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[54] **USE OF SUCRALFATE TO TREAT BALDNESS**

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[63] Continuation of Ser. No. 47,078, Apr. 16, 1993, abandoned, which is a continuation of Ser. No. 613,559, Nov. 21, 1990, abandoned.

[30] **Foreign Application Priority Data**

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[58] **Field of Search** 514/23, 25, 53, 514/59

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[57] **ABSTRACT**

A method of treating and/or preventing alopecia (baldness, deficient hair growth) comprises administering to a patient in need thereof a therapeutically or prophylactically effective amount of a sulfated mono-, di- or oligosaccharide or a derivative, salt or complex thereof. The saccharide is preferably polysulfated, such as a polysulfated disaccharide, in particular sucrose, or a derivative, complex or salt thereof. Especially interesting polysulfated disaccharides are sucrose pentasulfate, sucrose hexasulfate, sucrose heptasulfate and sucrose octasulfate, e.g. in the form of a potassium or sodium salt, or in the form of sucralfate.

15 Claims, No Drawings

USE OF SUCRALFATE TO TREAT BALDNESS

This application is a continuation of application Ser. No. 08/047,078 filed Apr. 16, 1993, now abandoned itself a continuation of application Ser. No. 07/613,559 filed Nov. 21, 1990, now abandoned which was the national stage of PCT/DK90/00104, filed Apr. 19, 1990.

Alopecia (baldness or deficient hair growth) is a condition which leads to more or less disabling or discomfort to the individual suffering therefrom, ranging from minor cosmetic disadvantages to severe psychological consequences.

Alopecia has a number of etiologies.

The most common form of alopecia is androgenetic alopecia, more accurately described as common baldness. Androgenetic alopecia occurs in chimpanzees, orang-outangs and other primates as well as in man.

As is implied by the name, androgenetic alopecia is induced by androgenic stimulation of hair follicles predisposed by the interdependent influences of genetic factors and of ageing. Despite its name, it affect both the male and the female.

The initial stage in the condemned follicles is probably the accumulation of 5α-dihydrotestosterone, the tissue-active androgen which inhibits the metabolism of such follicles.

There is a marked racial variation in the incidence of androgenetic alopecia. The disease is most frequent and severe in Caucasoids.

The earliest histological change is the appearance of foci of degeneration in the lower part of the connective-tissue sheath of the follicles, with perivascular basophilic change. The follicle gradually shrinks, leaving beneath it a strand of sclerosed and hyaline connective tissue. However, even in areas of scalp in which almost all follicles are short and small, producing at best only tiny vellus hairs, there remain a few quiescent terminal follicles which can be stimulated into growth to give false hopes of a cure.

Androgenetic alopecia is a very widespread condition, at least in its less severe forms. Thus, during adolescence, uniform recession of the frontal hair-line occurs in 96% of males and about 80% of females.

As mentioned above, there are a number of other etiologies of alopecia, such as the administration of chemicals, such as drugs. As examples of these may be mentioned anticoagulants such as large doses of heparin, heparinoids and coumarins, cytostatic agents, triparanol and fluorobutyrophenone, excessive consumption of vitamin A, occupational exposure to sodium borate, potassium thiocyanate, large amounts of bismuth. Also, oral contraceptives have been suspected of giving rise to the disease, and the same applies to propranolol, metoprolol, levodopa, and ibuprofen.

Also, alopecia may have nutritional or metabolic origin, or it may be caused by disorders of the central nervous system. Furthermore, the significant association of the atrophic state with alopecia areata has been stressed relatively recently in some populations. Also, an association between autoimmunity and alopecia areata has long been recognized. Alopecia including areata is also often seen in association with skin disease such as scalp eczema, psoriasis and other dermatosis and also in association with systemic disease such as LE.

Today, no completely satisfactory treatment or prophylaxis of alopecia exists. Although topical administration of minoxidil can induce regrowth, it is not considered the definitive therapy.

Heparin, heparinoids and related glycosaminoglycans have been suggested as effective in stimulating hair growth (e.g. DE 3543221 A1, GB 936 916, GB 1 098 935, EP 35 919, EP 182 756, EP 277 428, EP 279 244, EP 295 092, EP 297 455).

