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(54) Title: METHOD OF REGULATING HAIR GROWTH USING METAL COMPLEXES OF OXIDIZED CARBOHYDRATES

(57) Abstract: A method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition comprising: (a) from about 0.001 % to about 99.9 %, by weight, of at least one metal complex of an oxidized carbohydrate, wherein the metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate; and (b) from about 0.1 % to about 99.999 %, by weight, of a vehicle.

METHOD OF REGULATING HAIR GROWTH USING METAL COMPLEXES OF OXIDIZED CARBOHYDRATES

TECHNICAL FIELD OF THE INVENTION

The present invention relates to a method of regulating hair growth comprising the administering, preferably topically, of compositions containing: (a) metal complexes of oxidized carbohydrates, but neither zinc gluconate nor manganese gluconate; and (b) a vehicle.

BACKGROUND OF THE INVENTION

The hair of a mammal has always been recognized as an important symbol of beauty, strength, vitality and fashion, whether it be a lion's mane, a dog's shiny coat, or a human's locks. The immense strength of the great Samson was reputedly drained as Delilah severed his hair. The Egyptian queen Cleopatra was known to immerse herself in luxuriant baths of milk and honey to revitalize her hair and skin. Upon the emergence of post-medieval English and French courts, those charged with administering the law were distinguished by wearing elaborate wigs.

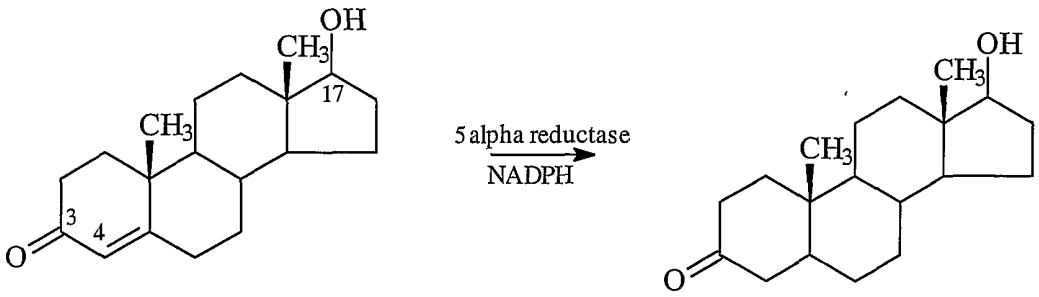
In contemporary times, the icon of an adult male lion with a brandishing mane is associated with pride, strength, and tradition. Prizes are awarded at shows for dogs having healthy, shiny coats. Humans are willing to invest much time and money to maintain their "do," for sundry reasons, including making a social or business appearance, "expressing" oneself, demonstrating political speech, being attractive, and being healthy. However, many do not enjoy a full amount of hair. Generally, the absence of hair from areas where it normally grows is referred to as "alopecia."

Because such importance has been placed on the quantity and quality of hair, as described above, those who suffer from some form of alopecia are often stigmatized. These men, women, and children often experience a self-consciousness related to their condition, and may feel an emotional trauma and lack of self-esteem. While perhaps issued in good humor, bald jokes manufactured by would-be comedians are sometimes received by the hair loss sufferer as injurious.

In most mammals, hair does not grow continuously, but rather, it undergoes a cycle of activity involving alternate periods of growth and rest. The hair growth cycle can typically be divided into three main stages, namely: (a) the growth phase known as anagen, during which the hair follicle penetrates deep into the dermis with the cells of the bulb dividing rapidly and differentiating to form the hair; (b) the transitional stage known as catagen, which is heralded by the cessation of mitosis, and during which the follicle regresses upwards through the dermis and hair growth ceases; and (c) the resting stage known as telogen, in which the regressed follicle contains a small secondary germ with an underlying ball of tightly packed dermal papilla cells. The initiation of a new anagen phase is revealed by rapid proliferation in the germ, expansion of the dermal papilla and elaboration of basement membrane components.

Alopecia may be initiated or aggravated by many factors or conditions. Alopecia may be hereditary, as in the case of male pattern baldness, or it may be due to disease, such as malnutrition, injury or insult, such as overdrying, bleaching, coloring, overbrushing, or treatment, such as chemotherapy, or it may occur in old age, or it may be due to physical, psychological or emotional stress, or still yet, it may be caused by hormonal imbalance, particularly during the advent of menopause. The rate of hair growth may decrease, the rate of hair loss may increase, or the structure, including thickness of the hair may be altered. Also, hair may fall out gradually, or in patches.

It is believed that androgenetic alopecia (commonly known as "male pattern baldness" or "female pattern baldness") is the result of hyperandrogenic stimulation caused by excessive accumulation of testosterone or similar androgenic hormones in the metabolic system. A principal mediator of androgenic activity is dihydrotestosterone (DHT), formed locally in the target area by the action of 5-α-reductase. Inhibitors of this enzyme will serve to diminish symptoms of hyperandrogenic stimulation in these target areas. The enzyme 5-α-reductase catalyzes the reduction of testosterone to the more potent androgen, DHT, as shown below:



testosterone DHT

Another mechanism believed to contribute to alopecia is inflammation of the hair follicle. During the inflammatory process, cytokines (e.g. interleukin-1-α, interleukin-1-β, and tumor necrosis factor) are released that have been demonstrated to inhibit hair growth. Antibodies produced by the immune system may also play a role in inhibiting hair growth. Accordingly, agents which inhibit inflammation, i.e. anti-inflammatories, may be used to regulate hair growth. Also, compounds that inhibit the immune system's ability to attach leukocytes to the follicle may be useful in regulating hair growth.

In response to consumer interest in combating alopecia, many products and methods have been advertised as being capable of providing benefits ranging from cosmetic masking of alopecia to "curing" hair loss. There are many internet websites which are dedicated to providing information on alopecia, which enable the purchase of products that are believed to combat alopecia, or which at least provides hyperlinks to other websites of these types. Various regimens are available for combating alopecia: (a) topical treatments for growing hair or for retarding the loss of hair (such as ROGAINE (RTM), available from Pharmacia & Upjohn); (b) oral treatments for growing hair or for retarding the loss of hair (such as PROPECIA (RTM), available from Merck Pharmaceuticals); (c) shampoos for making hair appear thicker and fuller (such as COUVRE (TM) Thickening Shampoo, available from Spencer Forrest, Inc.); (d) hair loss concealers for creating a cosmetic appearance that hair is not as thin as it really is (such as PROTHIK (TM) Spray, available from Aquila); (e) artificial hairpieces (such as toupees or weaves); (f) and surgical transplanting. While these regimens may partially address alopecia for certain individuals, they have various limitations.

For instance, not all people respond to ROGAINE (RTM) (active ingredient is minoxidil (6-(1-piperidinyl)-2,4-pyrimidinediamine 3-oxide)) (see U.S. Pat. Nos. 3,461,461; 3,973,061; 3,464,987; and 4,139,619), and the efficacy level is limited in those who do exhibit a response. Many people find ROGAINE (RTM) to be expensive, and its side effects include itching, scaling and scalp irritation. Thickening shampoos and concealers do not actually increase hair growth or retard hair loss. Rather, these regimens merely cosmetically mask hair loss, oftentimes by coloring the scalp to reduce the contrast between hair and scalp. Many products of this type are ineffective in providing a natural look, may be difficult to remove, and may run or dilute when exposed to moisture. Artificial hair pieces may come unattached causing an embarrassing moment, and oftentimes fail to provide a natural look. Surgical transplanting of "hair plugs," vulgarly known as "sodding," may be very time consuming, expensive, painful, and during the period after the surgery may appear unattractive. Recently, there has been an explosion of new products on the market which claim to be inexpensive, all-natural, and are supported by one or two testimonials of persons who believe to have seen an increase in hair growth. Such products are usually comprised of plant extracts, vitamins, amino acids, plant proteins, herbs, plant oils, and berries. Many of these products are speculative and have yet to be proven clinically.

PROPECIA (RTM) (finasteride) is a synthetic 4-azasteroid compound, that is a specific inhibitor of steroid Type II 5-α-reductase, an intracellular enzyme that converts the androgen testosterone into 5-α-dihydrotestosterone (DHT). A reduction in DHT level is believed to correlate to a reduction in alopecia. Finasteride is 4-azaandrost-1-ene-17-carboxamide,N-(1,1-dimethylethyl)-3-oxo-,(5α,17β)-, (see U.S. Pat. No. 5,670,643; EP 823,436; WO 97/15558; and WO 97/15564). There are a limited number of people which respond to PROPECIA (RTM), and its efficacy level is limited in those who exhibit a response. Also, many people find PROPECIA (RTM) to be expensive. It is for use by men only, and due to the severe risk of teratogenic effects, the manufacturer warns that women who are or who may potentially be pregnant should not even handle broken pills. The manufacturer also reports that in clinical studies a small number of men experienced certain sexual side effects.

Accordingly, there exists a need for a method for regulating the growth of hair which appeals to a larger number of consumers, at a reasonable price, which provides good results, with few, if any, undesirable side effects. Applicants have found, surprisingly, that by applying compositions containing certain metal complexes of oxidized carbohydrates, the growth of hair in mammals

can be regulated, and as such, alopecia can be combated. It is believed that zinc and other metals may regulate hair growth by (a) inhibiting activity of 5-α-reductase which converts testosterone to DHT, and (b) inhibiting DHT binding to the androgen receptor in the cytosol. Zinc and other metals may also have an anti-inflammatory effect on hair follicles, which is believed to correlate to a reduction in alopecia. Applicants have discovered that certain metal complexes of oxidized carbohydrates can (a) disrupt DHT activity; and/or (b) stimulate the transition of follicles from the resting telogen phase into the active anagen phase and/or from earlier anagen phase to later anagen phase; and/or (c) retard the transition of follicles from anagen phase to catagen phase; and/or (d) may also have an anti-inflammatory effect on hair follicles.

SUMMARY OF THE INVENTION

The present invention relates to a method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition comprising: (a) from about 0.001% to about 99.9%, by weight, of at least one metal complex of an oxidized carbohydrate, wherein the metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate; and (b) from about 0.1% to about 99.999%, by weight, of a vehicle.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a method for regulating the growth of hair. Particularly, these compositions comprise (a) at least one metal complex of an oxidized carbohydrate, but neither zinc gluconate nor manganese gluconate; and (b) a vehicle. These compositions, when applied to a mammal, may disrupt DHT activity, stimulate the transition of follicles from the resting telogen phase into the active anagen phase, and may, in some cases, also have an anti-inflammatory effect. These characteristics are important to regulating the growth of hair.

Such compositions of the present invention can comprise, consist of, or consist essentially of the essential elements and limitations of the invention described herein, as well as any of the additional or optional ingredients, components or limitations described herein. The components of the compositions of the present invention, including those which may optionally be added, as well as methods for preparation, and methods for use thereof, are described in detail below.

As used herein the term "hair" is meant to encompass all mammalian hair. Preferably, the hair is that of a human, however, animal hair, such as dog hair and cat hair are suitable. While the hair

whose growth is to be regulated is typically located upon the head, it is contemplated that the inventive method and compositions described herein may be applied to hair located anywhere on the body, including, eyebrows, mustaches, beards, the pubic area, and anywhere else the consumer prefers.

As used herein, the terms "regulating hair growth," "hair growth regulation," and "regulating the growth of hair," are meant to include: stimulating hair growth; stimulating hair thickening; preventing, reducing, arresting and/or retarding the loss of hair; preventing, reducing, arresting and/or retarding the thinning of hair; increasing the rate of hair growth; inducing the formation of a greater number of hair strands; increasing the diameter of the hair strand; lengthening the hair strand; changing the hair follicle from vellus follicle to terminal follicle; inducing the formation of vellus follicles; converting follicles from telogen to anagen phase (thereby increasing the overall ratio of anagen phase follicles relative to telogen phase follicles); advancing a follicle from an earlier stage of anagen to a later stage of anagen; reducing the conversion from anagen to catagen phase; treating alopecia; and any combination thereof.

As used herein, the term "vellus follicle" means a hair follicle which produces a soft, short, and often colorless hair fiber. The size of the vellus follicle is considerably smaller than the terminal hair follicle. In an adult, vellus follicles can be found on the forehead (i.e., receding hair line area) and bald scalp.

