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(71) Applicant (for all designated States except US): **GLEN-MARK PHARMACEUTICALS LIMITED** [IN/IN]; Glenmark House, HDO-Corporate Bldg, Wing-A, B.D Sawant Marg, Chakala, Andheri (East), Maharashtra (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DHUPPAD, Ulhas Rameshchandra** [IN/IN]; Bunglow No. B-3, Coral Apt., Resi 1 -Phase, Shahu Nagar, Motwani Factory Road, Nashik Road, Maharashtra, Nashik 422101 (IN). **KHACHANE, Vasant Sitaram** [IN/IN]; Flat no 6A, Niwas Plaza, behind HDFC, Sharanpur-Trimbak Link Road, Maharashtra, Nashik 422005 (IN). **BHAMRE, Nitin Babulal** [IN/IN]; 1, Sanjay Apt., Racca Colony, Sharanpur Road, Maharashtra, Nashik 422 002 (IN). **PAL, Santosh Kumar** [IN/IN]; Sudhanshu Parida, Patkura Medical Stores, At / Post - Patkura, District - Kendrapara, Orissa (IN).

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(54) Title: TOPICAL PHARMACEUTICAL COMBINATION COMPRISING MINOXIDIL AND AMINEXIL

(57) Abstract: The present invention relates to a fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil, processes for preparing such formulation and their method of use for the treatment of alopecia in human.



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**TOPICAL PHARMACEUTICAL COMBINATION COMPRISING
MINOXIDIL AND AMINEXIL**

PRIORITY DETAILS

5 This patent application claims priority to Indian Patent Application No. 285/MUM/2008, filed on February 11, 2008, the contents of which are hereby incorporated as reference.

TECHNICAL FIELD OF THE INVENTION

10 The present invention relates to topical pharmaceutical compositions, their uses and methods of manufacturing. Specifically, the present invention relates to topical pharmaceutical combination comprising minoxidil and aminexil

INTRODUCTION OF THE INVENTION

15 The present invention relates to a topical pharmaceutical combination comprising minoxidil and aminexil for the treatment of alopecia in a mammal. More particularly, the present invention relates to a fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil, processes for preparing such formulation and their method of use for the treatment of alopecia in human.

20 Androgenetic alopecia ("AGA") is the most common form of alopecia. The first signs of AGA may start after puberty. In the so-called bald person there is a noticeable absence of terminal hair; however, the skin does contain vellus or fine colorless hair which may require microscopic examination to determine its presence.

25 AGA has been reported to be a polygenic trait believed to involve several genes for both sexes. It is an androgen hormone-dependent process with continuous miniaturization of hair follicles in both genetically predisposed men and women.

30 Systemically and also in the hair follicle cells, testosterone is converted into the more active androgen dihydrotestosterone ("DHT") by 5 α -reductase enzyme. The androgens bind to androgen receptors ("AR") in the hair follicle, which triggers a process reducing the anagen phase of the hair cycle. Gradually, over

succeeding cycles, the terminal hair converts into a thinner and shorter vellus hair. The density of the AR in the hair follicles varies according to location, which is genetically determined. Age also plays an important role in AGA.

Until recently the absence of a truly effective treatment for AGA led to a general lack of interest in it as a clinical condition. Fortunately, currently drug therapies of proven efficacy are available. Current treatments for alopecia and other hair growth disorders include those seeking to convert the fine colorless vellus-like hairs into thicker, broader terminal hairs. Currently there are two treatments approved by the Food and Drug Administration in the United States for the treatment of androgenetic alopecia in men: topical minoxidil and oral finasteride. The androgen receptor antagonists used to treat women are not suitable for men because of the potential risks of gynaecomastia, feminisation, and impotence.

Minoxidil, chemically known as 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-piperidinopyrimidine, prolongs the anagen phase of the hair cycle. Minoxidil (a) increases the rate of growth of terminal hair, and (b) converts vellus-like hair to grow as terminal hair.

When applied topically, Minoxidil topical solution has been shown to stimulate hair growth in individuals with alopecia androgenetica (male pattern baldness) and hair loss occurring on the crown of the scalp. It is well established that the effectiveness of topical minoxidil in treating male pattern baldness is dose dependant. It is thus desirable to deliver a pharmaceutical composition comprising high percentages of minoxidil.

