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ANTI-ENZYME COMPOSITIONS COMPRISING ETHYLENEDIAMINE DISUCCINIC ACID

The invention relates to compositions, which can be administered or applied to a human or animal, to inhibit or reduce the enzyme activity.

Background

Various types of enzymes are present in the our body or on our skin, including enzymes form bacteria's, enzymes derived from our diet and enzymes produced by the body.

It is know that some of these enzymes can have undesirable side-effects. For example, lipase enzymes are present in the body exudates and these enzymes are known to cause dermatitis or skin rash, which for example, has always been a problem encountered by the users of disposable absorbent articles, such as diapers, incontinence articles, sanitary towels, training pants etc.

Manufacturers of diapers and skin care products have developed various products over the past decades which help reduce the occurrence of diaper rash (or skin rash). The main focus thereby has been to reduce the exposure of the skin to the body exudates. This is for example done by introduction to the diaper of absorbing or better absorbing materials. The amount of water which is in contact with the skin is thus reduced.

Lipase enzymes are also responsible for the production of fatty acids, which are partially eliminated from the body in the body exudates. These fatty acids can cause a malodour of the body.

EP 0117632-B relates to disposable articles which comprise lipase inhibiting agents, preferably zinc containing components, and a vehicle material. US 3,091,241 relates to the use of triacetine in vaginal tampons to inhibit lipase enzyme activity. US 3, 961,486 teaches the use of adipic acid to reduce the lipase enzyme activity and to reduce the skin rash.

It is known that the activity of various enzymes, such as lipase enzymes, is depended on the presence of certain metal ion, such as iron and copper, a so-called metallic cofactor. It has been



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suggested to use EDTA complexing agents to react with the metallic cofactors, to reduce the enzyme activity (for example in NL 7506962).

However, it has been found that EDTA is not an effective complexing agents for the metal ions of the metallic cofactors, in particularly when other metal ions are present on the skin or in the compositions.

The inventors now found that certain complexing agents, in particular ethylene diamine disuccinic acid (EDDS), can very effectively inactivate or inhibit the enzymes, by interacting with the metallic cofactor, containing metal ions such as copper and iron, and particularly when other ions, such as calcium ions, are present. Since calcium ion concentrations are generally high in body exudates or on the surface of the skin or hair, the complexing agents of the invention will be more effective when administered to humans or animals or applied to their skin or hair, than known complexing agents such as EDTA.

Thus, for example, it has been found that the use of the complexing agents in compositions of the invention, results in a very effective reduction or a prevention of dermatitis or malodour of the body, also when calcium ions are present in the compositions or on the skin, and for example, it has been found that even very small amounts of these complexing agents in these compositions can effectively give the required prevention or reduction of dermatitis or malodour of the body.

Summary of the Invention

The invention provides a composition comprising ethylene diamine disuccinic acid or a salt (EDDS) for reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body, in particular of enzymes present in the exudates.

The invention also provides compositions for reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body, comprising a complexing agent, and in use additionally comprising calcium ions and one or more metal ions, selected from the group

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consisting of Cu, Fe, Zn, Ni, Co (herein referred to as 'the selected metal ions'), whereby the $-\log_{10}C_T$ is equal to or greater than the smallest value of A or B, where

A is $-\log_{10}(L_T - M_T)$ and B is $K_1(1 - K_2\sqrt{I})(1 - K_3 \cdot \exp(-K_4 \cdot P))$,

C_T is the total concentration of calcium ions, L_T is the total concentration of complexing agent, M_T is the total concentration of the metal ions, selected from the group consisting of Cu, Fe, Zn, Ni and Co; P is the pH of the composition, I is the ionic strength of the composition, wherein all concentrations are in moles/litre, where K_1 , K_2 , K_3 and K_4 are the following constants for the metals ions:

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	Cu^{++}	Fe^{+++}	Zn^{++}	Ni^{++}	Co^{++}
K1	11.062	5.754	7.963	13.098	7.642
K2	0.496	0.479	0.619	0.535	0.652
K3	2.479	9385.0	24.202	1.473	32.069
K4	0.227	1.092	0.506	0.126	0.532

The invention also provides the use of the complexing agents as defined above , including ethylene diamine disuccinic acid or a salt (EDDS) for preparation of a composition for reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body, in particular of enzymes present in the exudates.

