without undesirable odor, texture, or appearance. Rheological properties such as gel viscosity should allow a gel to be applied externally to skin and thereafter remain at that location of application for a period of uptake of the testosterone through the skin. Tactile properties relate to the feel and texture of the gel when touched and applied by a user, with preferred gels exhibiting a smooth feel. Good delivery properties (*e.g.*, uptake) allow an effective amount of testosterone from the applied gel to be absorbed through skin during the time that the gel remains located at the skin surface.

Certain specific ingredients are included in commercial testosterone gel products to achieve desired properties of viscosity and uptake, such as enhancers, that is, a material which is capable of increasing the rate of passage of an androgen through a body membrane. For example, Testim® testosterone gel includes the chemically complex, cyclic oxacyclohexadecane-2-one.

Doctors and patients continue to need improved testosterone gel products having good stability, cosmetic properties, and efficacy, especially such products that also benefit from cost advantages or improved performance relative to current available product options.

SUMMARY

The following description relates to pharmaceutical compositions, such as compositions in the form of a gel ("gel compositions"), that include an active pharmaceutical ingredient ("active ingredient") that can be applied to the skin to transdermally administer the active ingredient to a patient. The active ingredient can be any that is desired for transdermal administration, though gel compositions of the ~~invention~~ disclosure that include testosterone as the active ingredient have been found to exhibit particularly useful or advantageous properties compared to other testosterone gel compositions currently marketed.

Examples of gel compositions as described can include a combination of ingredients that includes a solvent, cosolvent, polyol, gel-forming polymer (*i.e.*, "thickener"), and optional pH adjusting ingredient (pH-modifier), to provide bioavailability of the active ingredient that is as good as, equivalent to, or better than certain currently-available commercial products such as Testim® testosterone gel and Androgel® testosterone gel. Advantageously, the gel compositions described

gel composition do not exhibit an undesired odor that can arise from the presence of a "Hseih enhancer."

Data show that testosterone gel compositions described herein can exhibit transdermal absorption of testosterone that is as good as, *e.g.*, equivalent to, or better than absorption of testosterone associated with commercial products such as the Testim® testosterone gel and Androgel® testosterone gel products. The testosterone gel compositions can also be stable, and can have desirable cosmetic, tactile properties (*e.g.*, texture), rheological properties including diminished, and reduced or suppressed undesirable odor, preferably an absence of any noticeable undesirable odor.

~~In one aspect,~~ T~~t~~he ~~invention~~ disclosure relates to a pharmaceutical composition that contains: about 0.5 to about 10 weight percent testosterone; solvent comprising ethyl alcohol; cosolvent system comprising a cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising a polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

In one aspect, the disclosure provides a pharmaceutical composition, comprising:

about 0.5 to about 10 weight percent testosterone;

solvent comprising ethyl alcohol;

cosolvent system comprising a cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof;

polyol system comprising a polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and

gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

In another aspect the ~~invention~~ disclosure relates to a pharmaceutical composition in the form of a gel, consisting essentially of: about 0.5 to about 10 weight percent testosterone; ethyl alcohol; diisopropyl adipate; methyl laurate; oleyl alcohol; glycerine; propylene glycol; polyethylene glycol polyol; gel-forming

polymer; purified water; and optional pH- modifier, wherein the weight is based on total weight of the pharmaceutical composition.

In another aspect, the ~~invention~~ disclosure relates to a pharmaceutical composition in the form of a gel, consisting of: about 0.5 to about 10 weight percent testosterone; ethyl alcohol; cosolvent system consisting of diisopropyl adipate, methyl laurate, and oleyl alcohol; polyol system consisting of glycerine, propylene glycol, polyethylene glycol; gel-forming polymer; purified water; and optional pH-adjuster, wherein the weight percent is based on total weight of the pharmaceutical composition.

~~In yet another aspect, t~~The ~~invention~~ disclosure relates to a package containing from 3 to 6 grams pharmaceutical composition. In another aspect, there is provided a package containing from 3 to 6 grams pharmaceutical composition as defined herein. The composition contains: about 0.5 to about

10 weight percent testosterone; solvent comprising ethyl alcohol; cosolvent system comprising cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

In another aspect, there is provided a package containing from 3 to 6 grams pharmaceutical composition comprising:

about 0.5 to about 10 weight percent testosterone;

solvent comprising ethyl alcohol;

cosolvent system comprising cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof;

polyol system comprising polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and

gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

In another aspect, there is provided a package containing from 3 to 6 grams pharmaceutical composition as defined herein, wherein the package is adapted for dispensing a single dose of the pharmaceutical composition. In another aspect, there is provided a package containing from 3 to 6 grams pharmaceutical composition as defined herein, wherein the package is adapted for dispensing a metered volume of the pharmaceutical composition.

In another aspect, there is provided a pharmaceutical composition consisting essentially of:

about 0.5 to about 2 weight percent testosterone;

about 75 to about 85 weight percent ethyl alcohol;

about 2 to about 10 weight percent cosolvent system, wherein the cosolvent system consists of diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof;

about 7 to about 14 weight percent polyol system, wherein the polyol system comprises a polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof;

about 0.5 to about 3 weight percent carbomer gel forming polymer; and

pH-modifier, wherein the weight percent is based upon the total weight of the pharmaceutical composition.

