limited to, hydrophilic molecules, large molecular structures (e.g., greater than a few hundred Daltons), genetic treatments, vaccines, etc. Prausnitz, M. R. & Langer, R. "Transdermal drug delivery," Nat Biotechnol. 26(11): 1261–1268 (2008).

[0004a] In one aspect of the present disclosure, there is provided a use of an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater in the manufacture of a medicament for treating or preventing a disease or disorder, wherein the medicament is to be applied to a site in combination with microneedle skin conditioning (MSC) of the site, wherein the emulsion composition is formulated so that the large agent can penetrate the site without use of a penetration enhancing agent.

[0004b] In another aspect of the present disclosure, there is provided a patch comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a plurality of microneedles, wherein the emulsion composition is formulated so that the large agent can penetrate the site without use of a penetration enhancing agent.

[0004c] In a further aspect of the present disclosure, there is provided a kit comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a patch comprising a plurality of microneedles, for use in applying the emulsion composition to a site, wherein the emulsion composition is formulated so that the large agent can penetrate the site without use of a penetration enhancing agent.

[0004d] In a further aspect of the present disclosure, there is also provided a kit comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a device for microneedle conditioning of a site, wherein the emulsion composition is formulated so that the large agent can penetrate the site without use of a penetration enhancing agent.

Claims

We claim:

1. Use of an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater in the manufacture of a medicament for treating or preventing a disease or disorder, wherein the medicament is to be applied to a site in combination with microneedle skin conditioning (MSC) of the site, wherein the emulsion composition is formulated so that the large agent can penetrate the site without use of a penetration enhancing agent.

2. The use of claim 1, wherein the composition comprising a large agent comprises a nanoemulsion comprising the large agent.

3. The use of claim 1, wherein the composition comprising a large agent comprises a macroemulsion comprising the large agent.

~~4. The use of any one of claims 1-3, wherein a non-irritating penetration enhancing agent is to be further administered.~~

~~5. The use of claim 4, wherein the non-irritating penetration enhancing agent is selected from carrier peptides and co-peptides.~~

~~6. The use of any one of claims 4-5, wherein the non-irritating penetration enhancing agent is selected from a cationic peptide and a positively charged carrier with the sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR.~~

~~7~~4. The use of any one of claims 1-~~4~~6, wherein the MSC of the site is to be performed before applying the medicament to the site.

~~8~~5. The use of any one of claims 1-~~4~~6, wherein the MSC of the site is to be performed after applying the medicament to the site.

~~9~~6. The use of any one of claims 1-~~4~~6, wherein the MSC of the site and applying the medicament to the site is to occur at substantially the same time.

~~10~~7. The use of any one of claims 1-~~6~~9, wherein the large agent is a botulinum toxin.

~~11~~8. The use of claim 7~~10~~, wherein the botulinum toxin is to be further delivered with a biologically active agent.

~~12~~9. The use of claim 8~~11~~, wherein the biologically active agent is selected from steroids, retinoids, anesthetics, fillers, silicone, and/or collagen.

~~13~~10. The use of claim 9~~12~~, wherein the biologically active agent is selected from hydrocortisone, retin A, and/or lidocaine.

~~14~~11. The use of any one of claims 1-~~6~~9, wherein the large agent is an antibody agent.

~~15~~12. The use of claim 11~~14~~, wherein the antibody agent is selected from an anti-TNFα antibody, an anti-CD2 antibody, an anti-CD4 antibody, an anti-IL-12 antibody, an anti-IL-17 antibody, an anti-IL-22 antibody, and an anti-IL-23 antibody.

~~16~~13. The use of any one of claims ~~14-15~~11-12, wherein the antibody agent is selected from an antibody having epitope binding elements found in one or more of infliximab, adalimumab, golimumab, etanercept, etanercept-szzs, certolizumab pegol, siplizumab, zanolimumab, briakinumab, secukinumab, brodalumab, fezakinumab, ustekinumab and/or guselkumab.

~~17~~14. The use of any one of claims 11-13~~14-16~~, wherein the antibody agent is to be further delivered with a biologically active agent.

~~18. The use of any one of claims 14-17, wherein the antibody agent is to be further delivered with a non-irritating penetration enhancing agent.~~

~~19. The use of claim 18, wherein the non-irritating penetration enhancing agent is selected from co-peptides, and carrier peptides.~~

~~20~~15. The use of any one of claims 1-14~~19~~, wherein the MSC of the site is to be performed with a device comprising a plurality of microneedles.

~~21~~16. The use of claim 15~~20~~, wherein the device is a patch, a roller, stamp, or pen.

~~22~~17. The use of any one of claims 1-16~~21~~, wherein the site is a skin surface overlying a muscle or muscle group of a subject.