As used herein, the term "terminal follicle" means a hair follicle which produces a coarse, long and often pigmented hair shaft. The size of the terminal follicle is considerably larger and thicker in diameter and longer than the vellus follicle. In an adult, terminal follicles can be found on the scalp, axilla and pubic areas.

As used herein, "anagen phase" refers to the period in the hair follicle growth cycle wherein the follicle is actively growing and producing new hair.

As used herein, "telogen phase" refers to the period in the hair growth cycle wherein the follicle is resting and not producing new hair.

As used herein, the term "oxidized carbohydrate" is meant to be inclusive of acids derived from carbohydrates. The adjective "oxidized" is meant to be inclusive of mono-, di-, and poly-oxidized. The term "carbohydrate" is meant to be inclusive of mono-, di-, oligo-, and poly-saccharides.

The term "safe and effective amount" as used herein, means an amount of an active ingredient high enough to modify the condition to be treated or to deliver the desired hair growth regulation benefit, but low enough to avoid serious side effects, at a reasonable benefit to risk ratio within the scope of sound medical judgment. What is a safe and effective amount of the active ingredient will vary with the specific active, the ability of the active to penetrate through the skin, hair, or relevant tissue of the digestive tract, the age, health condition, and skin, hair or digestive condition of the user, and other like factors.

I. Components

The method of the present invention utilizes compositions which comprise at least one metal complex of an oxidized carbohydrate and a vehicle. Such compositions can be administered topically, orally or parenterally, preferably topically. Such compositions can be in any form which delivers a sufficient amount of the metal complex of an oxidized carbohydrate to effectively regulate hair growth. Such forms include, but are not limited to tablets, capsules, caplets, creams, gels, hydrogels, lotions, shampoos, rinses, tonics, sprays, ointments, mousses or pomade.

The ingredients comprising the compositions herein, as well as other optional components, are described in detail as follows. As is known in the art, many cosmetic ingredients have multiple functions in formulations and therefore may be included in several functional groupings. Accordingly, it should be understood that although the active ingredients useful herein are categorized by their therapeutic benefit or their postulated mode of action, some such ingredients can in some instances provide more than one cosmetic and/or therapeutic benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit the active ingredient to that particular application or applications listed. Also, where not stated otherwise, cosmetically and pharmaceutically acceptable salts of these active ingredients are useful herein.

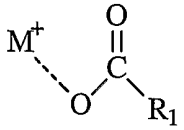
It is to be understood that the percentage weights of the composition components herein are expressed in terms of the total composition, and includes the composition in the form of intended use.

A. Metal complex of an oxidized carbohydrate

The method of the present invention utilizes compositions which comprise as an essential component, at least one metal complex of an oxidized carbohydrate in an amount which is sufficiently effective to regulate hair growth, wherein the at least one metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate. As described below, however, zinc gluconate and manganese gluconate may optionally be included as additional ingredients. Typically an amount effective to regulate hair growth will range from about 0.001% to about 99.9%, by weight of the composition, preferably from about 0.001% to about 75%, more preferably from about 0.001% to about 50%, more preferably from about 0.001% to about 25%, more preferably from about 0.001% to about 15%.

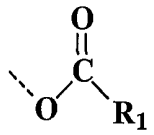
The metal complexes of oxidized carbohydrates are believed to: (a) disrupt DHT activity; and/or (b) stimulate the transition of follicles from the resting telogen phase into the active anagen phase and/or from earlier anagen phase to later anagen phase; and/or (c) retard the transition of follicles from anagen phase to catagen phase; and/or (d) may also have an anti-inflammatory effect on hair follicles. These characteristics are important to regulating hair growth.

The metal complexes of oxidized carbohydrates, are the result of an equilibrium reached between metal ions, and deprotonated carboxylic acids of carbohydrates, as shown, without regard to stereochemistry, in formulae (I) and (II), below. This equilibrium may be achieved during or before, preferably before, administration of the composition according to the method described herein.

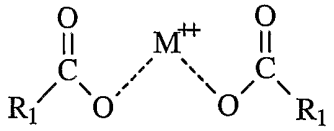


(I)

wherein **M** is a monovalent metal ion, and

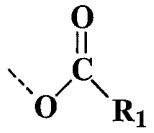


is an oxidized carbohydrate, $\mathbf{R_1}$ being the remainder of the carbohydrate moiety;



(II)

wherein **M** is a bivalent metal ion, and



is an oxidized carbohydrate, $\mathbf{R_1}$ being the remainder of the carbohydrate moiety;

The metal complex of an oxidized carbohydrate component of the compositions herein may be prepared by any suitable means. For example: metal-salt + carboxylic acid of carbohydrate yields metal complex of an oxidized carbohydrate and the conjugate acid of the metal's counter ion. The pH of the resulting product may be adjusted using any suitable pH adjuster. A non-limiting example of this preparation is: zinc sulfate + lactobionic acid yields zinc lactobionate and sulphuric acid, with the pH being adjusted to the desired level with sodium hydroxide. Other non-limiting examples may be constructed using the metals, salts, oxidized carbohydrates, and pH adjusters described as suitable in the disclosure herein. Typically, from about 0.5% to about 50%, preferably about 1% to about 25%, more preferably from about 3% to about 10%, of metal-salt will be added to typically about 0.5% to about 50%, preferably from about 1% to about 30%, more preferably from about 5% to about 25%, of carboxylic acid.

Suitable salts for use herein include, but are not limited to: the chlorides, sulfates, acetates, or oxides of sodium, lithium, potassium, silver, gold, zinc, copper, nickel, iron, chromium, calcium, magnesium, molybdenum, manganese, cobalt, palladium, platinum, and tin. Non-limiting examples of preferred salts are zinc sulfate, zinc acetate, zinc oxide, cupric chloride, cupric sulfate, cupric acetate, and copper oxide.

1. **Monovalent metal**

The metal complex of an oxidized carbohydrate component of the compositions herein comprises metals. Such metals may be in an oxidation state or valence of 1^+. Monovalent metals which are suitable for use herein include: lithium; silver; gold; sodium; and mixtures thereof. Preferred metals are sodium and lithium.

2. **Bivalent metal**

The metal complex of an oxidized carbohydrate component of the compositions herein comprises metals. Such metals may preferably be in an oxidation state or valence of 2^+. Bivalent metals which are suitable for use herein include: zinc, copper, nickel, iron, chromium, calcium, magnesium, molybdenum, manganese, cobalt, palladium, platinum, tin, and mixtures thereof. Preferred metals include: zinc, copper, and mixtures thereof.

3. **Oxidized carbohydrate**

The metal complex of an oxidized carbohydrate component of the compositions herein comprise oxidized carbohydrates. The oxidized carbohydrates may be used either in the dextro-rotary (D) or the levo-rotary (L) form. They may be substituted or un-substituted. When substituted, the oxidized carbohydrates useful herein may be amino-substituted, amido-substituted, phospho-substituted, or any mixture thereof. As described below, oxidized carbohydrates which are sulpho-substituted may optionally be included as additional ingredients.

The oxidized carbohydrates for use herein include substituted or un-substituted monosaccharides, disaccharides, oligosaccharides, polysaccharides, and mixtures thereof. Suitable oxidized carbohydrates for use herein include, but are not limited to: oxidized aldoses, oxidized ketoses, oxidized trioses, oxidized tetroses, oxidized pentoses, oxidized hexoses, and mixtures thereof.

Specific examples of oxidized monosaccharides for use herein include, but are not limited to: ribonic acid, ribulonic acid, arabinonic acid, xylonic acid, xylulonic acid, lyxonic acid, allonic acid, altronic acid, gluconic acid, mannonic acid, gulonic acid, idonic acid, galactonic acid, talonic acid, glucoheptonic acid, psiconic acid, fructonic acid, sorbonic acid, tagatonic acid, and mixtures thereof.

Specific examples of oxidized disaccharides for use herein include, but are not limited to: lactobionic acid, maltobionic acid, isomaltobionic acid, cellobionic acid, and mixtures thereof.

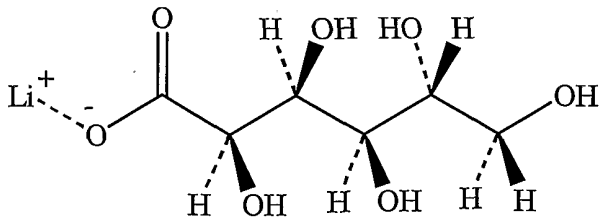
Specific examples of oxidized oligosaccharides for use herein include, but are not limited to: oxidized malto-oligosaccharide, oxidized cello-oligosaccharide, and mixtures thereof.

Specific examples of oxidized polysaccharides for use herein include, but are not limited to: oxidized cellulose; chitin; gum arabic; gum karaya; gum xanthan; oxidized gum guar; oxidized locust bean gum; oxidized agars; oxidized algins; oxidized gellan gum; and mixtures thereof.

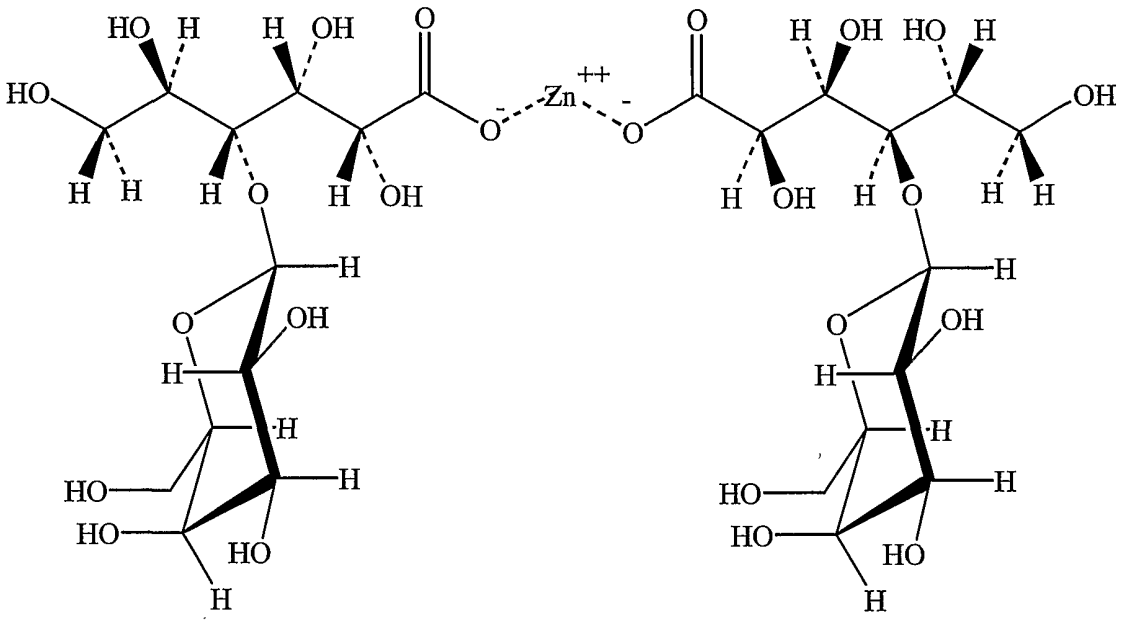
4. Preferred metal complexes of oxidized carbohydrates

Specific examples of preferred metal complexes of oxidized carbohydrates for use herein include, but are not limited to: lithium gluconate; copper gluconate; zinc galactonate; copper galactonate; zinc glucuronate; copper glucuronate; zinc galacturonate; copper galacturonate; zinc glucarate; copper glucarate; zinc galactarate; copper galactarate; zinc glucoheptonate; copper glucoheptonate; lithium lactobionate; sodium lactobionate; zinc lactobionate; copper lactobionate; lithium maltobionate; zinc maltobionate; copper maltobionate; lithium cellobionate; zinc cellobionate; copper cellobionate; and zinc alginate. Preferred are lithium lactobionate; sodium lactobionate; zinc lactobionate; copper lactobionate; lithium maltobionate; zinc maltobionate; copper maltobionate; lithium cellobionate; zinc cellobionate; and copper cellobionate. Highly preferred is zinc lactobionate. As described below, zinc gluconate and manganese gluconate are preferred metal complexes of oxidized carbohydrates for use as additional optional ingredients.