However, minoxidil has poor solubility in water and ethanol, and thus the dose of minoxidil in solutions remains relatively low. Minoxidil solutions of the prior art comprise a maximum of 5% to 6.5%w/v minoxidil, depending on the solvent used. The final solution is a watery, runny composition, that will either quickly dry or will evaporate once applied.

U.S. Patent Nos. 7442369, 6946120, 4139619 and 3382247 describe compositions comprising minoxidil.

Tsai, JC, et al., (Drug and vehicle deposition from topical applications: Use of in vitro mass balance technique with minoxidil solutions, *J. Pharm. Sci.*, 81 (8), 2006, 736-743) demonstrated the disposition of minoxidil and propylene glycol from topical solutions as measured by an in vitro mass balance technique. They
5 concluded that the evaporation of propylene glycol concentrated the solution to supersaturation and precipitated out the minoxidil. The amount of formulation applied influenced the rate of concentration and, thus, the time at which minoxidil precipitates. The precipitation limits the amount of minoxidil that can be absorbed and leads to poor percutaneous absorption of drug from the formulation.

10 Aminexil, an analogue of minoxidil is an antifibrotic agent that inhibits collagen formation around the hair follicle and maintains the follicle survival. Aminexil's primary use is prevention of further hair loss. Perifollicular fibrosis is a condition that accompanies all alopecia whereby the collagen around the hair root becomes rigid and tightens, pushing the root to the surface and causing
15 premature hair loss. Aminexil has been shown to increase hair density and hair growth by preventing perifollicular fibrosis.

U.S. Patent Nos. 5328914 and 5846552" relate to compositions comprising aminexil.

In the present invention, without being bound by any theory, it is believed
20 that the addition of aminexil to topical pharmaceutical compositions comprising minoxidil would lead to a synergistic effect on the hair growth response, thus accenting the dose response curve of minoxidil alone. The combination therapy besides improving the rate of hair growth and vellus to terminal hair conversion would also bypass the deficiency in said dose response curve caused by
25 minoxidil's poor solubility in water and alcohol. Thus, the combination of minoxidil and aminexil is expected to result in greater hair growth effect using low concentrations of minoxidil. Further, the use of bioadhesive polymer such pharmaceutical combination would lead to increased contact time of both the active ingredients at the scalp. Moreover, such bioadhesive polymer also
30 prevents/minimizes the precipitation of minoxidil for the topical formulation, thereby further promoting hair growth.

SUMMARY OF THE INVENTION

The present invention relates to a fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil, processes for preparing such formulation and their method of use for the treatment of alopecia in human.

5 In an aspect, the present invention provides a fixed dose pharmaceutical composition comprising effective amounts of minoxidil and aminexil.

In another embodiment, the present invention provides a topical pharmaceutical formulation comprising about 1.0% w/v to about 6.0 % w/v of minoxidil, and about 1.0% w/v to about 3.0 % w/v of aminexil, preferably from
10 about 2.0% w/v to about 5.0 % w/v of minoxidil, and about 1.5 to about 2.0 % w/v of aminexil.

In another aspect, the fixed dose topical pharmaceutical formulation of the present invention comprises effective amounts of minoxidil and aminexil along with a bioadhesive polymer, preferably selected from cellulose polymers.

15 In an embodiment, the concentration of the bioadhesive polymer in the fixed dose topical pharmaceutical formulation of the present invention ranges between about 0.1 % w/v to about 2 % w/v.

In another aspect, the fixed dose topical pharmaceutical formulation of the present invention comprises effective amounts of minoxidil and aminexil along
20 with silicone oil.

In an embodiment, the concentration of the silicone oil in the fixed dose topical pharmaceutical formulation of the present invention ranges from about 10 % w/v to about 80 % w/v.

In a further aspect, the present invention provides a process to prepare the
25 fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil as described herein.

In yet another aspect, the present invention provides use of fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil for the treatment of alopecia.

30

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a fixed dose topical pharmaceutical formulation comprising minoxidil and aminexil, processes for preparing such formulation and their method of use for the treatment of alopecia in human.

5 "Topical pharmaceutical formulation" in the context of present invention refers to a composition that is employed to prevent, reduce in intensity, cure or otherwise treat a target condition or disease. Such formulations typically include gel, lotion, cream, ointments and the like for topical application. The terms "topical" or "local" conventionally mean delivery of a drug or pharmacologically
10 active agent to the skin or mucosa. Topical pharmaceutical formulation encompasses various dosage forms like lotions, solutions, ointments, creams, pastes and gels.