In another aspect, there is provided a pharmaceutical composition consisting essentially of:

about 0.5 to about 2 weight percent testosterone;

about 75 to about 85 weight percent ethyl alcohol;

about 1 to about 2 weight percent diisopropyl adipate;

about 0.2 to about 0.4 weight percent methyl laurate;

about 1 to about 2 weight percent oleyl alcohol;

about 3 to about 7 weight percent glycerine;

about 3 to about 7 weight percent propylene glycol;

about 0.3 to about 0.7 weight percent polyethylene glycol;

about 1 to about 3 weight percent weight percent gel-forming polymer; and

pH-modifier, wherein the weight percent is based upon the total weight of the pharmaceutical composition.

In another aspect, there is provided a pharmaceutical composition consisting essentially of:

about 0.5 to about 2 weight percent testosterone;

about 75 to about 85 weight percent ethyl alcohol;

about 1 to about 2 weight percent diisopropyl adipate;

about 0.2 to about 0.4 weight percent methyl laurate;

about 1 to about 2 weight percent oleyl alcohol;

about 3 to about 7 weight percent glycerine;

about 3 to about 7 weight percent propylene glycol;

about 0.3 to about 0.7 weight percent polyethylene glycol;

about 1 to about 3 weight percent weight percent gel-forming polymer;

purified water; and

pH-modifier, wherein the weight percent is based upon the total weight of the pharmaceutical composition.

In another aspect, there is provided a pharmaceutical composition consisting essentially of:

about 0.5 to about 2 weight percent testosterone;

about 75 to about 85 weight percent ethyl alcohol;

about 1 to about 2 weight percent diisopropyl adipate;

about 0.2 to about 0.4 weight percent methyl laurate;

about 1 to about 2 weight percent oleyl alcohol;

about 3 to about 7 weight percent glycerine;

about 3 to about 7 weight percent propylene glycol;

about 0.3 to about 0.7 weight percent polyethylene glycol;

about 1 to about 3 weight percent gel-forming polymer;

and

about 0.1 weight percent tromethamine , wherein the weight percent is based upon the total weight of the pharmaceutical composition.

In another aspect, there is provided a package containing a pharmaceutical composition consisting essentially of:

about 0.5 to about 2 weight percent testosterone;

about 75 to about 85 weight percent ethyl alcohol;

about 2 to about 10 weight percent cosolvent system, wherein the cosolvent system consists of diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof;

about 7 to about 14 weight percent polyol system, wherein the polyol system comprises a polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof;

about 0.5 to about 3 weight percent carbomer gel forming polymer; and

pH-modifier, wherein the weight percent is based upon the total weight of the pharmaceutical composition.

~~In another aspect, t~~The ~~invention~~ disclosure relates to a method for treating a condition associated with a deficiency of endogenous testosterone in a male patient.

The method includes administering to the patient a pharmaceutical composition that contains: about 0.5 to about 10 weight percent testosterone; solvent comprising ethyl alcohol; cosolvent system comprising cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

~~In yet another aspect t~~The ~~invention~~ disclosure relates to a method for transdermal delivery of testosterone to a patient. The method includes administering to the patient a pharmaceutical composition in the form of a gel, which contains: about 0.5 to about 10 weight percent testosterone; solvent comprising ethyl alcohol; cosolvent system comprising cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

~~In yet another aspect t~~The ~~invention~~ disclosure relates to a method for treating hypogonadism in a patient. The method includes administering to the patient a pharmaceutical composition in the form of a gel, which contains: about 0.5 to about 10 weight percent testosterone; solvent comprising ethyl alcohol; cosolvent system comprising cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-

forming polymer, wherein the weight percent is based on total weight of the pharmaceutical composition.

~~In yet another aspect t~~The ~~invention~~ disclosure relates to a method for maintaining an effective concentration of testosterone in the blood serum of a male for treating hypogonadism. The method includes transdermally delivering to the male by applying to the skin a pharmaceutical composition in the form of a gel. The gel contains: about 0.5 to about 10 weight percent testosterone based on total weight of the pharmaceutical composition; solvent comprising ethyl alcohol; cosolvent system comprising a cosolvent selected from diisopropyl adipate, methyl laurate, oleyl alcohol, and combinations thereof; polyol system comprising a polyol selected from glycerine, propylene glycol, polyethylene glycol, and combinations thereof; and gel-forming polymer. The pharmaceutical composition is applied to skin of the male in the form of a unit dose that contains about 25 mg to about 200 mg of testosterone and is maintained on the skin for a period of time sufficient for delivery of the testosterone to the male's systemic circulation such that, following a single application of the unit dose to the skin, the amount of circulating testosterone (AUC_{0-24}) in blood serum of the male achieved in a 24-hour period following the application is about 1,000 to about 350,000 pg•h/mL (picogram- hour/milliliter) greater than the amount of circulating testosterone (AUC_{0-24}) in the blood serum of the male that would have been achieved in the same 24-hour period had the dose not been administered.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graph showing flux of active ingredient of testosterone gel compositions, relative to time.

Figure 2 is a graph showing flux of active ingredient of testosterone gel compositions, relative to time.

DETAILED DESCRIPTION

While the present invention may be embodied in many different forms, the following description includes certain specific testosterone gel composition embodiments that particularly relate to treating hormone deficiency or