Lithium gluconate can be represented by the following structure:



Zinc lactobionate can be represented by the following structure:



5. **Solubility of metal complexes of oxidized carbohydrates**

While not being limited by theory, it is believed that there may be a positively proportional relationship between the solubility in water of metal complexes of oxidized carbohydrates and their hair growth regulation efficacy, i.e. the greater the solubility in water, the greater the efficacy. Further, it is believed that metal complexes of oxidized polysaccharides have a greater solubility in water than metal complexes of oxidized disaccharides, which are believed to have a greater solubility in water than metal complexes of monosaccharides. Typically the metal complexes of oxidized carbohydrates of the present invention, will have a solubility, at ambient conditions, in water of at least about 5%, by weight, preferably at least about 10%, more preferably at least about 40%, more preferably at least about 50%, more preferably at least about 60%. As used herein, the "solubility" of a solute is a quantity that will dissolve in a given amount of solvent.

B. Vehicle

The method of the present invention utilizes compositions which comprise as an essential component, a vehicle for the metal complex of an oxidized carbohydrate, in an amount sufficient to carry an effective amount of at least one metal complex of an oxidized carbohydrate onto or into the body in an amount which is sufficiently effective to regulate hair growth. Typically such amount will range from about 0.1% to about 99.999%, by weight of the composition, preferably

from about 25% to about 99.99%, more preferably from about 50% to about 99.9%, more preferably from about 75% to about 99%, more preferably from about 85% to about 99%.

The vehicle can comprise a solid, semi-solid or liquid cosmetically and/or physiologically acceptable vehicle, to enable the metal complex of an oxidized carbohydrate to be conveyed to the skin at an appropriate concentration. As used herein, "pharmaceutically-acceptable" means that drugs, medications or inert ingredients which the term describes are suitable for use in humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response, and the like. As used herein, "cosmetically acceptable" means that ingredients which the term describes are suitable for use in contact with the skin or hair of humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response and the like.

The nature of the vehicle will depend upon the method chosen for administration of the composition. The vehicle can itself be inert or it can possess cosmetic or pharmaceutical benefits of its own. When the compositions are to be applied topically, such vehicles will act as diluents, dispersants, or solvents for the metal complex of an oxidized carbohydrates, which therefore ensure that they can be applied to and distributed evenly over the hair and/or scalp at an appropriate concentration. The vehicle will preferably be one which can aid penetration of the metal complex of an oxidized carbohydrates into the skin to reach the immediate environment of the hair bulb. For all types of application, such vehicles should be physically and chemically compatible with the essential components described herein, and should not otherwise unduly impair product stability, aesthetics or performance. Vehicles suitable for use herein alone or in combination include: solvents; thickeners; propellants; powders; fillers; plasticizers; lubricants; and emollients and humectants.

1. Solvents

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, solvents. Generally, solvents suitable for use in the compositions herein are either water or are selected to be miscible with water and innocuous to the skin. Solvents suitable for use herein include, but are not limited to: water; C_1 to C_{20} mono- or poly-hydric alcohols and their ethers, preferred are C_2 to C_3 mono- and di- hydric alcohols, particularly ethanol, isopropanol, *n*-propanol, and butanol; propylene glycol; ethylene glycol monoethyl

ether; glycerine; methylene chloride; diethylene glycol monobutyl ether; diethylene glycol monoethyl ether; dimethyl sulphoxide; dimethyl formamide; tetrahydrofuran; propylene glycol; and mixtures thereof. Preferred solvents for use herein include: water, ethanol, isopropanol, propylene glycol, and mixtures thereof. When the solvent includes propylene glycol, it will typically contain it at a level of at least about 5%, by weight, preferably at least about 8%, more preferably at least about 10%, and typically the level will range from about 5% to about 20%, preferably from about 8% to about 15%, more preferably from about 10% to about 15%. It is believed that the presence of at least about 5% propylene glycol may improve penetration, and thereby, efficacy, of the metal-oxidized carbohydrate complex. When topically applied, propylene glycol's presence may also improve the appearance and/or the feel of the composition, on skin after drying.

2. Thickeners

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, thickening agents. Typically, such thickening agents when present, will be present at a level of from about 0.05% to about 20%, by weight of the composition, preferably from about 0.1% to about 10%, more preferably from about 0.5% to about 5%. It should be understood that under certain circumstances the thickening function may be accomplished by a material also serving as a silicone or emollient. For instance, silicone gums in excess of 10 centistokes and esters such as glycerol stearate impart this dual functionality.

Thickening agents suitable for use in the compositions herein include, but are not limited to: oleic acid; cetyl alcohol; oleyl alcohol; sodium chloride; cetearyl alcohol; stearyl alcohol; synthetic thickeners such as those available under the tradenames ACULYN (RTM) and SALCARE (RTM) and ELFACOS (RTM), and those cross-linked polyacrylate materials available under the trademark Carbopol (RTM) from the B. F. Goodrich Company; and mixtures thereof. Some particular thickeners for use herein are ACULYN (RTM) 22 steareth-20 methacrylate copolymer, ACULYN (RTM) 33 anionic acrylic copolymer, ACULYN (RTM) 44 polyurethane resin, and ACULYN (RTM) 46 hydrophobically modified nonionic polyol and others, which are available from ISP (International Specialty Products). Also suitable are the SALCARE (RTM) series of thickeners (SC80, 81, 91, 92, 95, 96 AST) available from Ciba Specialty Chemicals. Also suitable are the series of thickeners available from Akzo Nobel such as ELFACOS (RTM) GT 282S ceteareth-60 myristyl glycol, ELFACOS (RTM) GT 282 L ceteareth-60 myristyl glycol,

ELFACOS (RTM) T211 PPG 14 Laureth-60 Isophoryl dicarbamate, and ELFACOS (RTM) T212 PPG-14 Palmeth-60 Hexyl Dicarbamate. Additional thickening agents suitable for use herein include: sodium alginate; gum arabic; cellulose derivatives, such as ethylcellulose, methylcellulose, hydroxypropyl cellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose, or the sodium salt of carboxymethylcellulose; acrylic polymers, such as carboxyvinyl polymer; acrylic resins, such as EUDRAGIT (RTM) RL30D, available from Rohm Pharma GmbH Weiderstadt, West Germany; polyvinylpyrrolidone or other commercially available film-coating preparations, such as DRI-KLEAR (RTM), available form Crompton & Knowles Corp., Mahwah, New Jersey, USA, or OPADRY (RTM), available from Colorcon, West Point, Pennsylvania, USA. Also suitable for use herein as thickening agents are: gums, such as xanthan gum, guar gum, locust bean gum; carrageenan; gelatin; karaya; pectin; Biopolymer PS 87; clays, such as hectorites and bentonites; and mixtures thereof.

Additional thickeners suitable for use herein are those disclosed in: WO 99/37,047 (nonionic polyurethanes and/or cationic polymers); EP 0,875,237A2 (hydrophobically modified nonionic polyols and polyethoxylated urethane); WO 99/36,047 (polyurethane polymers and/or cationic conditioning agents); WO 98/03,150 (nonionic amphophilic polymers having at least one fatty chain); and U.S. Pat. No. 5,281,654 (mixture of polyurethanes), all of which descriptions are incorporated herein by reference.

3. Propellants

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, propellants. Propellants suitable for use herein include, but are not limited to: propane; butane; isobutane; dimethyl ether; carbon dioxide; nitrogen; nitrous oxide; and mixtures thereof.

4. Powders

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, powders. Powders suitable for use herein include, but are not limited to: chalk; talc; fullers earth; kaolin; starch; gums; colloidal silicon dioxide; sodium polyacrylate; tetra alkyl and/or trialkyl aryl ammonium smectites; chemically modified magnesium aluminum silicate; organically modified montmorillonite clay; hydrated aluminum silicate; fumed silica; TiO_2 and TiO_2-coated mica, and mixtures thereof.

5. Fillers

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, fillers. Fillers suitable for use herein include, but are not limited to: lactose, sucrose, maltodextrin, mannitol, starch, dicalcium phosphate and microcrystalline cellulose.

6. Plasticizers

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, plasticizers. Plasticizers suitable for use herein include, but are not limited to: polyethylene glycol; propylene glycol; dibutyl phthalate; castor oil; acetylated monoglycerides; triacetin; and mixtures thereof.

7. Lubricants

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, lubricants. Lubricants suitable for use herein include, but are not limited to: magnesium stearate; stearic acid; talc; and mixtures thereof.

8. Emollients and Humectants

The vehicle of the compositions of the present invention can comprise alone or in combination with other vehicle ingredients, emollients and humectants. Some emollients and humectants which are useful as being all or part of the vehicle herein include, but are not limited to: esters; fatty alcohols and acids; polyols; hydrocarbons; non-volatile silicones; waxes; animal fats; vegetable oils; and mixtures thereof.

One class of emollients and humectants suitable for use herein are esters, such class includes: C1-C30 alcohol esters of C1-C30 carboxylic acids and of C2-C30 dicarboxylic acids, including straight and branched chain materials as well as aromatic derivatives can also be used herein. Also useful herein are esters such as monoglycerides of C1-C30 carboxylic acids, diglycerides of C1-C30 carboxylic acids, triglycerides of C1-C30 carboxylic acids, ethylene glycol monoesters of C1-C30 carboxylic acids, ethylene glycol diesters of C1-C30 carboxylic acids, propylene glycol monoesters of C1-C30 carboxylic acids, and propylene glycol diesters of C1-C30 carboxylic

acids. Straight chain, branched chain and aryl carboxylic acids are included herein. Also useful are propoxylated and ethoxylated derivatives of these materials.

Non-limiting examples of esters useful herein include, but are not limited to: diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl palmitate, myristyl propionate, ethylene glycol distearate, 2-ethylhexyl palmitate, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl palmitate, myristyl myristate, stearyl stearate, cetyl stearate, behenyl behenrate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate, diisopropyl dilinoleate, caprylic/capric triglyceride, PEG-6 caprylic/capric triglyceride, PEG-8 caprylic/capric triglyceride, and mixtures thereof.

Also useful herein are various C1-C30 monoesters and polyesters of sugars and related materials. These esters are derived from a sugar or polyol moiety and one or more carboxylic acid moieties. Depending on the constituent acid and sugar, these esters can be in either liquid or solid form at room temperature. Examples of liquid esters include, but are not limited to: glucose tetraoleate, the glucose tetraesters of soybean oil fatty acids (unsaturated), the mannose tetraesters of mixed soybean oil fatty acids, the galactose tetraesters of oleic acid, the arabinose tetraesters of linoleic acid, xylose tetralinoleate, galactose pentaoleate, sorbitol tetraoleate, the sorbitol hexaesters of unsaturated soybean oil fatty acids, xylitol pentaoleate, sucrose tetraoleate, sucrose pentaoletate, sucrose hexaoleate, sucrose hepatoleate, sucrose octaoleate, and mixtures thereof. Examples of solid esters include, but are not limited to: sorbitol hexaester in which the carboxylic acid ester moieties are palmitoleate and arachidate in a 1:2 molar ratio; the octaester of raffinose in which the carboxylic acid ester moieties are linoleate and behenate in a 1:3 molar ratio; the heptaester of maltose wherein the esterifying carboxylic acid moieties are sunflower seed oil fatty acids and lignocerate in a 3:4 molar ratio; the octaester of sucrose wherein the esterifying carboxylic acid moieties are oleate and behenate in a 2:6 molar ratio; and the octaester of sucrose wherein the esterifying carboxylic acid moieties are laurate, linoleate and behenate in a 1:3:4 molar ratio. A preferred solid material is sucrose polyester in which the degree of esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-unsaturated and behenic, in a molar ratio of unsaturates:behenic of 1:7 to 3:5. A particularly preferred solid sugar polyester is the octaester of sucrose in which there are about 7 behenic fatty acid moieties and about 1 oleic acid moiety in the molecule. Other materials include cottonseed oil or soybean oil fatty acid esters of sucrose. The ester materials are further described in, U.S. Patent No. 2,831,854, U.S. Patent No.

4,005,196, to Jandacek, issued January 25, 1977; U.S. Patent No. 4,005,195, to Jandacek, issued January 25, 1977, U.S. Patent No. 5,306,516, to Letton et al., issued April 26, 1994; U.S. Patent No. 5,306,515, to Letton et al., issued April 26, 1994; U.S. Patent No. 5,305,514, to Letton et al., issued April 26, 1994; U.S. Patent No. 4,797,300, to Jandacek et al., issued January 10, 1989; U.S. Patent No. 3,963,699, to Rizzi et al, issued June 15, 1976; U.S. Patent No. 4,518,772, to Volpenhein, issued May 21, 1985; and U.S. Patent No. 4,517,360, to Volpenhein, issued May 21, 1985; all of which are incorporated by reference herein in their entirety.