As used herein the term "subject" or "a patient" or "a host" as used herein refers to mammal, particularly human.

15 As used herein, the terms "treating" or "treatment" of a state, disorder or condition as used herein means: (1) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a mammal that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder
20 or condition, (2) inhibiting the state, disorder or condition, i.e., arresting or reducing the development of the disease or at least one clinical or subclinical symptom thereof, or (3) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms. The benefit to a subject to be treated is either statistically significant or at least
25 perceptible to the patient or to the physician.

As used herein, the term "pharmaceutically acceptable" such as in the recitation of a "pharmaceutically acceptable carrier" or a "pharmaceutically acceptable derivative" is meant a compound that is not biologically or otherwise undesirable, i.e., the compound may be incorporated into a topical formulation of
30 the invention and administered to a patient without causing any undesirable

biological effects or interacting in a deleterious manner with any of the other components of the formulation in which it is contained.

As used herein, the terms "carriers" or "vehicles" as used herein refer to pharmaceutically acceptable carrier materials suitable for topical drug administration. Carriers and vehicles useful herein include any such materials known in the art that are nontoxic and do not interact with other components of the composition in a deleterious manner.

In another embodiment, the present invention provides the topical pharmaceutical formulation comprising about 1.0 to about 6.0 % w/v of minoxidil, and about 1.0 to about 3.0 % w/v of aminexil.

As used herein, the terms "effective amount" or a "therapeutically effective amount" of a pharmacologically active agent is meant a non-toxic but sufficient amount of the drug or agent to provide the desired effect. The "effective amount" will vary depending on the compound, the disease and its severity and the age, weight, physical condition and responsiveness of the mammal to be treated. Thus, it is not always possible to specify an exact "effective amount." However, an appropriate "effective amount" in any individual case may be determined by one of ordinary skill in the art using routine experimentation. In the present invention, the effective amount of the active ingredients such as minoxidil ranges from about 1 to about 6 % w/v, or about 2 to about 5 % w/v, and for aminexil, ranges from about 1 to about 4 % w/v, or about 2 to about 3 % w/v.

As used herein, the terms "active agent" or "active pharmaceutical ingredient" or "drug" are used interchangeably herein to refer to a chemical material or compound that induces a desired pharmacological, physiological effect, and include agents that are therapeutically effective, prophylactically effective, or cosmeceutically effective. The active ingredients, for example, retinoids such as adapalene and antibiotics such as clindamycin and the like are used in the present invention.

Creams, as also well known in the art, are viscous liquids or semisolid emulsions, either oil-in-water or water-in-oil. Cream bases are water-washable,

and contain an oil phase, an emulsifier, and an aqueous phase. The oil phase, also called the "internal" phase, is generally comprised of petrolatum and a fatty alcohol such as cetyl or stearyl alcohol. The aqueous phase usually, although not necessarily, exceeds the oil phase in volume, and generally contains a humectant.

As will be readily be understood by those skilled in the field of pharmaceutical formulation, gels are semisolid, suspension-type systems. Gel forming agent for use herein can be any gelling agent typically used in the pharmaceutical art for topical semi solid dosage forms. Single-phase gels contain organic macromolecules distributed substantially uniformly throughout the carrier liquid, which is typically aqueous, but also, preferably, contain an alcohol and, optionally, an oil. Preferred "organic macromolecules," i.e., gelling agents, are crosslinked acrylic acid polymers such as the "carbomer" family of polymers, e.g., carboxypolyalkylenes that may be obtained commercially under the CARBOPOL® such as CARBOPOL 940.

In another aspect, the fixed dose topical pharmaceutical formulation of the present invention comprises effective amounts of minoxidil and aminexil along with a bioadhesive polymer that improves the contact time of the formulation when applied onto the needed surface.

In an embodiment, the concentration of the bioadhesive polymer in the fixed dose topical pharmaceutical formulation of the present invention ranges between about 0.1 % w/v to about 2 % w/v.