~~23~~18. The use of any one of claims 1-17~~22~~, wherein the site is a skin surface that contains sweat glands.

~~24~~19. The use of any one of claims 1-18~~23~~, wherein the site is a skin surface that contains sebaceous glands.

~~25~~20. The use of any one of claims 1-19~~24~~, wherein the site is a skin surface that contains hair follicles.

~~26~~21. The use of any one of claims 15-20~~-25~~, wherein the microneedles have a length sufficient to project through the stratum corneum of the skin.

~~27~~22. The use of any one of claims 15-21~~20-26~~, wherein the microneedles have a length insufficient to reach nerves in the dermis of the skin.

~~28~~23. The use of any one of claims 15-22~~20-27~~, wherein the microneedles have a length between 10 and 4000 µm.

~~29~~24. The use of any one of claims 15-23~~20-28~~, wherein the microneedles have a length equal to or greater than 100 µm.

~~30~~25. The use of any one of claims 15-23~~20-28~~, wherein the microneedles have a length equal to or greater than 25 µm.

~~31~~26. The use of any one of claims 15-23~~20-28~~, wherein the microneedles have a length equal to or greater than 300 µm, 500 µm, 800 µm, 1000 µm, 1500 µm, 2000 µm, or 4000 µm.

~~32~~27. The use of any one of claims 15-26~~20-31~~, wherein the microneedles are composed of a biocompatible material.

~~33~~28. The use of any one of claims 15-26~~20-31~~, wherein the microneedles are composed of a metal.

~~34~~29. The use of any one of claims 15-28~~1-33~~, wherein the MSC of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 microneedles or microneedle array impressions is to be administered.

~~35~~30. The use of claim 29~~34~~, wherein the microneedle array is rotated between one or more impressions.

~~36~~31. The use of claim 29~~34~~, wherein the microneedle array is not rotated between one or more impressions.

~~37~~32. The use of any one of claims 29-31~~34-36~~, wherein the impressions are made on approximately the same site.

~~38~~33. The use of any one of claims 29-31~~34-36~~, wherein the impressions are made on overlapping sites.

~~39~~34. The use of any one of claims 29-31~~34-36~~, wherein the impressions are made on different sites.

~~40~~35. The use of any one of claims 29-34~~34-39~~, wherein the microneedle array is in the form of a stamp or roller.

~~41~~36. The use of claim 35~~40~~, wherein the impressions are made by stamping or rolling.

~~42~~37. The use of any one of claims 1-36~~41~~, wherein the large agent penetrates the skin within 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 minutes of administration.

~~43~~38. The use of any one of claims 1-36~~41~~, wherein the large agent penetrates the skin within 5 to 60 minutes, 5 to 12 minutes, 5 to 15 minutes, or 15 to 30 minutes of administration.

~~44~~39. The use of any one of claims 1-36~~41~~, wherein the large agent penetrates the skin within 1, 2, 3, 4, 5, or 6 hours of administration.

~~45~~40. The use of any one of claims 15-27~~20-32~~, wherein the microneedles are composed of a dissolving polymer.

~~46~~41. The use of any one of claims 1-40~~45~~, wherein the medicament is to be administered at a lower dose as compared to a reference topical treatment regimen where microneedles are not employed.

~~47~~42. The use of any one of claims 1-41~~46~~, wherein more than one dose of the medicament is to be administered over time.

~~48~~43. The use of claim 42~~47~~, wherein fewer doses of the medicament is to be administered over a fixed treatment period as compared to a reference treatment regimen where microneedles are not employed to generate comparable treatment effects.

~~49~~44. The use of claim 42~~47~~ or claim 43~~48~~, wherein each dose of the medicament is separated by a specified period of time.

~~50~~45. The use of claim 44~~49~~, wherein the specified period of time is longer as compared to the specified period of time for administering a reference treatment regimen where microneedles are not employed.

~~51~~46. The use of any one of claims ~~46-50~~41-45, wherein the reference treatment regimen comprises administering the medicament without MSC.

~~52~~47. The use according to any one of claims 1-46~~51~~, wherein the medicament is for treating a dermatological disorder.

~~53~~48. The use of claim 47~~52~~, wherein the dermatological disorder is selected from acne, unwanted sweating , body odor, hyperhidrosis, bromhidrosis, chromhidrosis, rosacea, hair loss , psoriasis, actinic keratosis, eczematous dermatitis, excess sebum-producing disorders, burns, lupus erythematosus, hyperpigmentation disorders, hypopigmentation disorders, skin cancer, dermal infection, facial wrinkles, unsightly facial expressions, neck lines, hyperfunctional facial lines, hyperkinetic facial lines, platysma bands, and/or combinations thereof.