Suitable fatty alcohols and acids for use herein include, but are not limited to those compounds having from 10 to 20 carbon atoms. Preferred are such compounds as cetyl, myristyl, palmitic and stearyl alcohols and acids.

Among the polyols which may comprise all or part of the vehicle herein are linear and branched chain alkyl polyhydroxyl compounds. Preferred polyols include propylene glycol, sugars having up to about 12 carbons atoms, sugar alcohols having up to about 12 carbon atoms, and mixtures thereof, glycerin, polypropylene glycols, polyethylene glycols, ethyl hexane diol, hexylene glycols, and mixtures thereof.

Specific examples of polyols useful herein include, but are not limited to: materials such as sucrose, fructose, glucose, eruthrose, erythritol, sorbitol, mannitol, glycerol, hexanetriol, propylene glycol, butylene glycol, hexylene glycol, and the like; polyethylene glycols such as PEG-2, PEG-3, PEG-30, PEG-50, polypropylene glycols such as PPG-9, PPG-12, PPG-15, PPG-17, PPG-20, PPG-26, PPG-30, PPG-34; alkoxylated glucose; hyaluronic acid; and mixtures thereof.

Also useful are materials such as: urea; guanidine; glycolic acid and glycolate salts (e.g. ammonium and quaternary alkyl ammonium); lactic acid and lactate salts (e.g. ammonium and quaternary alkyl ammonium); cholesterol; and mixtures thereof.

Also useful are materials such as aloe vera in any of its variety of forms (e.g., aloe vera gel), chitin, starch-grafted sodium polyacrylates such as SANWET (RTM) IM-1000, IM-1500, and IM-2500 (available from Celanese Superabsorbent Materials, Portsmouth, Virginia, USA); lactamide monoethanolamine; acetamide monoethanolamine; and mixtures thereof. Also useful

are propoxylated glycerols described in U.S. Patent No. 4,976,953, to Orr et al., issued December 11, 1990, which is incorporated by reference herein in its entirety.

Suitable hydrocarbons for use in the vehicle herein are straight and branched chain hydrocarbons having from 7 to 40 carbon atoms. Non-limiting examples include mineral oil, petrolatum, squalene, isoparaffins. dodecane, isododecane, hydrogenated polyisobutylene, docosane (i.e. a C_{22} hydrocarbon), hexadecane, isohexadecane (a commercially available hydrocarbon sold as PERMETHYL (RTM) 101A by Presperse, South Plainfield, New Jersey, USA).

Mineral oil, which is also known as petrolatum liquid, is a mixture of liquid hydrocarbons obtained from petroleum. See The Merck Index, Tenth Edition, Entry 7048, p. 1033 (1983) and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p.415-417 (1993), which are incorporated by reference herein in their entirety.

Petrolatum, which is also known as petroleum jelly, is a colloidal system of non-straight-chain solid hydrocarbons and high-boiling liquid hydrocarbons, in which most of the liquid hydrocarbons are held inside the micelles. See The Merck Index, Tenth Edition, Entry 7047, p. 1033 (1983); Schindler, Drug. Cosmet. Ind., vol. 89, 36-37, 76, 78-80, 82 (1961); and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p. 537 (1993), which are incorporated by reference herein in their entirety.

Non-volatile silicones such as polydialkylsiloxanes, polydiarylsiloxanes, and polyalkarylsiloxanes are also useful herein. These silicones are disclosed in U.S. Patent No. 5,069,897, to Orr, issued December 3, 1991, which is incorporated by reference herein in its entirety. The polyalkylsiloxanes correspond to the general chemical formula $R_3SiO[R_2SiO]_xSiR_3$ wherein **R** is an alkyl group (preferably **R** is methyl or ethyl, more preferably methyl) and **x** is an integer up to about 500, chosen to achieve the desired molecular weight. Commercially available polyalkylsiloxanes include the polydimethylsiloxanes, which are also known as dimethicones, non-limiting examples of which include the VISCASIL (RTM) series sold by General Electric Company and the DOW CORNING (RTM) 200 series sold by Dow Corning Corporation. Specific examples of polydimethylsiloxanes useful herein include DOW CORNING (RTM) 225 fluid having a viscosity of 10 centistokes and a boiling point greater than 200°C, and DOW CORNING (RTM) 200 fluids having viscosities of 50, 350, and 12,500 centistokes, respectively,

and boiling points greater than 200°C. Also useful are materials such as trimethylsiloxysilicate, which is a polymeric material corresponding to the general chemical formula $[(CH_2)_3SiO_{0.5}]_x[SiO_2]_y$, wherein **x** is an integer from about 1 to about 500 and **y** is an integer from about 1 to about 500. A commercially available trimethylsiloxysilicate is sold as a mixture with dimethicone as DOW CORNING (RTM) 593 fluid. Also useful herein are dimethiconols, which are hydroxy terminated dimethyl silicones. These materials can be represented by the general chemical formulas $R_3SiO[R_2SiO]_xSiR_2OH$ and $HOR_2SiO[R_2SiO]_xSiR_2OH$ wherein **R** is an alkyl group (preferably **R** is methyl or ethyl, more preferably methyl) and **x** is an integer up to about 500, chosen to achieve the desired molecular weight. Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. DOW CORNING (RTM) 1401, 1402, and 1403 fluids). Also useful herein are polyalkylaryl siloxanes, with polymethylphenyl siloxanes having viscosities from about 15 to about 65 centistokes at 25°C being preferred. These materials are available, for example, as SF 1075 methylphenyl fluid (sold by General Electric Company) and 556 Cosmetic Grade phenyl trimethicone fluid (sold by Dow Corning Corporation).

Waxes which are useful in being all or part of the vehicle in the compositions herein include those set forth in CTFA Cosmetic Ingredient Handbook, Second Edition, 1992, pp. 535, which is herein incorporated by reference. Specific examples include beeswax, carnauba, candelilla wax, jojoba wax, lanolin wax, ozokerite, paraffin wax, and mixtures thereof.

Animal fats, vegetable oils and hydrogenated vegetable oils, and vegetable oil adducts are also potentially useful herein as all or part of the vehicle.

Examples of vegetable oils and hydrogenated vegetable oils include, but are not limited to: safflower oil, castor oil, coconut oil, cottonseed oil, menhaden oil, palm kernel oil, palm oil, peanut oil, soybean oil, rapeseed oil, linseed oil, rice bran oil, pine oil, sesame oil, sunflower seed oil, hydrogenated safflower oil, hydrogenated castor oil, hydrogenated coconut oil, hydrogenated cottonseed oil, hydrogenated menhaden oil, hydrogenated palm kernel oil, hydrogenated palm oil, hydrogenated peanut oil, hydrogenated soybean oil, hydrogenated rapeseed oil, hydrogenated linseed oil, hydrogenated rice bran oil, hydrogenated sesame oil, hydrogenated sunflower seed oil, and mixtures thereof.

Some preferred emollients and humectants for use herein include, but are not limited to: glycerine; sorbitol; sodium 2-pyrrolidone-5-carboxylate; soluble collagen; dibutyl phthalate; gelatin; stearyl alcohol; glyceryl monoricinoleate; glyceryl monostearate; propane-1,2-diol; butane-1,3-diol; mink oil; cetyl alcohol; isopropyl isostearate; stearic acid; isobutyl palmitate; isocetyl stearate; oleyl alcohol; isopropyl laurate; hexyl laurate; decyl oleate; octadecan-2-ol; isocetyl alcohol; cetyl palmitate; dimethylpolysiloxane; di-*n*-butyl sebacate; isopropyl myristate; isopropyl palmitate; isopropyl stearate; butyl stearate; polyethylene glycol; triethylene glycol; lanolin; sesame oil; coconut oil; arachis oil; castor oil; acetylated lanolin alcohols; petroleum; mineral oil; butyl myristate; isostearic acid; palmitic acid; isopropyl linoleate; lauryl lactate; myristyl lactate; decyl oleate; myristyl myristate; and mixtures thereof.

II. Optional Components

The compositions of the present invention may, in some embodiments, further comprise additional optional components known or otherwise effective for use in topically applied personal care products. Surfactants, conditioning agents, cationic polymers, anti-dandruff actives, activity enhancers, penetration enhancers, suspending agents, non-steroidal anti-inflammatory drugs, topical anesthetics, and other optional components are described in detail below. Any optional component(s) should be physically and chemically compatible with the essential components of the composition, and should not otherwise unduly impair product stability, aesthetics or performance. Zinc gluconate and manganese gluconate are preferred metal complexes of oxidized carbohydrates for use as additional optional ingredients.

A. Surfactant

The compositions utilized in the method of the present invention, may, in some embodiments contain a surfactant suitable for application to the hair or skin, particularly when the compositions are to be applied topically, although surfactant may be used in any other form, adjusting the amount of surfactant present according to the desired effect for that particular form. Typically, such concentrations will range from about 5% to about 50%, by weight of the composition, preferably from about 8% to about 30%, more preferably from about 10% to about 25%, most preferably from about 12% to about 18%. When present, the surfactant is believed to provide cleaning and lather performance to the composition. Additionally, when an anionic detersive surfactant is used in combination with a cationic polymer, a coacervate is formed upon aqueous dilution, which is believed to be important in providing efficacy benefits.

The anionic surfactant component can comprise an anionic detersive surfactant, a zwitterionic or an amphoteric detersive surfactant having an attached moiety that is anionic at the pH of the composition, or a combination thereof; preferably an anionic surfactant.

Suitable surfactants for use herein include, but are not limited to alkyl and alkyl ether sulfates, e.g. ammonium lauryl sulfate and ammonium laureth sulfate; olefin sulfonates; sarcosinates and sarcosine derivatives; alkoyl isethionates; soaps of fatty acids; and taurates; C_{12} to C_{14} fatty acid mono-and di- ethanolamides, sucrose polyesters, polyhydroxy fatty acid amides, water soluble vegetable and animal-derived emollients, polyethylene glycol based polyethoxylated C_9-C_{15} fatty alcohol nonionic surfactants containing an average of from about 5 to about 50 ethyleneoxy moieties per mole of surfactant, and amine oxides; betaines, sultaines, hydroxysultaines, alkyliminoacetates, iminodialkanoates, and aminoalkanoates; surfactants disclosed in McCutcheon's, Detergents and Emulsifiers, North American edition (1986), published by allured Publishing Corporation; and McCutcheon's, Functional Materials, North American Edition (1992); and *Surfactant Encyclopedia*, Martin Reiger, (published by Cosmetics and Toiletries, ISBN 0-931710-29-4), all of whose descriptions are incorporated herein by reference; surfactants containing quaternary nitrogen moieties; amino-amides; quaternary ammonium salt cationic surfactants; and mixtures thereof.

B. Conditioning agent

The compositions herein may comprise from about 0.01% to about 30%, by weight of the composition, preferably from about 0.1% to about 20%, more preferably from about 0.1% to about 10%, most preferably from about 0.2% to about 6%, of a conditioning agent suitable for application to the hair or skin. It is believed that the conditioning agent provides improved conditioning benefits to the hair, particularly clean hair feel and wet rinse feel.

Suitable conditioning agents for use in the compositions herein are those conditioning agents characterized generally as silicones (e.g. silicone oils, cationic silicones, silicone gums, high refractive silicones, and silicone resins), organic conditioning oils (e.g. hydrocarbon oils, polyolefins, and fatty esters) or combinations thereof, or those conditioning agents which otherwise form liquid, dispersed, particles in the aqueous surfactant matrix herein.

The concentration of the conditioning agent in the composition should be sufficient to provide the desired conditioning benefits, and as will be apparent to one of ordinary skill in the art. Such concentration can vary with the conditioning agent, the conditioning performance desired, the

average size of the conditioning agent particles, the type and concentration of other components, and other like factors.

