CLAIMS

1. A transdermal adhesive composition comprising:

an adhesive comprising a washed polymerization reaction product of at least two ethylenically unsaturated monomers; and

at least one pharmaceutically active compound which is susceptible to oxidative degradation;

wherein the at least two ethylenically unsaturated monomers, if present in the adhesive as unreacted monomers, are present at a level of less than 200 ppm of total unreacted monomer, based upon the total weight of the adhesive; and

wherein any free radical initiator, if present in the adhesive, is present at a level of less than 20 ppm, based upon the total weight of the adhesive; and

wherein any free radical initiator, if present in the adhesive, is present at a level of less than 20 ppm, based upon the total weight of the adhesive.

2. A transdermal adhesive composition comprising:

an adhesive comprising a washed polymerization reaction product of at least two ethylenically unsaturated monomers; and

(*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate or a pharmaceutically acceptable salt thereof;

wherein the at least two ethylenically unsaturated monomers, if present in the adhesive as unreacted monomers, are present at a level of less than 200 ppm of total unreacted monomer, based upon the total weight of the adhesive; and

wherein any free radical initiator, if present in the adhesive, is present at a level of less than 20 ppm, based upon the total weight of the adhesive.

3. The composition of any one of claims 1and 2, wherein the at least two ethylenically unsaturated monomers, if present in the adhesive, are present at a level of less than 100 ppm of total unreacted monomer.

4. The composition of any one of claims 1 through 3, wherein the at least two ethylenically unsaturated monomers comprise an ethylenically unsaturated group selected from the group consisting of acryloyl, methacryloyl, vinyl, and a combination thereof.

5. The composition of any one of claims 1 through 4, wherein the adhesive comprises the copolymerization product of at least one first monomer selected from the group consisting C_4 to C_{12} alkyl acrylate monomers, C_4 to C_{12} alkyl methacrylate monomers, and combinations thereof; and at least one second monomer selected from the group consisting of acrylamide, N,N-diethylacrylamide, methacrylamide, vinyl acetate, vinyl alcohol, N-vinyl-2-pyrrolidone, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, hydroxpropyl acrylate, glyceryl acrylate, 2-ethoxyethyl acrylate, 2-ethoxyethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, methacrylic acid, pyrrolidonylethyl acrylate, 2-carboxyethyl acrylate, and combinations thereof.

6. The composition of claim 5, wherein the at least one first monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, cyclohexyl acrylate, 2-methylbutyl acrylate, butyl acrylate, and combinations thereof.

7. The composition of any one of claims 1 through 6, wherein the adhesive comprises the co-polymerization product of isooctyl acrylate, acrylamide, and vinyl acetate.

8. The composition of any one of claims 1 and 3 through 7 except as dependent on claim 2, wherein the pharmaceutically active compound includes at least one group selected from the group consisting of tertiary amino, secondary amino, benzylic hydrogen-containing group, and combinations thereof.

9. The composition of any one of claims 1, 3 through 7 except as dependent on claim 2, and 8, wherein the pharmaceutically active compound is selected from the group consisting of: rivastigmine ((*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate), buprenorphine, etidocaine, ropivacaine, clonidine, lidocaine, letrozole, fentanyl, indapamide, apomorphine, propylnorapomorphine, salbutamol, lisuride, dihydroergotamine, pergolide,

terguride, proterguride, propranolol, imipramine, guanethidine, cyproheptadine and a pharmaceutically acceptable salt of any one of the preceding compounds.

10. The composition of claim 9, wherein the pharmaceutically active compound is (*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate or a pharmaceutically acceptable salt thereof.

11. The composition of any one of claims 1 through 10, wherein the composition is essentially free of any added antioxidant.

12. A transdermal drug delivery device comprising:

a transdermal adhesive composition comprising:

an adhesive comprising a washed polymerization reaction product of at least two ethylenically unsaturated monomers; and

at least one pharmaceutically active compound which is susceptible to oxidative degradation;

wherein the at least two ethylenically unsaturated monomers, if present in the adhesive as unreacted monomers, are present at a level of less than 200 ppm of total unreacted monomer, based upon the total weight of the adhesive; and

wherein any free radical initiator, if present in the adhesive, is present at a level of less than 20 ppm, based upon the total weight of the adhesive; and

a backing sheet coated with the transdermal adhesive composition, wherein the transdermal adhesive composition coating covers at least a portion of a major surface of the backing sheet.