According to one aspect of the present invention, there is provided a use of a composition as described above in the preparation of a medicament useful in reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body.

According to another aspect of the present invention, there is provided a use of a composition as described above in the preparation of a medicament for the treatment of enzymatic dermatitis.

According to an another aspect of the present invention, there is provided a use of a composition as described above in the preparation of a medicament for the treatment of malodour of the body.

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Detailed Description of the Invention

The compositions of the invention reduce the enzyme activity of various enzymes, which require a metallic cofactor, in particular cofactors containing iron, copper, cobalt, zinc or nickel metal ions, by inhibiting or inactivating the enzymes.

The enzymes can be from bacteria's, fungi or algae, or can be produced by the human or animal body, or can be derived from the diet.

In particular esterase enzymes, including lipase enzymes, are very effectively inhibited or inactivated by the compositions of the invention.

The compositions can be used in any application where reduction of the enzyme activity of these enzymes is required. In particular, the compositions are used for reduction of the enzyme activity of enzymes in contact with the human or animal body, in particular the skin.

According to a preferred aspect of the invention, in use a source of calcium ions is also present in the composition. Hereby is meant that the calcium ions can be present in the composition containing the EDDS prior to use or in use, the calcium ion can be introduced in the

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compositions, e.g. by the application of the compositions to the skin, which contains calcium ions.

In a highly preferred aspect of the invention, the compositions are used for reduction of the enzyme activity of enzymes present in the exudates, in particular esterase enzymes, including lipase enzymes.

The compositions are particularly useful when calcium ions are present in the compositions and/ or in contact with the human or animal body.

In preferred embodiments of the invention, the compositions comprising the complexing agents are useful for the treatment of enzymatic dermatitis or the treatment of formation of a malodour of the body, caused by enzymes, in particular for reduction of the enzyme activity of lipase enzymes.

The compositions may be cosmetic compositions, preferably in the form of a spray, cream, foam, lotion, gel, oil, ointment or powder or tablet, preferably in the form of a water-in-oil emulsion.

Highly preferred are compositions are comprised in a deoderant or absorbent articles, such as diapers, wet wipes, as described herein.

By treatment is meant herein an improvement of the affected condition of the human or animal body, caused by the enzyme activity. Thus includes in one preferred aspect of the invention, the reduction or at least stabilisation of the malodour of the body, which is caused by enzymes; in another preferred aspect of the invention, the reduction or at least stabilisation of the enzymatic dermatitis or the rash of the skin, caused by enzymes.

The amount of the composition of the invention used for the reduction of the enzyme activity or in the treatment, will vary with the particular location of the condition being treated, the severity of the condition being treated, the expected duration of the treatment, any specific sensitivity to either the composition specific to the user, the condition of the user, concurrent therapies being administered, other conditions present in the user.

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For the present invention it is preferred that a minimum inhibitory concentration of the compositions containing the complexing agent is, preferably topically, applied to act as a complexing agent for selected metal ions present on the skin, which are required by the enzymes for their enzymatic performance, in an amount and form such that it is available to inhibit the activity of the enzymes present, particularly in the presence of calcium ions.

The complexing agents or compositions are in particular useful for the reduction of the enzyme activity of esterase enzymes, and thus for inhibition or inactivation of esterases, such as lipases or lipolytic enzymes. Their general activity is to hydrolyse fats present in the ester form (such as the glycerides found in human skin), and accordingly generate fatty acids and glycerol, which can cause irritation and malodour of the body. Because this group of enzymes is so widely distributed in plants, moulds, bacteria, milk, and milk-products, as well as in almost all animal tissues, and because moreover human lipase enzymes are present in the pancreatic exudates, they are almost always present in or on the human or animal body.