Conditioning agents suitable for use herein include, but are not limited to: insoluble silicones comprising volatile silicone, non-volatile silicone, or combinations thereof; silicone oils, e.g. polyalkyl or polyaryl siloxanes; non-volatile polyalkylsiloxane fluids; alkylamino substituted silicones; insoluble silicone gums, such as those described in U.S. Pat. No. 4,152,416, Noll and Walter, *Chemistry and Technology of Silicones*, New York: Academic Press (1968), and in General Electric Silicone Rubber Product Data Sheets SE 30, SE 33, SE 54 and SE 76, all of whose descriptions are incorporated herein by reference; high refractive index silicones; silicone fluids disclosed in U.S. Pat. No. 2,826,551, U.S. Pat. No. 3,964,500, U.S. Pat. No. 4,364,837, British Pat. No. 849,433, and *Silicon Compounds*, Petrarch Systems, Inc. (1984), all of which descriptions are incorporated herein by reference; and silicone resins, i.e. highly cross-linked polymeric siloxane systems.

The conditioning component of the compositions of the present invention may also comprise from about 0.05% to about 3%, by weight of the composition, preferably from about 0.08% to about 1.5%, more preferably from about 0.1% to about 1%, of at least one organic conditioning oil as the conditioning agent, either alone or in combination with other conditioning agents, such as the silicones (described above). The conditioning oils may add shine and luster to the hair. Additionally, they may enhance dry combing and dry hair feel.

The organic conditioning oils suitable for use as the conditioning agent herein are preferably low viscosity, water insoluble, liquids selected from the hydrocarbon oils, polyolefins, fatty esters, and mixtures thereof. The viscosity, as measured at 40°C, of such organic conditioning oils is preferably from about 1 centipoise to about 200 centipoise, more preferably from about 1 centipoise to about 100 centipoise, most preferably from about 2 centipoise to about 50 centipoise.

Suitable organic conditioning oils for use herein include, but are not limited to: hydrocarbon oils having at least about 10 carbon atoms; e.g. cyclic hydrocarbons; straight chain aliphatic hydrocarbons (saturated or unsaturated); branched chain aliphatic hydrocarbons (saturated or unsaturated); including polymers and mixtures thereof. Also suitable are liquid polyolefins, more preferably liquid poly-α-olefins, most preferably hydrogenated liquid poly-α-olefins. Also suitable are fatty esters, typically having at least 10 carbon atoms, including esters with

hydrocarbyl chains derived from fatty acids or alcohols (e.g. mono-esters, polyhydric alcohol esters, and di- and tri-carboxylic acid esters); polyhydric alcohol esters; glycerides; polyol fatty acid polyesters;

The hair growth regulating compositions of the present invention may comprise from about 0.005% to about 1.5%, by weight of the composition preferably from about 0.025% to about 0.1%, more preferably from about 0.05% to about 1%, more preferably from about 0.1% to about 0.5%, most preferably from about 0.1% to about 0.3%, of selected polyalkylene glycols suitable for application to the hair or skin. Also suitable for use in the compositions herein are the conditioning agents described by the Procter & Gamble Company in U.S. Pat. Nos. 5,674,478, and 5,750,122, both of which are incorporated herein in their entirety by reference. Yet other conditioning agents suitable for use herein are the series of conditioners available from International Specialty Chemicals, such as the GAFQUAT (RTM) series of quaternary copolymers, and the ARQUAD (RTM) series of quaternary ammonium salts, available from Akzo Nobel. Also suitable for use herein are those conditioning agents described in U.S. Pat. Nos. 4,529,586 (Clairol), 4,507,280 (Clairol), 4,663,158 (Clairol), 4,197,865 (L'Oreal), 4,217, 914 (L'Oreal), 4,381,919 (L'Oreal), and 4,422, 853 (L'Oreal), all of which descriptions are incorporated herein by reference.

C. <u>Cationic polymer</u>

The compositions of the present invention may comprise from about 0.02% to about 5%, by weight of the composition, preferably from about 0.05% to about 3%, more preferably from about 0.1% to about 2%, most preferably from about 0.5% to about 1%, of at least one organic, cationic deposition and conditioning polymer suitable for application to the hair or skin. Cationic polymers suitable for use herein include, but are not limited to: cationic polysaccharides; e.g. those described in the *CTFA Cosmetic Ingredient Dictionary*, 3d ed., edited by Estrin, Crosley, and Haynes, (The Cosmetic, Toiletry, and Fragrance Association, Inc., Washington, D.C. (1982), which description is incorporated herein by reference; cationic cellulose derivatives and cationic starch derivatives; cationic guar polymers; copolymers of vinyl monomers, having cationic protonated amine or quaternary ammonium functionalities, reacted with water soluble monomers; vinyl pyrrolidone copolymers; cationic modified proteins, e.g. lauryldimonium hydroxypropyl collagen; and mixtures thereof.

D. Anti-dandruff active

The hair growth regulating compositions of the present invention may, in some embodiments, comprise from about 0.1% to about 4%, by weight of the composition, preferably from about 0.1% to about 3%, most preferably from about 0.3% to about 2%, of an anti-dandruff active suitable for application to the hair or skin, which active may be particulate or soluble. The anti-dandruff active provides the compositions with anti-microbial activity. Suitable, non-limiting examples of anti-dandruff particulate actives include: pyridinethione salts, selenium sulfide, particulate sulfur, and mixtures thereof. Preferred are pyridinethione salts. Soluble anti-dandruff actives are described below along with other anti-microbials.

The hair growth regulating compositions of the present invention, may in some embodiments, comprise pyridinethione anti-dandruff particulates, especially 1-hydroxy-2-pyridinethione salts, are preferred particulate anti-dandruff agents for use. The concentration of pyridinethione anti-dandruff particulate typically ranges from about 0.1% to about 4%, by weight of the composition, preferably from about 0.1% to about 3%, most preferably from about 0.3% to about 2%. Preferred pyridinethione salts include those formed from heavy metals such as zinc, tin, cadmium, magnesium, aluminum and zirconium, preferably zinc, more preferably the zinc salt of 1-hydroxy-2-pyridinethione (known as "zinc pyridinethione" or "ZPT"), most preferably 1-hydroxy-2-pyridinethione salts in platelet particle form, wherein the particles have an average size of up to about 20μ, preferably up to about 5μ, most preferably up to about 2.5μ. Salts formed from other cations, such as sodium, may also be suitable. Pyridinethione anti-dandruff agents are described, for example, in U.S. Pat. No. 2,809,971; U.S. Pat. No. 3,236,733; U.S. Pat. No. 3,753,196; U.S. Pat. No. 3,761,418; U.S. Pat. No. 4,345,080; U.S. Pat. No. 4,323,683; U.S. Pat. No. 4,379,753; and U.S. Pat. No. 4,470,982, all of which are incorporated herein by reference. It is contemplated, as noted below, that ZPT may also function as an agent that regulates hair growth as an activity enhancer. Also suitable for use herein are selenium sulfide and sulfur.

E. Activity enhancer

The compositions herein may also optionally comprise in some embodiments one or more activity enhancers. Such agents can be chosen from a wide variety of molecules which can function in different ways to enhance the hair growth effects of a metal complex of an oxidized carbohydrate, of the present invention. Some activity enhancers may have a direct effect on the

regulation of hair growth themselves, others may work synergistically with the metal complexes of oxidized carbohydrates of the present invention to affect the regulation of hair growth. Some activity enhancers can also function as vehicles for the metal complex of an oxidized carbohydrate, as noted above. It should be understood that the activity enhancers described below, while imparting some effect on the activity of the metal complexes of oxidized carbohydrates of the present invention, will continue to impart their commonly known effect to the compositions described herein, e.g. while an anti-microbial agent such as zinc pyrithione may affect the growth of hair, it will still impart a deleterious effect on microbes, such as those relating to dandruff. The activity enhancers, when present, are typically employed in the compositions herein at a level ranging from about 0.001% to about 15%, preferably from about 0.1% to about 10%, more preferably from about 0.5% to about 5% by weight of the composition. Non-limiting examples of activity enhancers are described below.

1. Vasodilators

Optional activity enhancers suitable for use herein include vasodilators, such as potassium channel agonists, including, for example, minoxidil and minoxidil derivatives, such as aminexil, and such as those described in U.S. Patent 3,382,247, U.S. Patent 5,756,092, issued May 26, 1998, U.S. Patent 5,772,990, issued June 30, 1998, U.S. Patent 5,760,043, issued June 2, 1998, U.S. Patent 328,914, issued July 12, 1994, U.S. Patent 5,466,694, issued November 14, 1995, 5,438,058, issued August 1, 1995, and U.S. Patent 4,973,474, issued November 27, 1990, and also minoxidil glucuronides, as described by Unilever in EP-A-0 242 967, minoxidil sulphates, as described by The Upjohn Co. in WO-A-86/04231, (all of which are herein incorporated by reference), and cromakalin and diazoxide can be used as optional hair growth regulating agents in the compositions herein.

2. Anti-androgens

Optional activity enhancers suitable for use herein include anti-androgens. Examples of suitable anti-androgens may include, but are not limited 5-α-reductase inhibitors such as finasteride and those described in U.S. Patent 5,516,779, issued May 14, 1996 (herein incorporated by reference) and in Nnane et al, Cancer Research 58, "Effects of Some Novel Inhibitors of C17,20-Lyase and 5α-Reductase *in Vitro* and *in Vivo* and Their Potential Role in the Treatment of Prostate Cancer., as well as cyproterone acetate, azelaic acid and its derivatives and those compounds described in U.S. Patent 5,480,913, issued January 2, 1996, flutamide, and those described in U.S. Patents

5,411,981, issued May 2, 1995, U.S. Patent 5,565,467, issued October 15, 1996 and U.S. Patent 4,910,226, issued March 20, 1990, all of which are herein incorporated by reference.

3. Immunosuppressants

Optional activity enhancers suitable for use herein include immunosuppressants such as 1) cyclosporin and cyclosporin analogs including those described in U.S. Provisional Patent Application No. 60/122,925, Fulmer et al., "Method of Treating Hair Loss Using Non-Immunosuppressive Compounds", filed March 5, 1999, herein incorporated by reference, and 2) FK506 analogs such as those described in U.S. Provisional Patent Application No. 60/102,449, McIver et al., "Heterocyclic 2-Substituted Ketoamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,448, McIver et al., "2-Substituted Ketoamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,539, McIver et al., "2-Substituted Heterocyclic Sulfonamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,458, Tiesman et al., "Method of Treating Hair Loss Using Ketoamides", filed September 30, 1998, and U.S. Provisional Patent Application No. 60/102,437, McIver et al., "Method of Treating Hair Loss Using Sulfonamides", filed September 30, 1998, all of which are herein incorporated by reference.

4. Anti-microbial and Anti-fungal Actives

Optional activity enhancers suitable for use herein include anti-microbial and anti-fungal actives. Examples of anti-microbial and anti-fungal actives useful herein include ß-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, 2,4,4'-trichloro-2'-hydroxy diphenyl ether, 3,4,4'-trichlorobanilide, phenoxyethanol, phenoxy propanol, phenoxyisopropanol, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, hexamidine isethionate, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin, miconazole, tetracycline hydrochloride, erythromycin, zinc erythromycin, erythromycin estolate, erythromycin stearate, amikacin sulfate, doxycycline hydrochloride, capreomycin sulfate, chlorhexidine gluconate, chlorhexidine hydrochloride, chlortetracycline hydrochloride, oxytetracycline hydrochloride, clindamycin hydrochloride, ethambutol hydrochloride, metronidazole hydrochloride, pentamidine hydrochloride, gentamicin sulfate, kanamycin sulfate, lineomycin hydrochloride, methacycline hydrochloride, methenamine hippurate, methenamine mandelate, minocycline hydrochloride,

neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, octopirox, parachlorometa xylenol, nystatin, tolnaftate, clotrimazole, cetylpyridinium chloride (CPC), piroctone olamine, selenium sulfide, ketoconazole, triclocarbon, triclosan, zinc pyrithione, itraconazole, asiatic acid, hinokitiol, mipirocin and those described in EPA 0,680,745 (herein incorporated by reference), clinacycin hydrochloride, benzoyl peroxide, benzyl peroxide, minocyclin, phenoxy isopropanol, and mixtures thereof.