In EP 295 092, it is described that hyaluronic acid fragments comprising from 7 to 50 monosaccharide units terminating either with a glucuronic acid unit and/or a N-acetyl glucosamine unit, or an unsaturated derivative of one or both of these terminal units are useful as hair stimulating agents when topically applied to the scalp. Such compounds can be characterized by being "naturally" occurring mucopolysaccharide moieties.

It has now surprisingly been observed that after 3–4 weeks of two daily applications of an ointment containing 10% w/w of sucralfate, there was appearance of hair in the otherwise bald lateral-frontal areas in a 40-year-old male who had a normal common male-pattern baldness. At the beginning, a "plume" appeared in the area, and after a few days the "plume" began turning into real hairs and 8 days after, there were dozens of real hairs which were indistinguishable from other hairs of the scalp, apart from being shorter and all coloured, in contrast to the existing hair, which was partially greyed.

This observation is most remarkable in view of the fact that sucralfate or sulfated mono-, di- or oligosaccharides have apparently not been suggested as means for treating or preventing alopecia. Also, the sulfated mono-, di- or oligosaccharides do not belong to any chemical or therapeutic group of compounds previously used or suggested for the treatment of alopecia, such as minoxidil, vitamin A, steroids, in particular triamcinolone, pyrimidine carbamate, squaric acid, allergens and psoralens in PUVA and naturally occurring mucopolysaccharides.

Sucralfate and other disaccharide polysulfate-aluminium compounds have been indicated as effective in alleviating the symptoms of anorectal disease when topically applied to human skin, and as effective in promoting the healing of wounds (WO 89/00047), and sulfated oligosaccharides, particularly mono- and disaccharides such as sucrose octasulfate, have been mentioned as wound healing agents (EP 230 023). WO 89/05645 and WO 89/05646 disclose a broad range of pharmacological effects of sucralfate and sucrose octasulfate such as anti-inflammatory, anti-infective, anti-malignant, skin-protective and anti-wrinkle and other effects after topical or systemic administration. WO 89/07932 discloses the use of sucralfate and sucrose octasulfate in the treatment of gingivitis and parodontosis.

Based upon the observations made in the present invention and the inventors' knowledge of sulfated saccharides, it is reasonable to contemplate that the hair growth stimulating effect will extend not only to sucralfate and the sodium salt of sucrose octasulfate, but also to other related sulfated mono-, di- and oligosaccharides, which are of a type not naturally occurring in glycosaminoglycan structures.

SUMMARY OF THE INVENTION

In one aspect, the invention provides a method of treating and/or preventing alopecia, the method comprising administering to a patient in need thereof a therapeutically or prophylactically effective amount of a sulfated mono-, di- or oligosaccharide or a derivative, salt or complex thereof.

In another aspect, the invention relates to the use of a sulfated mono-, di- or oligosaccharide for preparing a composition for use in the treatment and/or prevention of alopecia.

In a further aspect, the invention relates to the cosmetic use of a sulfated mono-, di- or oligosaccharide for combating or preventing hair loss and/or preserving the natural colour of the hair.

DETAILED DISCLOSURE OF THE INVENTION

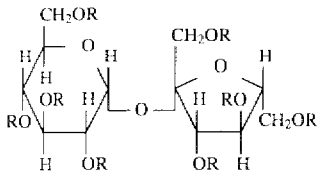
The sulfated saccharide used in accordance with the invention may be a sulfated monosaccharide, for instance sulfated xylose, fructose, glucose, ribose, arabinose, galactose, rhamnose, fucose, sorbose, psicose, tagatose or gulose, a sulfated disaccharide such as sulfated sucrose, lactose, maltose or cellobiose, or a sulfated oligosaccharide such as sulfated maltotriose, maltertreose, or a sulfated raffinose, which is an oligosaccharide comprising a sulfated sucrose moiety together with a galactose moiety, or a sulfated melezitose, which is a sulfated sucrose moiety together with a glucose moiety. In the present context, the term "an oligosaccharide" is a saccharide consisting of 3–20 monosaccharide units in accordance with the generally accepted terminology.

The sulfated mono-, di- or oligosaccharide is preferably a polysulfated or persulfated saccharide, which means that two or more, possibly all, sulfur-containing moieties are present as substituents on hydroxy groups of the carbohydrate moiety.