The activity of these lipases contributes to almost all skin rash or in particular diaper rash, causing irritation by the digestive degenerative action of lipase on the skin per se and by breaking down the lipid skin-components compromises the barrier property of the skin in the affected area. This breakdown of the integrity of the skin allows other components of the body exudates (urine and faeces in particular), which may not, by themselves, be irritating, to migrate through the compromised skin. At this point normally harmless components may then become irritating.

Highly preferred additional components of the compositions of the invention may be bactericidal or fungicidal agents, and/ or other enzyme inhibitors. Highly preferred can be the inclusion of cationic organic compounds, such as cationic surfactants.

pH Measurement

The pH as used herein can be determined by any known method of calculating or measuring the pH of an aqueous solution.

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Ionic Strength Measurement

The ionic strength (I) can be determined by the following equation:

$$I = \frac{1}{2} \sum c_i z_i^2,$$

wherein c is the molecular concentration of the soluble ion (i) and z is the charge of the soluble ion (i).

Complexing Agent

A highly preferred complexing agent for use in compositions of the invention is N, N'- ethylene diamine disuccinic acid or its salt (EDDS).

It is known that the (S,S) EDDS isomer is more readily biodegradable than the (R,R) isomer. Thus, depending of the application of the aqueous compositions of the invention, it may be desirable to use only one of the isomers of EDDS. It may be preferred that a racemic mixture of the isomers is used in the aqueous compositions, for example because the racemic mixture is less expensive.

The exact level of incorporation of the complexing agents in the compositions of the invention will depend on the nature of the compositions and the mode of applications. However, in general even small amounts of complexing agents can be sufficient to obtain the required prevention or reduction of dermatitis. Typical amount of complexing agents can be from 0.001% by weight to 30% by weight, more preferably from 0.005% to 10%, more preferably from 0.01% to 5% by weight of the composition..

Method of Preparation of the Compositions

The compositions can be prepared by any method known in the art for preparation for cosmetic compositions or medicament. The exact method will depend on the nature of the composition. The complexing agent can be added to the compositions in its acid or salt form, or be combined

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with other ingredients commonly used in cosmetic compositions or medicaments, or dispersed or dissolved in water or oil or a water-in-oil emulsion prior to addition to the composition.

Method of Use of Compositions

The composition of the invention can be administered to the patient or user by any method known in the art, but preferably the composition is applied to the skin or hair, which will be in contact with, or the vicinity of the enzymes.

The compositions can also be applied (firstly) to an article, such as a wipe or tissue, which will then be applied to the skin.

When the composition is used for treatment of malodour of the body, the composition may preferably be in the form of a deodorant composition, in the form of a fluid, gel, cream or powder, contained in a stick or spray .

Absorbent Articles

The compositions of the present invention can be comprised in an absorbent article, preferably a disposable absorbent article. Particularly preferred absorbent articles therefor is a wipe or a diaper. The diaper preferably comprises the composition in the topsheet of the diaper.

As used herein, the term "absorbent articles" refers to devices which absorb and contain body exudates, and, more specifically, refers to devices which are placed against or in proximity to the body of the wearer to absorb and contain the various exudates discharged from the body. The term "disposable" is used herein to describe absorbent articles which are not intended to be laundered or otherwise restored or reused as an absorbent article (i.e., they are intended to be discarded after a single use and, preferably, to be recycled, composted or otherwise disposed of in an environmentally compatible manner).

The structure of the disposable absorbent article is not critical to the practice of the present invention.

Normally, the composition is incorporated into the absorbent article or diaper in particular in an amount which will deliver the required treatment or reduction or inhibition of the enzyme activity, whereby it may be preferred that this is achieved after frequent use.

The disposable absorbent article preferably contains the composition according to the invention at a level such that the complexing agents therein are present at a level of from 0.01% to 30%, more preferably from 0.01% to 10%, most preferably from 0.05% to 5% by weight of the article.

Additional Ingredients

The composition of the invention can comprise additional ingredients. Which ingredients are present and at which level depends on the character of the composition and the use thereof. Thus for example lotions will generally comprise different additional ingredients to powders.

