Raynaud's Phenomenon (including CREST syndrome), leprosy and autoimmune diseases such as erythromatosis and rheumatoid diseases.

[0005] Some neuropathies are caused by toxic agents. These toxic agents may include therapeutic agents, particularly those used to treat neoplastic diseases. In certain cases, peripheral neuropathy is a major complication of cancer treatment and a main factor limiting the dosage of chemotherapeutic agents that can be administered to a patient. Treatment options for patients having peripheral neuropathies are currently limited, with most methods generally consisting of analgesics for managing pain, for example to decrease the perception of pain, decrease reactions to pain, or to increase pain tolerance.

SUMMARY

[0006] Accordingly, the disclosure relate to treatment of peripheral neuropathies with topical formulations of muscarinic M1 receptor antagonists, such as pirenzepine. In some examples, the formulations comprise a muscarinic receptor subtype 1 antagonist, and a topical vehicle. The topical vehicle may include a low volatility solvent and a polyether surfactant.

[0007] The disclosure relates to a topical formulation. In some examples, the topical formulation includes (i) a muscarinic acetylcholine receptor antagonist or a salt or derivative, (ii) DMSO, and/or (iii) a polyalkylene glycol alkyl ether. ~~In one aspect, the present disclosure relates to a topical formulation comprising: (i) a muscarinic acetylcholine receptor antagonist or a salt or derivative, (ii) a low volatility solvent, and (iii) a polyalkylene glycol alkyl ether.~~ In some examples, the muscarinic acetylcholine receptor antagonist is pirenzepine, pirenzepine free base, or a pirenzepine salt. In one aspect, the present disclosure relates to a topical formulation comprising: (i) pirenzepine, pirenzepine free base, or a pirenzepine salt, (ii) a low volatility solvent, and (iii) a polyalkylene glycol alkyl ether. In some examples, the polyalkylene glycol alkyl ether is a polyethylene glycol alkyl ether. Some examples include a fatty acid ester. In some examples , the fatty acid ester is lauryl lactate. Some examples include benzyl alcohol. Some examples include dimethyl isosorbide. In some examples , the muscarinic acetylcholine receptor antagonist is a pirenzepine salt or pirenzepine free base, and the composition comprises less than 10% pirenzepine salt or pirenzepine free base, respectively. Some examples include about 1% to 5% pirenzepine salt or pirenzepine free base. In some examples , the topical formulation is a topical gel formulation.

WHAT IS CLAIMED IS:

1. A topical formulation comprising: (i) pirenzepine, pirenzepine free base, or a pirenzepine salt~~a muscarinic acetylcholine receptor antagonist or a salt or derivative~~, (ii) a low volatility solvent, and (iii) a polyalkylene glycol alkyl ether.

~~2. The topical formulation of Claim 1, wherein the muscarinic acetylcholine receptor antagonist is selected from the group consisting of: pirenzepine, pirenzepine free base, and a pirenzepine salt.~~

~~3.~~2.The topical formulation of ~~any of~~ Claim~~s~~ 1~~-2~~, wherein said low volatility solvent is DMSO.

~~4.~~3.The topical formulation of ~~any of~~ Claim~~s~~ 1 or 2~~-3~~2, wherein said polyalkylene glycol alkyl ether ~~polyether surfactant~~ is a polyethylene glycol alkyl ether.

~~5.~~4.The topical formulation of any of Claims 1-~~4~~3, further comprising a fatty acid ester.

~~6.~~5.The topical formulation of Claim ~~5~~4, wherein the fatty acid ester is lauryl lactate.

~~7.~~6.The topical formulation of any of Claims 1-~~6~~ 5 further comprising a capric triglyceride.

~~8.~~7.The topical formulation of any of Claims 1-~~6~~7, further comprising benzyl alcohol.

~~9.~~8.The topical formulation of any of Claims 1-~~7~~8, further comprising dimethyl isosorbide.

~~10.~~9. The topical formulation of any of Claims 1-~~8~~9, wherein ~~the muscarinic acetylcholine receptor antagonist is pirenzepine salt, and~~ the composition comprises less than 20% pirenzepine salt.

~~11.~~10. The topical formulation of Claim ~~2~~1, wherein ~~the muscarinic acetylcholine receptor antagonist is pirenzepine free base, and~~ the composition comprises less than 10% pirenzepine free base.

~~12.~~11. The topical formulation of Claim ~~11~~10, wherein the topical formulation comprises ~~about~~ between ~~about~~ 1 – 5% pirenzepine free base.

~~13.~~12. The topical formulation of any of Claims 1-~~12~~11, wherein the topical formulation is selected from a gel, lotion, cream, ointment, and liquid formulation.

~~14.~~13. The topical formulation of any of Claims 1-~~13~~12, further comprising a muscle relaxant or cramping relief compound.

~~15.~~14. The topical formulation of Claim ~~12~~13, wherein the muscle relaxant or cramping relief compound is selected from a magnesium ion, vitamin B1, B2, B6 and/or vitamin B12.

~~16.~~15. The topical formulation of any of Claims 1-~~15~~14, further comprising a compound which aids in a person's sleep.

~~17.~~16. The topical formulation of any of Claims 1-~~16~~15, further comprising an anaesthetic or analgesic compound.

~~18.~~17. The topical formulation of Claim ~~17~~16, wherein said analgesic compound is an amino ester or amide.

~~19.~~18. The topical formulation of Claim ~~17~~16, wherein said analgesic compound is a cannabinoid.

~~20.~~19. The topical formulation of claim 1, wherein a drying time of the formulation ranges from ~~about~~ 30 seconds to ~~about~~ 30 minutes.

~~21.~~20. The topical formulation of Claim 1, wherein a viscosity of the formulation ranges from ~~about~~ 300 mPa.s to ~~about~~ 15,000 mPa.s.

~~22.~~21. The topical formulation of Claim 1, wherein the formulation comprises a dose of pirenzepine of ~~about~~ 40 μg/cm^2 to ~~about~~ 120 μg/cm^2.

~~23.~~22. The topical formulation of Claim ~~22~~21, wherein the formulation is a dose of pirenzepine of ~~about~~ 40 μg/cm^2 to ~~about~~ 120 μg/cm^2 formulated to be delivered via the epidermis.

~~24.~~23. The topical formulation of Claim ~~23~~22, wherein the formulation is configured to be delivered to the epidermis within ~~about~~ 18 hours to ~~about~~ 24 hours.

~~25.~~24. The topical formulation of Claim ~~24~~23, wherein the formulation is configured to be delivered via the epidermis within about 22 hours.

~~26.~~25. Use of the topical formulation of any of Claims 1-24 in the manufacture of a medicament for inhibiting, ameliorating, reducing a severity of, treating, delaying the onset of, or preventing one or more symptoms of peripheral neuropathy in a subject, wherein said topical formulation is to be administered topically to the subject.

~~27.~~26. The use of Claim ~~26~~25, wherein the peripheral neuropathy is selected from the group consisting of type I diabetic peripheral neuropathy, type II diabetic peripheral neuropathy, diabetes mellitus insulin dependent peripheral neuropathy, surgically induced peripheral neuropathy, chemotherapy induced peripheral neuropathy, infectious disease induced peripheral neuropathy, and idiopathic peripheral neuropathy.

~~28.~~27. The use of Claim ~~27~~26, wherein the infectious diseases is HIV.