In some cases, the sulfated mono-, di- or oligosaccharide may be complexed with or form a salt with a metal, e.g. an alkali or alkaline earth metal such as Na, K, Ca, Mg or Ba, or Al, Zn, Cu, Zr, Ti, Bi, Mn or Os, or with an organic base (e.g. an amino acid). The currently preferred salts are potassium and sodium salts, and the preferred complex is the aluminium complex. Furthermore, the mono-, di- or oligosaccharide may be in the form of a suitable derivative, e.g. a mono-, di- or polyester of aliphatic carboxylic acids such as formic, acetic, propionic, butanoic, myristic or stearic acid.

Preferably, the composition of the invention contains a persulfated disaccharide, for example sucrose octasulfate.

The preferred sulfated disaccharide can be represented by the following formula:



wherein R is H, $SO_3[Al_2(OH)_5]$, SO_3H or an acyl residue of the above-mentioned carboxylic acids, the groups designated R being the same or different, with the proviso that at least one R represents a sulfate group,

or physiologically acceptable salts or complexes thereof.

The particular preferred compounds according to the invention are sucralfate and the potassium or sodium salt of sucrose octakis(hydrogen sulfate).

Sucralfate may also be termed sucrose octakis(hydrogen sulfate) aluminium complex. Its CAS number is 54182-58-0. The commercial product is a white powder which is practically insoluble in water and most organic solvents; it is soluble in acids and alkalis. In practice, there may be slight variations in the chemical composition, e.g., due to the fact that the sulfation may be slightly incomplete so that the product may, e.g., contain a certain proportion of molecules which are not octasulfated (persulfated), but rather less sulfated such as heptasulfated. Such minor variations in the commercial product are well known and are reflected in the fact that e.g., the aluminium content in commercial products may range from 17 to 21% and sulfur from 9.5 to 12.5%. In the present context, the term "sucralfate" also comprises such generally accepted minor variations.

Sucralfate may, for instance, be prepared as disclosed in U.S. Pat. No. 3,432,489 by reacting a 1–10% w/w aqueous solution of sucrose octasulfate or an alkali metal or alkaline earth metal salt thereof with a 1–10% w/w aqueous solution containing aluminium ions, preferably $AlCl(OH)_2$ at room temperature and a pH of 4–4.5. The sucrose octasulfate may be prepared by reacting sucrose with $ClSO_3H$, H_2SO_4 or H_2SO_4—C_5H_5N.

The sulfated saccharides may otherwise be prepared, for example, as disclosed in EP 230023.

The sulfated sucrose is preferably selected from the group consisting of sucrose pentasulfate, sucrose hexasulfate, sucrose heptasulfate and sucrose octasulfate.

The administration form in which the sulfated saccharide is administered will normally be a form suitable for topical application to the affected area. However, also administration into the skin or administration under the skin, e.g. by injection (by needle or dermajet) or other methods, are contemplated.

Although there may be cases where the sulfated saccharide may be administered as such, it will typically be compounded with one or more pharmaceutically acceptable carriers or excipients to present it in a form which is suitable for topical application or for injection or other form of introduction into or under the skin. In other words, it will be in the form of a liquid, semi-solid or solid topical or systemic preparation such as an ointment, lotion, gel, cream, emulsion, solution, suspension, microemulsion, liposomes or as a roll-ball applicator, sponge applicator or a spray device; a shampoo, hair tonic, hair conditioner, soap, balm, spray, paste, powder, sponge, strip, plaster, pad, dressing, or a comb or brush impregnated with or carrying the sulfated saccharide in such a manner that it is released when the comb or brush is used at the affected area.

The above-mentioned compositions are also suitable for cosmetic purposes where the compositions are applied to the hair or the skin areas normally covered with hair in order to prevent hair loss and/or to preserve the natural colour of the hair. Preferred compositions for cosmetic use are e.g. gels, emulsions, suspensions, liposomes, shampoos, hair tonics, hair conditioners, soaps, balms or sponges.