It can be preferred that the compositions comprise one or more other ingredient which can reduce dermatitis, or compounds which can help the healing of the skin, such as vitamins (vitamin E) and cortisone's, and also compounds to soften the skin such as vaseline, glycerin, triethyleneglycol, lanolin, paraffin and another group of polymers extensively employed by pharmaceutical and cosmetic manufactures, as also described herein.

Depending on the application of the compositions of the invention, a preferred additional ingredient can be one or more builders or dispersants. It can be preferred that a crystal growth inhibitor is present, preferably in addition to dispersants.

Suitable examples of water-soluble phosphates, suitable as crystal growth inhibitors or builders, are the alkali metal tripolyphosphates, sodium, potassium and ammonium pyrophosphate, sodium and potassium and ammonium pyrophosphate, sodium and potassium orthophosphate, sodium polymeta/phosphate in which the degree of polymerization ranges from about 6 to 21, and salts of phytic acid.

Any builder or dispersant material known in the art can be used. Particularly useful builders or dispersants can be monomeric, oligomeric and polycarboxylate-containing components,

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polymeric components, borate-containing components and phosphate-containing components and silicate and aluminosilicate-containing components.

Suitable polycarboxylates or polycarboxylic acids can be succinic acid, malonic acid, (ethylenedioxy) diacetic acid, maleic acid, diglycolic acid, tartaric acid, tartronic acid and fumaric acid; citrates, aconitrates and citraconates as well as succinate derivatives such as the carboxymethyloxysuccinates described in British Patent No. 1,379,241, lactoxysuccinates described in British Patent No. 1,389,732, and aminosuccinates described in Netherlands Application 7205873, and the oxypolycarboxylate materials such as 2-oxa-1,1,3-propane tricarboxylates described in British Patent No. 1,387,447; oxydisuccinates disclosed in British Patent No. 1,261,829, 1,1,2,2-ethane tetracarboxylates, 1,1,3,3-propane tetracarboxylates and 1,1,2,3-propane tetracarboxylates; sulfosuccinate derivatives disclosed in British Patent Nos. 1,398,421 and 1,398,422 and in U.S. Patent No. 3,936,448, and the sulfonated pyrolysed citrates described in British Patent No. 1,439,000;

Polymeric components include the water soluble organic homo- or co-polymeric polycarboxylic acids or their salts in which the polycarboxylic acid comprises at least two carboxyl radicals separated from each other by not more than two carbon atoms. Polymers of the latter type are disclosed in GB-A-1,596,756. Examples of such salts are polyacrylates of MWt 1000-5000 and their copolymers with maleic anhydride, such copolymers having a molecular weight of from 2000 to 100,000, especially 40,000 to 80,000.

The polyamino components are useful herein including those derived from aspartic acid such as those disclosed in EP-A-305282, EP-A-305283 and EP-A-351629.

Terpolymers containing monomer units selected from maleic acid, acrylic acid, polyaspartic acid and vinyl alcohol, particularly those having an average molecular weight of from 5,000 to 10,000, are also suitable herein.

Other polymeric components suitable for incorporation in the compositions herein include cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxypropylmethylcellulose and hydroxyethylcellulose.

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Further useful polymeric components are the polyethylene glycols, particularly those of molecular weight 1000-10000, more particularly 2000 to 8000 and most preferably about 4000

Other preferred ingredients are amorphous or crystalline, preferably layered, silicate or aluminosilicate materials or builders. Suitable aluminosilicate zeolites have the unit cell formula $\text{Na}_2[(\text{AlO}_2)_z(\text{SiO}_2)_y] \cdot x\text{H}_2\text{O}$ wherein z and y are at least 6; the molar ratio of z to y is from 1.0 to 0.5 and x is at least 5, preferably from 7.5 to 276, more preferably from 10 to 264. The aluminosilicate materials are in hydrated form and are preferably crystalline, containing from 10% to 28%, more preferably from 18% to 22% water in bound form.