13. The device of claim 12, wherein the at least two ethylenically unsaturated monomers, if present in the adhesive, are present at a level of less than 100 ppm of total unreacted monomer.

14. The device of any one of claims 12 and 13, wherein the at least two ethylenically unsaturated monomers comprise an ethylenically unsaturated group selected from the group consisting of acryloyl, methacryloyl, vinyl, and a combination thereof.

15. The device of any one of claims 12 through 14, wherein the adhesive comprises the copolymerization product of at least one first monomer selected from the group consisting C_4 to C_{12} alkyl acrylate monomers, C_4 to C_{12} alkyl methacrylate monomers, and combinations thereof; and at least one second monomer selected from the group consisting of acrylamide, N,N-diethylacrylamide, methacrylamide, vinyl acetate, vinyl alcohol, N-vinyl-2-pyrrolidone, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, hydroxpropyl acrylate, glyceryl acrylate, 2-ethoxyethyl acrylate, 2-ethoxyethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, methacrylic acid, pyrrolidonylethyl acrylate, 2-carboxyethyl acrylate, and combinations thereof.

16. The device of claim 15, wherein the at least one first monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, cyclohexyl acrylate, 2-methylbutyl acrylate, butyl acrylate, and combinations thereof.

17. The device of any one of claims 12 through 16, wherein the adhesive comprises the co-polymerization product of isooctyl acrylate, acrylamide, and vinyl acetate.

18. The device of any one of claims 12 through 17, wherein the pharmaceutically active compound includes at least one group selected from the group consisting of tertiary amino, secondary amino, benzylic hydrogen-containing group, and combinations thereof.

19. The device of any one of claims 12 through 18, wherein the pharmaceutically active compound is selected from the group consisting of: rivastigmine ((*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate), buprenorphine, etidocaine, ropivacaine, clonidine, lidocaine, letrozole, fentanyl, indapamide, apomorphine, propylnorapomorphine, salbutamol, lisuride, dihydroergotamine, pergolide, terguride, proterguride, propranolol, imipramine,

guanethidine, cyproheptadine and a pharmaceutically acceptable salt of any one of the preceding compounds.

20. The device of claim 19 wherein the pharmaceutically active compound is (*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate or a pharmaceutically acceptable salt thereof.

21. The device of any one of claims 12 through 20, wherein the composition is essentially free of any added antioxidant.

22. A method of making a stable transdermal adhesive composition comprising:

providing a polymerization reaction product of at least two ethylenically unsaturated monomers; and wherein the polymerization reaction product is dissolved and/or dispersed in a first liquid;

separating at least a portion of the polymerization reaction product from the first liquid to provide a first washed polymerization reaction product;

dissolving or dispersing the first washed polymerization reaction product in a second liquid;

separating at least a portion of the first washed polymerization reaction product from the second liquid to provide a second washed polymerization reaction product;

wherein the at least two ethylenically unsaturated monomers, if present in the second washed polymerization reaction product, are present at a level of less than 200 ppm of total unreacted monomer, based upon the total weight of the second washed polymerization reaction product; and

wherein any free radical initiator, if present in the washed polymerization product combined with the at least one pharmaceutically active compound, is present at a level of less than 20 ppm, based upon the total weight of the washed polymerization reaction product; and

combining the second washed polymerization reaction product with at least one pharmaceutically active compound which is susceptible to oxidative degradation to form a stable transdermal adhesive composition.

23. The method of claim 22, further comprising:

dissolving or dispersing the second washed polymerization reaction product in a third liquid;

separating at least a portion of the second washed polymerization reaction product from the third liquid to provide a third washed polymerization reaction product, and

combining the third washed polymerization reaction product instead of the second washed polymerization reaction product with the at least one pharmaceutically active compound which is susceptible to oxidative degradation to form the stable transdermal adhesive composition

24. The method of claim 22 or claim 23, wherein the separating, in each instance, is carried out by adding a wash liquid to the dissolved polymerization reaction product, allowing polymerization reaction product to precipitate, and separating the precipitate from the liquid, to provide washed polymerization reaction product.

