drying. Further, many active agents are less stable in neutral form than in salt form. Therefore, there exists a need for compositions, systems and medicaments having an adhesive matrix as a component layer that can consistently and effectively deliver a therapeutic amount of an active agent over a prolonged period of time.

[0006] The foregoing examples of the related art and limitations related therewith are intended to be illustrative and not exclusive. Other limitations of the related art will become apparent to those of skill in the art upon a reading of the specification and a study of the drawings.

SUMMARY

[0007] The following aspects and examples thereof described and illustrated below are meant to be exemplary and illustrative, not limiting in scope.

[0008] In a first example, a transdermal delivery system is provided, the system comprising a skin contact adhesive layer to attach the system to the skin of a user; a drug reservoir layer comprising an active agent and a drug carrier composition; and a microporous membrane disposed between the adhesive layer and the drug reservoir layer, the microporous membrane comprising a plurality of pores and a membrane treatment composition, wherein the membrane treatment composition occupies at least a portion of the pores.

[0008a] In one aspect, the present disclosure refers to a transdermal delivery system, comprising: a skin contact adhesive layer to attach the system to the skin of a user; a drug reservoir layer comprising an adhesive polymer, a salt form of donepezil, and a drug carrier composition; and a microporous membrane disposed between the adhesive layer and the drug reservoir layer, the microporous membrane comprising a plurality of pores filled with a membrane treatment composition different from the drug carrier composition, wherein the skin contact adhesive layer comprises an acrylic acid/vinyl acetate copolymer adhesive, a nonionic surfactant, a long-chain aliphatic alcohol, and a citric acid ester, wherein the drug carrier composition comprises a nonionic surfactant, a long-chain aliphatic alcohol, a citric acid ester and a hydrophilic solvent, wherein the membrane treatment composition excludes the hydrophilic solvent and comprises sorbitan monolaurate, lauryl lactate, and triethyl citrate, wherein the sorbitan monolaurate comprised is between 8-25 wt%, wherein the lauryl lactate comprised is between 10-30 wt%, and wherein the triethyl citrate comprised is between 55-80 wt%.

[0009] In some examples, the microporous membrane is and/or the pores of the microporous membrane are saturated with the membrane treatment composition. In another example, the membrane treatment composition is sequestered in or within the pores of the microporous membrane. In another example, the membrane treatment composition fills the pores of the microporous membrane. In one example, the microporous membrane is a flat sheet microporous membrane.

[0010] In some examples, the drug carrier composition and the membrane treatment composition are the same. In another example, the drug carrier composition and the membrane treatment composition are different. In one example, the drug carrier composition and the membrane treatment composition are different. In one example, the membrane treatment composition and the contact adhesive layer drug carrier composition are the same, and both are different from the drug carrier composition that is disposed in the drug reservoir layer. In one example, the drug carrier composition differs from the membrane treatment composition and the contact adhesive layer drug carrier composition by the presence of a hydrophilic solvent.

[0011] In some examples, the membrane treatment composition comprises a nonionic surfactant, a long-chain aliphatic alcohol, a citric acid ester, and/or combinations thereof.

[0012] In some examples, the active agent is a water insoluble base and the drug carrier composition comprises a nonionic surfactant, a long-chain aliphatic alcohol, a citric acid ester, and/or combinations thereof.

[0013] In some examples, the microporous membrane is a microporous polypropylene.

IT IS CLAIMED:

1. A transdermal delivery system, comprising:

a skin contact adhesive layer to attach the system to the skin of a user;

a drug reservoir layer comprising an adhesive polymer, a salt form of donepezil, and a drug carrier composition; and

a microporous membrane disposed between the adhesive layer and the drug reservoir layer, the microporous membrane comprising a plurality of pores filled with a membrane treatment composition different from the drug carrier composition,

wherein the skin contact adhesive layer comprises an acrylic acid/vinyl acetate copolymer adhesive, a nonionic surfactant, a long-chain aliphatic alcohol, and a citric acid ester,

wherein the drug carrier composition comprises a nonionic surfactant, a long-chain aliphatic alcohol, a citric acid ester and a hydrophilic solvent,

wherein the membrane treatment composition excludes the hydrophilic solvent and comprises sorbitan monolaurate, lauryl lactate, and triethyl citrate,

wherein the sorbitan monolaurate comprised is between 8-25 wt%,

wherein the lauryl lactate comprised is between 10-30 wt%, and

wherein the triethyl citrate comprised is between 55-80 wt%.

2. The system of claim 1, wherein the plurality of pores are filled with the membrane treatment composition prior to the microporous membrane being disposed between the adhesive layer and the drug reservoir layer.

3. The system claim 1, wherein the hydrophilic solvent in the drug carrier composition is glycerine.

4. The system of claim 1, wherein the nonionic surfactant is sorbitan monolaurate, the long-chain aliphatic alcohol is lauryl lactate or octyldodecanol, and the citric acid ester is triethyl citrate.

5. The system of any one of the preceding claims, wherein the drug reservoir layer further comprises an amphoteric base compound.

6. The system of claim 5, wherein the salt form of donepezil and the amphoteric base compound react *in situ* in the drug reservoir layer after the system is applied to skin of a user to generate a base form of donepezil.

7. The system of claim 1, wherein the skin contact adhesive layer excludes the hydrophilic solvent.

8. The system of claim 7, wherein the hydrophilic solvent is a polyol.

9. The system of claim 8, wherein the drug carrier composition comprises between 1.5-2.5 wt% sorbitan monolaurate, between 8-12 wt% triethyl citrate, and between 5-15 wt% polyol.

10. The system of claim 9, wherein the membrane treatment composition comprises between 10-17 wt% sorbitan monolaurate, between 15-25 wt% lauryl lactate, and between 60-75 wt% triethyl citrate.

11. The system of claim 10, wherein the contact adhesive layer comprises sorbitan monolaurate, lauryl lactate, and triethyl citrate.

12. A transdermal delivery system according to any one of claims 1-11, for use in treating Alzheimer's disease, wherein the system when applied to skin of a subject generates a base form of the salt form of donepezil for delivery to the skin.

13. A transdermal delivery system according to any one of claims 1-11 for delivery of a base form of donepezil,

wherein the transdermal delivery system when secured to the skin of a user delivers the base form of donepezil from the system to the skin, whereby (i) the time to reach steady state flux is at least about 20% faster compared to a system with no membrane treatment composition in the pores of the microporous membrane, (ii) the system achieves its steady state equilibrium flux at least 20% faster compared to a system with no membrane treatment composition in the pores of the microporous membrane; and/or (iii) donepezil diffuses from the system to the skin at least 20% faster compared to a system with no membrane treatment composition in the pores of the microporous membrane.

14. Use of donepezil in the manufacture of a transdermal delivery system according to any one of claims 1-11, for treating Alzheimer's disease, wherein the system when applied to skin of a subject generates a base form of the salt form of donepezil for delivery to the skin.