~~54~~49. The use according to any one of claims 1-47~~52~~, wherein the medicament is for treating or preventing a disorder selected from unwanted sweating, body odor, hyperhidrosis, bromhidrosis, chromhidrosis, hair loss, Raynaud's phenomenon, rheumatoid arthritis, psoriatic arthritis, osteoarthritis, lupus erythematosus, systemic lupus , discoid lupus, drug-induced lupus, neonatal lupus, Crohn's disease, inflammatory bowel disease, ulcerative colitis, pulmonary disorders, asthma, chronic obstructive pulmonary disorder, amyloidosis, systemic amyloidosis, cutaneous amyloidosis, cancer, skin cancer, blood cancer, breast cancer, colon cancer, lung cancer, prostate hyperplasia, dyslipidemia, hypercholesterolemia, infection, *C. difficile* infection, *Staphylococcus* infection, dystonia, headache, pain, arthritis associated pain, rheumatoid arthritis associated pain, psoriatic arthritis associated pain, osteoarthritis associated pain, certain ophthalmologic conditions, certain urologic conditions, neuromuscular disorders, conditions involving muscular spasm and/or contracture, strabismus, hemifacial spasm, tremor, spasticity such as that resulting from multiple sclerosis, retroorbital muscle, neurologic conditions, Alzheimer's Disease, Parkinson's Disease, or stroke.

~~55~~50. The use of any one of claims 1-49~~54~~, wherein the medicament is formulated as a lotion, cream, powder, ointment, liniment, gel, or drops.

~~56~~51. A patch comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a plurality of microneedles, wherein the

emulsion composition is formulated so that the large agent can penetrate a site of a subject without use of a penetration enhancing agent.

~~57~~52. The patch of claim 51~~56~~, wherein the composition comprising a large agent comprises a nanoemulsion.

~~58~~53. The patch of claim 51~~56~~, wherein the composition comprising a large agent comprises a macroemulsion.

~~59~~54. The patch of any one of claims ~~56-58~~51-53, wherein the microneedles have a length sufficient to project through the stratum corneum of the skin.

~~60~~55. The patch of any one of claims 52-54~~57-59~~, wherein the microneedles have a length insufficient to reach nerves in the dermis of the skin.

~~61~~56. The patch of any one of claims 52-55~~57-60~~, wherein the microneedles have a length between 10 and 1000 μm.

~~62~~57. The patch of any one of claims 52-56~~57-61~~, wherein the microneedles have a length equal to or greater than 100 μm.

~~63~~58. The patch of any one of claims 52-57~~57-62~~, wherein the microneedles have a length equal to or greater than 300 μm.

~~64~~59. The patch of any one of claims 52-58~~57-63~~, wherein the microneedles are composed of a biocompatible material.

~~65~~60. The patch of any one of claims 52-59~~57-64~~, wherein the microneedles are composed of a metal.

~~66~~61. The patch of any one of claims 52-59~~57-64~~, wherein the microneedles are composed of a dissolving polymer.

~~67~~62. The patch of any one of claims 52-61~~57-66~~, wherein the large agent is a botulinum toxin.

~~68~~63. The patch of any one of claims 52-61~~57-66~~, wherein the large agent is an antibody agent.

~~69~~64. A kit comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a patch comprising a plurality of microneedles, for use in applying the emulsion composition to a site, wherein the emulsion composition is formulated so that the large agent can penetrate a site of a subject without use of a penetration enhancing agent.

~~70~~65. The kit of claim 64~~69~~, wherein the emulsion composition is incorporated into the patch.

~~71~~66. A kit comprising an emulsion composition comprising a large agent having a molecular weight of 100,000 Da or greater, and a device for microneedle conditioning of a site, wherein the emulsion composition is formulated so that the large agent can penetrate a site of a subject without use of a penetration enhancing agent.

~~72~~67. The kit of any one of claims 64-66~~69-71~~, wherein the emulsion composition comprises a nanoemulsion.

~~73~~68. The kit of any one of claims 64-66~~69-71~~, wherein the emulsion composition comprises a macroemulsion.

~~74~~69. The kit of any one of claims 66-68~~71-73~~, wherein the device comprises a plurality of microneedles.

~~75~~70. The kit of any one of claims 66-69~~71-74~~, wherein the device is a patch, a roller, a stamp, or a pen.

~~76~~71. The kit of any one of claims 64~~69~~ or 65~~70~~, comprising a patch of any one of claims ~~56-68~~51-63.

~~77~~72. The kit of any one of claims 64~~69~~ or 66-71~~71-76~~, wherein the emulsion composition is formulated as a lotion, cream, powder, ointment, liniment, gel, or drops.