The bioadhesive polymer of the present invention typically includes hydrophilic polymers such as cellulosic polymers such as hydroxypropyl cellulose, hydroxyethyl cellulose, Kulcel LF, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, carboxy methyl cellulose and methyl cellulose; polyethylene oxides, polyoxyethylene-polyoxypropylene copolymers; polyvinylalcohol; gums such as tragacanth and xanthan gum; sodium alginate; and gelatin. The amount of bioadhesive polymer varies widely and ordinarily ranges from about 0.1 % to about 2.0 % by weight, based on the total weight of the composition.

In another aspect, the fixed dose topical pharmaceutical formulation of the present invention comprises effective amounts of minoxidil and aminexil along with silicone oil.

Silicone oils used according to the present invention may be of the volatile or nonvolatile and are selected from dimethicone, cyclomethicone, cyclomethicone and dimethicone crosspolymer, and dimethiconol 40, dimethicone copolyol, polyalkyl siloxanes, polyalkylaryl siloxanes, polyether siloxane, copolymers, polyalkyl siloxanes, polydimethyl siloxanes, polydimethyl cyclosiloxane, diethylpolysiloxane, dimethylpolysiloxane-diphenylpolysiloxane, trimethylpolysiloxane, diphenylpolysiloxane, disiloxane, trisiloxane, amodiethione, trimethylsilyl amodimethicone, divinyl dimethicone, cyclopentasiloxane, stearyl dimethicone, cyclopentasiloxane, trimethylsiloxysilicate and other silicone oils available from Union Carbide Corporation, SWS Silicones and Dow Corning and mixtures thereof.

Silicone oils used according to the present invention have one or more of the following properties: as a skin protectant, emollient, conditioner, moisturizer, lubricity which softens and moisturizes the skin, capable of allowing the formation of thin films on the skin in order that no greasy or sticky feeling is imparted to the skin from the personal care product.

The amount of silicone oil used according to the present invention varies widely and ranges from about 10 % to about 80.0 % by weight, based on the total weight of the composition.

The topical pharmaceutical formulation of the present invention can be prepared using various techniques known in the art. Different dosage forms like creams, gels, lotions, solutions and pastes can be formulated based on the teachings of known references, e.g., Pharmaceutical Dosage Forms and Drug Delivery Systems, (7th Ed. 1999); Remington: The Science and Practice of

Pharmacy, (20th Ed. 2000); and Handbook of Pharmaceutical Excipients, (3rd Ed. 2000), the contents of which are incorporated by reference herein.

The pharmaceutical formulation of the present invention can further contain pharmaceutically acceptable excipients. The pharmaceutically acceptable excipients include, but are not limited to, polymers, chelating agents, gelling agents, preservatives, surfactants, buffering agents and the like and mixtures thereof that are typically used in the art for locally applied semisolid dosage forms. Most of these excipients are described in detail in, e.g., Howard C. Ansel et. al., Pharmaceutical Dosage Forms and Drug Delivery Systems, (7th Ed. 1999); Alfonso R. Gennaro et al., Remington: The Science and Practice of Pharmacy, (20th Ed. 2000); and A. Kibbe, Handbook of Pharmaceutical Excipients, (3rd Ed. 2000), the contents of which are incorporated by reference herein.

Suitable polymers include, by way of example and without limitation, those known to one of ordinary skill in the art such as gum arabic, sodium based lignosulfonate, methyl methacrylate, methacrylate copolymers, isobutyl methacrylate, ethylene glycol dimethacrylate and the like and mixtures thereof.

Suitable buffering agents include, by way of example and without limitation, sodium hydroxide, potassium hydroxide, ammonium hydroxide and the like and mixtures thereof.

Suitable elastomers include, by way of example and without limitation, silicone elastomers, DC ST elastomer, crosslinked elastomeric organopolysiloxanes, methylpolysiloxane, methylphenylpolysiloxane, ethylpolysiloxane, ethylmethylpolysiloxane, ethylphenylpolysiloxane, hydroxymethylpolysiloxane, alkylpolydimethylsiloxane and cyclic polysiloxanes and other elastomers available from Dow Corning and mixtures thereof.

Suitable surfactants include, by way of example poloxamer and the like and mixtures thereof.

Suitable chelating agents include mild agents, such as for example, ethylenediaminetetraacetic acid (EDTA), disodium edetate and EDTA derivatives, and the like and mixtures thereof.