5. Anti-inflammatories

Anti-inflammatories can also be incorporated into the compositions herein as an optional activity enhancer. Examples of suitable anti-inflammatories may include glucocorticoids such as hydrocortisone, mometasone furoate and prednisolone, nonsteroidal anti-inflammatories including cyclooxygenase or lipoxygenase inhibitors such as those described in U.S. Patent 5,756,092, and benzydamine, salicylic acid, those compounds described in EPA 0,770,399, published May 2, 1997, WO 94/06434, published March 31, 1994 and FR 2,268,523, published November 21, 1975, all of which are herein incorporated by reference, aspirin, ibuprofen, naproxen, indomethacin, piroxicam, flurbiprofen, meclofenamate sodium, ketoprofen, tenidap, tebufelone, and ketorolac.

6. Thyroid hormones

Optional activity enhancers suitable for use herein include thyroid hormones and derivatives and analogs thereof. Examples of suitable thyroid hormones for use herein may include triiodothyrionine. Examples of thyroid hormone analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No. 60/136,996, Zhang et al., "Method of Treating Hair Loss", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating Hair Loss Using Biphenyl Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating Hair Loss Using Carboxyl Derivatives", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating Hair Loss Using Sulfonyl Thyromimetic Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed June 1, 1999, and U.S.

Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed June 1, 1999.

7. Prostaglandin agonists

Prostaglandin agonists (also known as "antagonists") can also be used as optional activity enhancers in the compositions herein. Examples of suitable prostaglandins agonists or antagonists include latanoprost and those described in WO 98/33497, Johnstone, published August 6, 1998, WO 95/11003, Stjernschantz, published April 27, 1995, JP 97-100091, and Ueno, JP 96-134242, Nakamura.

8. Retinoids

Optional activity enhancers suitable for use herein include retinoids. Suitable retinoids may include isotretinoin, acitretin, and tazarotene.

9. Other activity enhancers

Suitable for use herein are: (i) nicotinic acid and esters thereof, particularly benzyl, nicotinate, methyl nicotinate and ethyl nicotinate; (ii) Panthenol (iii) alpha-1,4 esterified disaccharides as described by Choay S.A. in EP-A-0 064 012, (iv) Oligosaccharide derivatives, as described by Unilever in EP-A-0 211 610, (v) Proteoglycanase inhibitors, glycosaminoglycan chain cellular uptake inhibitors and glycosaminoglycanase inhibitor other than those disclosed herein, as described by Unilever in EP-A-0 277 428, (vi) Ethylenediaminetetraacetic acid or salts thereof, as described by Redken Laboratories, Inc. in U.S. Pat. No. 4,814,351, (vii) Esters of pyroglutamic acid, as described by Lever Brothers Company in U.S. Pat. No. 4,774,255, especially: pyroglutamic acid n-hexyl ester, pyroglutamic acid n-octyl ester, ethyl-2-[pyroglutamoyloxy]-n-propionate, linoleyl-2-[pyroglutamoyloxy]-n-caprylate, lauryl-2-[pyroglutamoyloxy]-n-caprylate, stearyl-2-[pyrogluta-moyloxy]-n-caprylate, glyceryl mono(2-[pyroglutamoyloxy]-n-propionate), glyceryl mono(2-[pyroglutamoyloxy]-n-caprylate), and glyceryl di(2-[pyroglutamoyloxy]-n-propionate); (viii) Aryl-substituted ethylenes, as described by Unilever in EP-A-0 403 238, (ix) Mono N-acylated amino acids, as described by Unilever in EP-A-0 415 598, especially: N-acetyl glycine (x) Saturated or unsaturated aliphatic alcohols having an odd number of carbon atoms of from 3 to 25 in number, especially: n-nonyl alcohol , (xi) Saturated or unsaturated aliphatic carboxylic acids having an odd number of carbon atoms of from 3 to 25 in number, especially: nonanoic acid; and (xii) mixtures thereof.

Still other activity enhancers suitable for use herein include flavinoids, ascomycin derivatives and analogs, histamine antagonists such as diphenhydramine hydrochloride, other triterpenes such as oleanolic acid and ursolic acid and those described in U.S. Patent 5,529,769, JP 10017431, WO 95/35103, U.S. Patent 5,468,888, JP 09067253, WO 92/09262, JP 62093215, U.S. Patent 5,631,282, U.S. Patent 5,679,705, JP 08193094, saponins such as those described in EP 0,558,509 to Bonte et al, published September 8, 1993 and WO 97/01346 to Bonte et al, published January 16, 1997 (both of which are herein incorporated by reference in their entirety), proeoglycanase or glycosaminoglycanase inhibitors such as those described in U.S. Patents 5,015,470, issued May 14, 1991, U.S. Patent 5,300,284, issued April 5, 1994 and U.S. Patent 5,185,325, issued February 9, 1993 (all of which are herein incorporated in their entirety by reference) estrogen agonists and antagonists, pseudoterins, cytokine and growth factor promotors, analogs or inhibitors such as interleukin-1 inhibitors, interleukin-6 inhibitors, interleukin-10 promotors, and tumor necrosis factor inhibitors, vitamins such as vitamin D analogs and parathyroid hormone antagonists, Vitamin B12 analogs and panthenol, interfuron agonists and antagonists, hydroxyacids such as those described in U.S. Patent 5,550,158, benzophenones and hydantoin anticonvulsants such as phenytoin.

Other activity enhancers are described in detail in, for example, JP 09-157,139 to Tsuji et al, published June 17, 1997; EP 0277455 A1 to Mirabeau, published August 10, 1988; WO 97/05887 to Cabo Soler et al, published February 20, 1997; WO 92/16186 to Bonte et al, published March 13, 1992; JP 62-93215 to Okazaki et al, published April 28, 1987; U.S. Patent 4,987,150 to Kurono et al, issued January 22, 1991; JP 290811 to Ohba et al, published October 15, 1992; JP 05-286,835 to Tanaka et al, published November 2, 1993, FR 2,723,313 to Greff, published August 2, 1994, U. S. Patent 5,015,470 to Gibson, issued May 14, 1991, U.S. Patent 5,559,092, issued September 24, 1996, U.S. patent 5,536,751, issued July 16, 1996, U.S. Patent 5,714,515, issued February 3, 1998, EPA 0,319,991, published June 14, 1989, EPA 0,357,630, published October 6, 1988, EPA 0,573,253, published December 8, 1993, JP 61-260010, published November 18, 1986, U.S. Patent 5,772,990, issued June 30, 1998, U.S. Patent 5,053, 410, issued October 1, 1991, and U.S. Patent 4,761,401, issued August 2, 1988, all of which are herein incorporated by reference.

10. Preferred activity enhancers

Some preferred activity enhancers for use in the hair growth regulating compositions of the present invention include: zinc salts of carboxylic acids, minoxidil, finasteride, cyclosporin, ketoconazole, triclocarbon, triclosan, zinc pyrithione, itraconazole, hinokitiol, mipirocin, hydrocortisone, tenidap, triiodothyrionine, latanoprost, isotretinoin, acitretin, tazarotene, nicotinic acid, niacinamide, glycosaminoglycanase inhibitors, ethylenediaminetetraacetic acid, oleanolic acid, ursolic acid, interleukin-1 inhibitors, interleukin-6 inhibitors, interleukin-10 promotors, saponins, triterpenes, betulinic acid, betulonic acid, crataegolic acid, celastrol, asiatic acid, inhibitors of 5-α-reductase, progesterone, 1,4-methyl-4-azasteroids, 17-β-N,N-diethylcarbamoyl-4-methyl-4-aza-5-α-androstan-3-one, androgen receptor antagonists, cyproterone acetate, azelaic acid, diazoxide, potassium channel openers, cromakalin, phenytoin, dutasteride, coal tar, zinc gluconate, manganese gluconate, glucocortisoids, macrolides, aminexil, ginkgo biloba, ivy, methyl salicylate, clinacycin hydrochloride, benzoyl peroxide, benzyl peroxide, minocyclin, and mixtures thereof.

F. <u>Penetration Enhancers</u>

The compositions according to the invention may also optionally comprise one or more penetration enhancers, which may potentiate the benefit of the metal complex of an oxidized carbohydrate by improving its delivery through the stratum corneum to its site of action in the immediate environment of the hair follicle close to the hair bulb.

Non-limiting examples of penetration enhancers which may be used herein include, for example: 2-methyl propan-2-ol; propan-2-ol; 1-propan-1,2-diol; ethyl-2-hydroxypropanoate; hexan-2,5-diol; POE(2) ethyl ether; di(2-hydroxypropyl) ether; pentan-2,4-diol; acetone; POE(2) methyl ether; 2-hydroxypropionic acid; 2-hydroxypropanoic acid; 2-hydroxyoctanoic acid; propan-1-ol; 1,4-dioxane; tetrahydrofuran; butan-1,4-diol; propylene glycol dipelargonate; polyoxypropylene 15 stearyl ether; octyl alcohol; POE ester of oleyl alcohol; oleyl alcohol; lauryl alcohol; dioctyl adipate; dicapryl adipate; di-isopropyl adipate, di-isopropyl sebacate, dibutyl sebacate, diethyl sebacate, dimethyl sebacate, dioctyl sebacate, dibutyl suberate, dioctyl azelate, dibenzyl sebacate, dibutyl phthalate, dibutyl azelate, ethyl myristate, dimethyl azelate, butyl myristate, dibutyl succinate, didecyl phthalate, decyl oleate, ethyl caproate, ethyl salicylate, *iso*-propyl palmitate, ethyl laurate, 2-ethyl-hexyl pelargonate, *iso*-propyl isostearate, butyl laurate, benzyl benzoate, butyl benzoate, hexyl laurate, ethyl caprate, ethyl caprylate, butyl stearate, benzyl salicylate, 2-hydroxypropanoic acid, 2-hyroxyoctanoic acid, methylsulfoxide, N,N-dimethyl acetamide, N,N-

dimethyl formamide, 2-pyrrolidone, 1-methyl-2-pyrrolidone, 5-methyl-2-pyrrolidone, 1,5-dimethyl-2-pyrrolidone, 1-ethyl-2-pyrrolidone, phosphine oxides, sugar esters, tetrahydrofurfural alcohol, urea, diethyl-*m*-toluamide, 1-dodecylazacycloheptan-2-one and those described in U.S. Patent 5,015,470, issued May 14, 1991 and U.S. Patent 5,496,827, issued July 15, 1994 (both of which are herein incorporated in its entirety by reference), dimethylsulfonyl oxide (DMSO), octonol, niacinamide, and mixtures thereof.

G. Suspending agent

The hair growth regulating compositions of the present invention may, in some embodiments, comprise from about 0.1% to about 10%, by weight of the composition, preferably from about 0.3% to about 5%, more preferably from about 0.3% to about 2.5%, of a suspending agent suitable for application to the hair or skin. It is believed that the suspending agent suspends water-insoluble, dispersed materials in the shampoo compositions. Examples of suspending agents which may be suitably employed in the compositions herein include, but are not limited to: acyl derivatives, long chain amine oxides, xanthan gum, carboxyvinyl polymers; primary amines having a fatty alkyl moiety having at least about 16 carbon atoms (e.g. palmitamine, and stearamine), and secondary amines having two fatty alkyl moieties each having at least about 12 carbon atoms (e.g. dipalmitoylamine, and di-(hydrogenated tallow)-amine). Also suitable are di-(hydrogenated tallow)-phthalic acid amide, and cross-linked maleic anhydride-methyl vinyl ether copolymer; cellulose ethers (e.g., methylcellulose, hydroxybutyl methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, hydroxyethyl ethylcellulose and hydroxyethylcellulose), guar gum, polyvinyl alcohol, polyvinyl pyrrolidone, hydroxypropyl guar gum, starch and starch derivatives, and other thickeners, viscosity modifiers, gelling agents, and mixtures thereof. A preferred viscosity modifier useful as a suspending agent is trihydroxystearin, (e.g. THIXIN (RTM) R, available from Rheox Company).

H. Non-Steroidal Anti-Inflammatory Actives (NSAIDS)

Examples of NSAIDS suitable for use herein include the following categories: propionic acid derivatives; acetic acid derivatives; fenamic acid derivatives; biphenylcarboxylic acid derivatives; and oxicams. All of these NSAIDS are fully described in U.S. Patent 4,985,459 to Sunshine et al., issued January 15, 1991, incorporated by reference herein in its entirety. Examples of useful NSAIDS include acetyl salicylic acid, ibuprofen, naproxen, benoxaprofen, flurbiprofen, fenoprofen, fenbufen, ketoprofen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, tiaprofenic acid, fluprofen and bucloxic acid.