Lotions, Creams, Oils, Foams, Ointments, Gels, Powders, Tablets and the like

The present compositions can be used for any suitable purpose. In particular, the present compositions are suitable for topical application to the skin or hair. In particular, the skin care compositions can be in the form of creams, sprays, lotions, gels, and the like. Preferably the cosmetic compositions herein are in the form of an oil-in-water emulsion of one or more oil phases in an aqueous continuous phase, each oil phase comprising a single oily component or a mixture of oily components in miscible or homogeneous form but said different oil phases containing different materials or combinations of materials from each other. The overall level of oil phase components in the compositions of the invention is preferably from about 0.1% to about 60%, preferably from about 1% to about 30% and more preferably from about 1% to about 10% by weight.

The present compositions preferably comprise, as either all or a portion of the oil phase or oil phases referred to above a first silicone-containing phase comprising a crosslinked polyorganosiloxane polymer and a silicone oil, wherein the composition comprises 0.1% to about 20%, preferably from about 0.5% to about 10%, more preferably from about 0.5% to about 5%, by weight of composition, of the combination of crosslinked silicone and silicone oil.

Compositions herein preferably also comprise a second non-crosslinked silicone-containing phase. In preferred embodiments the second silicone-containing phase is present in a level of from about 0.1% to about 20%, especially from about 0.1% to about 10% by weight of composition.

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Suitable silicone fluids for use in the second silicone-containing phase herein include water-insoluble silicones inclusive of non-volatile polyalkyl and polyaryl siloxane gums and fluids, volatile cyclic and linear polyalkylsiloxanes, polyalkoxylated silicones, amino and quaternary ammonium modified silicones, and mixtures thereof.

In preferred embodiments the second silicone-containing phase comprises a silicone gum or a mixture of silicones including the silicone gum. As used herein, the term "silicone gum" means high molecular weight silicone-based fluids having a mass-average molecular weight in excess of about 200,000 and preferably from about 200,000 to about 400,000. Silicone oils generally have a molecular weight of less than about 200,000. Typically, silicone gums have a viscosity at 25°C in excess of about 1,000,000 mm².s⁻¹. The silicone gums include dimethicones as described by Petrarch and others including US-A-4,152,416, May 1, 1979 to Spitzer, et al, and Noll, Walter, Chemistry and Technology of Silicones, New York: Academic Press 1968. Also describing silicone gums are General Electric Silicone Rubber Product Data Sheets SE 30, SE 33, SE 54 and SE 76.

In preferred embodiments, another, third, oil phase is present in an amount of from about 0.1% to about 15%, more preferably from about 1% to about 10% by weight of composition. The third oil phase can be either a separate phase or can form one phase together with either or both of the first and second silicone phases. Preferably, the third oil phase is a separate phase.

This oil phase preferably comprises a non-silicone organic oil, such as a natural or synthetic oil selected from mineral, vegetable, and animal oils, fats and waxes, fatty acid esters, fatty alcohols, fatty acids and mixtures thereof, which ingredients are useful for achieving emollient cosmetic properties.

Suitable first oil phase components for use herein include, for example, optionally hydroxy-substituted C₈-C₅₀ unsaturated fatty acids and esters thereof, beeswax, saturated and unsaturated fatty alcohols such as behenyl alcohol and cetyl alcohol, hydrocarbons such as mineral oils, petrolatum and squalane, fatty sorbitan esters (see US-A-3988255, Seiden, issued October 26 1976), lanolin and lanolin derivatives, animal and vegetable triglycerides such as almond oil, peanut oil, wheat germ oil, linseed oil, jojoba oil, oil of apricot pits, walnuts, palm

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nuts, pistachio nuts, sesame seeds, rapeseed, cade oil, corn oil, peach pit oil, poppyseed oil, pine oil, castor oil, soybean oil, avocado oil, safflower oil, coconut oil, hazelnut oil, olive oil, grapeseed oil, shea butter, shorea butter, and sunflower seed oil and $C_{1-C_{24}}$ esters of dimer and trimer acids such as diisopropyl dimerate, diisostearylmalate, diisostearyldimerate and triisostearyltrimerate. Of the above, highly preferred are the mineral oils, petrolatums, unsaturated fatty acids and esters thereof and mixtures thereof.