Suitable gelling agents/viscosifying agents include, by way of example and without limitation, carbomers (carbopol), modified cellulose derivatives, naturally-occurring, synthetic or semi-synthetic gums such as xanthan gum, acacia and tragacanth, sodium alginate, gelatine, modified starches, cellulosic polymers such as hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, and methyl cellulose; co-polymers such as those formed between maleic anhydride and methyl vinyl ether, colloidal silica and methacrylate derivatives, polyethylene oxides, polyoxyethylene-polyoxypropylene copolymers, polyvinylalcohol and the like and mixtures thereof.

Suitable preservatives include, by way of example and without limitation, phenoxyethanol, parabens such as methylparaben and propylparaben, propylene glycols, sorbates, urea derivatives such as diazolidinyl urea, and the like and mixtures thereof.

The pharmaceutical formulation of the present invention can further contain one or more suitable solvents. Examples of such solvents include, but are not limited to, water, tetrahydrofuran, isopropyl alcohol, propylene glycol, liquid petrolatum, ether, petroleum ether, alcohols, e.g., methanol, ethanol and higher alcohols, aromatics, e.g., benzene and toluene, alkanes, e.g., pentane, hexane and heptane, ketones, e.g., acetone and methyl ethyl ketone, chlorinated hydrocarbons, e.g., chloroform, carbon tetrachloride, methylene chloride and ethylene dichloride, acetates, e.g., ethyl acetate, oils, e.g., isopropyl myristate, diisopropyl adipate and mineral oil and the like and mixtures thereof.

The pharmaceutical formulation of the present invention may further comprise surfactants. Examples of such surfactants include, but are not limited to, methyl glucose sesquistearate, PEG-20 methyl glucoside sesquistearate, Steareth-21, polyethylene glycol 20 sorbitan monostearate, polyethylene glycol 60 sorbitan monostearate, polyethylene glycol 80 sorbitan monostearate, Steareth-20, Ceteth-20, PEG-100 stearate, sodium stearyl sarcosinate, hydrogenated lecithin, sodium cocoylglyceryl sulfate, sodium stearyl sulfate, sodium stearyl lactylate, PEG-20 glyceryl monostearate, sucrose monostearate, sucrose polystearates, polyglyceryl 10 stearate, polyglyceryl 10 myristate, steareth 10,

DEA oleth 3 phosphate, DEA oleth 10 phosphate, PPG-5 Ceteth 10 phosphate sodium salt, PPG-5 Ceteth 10 phosphate potassium salt, steareth-2, PEG-5 soya sterol oil, PEG-10 soya sterol oil, diethanolamine cetyl phosphate, sorbitan monostearate, diethyleneglycol monostearate, glyceryl monostearate, and the like and mixtures thereof.

The pharmaceutical formulation of the present invention may further comprise humectants. Examples of such humectants include, but are not limited to, propylene glycol, glycerin, butylene glycol, sorbitol, triacetin and the like and mixtures thereof.

It will be understood that various modifications may be made to the embodiments disclosed herein. Therefore the above description should not be construed as limiting, but merely as exemplifications of preferred embodiments. For example, the functions described above and implemented as the best mode for operating the present invention are for illustration purposes only. Other arrangements and methods may be implemented by those skilled in the art without departing from the scope and spirit of this invention.

The following examples are provided to enable one skilled in the art to practice the invention and are merely illustrative of the invention. The examples should not be read as limiting the scope of the invention.

EXAMPLES

EXAMPLES 1-2: Topical solution formulation comprising minoxidil and aminexil

Ingredients	Quantity (% w/v)	
	Example 1	Example 2
Propylene glycol	30	20
Purified water	15	10
Hydroxypropyl cellulose (Kulcel LF)	0.5	0.5
Minoxidil	5.0	2
Aminexil	1.5	1.5

Ethanol (v/v)	40	63
Fragrance GFL LQ43719	0.2	0.8

Manufacturing process:

1. Propylene glycol and purified water were heated to about 72°C to 75°C, and hydroxypropyl cellulose was added to it.
- 5 2. Minoxidil and aminexil were added to step 1 at 72°C to 75°C and stirred to dissolve completely.
3. The solution of step 2 was mixed for 15 minutes and allowed cooled to room temperature.
- 10 4. Alcohol and fragrance were added to the bulk of step 3 at about 35°C and mixed to get colorless to slight yellow colored topical solution.

EXAMPLE 3: Topical formulation comprising minoxidil and aminexil.