I. Topical Anesthetics

Examples of topical anesthetic drugs suitable for use herein include benzocaine, lidocaine, bupivacaine, chlorprocaine, dibucaine, etidocaine, mepivacaine, tetracaine, dyclonine, hexylcaine, procaine, cocaine, ketamine, pramoxine, phenol, and pharmaceutically acceptable salts thereof.

J. Preferred Combinations of Ingredients

Some preferred embodiments of the compositions described herein may be comprised of the following optional ingredients: conditioning agents selected from polydimethylsiloxane, polydiethylsiloxane, polymethylphenylsiloxane, amodimethicone, trimethylsilylamodimethicone, paraffin oil, mineral oil, polydecene, 1-decene homopolymer, C_8-C_{10} triester of trimethylolpropane, polyethylene glycol, and mixtures thereof; cationic polymers selected from Polyquaternium 10, Polyquaternium 24, guar hydroxypropyltrimethylammonium chloride, Polyquaternium 16, and mixtures thereof; anti-dandruff actives selected from zinc pyrithione, selenium sulfide, sulfur, ketoconazole, climbazole, and mixtures thereof; activity enhancers selected from minoxidil, finasteride, cyclosporin, ketoconazole, triclocarbon, triclosan, zinc pyrithione, itraconazole, hinokitiol, mipirocin, hydrocortisone, tenidap, triiodothyrionine, latanoprost, isotretinoin, acitretin, tazarotene, nicotinic acid, niacinamide, glycosaminoglycanase inhibitors, ethylenediaminetetraacetic acid, oleanolic acid, ursolic acid, interleukin-1 inhibitors, interleukin-6 inhibitors, interleukin-10 promotors, saponins, triterpenes, betulinic acid, betulonic acid, crataegolic acid, celastrol, asiatic acid, inhibitors of 5-α-reductase, progesterone, 1,4-methyl-4-azasteroids, 17-β-N,N-diethylcarbamoyl-4-methyl-4-aza-5-α-androstan-3-one, androgen receptor antagonists, cyproterone acetate, azelaic acid, diazoxide, potassium channel openers, cromakalin, phenytoin, dutasteride, coal tar, zinc gluconate, manganese gluconate, glucocortisoids, macrolides, aminexil, ginkgo biloba, ivy, methyl salicylate, clinacycin hydrochloride, benzoyl peroxide, benzyl peroxide, minocyclin, and mixtures thereof; penetration enhancers selected from propan-2-ol; 1-propan-1,2-diol; propan-1-ol; di-isopropyl adipate; dimethylsulfonyl oxide; octonol; niacinamide; and mixtures thereof; suspending agents selected from ethylene glycol monostearate, ethylene glycol distearate, stearyl stearate, cetyl palmitate, xanthan gum, copolymers of acrylic acid crosslinked with polyallylsucrose, methylcellulose, hydroxybutyl methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose,

hydroxyethyl ethylcellulose, hydroxyethylcellulose, guar gum, polyvinyl alcohol, polyvinyl pyrrolidone, hydroxypropyl guar gum, starch, trihydroxystearin, and mixtures thereof.

K. Other Optional Ingredients

The hair growth regulating compositions of the present invention may, in some embodiments, further comprise additional optional components known or otherwise effective for use in hair care or personal care products. The concentration of such optional ingredients generally ranges from zero to about 25%, more typically from about 0.05% to about 25%, even more typically from about 0.1% to about 15%, by weight of the composition. Such optional components should also be physically and chemically compatible with the essential components described herein, and should not otherwise unduly impair product stability, aesthetics or performance.

Non limiting examples of optional components for use in the shampoo composition include anti-static agents (e.g. tricetyl methyl ammonium chloride), foam boosters (e.g. fatty ester (e.g. C_8-C_{22}) mono- and di (C_1-C_5, especially C_1-C_3) alkanol amides, preferably coconut monoethanolamide, coconut diethanolamide, and mixtures thereof), viscosity modifiers and thickeners (e.g. sodium chloride, sodium sulfate, and magnesium sulfate), pH adjusting agents (e.g. sodium citrate, citric acid, succinic acid, phosphoric acid, sodium hydroxide, and sodium carbonate), dyes, organic solvents or diluents, pearlescent aids, perfumes, fatty alcohols, proteins, skin active agents, vitamins, abrasives, absorbents, anti-caking agents, anti-oxidants (e.g. sodium sulphite, hydroquinone, sodium bisulphite, sodium metabisulphite and thyoglycolic acid, sodium dithionite, erythrobic acid and other mercaptans, which such anti-oxidants may be delivered using encapsulation techniques described in U.S. Pat. No. 5,053,051 (Goldwell), which description is incorporated herein by reference), biological additives, bulking agents, chelating agents, chemical additives, colorants, cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers, opacifying agents, reducing agents, skin bleaching agents, sunscreen agents, flavoring agents, sweeteners, preservatives, dyes, and moisturizing agents (e.g. hyaluronic acid, chitin, and starch-grafted sodium polyacrylates such as SANWET (RTM) IM-1000, IM-1500 and IM-2500 available from Celanese Superabsorbent Materials, Portsmith, Virginia, USA, and described in U.S. Pat. No. 4,076,663, which description is incorporated herein by reference). Furthermore, the CTFA International Cosmetic Ingredient Dictionary and Handbook, 8th ed., 1999, which is incorporated by reference herein in its entirety, describes a wide variety of non-limiting cosmetic and pharmaceutical ingredients commonly

used in the hair and skin care industry, which are suitable for use in the compositions of the present invention.

Methods of Manufacture

The metal complexes of oxidized carbohydrates of the present invention may be synthesized using any conventional method. Some typical methods are: (a) multiple synthesis method, as described in "The Synthesis and Analysis of Copper (II) Carboxylates," Yoder, et al., Journal of Chemical Education (1995), vol. 72, pages 267 et seq.; (b) bivalent metal oxide method, as described in "Complex Formation Between D-lactobionate and Bivalent Metal Ions," Frutos, et al., Canadian Journal of Chemistry, (1977), vol. 75, pages 405 - 413; and (c) ion exchange method, as described "Preparation of Zinc Gluconate by Ion Exchange Resin", Dy, et al., Zhongguo Yiyao Gongye Zazhi Journal, (1992), vol. 23(4), page 156; all of which descriptions are incorporated herein by reference.

The compositions containing the metal complexes of oxidized carbohydrates of the present invention may be the form of a tablet, capsule, caplet, cream, gel, hydrogel, foam, mousse, liquid, solid, powder, tonic, rinse, shampoo, spray, paste, or other suitable form.

Alternatively, the compositions according to the present invention can be packaged in a kit, as follows: one article of the kit comprises an individually packaged component containing at least one metal complex of an oxidized carbohydrate, while further kit articles could comprise one or more components for use in pre-treatment or post-treatment steps as part of a regimen for regulating hair growth regulating, for further enhancing hair growth performance, for creating special and individualized hair growth regulation effects, or for addressing specific needs of the consumer.

Methods of Use

The method of the present invention involves the administration of the compositions described herein for regulating hair growth in mammals (e.g., humans and domestic animals). It is also contemplated that the compositions may be administered to the skin for achieving skin benefits, and to the finger nails or toe nails for nail growth benefits.

The compositions of the present invention can be administered topically, orally or parenterally. A preferred method of using the present invention involves the topical application of the compositions described herein to the scalp, skin, and/or hair, more preferably to the scalp, skin, and/or hair where the scalp is already bald or balding. The amount of the composition and the frequency of application to scalp, skin, and/or hair can vary widely, depending on the desired effect and/or personal needs. Typically the composition is applied from about 1 to about 10 times per day, more typically from about 1 to about 6 times per day and most typically from 1 to 3 times per day. The compositions of the present invention can be also be used as a pre-treatment or post-treatment step to additional hair growth regulating processes taking place in order to further enhance hair growth performance or to create special and individualized hair growth regulation effects or to address specific needs of the consumer.

The topical compositions can be delivered the hair/scalp/skin from a variety of delivery devices. For example, the compositions can be incorporated into a medicated cleansing pad. Preferably these pads comprise form about 50% to about 75% of a substrate and from about 25% to about 50% of a liquid composition deliverable from the substrate. Suitable pads are described, for example, in U.S. Patent 4,891,228; Thurman et al.; issued January 2, 1990; and U.S. Patent 4,891,227; Thaman et al.; issued January 2, 1990, both of which are incorporated by reference.

Topical compositions of the present invention can also be delivered via any conventional hair care products, including, but not limited to shampoos, conditioners, styling products or other leave-in or rinse-off products.

EXAMPLES

The following are non-limiting examples of the hair growth regulating compositions of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention, which would be recognized by one of ordinary skill in the art. In the examples, all concentrations are listed as weight percent, unless otherwise specified. As used herein, "minors" refers to those optional components such as preservatives, viscosity modifiers, pH modifiers, fragrances, foam boosters, and the like. As is apparent to one of ordinary skill in the art, the selection of these minors will vary depending on

the physical and chemical characteristics of the particular ingredients selected to make the present invention as described herein.

Examples 1-8 are non-limiting examples of topical compositions used in the method of the present invention:

Ingredient	1	2	3	4	5	6	7	8
zinc lactobionate	10.0	5.0	5.0	---	6.0	0.1	1.0	15.0
sodium lactobionate	---	---	1.0	5.0	---	---	---	---
zinc gluconate	---	3.0	---	---	---	---	6.0	---
minoxidil	---	2.5	---	---	2.0	2.5	---	---
ketoconazole	---	---	---	---	---	2.0	---	---
Tween 20	1.0	---	0.20	---	---	---	---	---
propylene glycol	10.0	8.0	15.0	20.0	25.0		15.0	10.0
dimethylisosorbide	18.0	19.0	---	18.0	18.0	---	---	---
C_{12}-C_{15} alkyl octanoate	---	---	19.0	---	---	---	---	---
hydroxypropyl cellulose	---	---	0.10	---	---	0.20	---	---
Silicone	---	---	---	1.0	---	5.0	---	2.0
polyquaternium 10	---	---	---	0.50	1.0	---	---	---
ethyl alcohol and minors	30.0	q.s. to 100	q.s. to 100	---	---	q.s. to 100	25.0	30.0
water and minors	q.s. to 100	---	---	q.s. to 100	q.s. to 100	10.0	q.s. to 100	q.s. to 100

Examples 1-8 may be prepared as follows:

1. Add the ethyl alcohol, if present, and water, if present, and polyquaternium 10, if present, into mixing container and mix for 1 to 2 hours.
2. Add the ethyl alcohol, if present, and Tween 20, if present, into mixing container and agitate until combined.
3. Add propylene glycol, if present, and dimethylisosobide, if present, and C12-C15 alkyl octanoate, if present, into mixing container and mix until in a clear solution.
4. Add the metal complex(es) of an oxidized carbohydrate and mix with a high shear mixer for 10 minutes.

5. Add hydroxypropyl cellulose, if present, to the mixture and mix with a standard mixer for 4 to 5 hours.
6. Add the remaining ingredients and mix an additional 10 minutes.

Examples 9-17 are non-limiting examples of topical compositions used in the method of the present invention:

Ingredient	9	10	11	12	13	14	15	16	17
zinc lactobionate	5.0	---	---	---	---	5.0	---	---	5.0
zinc gluconate	1.0	---	---	1.0	---	---	---	1.0	---
copper lactobionate	---	5.0	---	---	---	---	---	---	---
lithium gluconate	---	---	5.0	---	---	---	---	---	---
copper galacturonate	---	---	---	5.0	---	---	---	---	---
zinc glucoheptonate	---	---	---	---	5.0	---	---	---	---
copper maltobionate	---	---	---	---	---	---	5.0	---	---
zinc alginate	---	---	---	---	---	---	---	5.0	---
Minoxidil	---	2.5	---	---	2.0	---	---	---	---
Finasteride	---	---	1.0	---	---	1.0	---	---	---
zinc pyrithione	1.0	---	---	---	---	---	---	---	1.0
Tween 20	1.0	---	0.20	---	---	---	---	---	1.0
propylene glycol	10.0	8.0	15.0	20.0	25.0	6.0	12.0	18.0	10.0
dimethylisosorbide	18.0	19.0	---	18.0	18.0	---	---	---	18.0
C_{12}-C_{15} alkyl octanoate	---	---	19.0	---	---	---	---	---	---
Hydroxypropyl cellulose	---	---	0.10	---	---	0.5	0.1	---	---
Polyquaternium 10	---	---	0.0	0.50	1.0	---	0.5	---	---
ethyl alcohol and minors	30.0	q.s. to 100	q.s. to 100	---	10.0	---	q.s. to 100	---	30.0
water and minors	q.s. to 100	---	---	q.s. to 100	q.s. to 100	q.s. to 100	10.0	q.s. to 100	q.s. to 100

Examples 9-17 may be prepared in the same manner as Examples 1-8.