25. The method of any one of claims 22, 23, and 24, further comprising polymerizing the at least two ethylenically unsaturated monomers dissolved in the first liquid to provide the polymerization reaction product dissolved and/or dispersed in the first liquid.

26. The method of any one of claims 22 through 25, wherein the at least two ethylenically unsaturated monomers, if present in the washed polymerization reaction product combined with the at least one pharmaceutically active compound, are present at a level of less than 100 ppm total unreacted monomer, based upon the total weight of the washed polymerization product.

27. The method of any one of claims 22 through 26, wherein the at least two ethylenically unsaturated monomer comprises an ethylenically unsaturated group selected from the group consisting of acryloyl, methacryloyl, vinyl, and a combination thereof.

28. The method of any one of claims 22 through 27, wherein the adhesive comprises the copolymerization product of at least one first monomer selected from the group consisting C_4 to C_{12} alkyl acrylate monomers, C_4 to C_{12} alkyl methacrylate monomers, and combinations thereof; and at least one second monomer selected from the group consisting of acrylamide, N,N-diethylacrylamide, methacrylamide, vinyl acetate, vinyl alcohol, N-vinyl-2-pyrrolidone, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, hydroxpropyl acrylate, glyceryl acrylate, 2-ethoxyethyl acrylate, 2-ethoxyethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, methacrylic acid, pyrrolidonylethyl acrylate, 2-carboxyethyl acrylate, and combinations thereof.

29. The method of claim 28, wherein the at least one first monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, cyclohexyl acrylate, 2-methylbutyl acrylate, butyl acrylate, and combinations thereof.

30. The method of any one of claims 22 through 29, wherein the adhesive polymer comprises the co-polymerization product of isooctyl acrylate, acrylamide, and vinyl acetate.

31. The method of any one of claims 22 through 30 wherein the pharmaceutically active compound includes at least one group selected from the group consisting of tertiary amino, secondary amino, benzylic hydrogen-containing group, and combinations thereof.

32. The method of any one of claims 22 through 31, wherein the pharmaceutically active compound is selected from the group consisting of: rivastigmine ((*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate), buprenorphine, etidocaine, ropivacaine, clonidine, lidocaine, letrozole, fentanyl, indapamide, apomorphine, propylnorapomorphine, salbutamol, lisuride, dihydroergotamine, pergolide, terguride, proterguride, propranolol, imipramine, guanethidine, cyproheptadine and a pharmaceutically acceptable salt of any one of the preceding compounds.

33. The method of claim 32, wherein the pharmaceutically active compound is (*S*)-*N*-ethyl-*N*-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate or a pharmaceutically acceptable salt thereof.

34. The method of any one of claims 22 through 33, wherein an antioxidant is not added to the stable transdermal adhesive composition.

35. A method of making a stable transdermal drug delivery device comprising:

providing a transdermal adhesive composition according to any one of claims 1 through 11 or a transdermal adhesive composition made according to any one of claims 22 through 34; and

coating a backing sheet with the transdermal adhesive composition, wherein the transdermal adhesive composition coating covers at least a portion of a major surface of the backing sheet.

36. A transdermal adhesive composition according to any one of claims 1 through 11, or a transdermal adhesive composition made according to any one of claims 22 through 34, or a device according to any one of claims 12 through 21, or a device made according to claim 35 for use in delivering a pharmaceutically active compound to a mammal, the delivery of the pharmaceutically active compound comprising the steps of:

providing the transdermal adhesive composition or device;

positioning the transdermal adhesive composition or device on the skin of the mammal; and

allowing the composition or device to remain on the skin for a time sufficient to permit systemic delivery of the pharmaceutically active compound;

wherein the pharmaceutically active compound is susceptible to oxidative degradation.

CLAIMS:

1. An invention not claimed in any divisional application.