Ingredients	Quantity (% w/v)
Minoxidil	5.00%
Aminexil	1.50%
Disiloxane	38.00%
Trisiloxane	40.50%
Dimethiconol 40	10.00%
Cyclomethicone and dimethicone crosspolymer	5.00%

15 Manufacturing process:

1. Disiloxane and dimethiconol 40 were mixed in a vessel.
2. Minoxidil and aminexil were added to step 1 and mixed to dissolve completely.
- 20 3. Cyclomethicone and dimethicone crosspolymer was added to the bulk of step 2 and mixed.

4. Trisiloxane was added to the bulk of step 3 and mixed.

EXAMPLES 4-6: Minoxidil (2%) + Aminexil (1.5%) topical solution.

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Ingredients	Quantity (% w/v)		
	Example 4	Example 5	Example 6
Propylene glycol	20.00	30.00	30.00
Purified water	12.40	1.80	27.40
Hydroxypropyl cellulose	0.50	0.50	0.50
Minoxidil	2.00	2.00	2.00
Aminexil	1.50	1.50	1.50
Ethanol	53.46	53.46	33.94
Fragrance GFL LQ43719	0.80	0.80	0.80

Manufacturing process is same as that given for Examples 1-2.

EXAMPLE 7: Minoxidil (5%) + Aminexil (1.5%) topical solution.

Ingredients	Quantity (% w/v)
Propylene glycol	30.00
Purified water	25.60
Hydroxypropyl cellulose	0.50
Minoxidil	5.00
Aminexil	1.50
Ethanol	33.94
Fragrance GFL LQ43719	0.20

10

Manufacturing process is same as that given for Examples 1-2.

We claim:

1. A fixed dose topical pharmaceutical composition comprising:
 - a) a therapeutically effective amount of minoxidil or its salts;
 - 5 b) a therapeutically effective amount of aminexil or its salts; and
 - c) a pharmaceutically acceptable carrier.
2. A fixed dose topical pharmaceutical composition comprising:
 - a) a therapeutically effective amount of minoxidil or its salts;
 - b) a therapeutically effective amount of aminexil or its salts; and
 - 10 c) a bioadhesive polymer, comprising cellulose polymers.
3. A fixed dose topical pharmaceutical composition comprising:
 - a) a therapeutically effective amount of minoxidil or its salts;
 - b) a therapeutically effective amount of aminexil or its salts; and
 - c) a silicone oil.
- 15 4. The topical pharmaceutical composition according to any of the claims 1-3, wherein said composition is in the form of a solution, shampoo, ointment, cream, lotion, emulsion, dispersion, suspension or gel.
5. The topical pharmaceutical composition according to any of the claims 1-4, wherein minoxidil constitutes from about 1.0% w/v to about 6.0 % w/v, and
- 20 aminexil constitutes from about 1.0% w/v to about 3.0 % w/v of the total weight of the composition.
6. The topical pharmaceutical composition according to any of the claims 1-4, wherein minoxidil constitutes about 2.0% w/v to about 5.0 % w/v, and aminexil constitutes about 1.5 to about 2.0 % w/v of the total weight of the composition.
- 25 7. The topical pharmaceutical composition according to any of the claims 1-4, wherein the weight ratio of aminexil to minoxidil ranges from about 1:1 to about 1:6.
8. The topical pharmaceutical composition according to any of the claims 1-4, further comprising a solvent, elastomer, vehicle, ointment base, cream base,

emulsifier, preservative, buffer, emollient, humectant, surfactant, and transport enhancer, or mixtures thereof.

9. A topical fixed dose pharmaceutical composition comprising: about 2.0% w/v to about 5.0 % w/v of minoxidil, about 1.0% w/v to about 3.0 % w/v aminexil, about 0.1% w/v to about 2.0% w/v of hydroxypropyl cellulose, about 15.0% w/v to about 35.0 % w/v propylene glycol, about 30.0% w/v to about 60.0 % w/v ethanol, fragrance and purified water.

10. A topical fixed dose pharmaceutical composition comprising: about 2.0% w/v to about 5.0 % w/v of minoxidil, about 1.0% w/v to about 3.0 % w/v aminexil, about 35% w/v to about 45% w/v of disiloxane, about 35.0% w/v to about 45.0 % w/v trisiloxane, about 5.0% w/v to about 15.0 % w/v dimethiconol 40, and about 2.0% w/v to about 10.0 % w/v of silicone elastomer.

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