toxin type B, botulinum toxin type C, botulinum toxin type D, botulinum toxin type E, botulinum toxin type F, abobotulinumtoxinA, BTX-A, daxibotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB, syntaxin, pharmaceutically acceptable salts thereof, and combinations thereof.

~~16. The use of claim 15, wherein the composition does not contain any extracellular matrix component or a fragment thereof having a molecular weight above 60,000 daltons in detectable amounts.~~

~~17. The use of claim 15, wherein said neurotoxin agent is selected from the group consisting of botulinum toxin type A, botulinum toxin type B, botulinum toxin type C, botulinum toxin type D, botulinum toxin type E, botulinum toxin type F, abobotulinumtoxinA, BTX-A, daxibotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB, syntaxin derivatives thereof, pharmaceutically~~

~~acceptable salts thereof, and combinations thereof.~~

~~18. A method of detecting an antigen noninvasively, comprising:~~

~~applying a transdermal patch to a surface tissue, the transdermal patch comprising a composition comprising an antibody or an antibody fragment, and about 0.001 wt. % to about 10 wt. % of at least one extracellular matrix component or a fragment thereof and having an average molecular weight of about 2,000 daltons to about 20,000 daltons; and~~

~~detecting the antibody or the antibody fragment by imaging.~~

~~19. The method of claim 18, wherein the antigen is a tumor antigen, a cancer antigen, an allergen, a bacterial antigen, a viral antigen, a drug, a hormone, a plant lectin, an endotoxin, and combinations thereof.~~