It may be interesting in certain cases to combine the sulfated saccharide with other forms of therapy, in particular therapies known to either produce hair growth by themselves such as vitamin A, minoxidil, squaric acid, allergens, irritants, corticosteroids, or agents which attack or modify the mechanism responsible for the alopecia, such as in the case of fungal infection, an ointment containing sucralfate and an antifungal agent such as ketoconazole, miconazole, clotrimazole, antiviral agents, such as acyclovir, antiinflammatory agents, antibacterial agents, etc. Also, it may advantageous to combine the sulfated saccharide with other pharmaceutical products known to have beneficial effects on the skin, such as vitamins, including vitamins B, vitamin E, lactic acid, astringents, emollients, or other agents, such as hyaluronic acid or other glycosaminoglycans, dermatan sulfate, chondroitin sulfate, keratan sulfate, heparan or heparan sulfate. Normally, the sulfate saccharide will be the predominant active component of the preparation.

Furthermore, advantages may be achieved by incorporating pharmaceutically acceptable amounts of penetration

enhancers in the formulations, such as salicylic acid and other keratolytics, amino acids, thioglycollates, dimethylsulfoxide, and hydrating agents, such as glycerol.

Plasters, sponges, strips, pads or other dressings may be prepared by impregnating a dressing material such as cotton wool or gauze or a polymeric substance with a solution or suspension of the sulfated saccharide followed by drying. Alternatively, a paste, lotion, cream or gel containing the sulfated saccharide may be spread over the dressing material.

Alternatively, the sulfated mono-, di- or oligosaccharide may in certain cases be injected or otherwise introduced into or under the skin or scalp.

For topical application, the preparation may be formulated in accordance with conventional pharmaceutical practice with pharmaceutical excipients conventionally used for topical applications. The nature of the vehicle employed in the preparation of any particular composition will depend on the method intended for administration of that composition. Vehicles other than water that can be used in compositions can include solids or liquids such as emollients, solvents, humectants, thickeners and powders. Examples of each of these types of vehicles, which can be used singly or as mixtures of one or more vehicles, are as follows:

Emollients, such as stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, propane-1,2-diol, butane-1,3-diol, 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, castor oil, acetylated lanolin alcohols, petroleum, mineral oil, butyl myristate, isostearic acid, palmitic acid, isopropyl linoleate, lauryl lactate, myristyl lactate, decyl oleate, myristyl myristate;

solvents, such as water, methylene chloride, isopropanol, castor oil, ethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoethyl ether, dimethyl sulfoxide, tetrahydrofuran, vegetable and animal oils, glycerol, ethanol, propanol, propylene glycol, and other glycols or alcohols, fixed oils;

humectants, such as glycerin, sorbitol, sodium 2-pyrrolidone-5-carboxylate, soluble collagen, dibutyl phthalate, gelatin;

powders, such as chalk, talc, kaolin, starch and derivatives thereof, gums, colloidal silicon dioxide, sodium polyacrylate, chemically modified magnesium aluminium silicate, hydrated aluminium silicate, carboxyvinyl polymer, sodium carboxymethyl cellulose, ethylene glycol monostearate;

gelling or swelling agents, such as pectin, gelatin and derivatives thereof, cellulose derivatives such as methyl cellulose, carboxymethyl cellulose or oxidised cellulose, guar gum, acacia gum, karaya gum, tragacanth gum, bentonite, agar, carbomer, bladderwrack, ceratonia, dextran and derivatives thereof, ghatti gum, hectorite, ispaghula husk, xanthan gum;

polymers, such as polylactic acid or polyglycolic acid polymers or copolymers thereof, paraffin, polyethylene, polyethylene oxide, polyethylene glycol, polypropylene glycol, polyvinylpyrrolidone;

surfactants, such as non-ionic surfactants, e.g. glycol and glycerol esters, macrogol ethers and esters, sugar ethers and esters, such as sorbitan esters, ionic surfactants, such as amine soaps, metallic soaps, sulfated fatty alcohols, alkyl ether sulfates, sulfated oils, and ampholytic surfactants and lecitins;

buffering agents, such as sodium, potassium, aluminium, magnesium or calcium salts (such as the chloride, carbonate, bicarbonate, citrate, gluconate, lactate, acetate, gluceptate or tartrate).

The preparation of the invention may also contain other additives such as stabilizing agents, preservatives, etc.

Furthermore, it may be advantageous to provide modified release preparations in which the sulfated saccharide is incorporated into a polymer matrix, or nanoparticles, or liposomes or micelles, or adsorbed on ion exchange resins, or carried by a polymer.