Examples 18 and 19 are non-limiting examples of tablet compositions which can be used in the method of the present invention:

Ingredient	Example 18 (mg)	Example 19 (mg)
Zinc lactobionate	100	0.25
Crospovidone	15	0.0
Lactose, hydrous	200	0.0
Microcrystalline cellulose	80	0.0
Magnesium stearate	5	2.0
Polyvinylpyrrolidone	0.0	3.0
Sodium starch glycolate	0.0	2.0
Dicalcium phosphate	0.0	75.0
Talc	0.0	2.75
Methanol	0.0	20.0
Starch 1500	0.0	15.0

Example 18 may be prepared as follows:

1. Add the zinc lactobionate, the crospovidone and the microcrystalline cellulose into a twin-shell blender and mix for 20 minutes.
2. Sieve the mixture through a 40 mesh screen and return to the twin-shell blender.
3. Add the lactose hydrous and mix for 25 minutes.
4. Add the magnesium stearate and mix for 5 minutes.
5. Compress into tablets on a standard rotary tablet press.

Example 19 may be prepared as follows:

1. Dissolve the zinc lactobionate and polyvinylpyrrolidone in the methanol under agitation.
2. Add the sodium starch glycolate, dicalcium phosphate, and strach 1500 into a high shear mixer and mix for 15 minutes.
3. Add the methanol solution to the high-shear blender over a 10 minute period and then mix for an additional 10 minutes until granules are formed.
4. Transfer the wetted mass into a fluid bed dryer and dry at 45°C for 2 hours.
5. Sieve the dried granules through a 30 mesh screen and transfer back to the high-shear blender.
6. Add the talc and magnesium stearate and mix for 3 minutes.
7. Compress into tablets on a standard rotary tablet press

Example 20 is a non-limiting example of a composition which can be injected subcutaneously according to the method of the present invention.

Ingredient	Example 20 (mg/mL)
Zinc lactobionate	1.0
Dibasic sodium phosphate	7.0
Monobasic sodium phosphate	3.0
Edetate disodium	0.1
Benzalkonium chloride	0.1
Water for injection	QS to 10 liters

Example 20 may be prepared as follows:

1. The zinc lactobionate is micronized in a jet mill and sterilized by exposing it to 2.5 Mrad of radiation from a cobalt 60 source.
2. The dibasic sodium phosphate, monobasic sodium phosphate, edetate disodium, and benzalkonium chloride are dissolved in 9 liters of water for injection in a standard mixing tank.
3. The solution is filtered through a 0.22 micron filter to achieve sterilization.
4. The zinc lactobionate is added and mixed for 30 minutes under agitation.
5. The suspension is aseptically filled into 3 mL flint glass vials, stoppered and sealed on standard filling equipment.

Examples 21 to 25 are non-limiting examples of shampoo compositions which embody the present invention.

Ingredient	**Example Number**				
	21	**22**	**23**	**24**	**25**
zinc lactobionate	10.0	5.0	15.0	---	1.0
copper maltobionate	---	---	---	5.0	---
zinc gluconate	---	2.0	---	---	---
ammonium laureth-3 sulfate	14.00	10.0	14.0	12.0	12.50
ammonium lauryl sulfate	---	6.0	---	6.0	---
Cocamidopropylbetaine	2.70	---	2.70	---	4.20
Polyquaternium-10	0.15	---	---	0.15	---
cocamide MEA	0.80	0.80	0.80	0.80	---
cetyl alcohol	---	0.42	0.42	0.42	---
ethylene glycol distearate	1.50	1.50	0.75	1.50	0.75
zinc pyrithione	1.0	1.0	---	---	---
Dimethicone	0.5	0.3	0.5	0.3	0.5
water and minors	--------- q.s. to 100% ---------				

Examples 21 to 25 may be prepared according to any conventional method for making shampoos.

Examples 26 to 30 are non-limiting examples of products prepared processes, which embody the present invention.

Ingredient	Example Number				
	26	**27**	**28**	**29**	**30**
zinc sulphate	3.8	-	3.8	3.8	3.8
sodium hydroxide	1.1	-	1.1	1.1	-
zinc oxide	-	1.1	-	-	-
lactobionic acid	9.5	9.5	-	-	-
gluconic acid	-	-	5.18	-	-
maltobionic acid	-	-	-	9.5	-
sodium lactobionate	-	-	-	-	10.0
water and minors	--------- q.s. to 100% ---------				

Examples 26 to 30 may be prepared as follows:

1. Add the metal-salt and the carboxylic acid of carbohydrate and the carrier, in any order, agitate and heat, if necessary, to make homogeneous.
2. Adjust the pH of the result with sodium hydroxide, if desired. The resulting formulation will contain from about 0.001% to about 99.9%, by weight, of at least one metal complex of an oxidized carbohydrate, as desired.

WHAT IS CLAIMED IS:

1. A method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition characterized in that it comprises:
   (a) from 0.001% to 99.9%, by weight, preferably from 0.001% to 15%, of at least one metal complex of an oxidized carbohydrate, wherein said metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate; and
   (b) from 0.1% to 99.999%, by weight, preferably from 85% to 99.999%, of a vehicle.

2. A method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition characterized in that it comprises:
   (a) from 0.001% to 99.9%, by weight, of at least one metal complex of an oxidized carbohydrate having a solubility in water of at least 10%, preferably 40%, more preferably 50%, more preferably 60%; and
   (b) from 0.1% to 99.999%, by weight, of a vehicle.

3. A method for regulating the growth of hair comprising administering to a mammal, an effective amount of a composition characterized in that it is the product of a process comprising the steps (a) to (c) in any order:
   (a) adding from 1% to 25%, by weight, preferably from 3% to 10%, of a metal salt, and mixing;
   (b) adding from 1% to 30%, by weight, preferably from 5% to 25%, of a carboxylic acid of a carbohydrate, and mixing; and
   (c) adding from 0.1% to 99.999%, by weight, of a vehicle, and mixing;

   wherein said product comprises from 0.001% to 99.9%, by weight, of at least one metal complex of an oxidized carbohydrate, wherein said metal complex of an oxidized carbohydrate is neither zinc gluconate nor manganese gluconate.

4. The method of any preceding claim, wherein the metal comprising said at least one metal complex of an oxidized carbohydrate is selected from the group consisting of lithium, sodium, silver, gold, zinc, copper, nickel, iron, chromium, calcium, magnesium,

molybdenum, cobalt, palladium, platinum, tin, and mixtures thereof, preferably lithium, sodium, zinc, copper, and mixtures thereof, more preferably zinc.

5. The method of claim 3, wherein said metal salt is selected from the group consisting of zinc sulfate, zinc acetate, zinc oxide, cupric chloride, cupric sulfate, cupric acetate, and copper oxide, preferably zinc sulfate.

6. The method of any preceding claim, wherein the oxidized carbohydrate comprising said metal complex of an oxidized carbohydrate is selected from the group consisting of ribonic acid; ribulonic acid; arabinonic acid; xylonic acid; xylulonic acid; lyxonic acid; allonic acid; altronic acid; gluconic acid; mannonic acid; gulonic acid; idonic acid; galactonic acid; talonic acid; glucoheptonic acid; psiconic acid; fructonic acid; sorbonic acid; tagatonic acid; lactobionic acid; maltobionic acid; isomaltobionic acid; cellobionic acid; oxidized malto-oligosaccharide; oxidized cello-oligosaccharide; oxidized cellulose; chitin; gum arabic; gum karaya; gum xanthan; oxidized gum guar; oxidized locust bean gum; oxidized agars; oxidized algins; oxidized gellan gum; and mixtures thereof, preferably lactobionic acid; maltobionic acid; isomaltobionic acid; cellobionic acid; and mixtures thereof, more preferably lactobionic acid.

7. The method of any preceding claim, wherein said composition further comprises zinc gluconate, manganese gluconate, or both.

8. The method of any preceding claim, wherein said vehicle comprises a solvent comprising:
   (a) from 50% to 70%, by weight, of water;
   (b) from 20% to 40%, by weight, of ethanol; and
   (c) from 5% to 20%, by weight, preferably from 10% to 15%, of propylene glycol.

9. The method of any preceding claim, wherein said composition further comprises at least one ingredient selected from the group consisting of surfactants, conditioning agents, cationic polymers, anti-dandruff actives, activity enhancers, penetration enhancers, dyes, suspending agents, non-steroidal anti-inflammatory drugs, topical anesthetics, sunscreen actives, flavoring agents, preservatives, sweeteners, and mixtures thereof.

10. The method of Claim 9, wherein:

(a) said conditioning agents are selected from the group consisting of polydimethylsiloxane, polydiethylsiloxane, polymethylphenylsiloxane, amodimethicone, trimethylsilylamodimethicone, paraffin oil, mineral oil, polydecene, 1-decene homopolymer, C_8-C_{10} triester of trimethylolpropane, polyethylene glycol, and mixtures thereof; and

(b) said cationic polymers selected from the group consisting of Polyquaternium 10, Polyquaternium 24, guar hydroxypropyltrimethylammonium chloride, Polyquaternium 16, and mixtures thereof; and

(c) said anti-dandruff actives selected from the group consisting of zinc pyrithione, selenium sulfide, sulfur, ketoconazole, climbazole, and mixtures thereof; and

(d) said activity enhancers selected from the group consisting of minoxidil, finasteride, cyclosporin, ketoconazole, triclocarbon, triclosan, zinc pyrithione, itraconazole, hinokitiol, mipirocin, hydrocortisone, tenidap, triiodothyrionine, latanoprost, isotretinoin, acitretin, tazarotene, nicotinic acid, niacinamide, glycosaminoglycanase inhibitors, ethylenediaminetetraacetic acid, oleanolic acid, ursolic acid, interleukin-1 inhibitors, interleukin-6 inhibitors, interleukin-10 promotors, saponins, triterpenes, betulinic acid, betulonic acid, crataegolic acid, celastrol, asiatic acid, inhibitors of 5-α-reductase, progesterone, 1,4-methyl-4-azasteroids, 17-β-N,N-diethylcarbamoyl-4-methyl-4-aza-5-α-androstan-3-one, androgen receptor antagonists, cyproterone acetate, azelaic acid, diazoxide, potassium channel openers, cromakalin, phenytoin, dutasteride, coal tar, zinc gluconate, manganese gluconate, glucocortisoids, macrolides, aminexil, ginkgo biloba, ivy, methyl salicylate, clinacycin hydrochloride, benzoyl peroxide, benzyl peroxide, minocyclin, and mixtures thereof;

(e) said penetration enhancers selected from the group consisting of propan-2-ol; 1-propan-1,2-diol; propan-1-ol; di-isopropyl adipate; dimethylsulfonyl oxide; octonol; niacinamide; and mixtures thereof; and

(f) said suspending agents selected from the group consisting of ethylene glycol monostearate, ethylene glycol distearate, stearyl stearate, cetyl palmitate, xanthan gum, copolymers of acrylic acid crosslinked with polyallylsucrose, methylcellulose, hydroxybutyl methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, hydroxyethyl ethylcellulose, hydroxyethylcellulose, guar gum,

polyvinyl alcohol, polyvinyl pyrrolidone, hydroxypropyl guar gum, starch, trihydroxystearin, and mixtures thereof.

11. The method of any preceding claim, wherein said at least one metal complex of an oxidized carbohydrate is zinc lactobionate.

12. The method of any preceding claim, wherein said composition is packaged as a component part of a kit, said kit containing at least one additional component for use in pre-treatment or post-treatment steps, said steps being part of a regimen for regulating hair growth performance.

13. The method of any preceding claim, wherein said composition is administered orally, parenterally, or topically.