The pharmacologically active element in sucralfate is probably the non-aluminium complexed sodium and/or potassium salt of sucrose octakis(hydrogen sulfate). Since such a salt is soluble in water, it would seem that a small particle size would be an important factor when preparing formulations of the sparingly soluble sucralfate. One way of achieving a small sucralfate particle size is by means of milling, grinding or disintegrating apparatus, e.g. a three roll mill, where the sucralfate powder is ground, preferably together with a suitable liquid vehicle having a viscosity adapted to effectively suspend the resulting fine particles, and preferably a relatively low vapour pressure so that no excessive evaporation with resulting agglomeration of the fine particles will occur, such as a polyalcohol, for example glycerin or polyethylene glycol, normally having a molecular weight in the range of 200–6000, such as PEG 400. The resulting preparation will normally contain up to 60–70% by weight of sucralfate particles with a fairly uniform particle size of about 5–10 μm or less (for 95% by weight of the sucralfate), the particles being substantially evenly suspended in the vehicle. Such a paste can then be further suspended in any suitable pharmaceutical preparation using well known pharmaceutical methods. Another starting point for a small particle size sucralfate formulation is sucralfate "filter cake", which is an intermediary product obtained from the synthesis of sucralfate. The "filter cake" comprises sucralfate with a content of water of about 50% by weight, and with a particle size of about 5–10 μm or less. This material can be mixed with, for instance, a water-miscible liquid which has a relatively low vapour pressure, such as glycerin, in order to prevent the water from evaporating, and the sucralfate particles will retain their small size. Another important factor to take into consideration when preparing formulations of sucralfate and other sulfated saccharides is the strong negative charge of salts of sucrose octakis(hydrogen sulfate), and probably of most sulfated saccharides. The pharmacological effect of sucralfate, salts of sucrose octakis(hydrogen sulfate) and other sulfated saccharides probably depends on this negatively charged entity, and the pharmacological effect of the drug may be reduced by the presence of positively charged mono- and divalent ions in the vehicle. The person skilled in the art will be able to take this into consideration, using guidelines from the relevant literature, e.g., Martindale, The Extra Pharmacopoeia, The Pharmaceutical Press, London, or other pharmaceutical textbooks.

In this connection it should be mentioned that while the incorporation of sucralfate or other water-insoluble or sparingly water-soluble sulfated saccharides is best performed as described herein taking into consideration the physical and chemical properties of the sulfated saccharide, in particular the particle size considerations mentioned below, the incorporation of water-soluble sulfated saccharides, such as sodium and potassium salts of sucrose oktakis (hydrogen sulfate) in preparations discussed herein will normally be extremely simple and will ordinarily consist in the addition

of the sulfated saccharide to the preparation or to constituents thereof in either dry or dissolved form.

The sulfated saccharide will normally be used in a preparation in an amount of 0.001–99%, typically about 0.1–75%, such as about 0.2–30%, preferably about 0.5–20%, such as about 2–20%, e.g., 3–15%, by weight of the total preparation. For therapeutic and/or prophylactic use, the sulfated saccharide may also be used in a preparation in an amount of about 0.001–99% w/w, typically about 0.01–50% w/w, such as about 0.05–30% w/w, preferably about 0.1–20% w/w, such as about 0.5–15% w/w.

The concentration of the sulfated saccharide to be used in each particular case will of course depend upon the type of preparation and the intended use, but also on the solubility characteristics of the sulfated saccharide and, for sparingly soluble and substantially insoluble sulfated saccharides, on the particle size thereof; the smaller the particle size, the faster will be the dissolution of even sparingly soluble or even substantially insoluble sulfated saccharides or complexes thereof. Insoluble or sparingly soluble salts or complexes of sulfated saccharides are preferably used in the form of a fine powder, for example having a particle size of 200 μm or less, such as 100 μm or less. Examples of very small particle sizes which may be desirable for certain purposes are e.g. 50 μm or less, such as 20 μm or less, in certain cases 10 μm or less, such as 5 μm or less.

A topical preparation containing the sulfated saccharide is normally administered between 1 and 10 times a day, depending on the formulation, the severity of the condition to be treated, the age of the patient, and other factors. Based upon experience with other substances used in the treatment of alopecia, in particular minoxidil, it is expected that the effect will depend on continuing application of the preparation, for several months, or even years. In view of the fact that sucralfate is remarkably free of side effects, there should be no adverse long term consequences of such a treatment.

The invention is further illustrated by the following non-limiting examples.

EXAMPLE 1

Preparation of Sodium and Potassium Sucrose Octasulfate

I. Sucrose octasulfate

254.7 g (1.6 mol) of sulfur trioxide pyridine were slurried in 1300 ml of water-free pyridine. With stirring, 68.5 g (0.2 mol) of sucrose were added. The reaction mixture was heated to 65° C. and kept at this temperature for 240 minutes. As the reaction proceeded, the substance was separated as a thick flowing oil. When the reaction was terminated, the agitator was stopped, the pyridine phase was decanted, and the oily phase was dissolved in 600 ml of ion-exchanged water.

II. Potassium sucrose octasulfate

One portion of sucrose octasulfate solution prepared as described in I above was adjusted with 10% w/w aqueous potassium hydroxide to pH=9 with stirring at room temperature. The solution was evaporated at 50° C. in vacuo to remove pyridine and water until 880 g were left. The warm solution was filtered, adjusted to pH=9.5, and the substance was precipitated with slow cooling to 5° C. The substance was filtered and washed with 300 ml of 1:1 ion-exchanged water/methanol and 300 ml of methanol. The wet filter cake was dried in vacuo at 50° C. The crude product was dissolved at 40° C. in 700 ml of ion-exchanged water. The liquid was filtered and adjusted to pH=9.5, and the substance was precipitated with slow cooling to 5° C. The precipitated substance was filtered and washed with 300 ml of 1:1 ion-exchanged water/methanol and 300 ml of methanol. The wet filter cake was dried in vacuo at 50° C. The substance was reprecipitated twice as mentioned above.

Yield: 137 g (about 53%) of potassium sucrose octasulfate.

III. Sodium sucrose octasulfate

One portion of sucrose octasulfate solution prepared as described in I above was adjusted with 10% w/w aqueous sodium hydroxide to pH=9 with stirring at room temperature. The solution was evaporated at 50° C. in vacuo to remove pyridine and water. When 250 ml were distilled, 580 ml of ethylene glycol were added and the evaporation was continued until 10 mm vacuum. 100 ml of ethanol were added to the solution. The solution was filtered, and pH was adjusted to 9.5. 350 ml of ethanol were slowly added with vigorous stirring at 30°–35° C., and the substance will then precipitate. After the addition was ended, the mixture was cooled to 10° C., and the solid substance was filtered and washed with 50 ml of 1:1 ethanol/ethylene glycol and 200 ml of methanol. The wet filter cake was dried in vacuo at 50° C. The crude product was dissolved in 520 ml of ethylene glycol and heated to 40° C., and 100 ml of ethanol were added. The solution was filtered and pH was adjusted to 9.5. 350 ml of ethanol were slowly added with vigorous stirring at 30°–35° C. and the substance will then precipitate. After the addition was ended, the mixture was cooled to 10° C. and the solid substance was filtered. It was washed with 50 ml of 1:1 ethanol/ethylene glycol and 200 ml of ethanol. The wet filter cake was dried in vacuo at 50° C. The substance was reprecipitated once as above and then dried for 2 hours at room temperature in 500 ml of ethanol. The substance was filtered, washed with 200 ml of ethanol and dried at 50° C. in vacuo.

Yield: 146 g (about 63%) of sodium sucrose octasulfate.

EXAMPLE 2

A cream consisting of the following ingredients is prepared (all percentages are by weight):

2:1 suspension of sucralfate* in polyethylene glycol 400 (10% sucralfate in the final product)		15.0%
Lanolin		10.0%
Vegetable oil (evening primrose oil)		20.0%
Polyethylene glycol 400 monostearate		10.0%
Water	to	100.0%

*Sucralfate provided by Guilini Chemie, W. Germany.

The vegetable oil, lanoline and polyethylene glycol 400 monostearate were melted and thoroughly mixed with the warmed water to form an ointment. The sucralfate suspension was incorporated into the ointment.

EXAMPLE 3

A lotion is prepared from the following ingredients (all percentages are by weight):

2:1 suspension of sucralfate* in polyethylene glycol 400 (10% sucralfate in the final product)		15.0%
Glycerol		10.0%
Ethanol		50.0%
Water	to	100.0%

*Sucralfate provided by Guilini Chemie, W. Germany.

The ingredients were mixed together in the order stated to obtain a lotion.

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