Amphiphilic Surfactant

A further preferred component of the compositions herein is an organic amphiphilic surfactant which is capable of forming smectic lyotropic crystals in product or when the product is being applied to the skin at ambient or elevated temperatures. Preferably the amphiphilic surfactant is capable of forming liquid crystals at a temperature in the range from about 20°C to about 40°C. Preferably the amphiphilic surfactant is capable of forming smectic lyotropic liquid crystals. Once application of the product to the skin has been completed, liquid crystals may not be identifiable on the skin surface or stratum corneum. The amphiphilic surfactant is preferably present at a level of from about 0.1% to about 20%, preferably from about 0.1% to about 10%, by weight.

Organic amphiphilic surfactants suitable for use herein include those having a weight average HLB (Hydrophilic Lipophilic Balance) in the range from about 2 to about 12, preferably from about 4 to about 8.

Preferred organic amphiphilic surfactants employed herein have a long saturated or unsaturated branched or linear lipophilic chain having from about 12 to about 30 carbon atoms such as oleic, lanolic, tetradecylic, hexadecylic, isostearyllic, lauric, coconut, stearic or alkyl phenyl chains. When the hydrophilic group of the amphiphilic material forming the liquid crystal phase is a nonionic group, a polyoxyethylene, a polyglycerol, a polyol ester, oxyalkylated or not, and, for example, a polyoxyalkylated sorbitol or sugar ester, can be employed. When the hydrophilic group of the amphiphilic surfactant forming the liquid crystal phase is an ionic group, advantageously there can be used, as the hydrophilic group, a phosphatidylcholine residue as found in lecithin.

The compositions can also comprise Amphoteric, anionic, nonionic and cationic surfactants.

A wide variety of optional ingredients such as non-occlusive moisturizers, humectants, gelling agents, neutralizing agents, perfumes, colouring agents and surfactants, can be added to the skin compositions herein.

The compositions herein can comprise a humectant. Suitable humectants for use herein include sorbitol, propylene glycol, butylene glycol, hexylene glycol, ethoxylated glucose derivatives, hexanetriol, glycerine, glycine, hyaluronic acid, arginine, Ajidew (NaPCA), water-soluble polyglycerylmethacrylate lubricants and panthenols. A preferred humectant herein is glycerine (sometimes known as glycerol or glycerin). Chemically, glycerine is 1,2,3-propanetriol and is a product of commerce. One large source of the material is in the manufacture of soap. Glycerine is especially preferred in the compositions of the invention from the viewpoint of boosting moisturisation. Also preferred for use herein is butylene glycol. Particularly preferred from the viewpoint of boosting moisturisation is a combination of glycerine and urea.

In the present compositions, the humectant is preferably present at a level of from about 0.1% to about 20%, more preferably from about 1% to about 15%, and especially from about 5% to about 15% by weight of composition.

The compositions of the invention can also contain a hydrophilic gelling agent at a level preferably from about 0.01% to about 10%, more preferably from about 0.02% to about 2%, and especially from about 0.02% to about 0.5%. The gelling agent preferably has a viscosity (1% aqueous solution, 20°C, Brookfield RVT) of at least about 4000 mPa.s, more preferably at least about 10,000 mPa.s and especially at least 50,000 mPa.s.

Suitable hydrophilic gelling agents can generally be described as water-soluble or colloiddally water-soluble polymers, and include cellulose ethers (e.g. hydroxyethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose), polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum and xanthan gum.

Preferred hydrophilic gelling agents herein, however, are acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers sold by the B.F. Goodrich Company under the trade mark of

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Carbopol resins. These resins consist essentially of a colloiddally water-soluble polyalkenyl polyether crosslinked polymer of acrylic acid crosslinked with from 0.75% to 2.00% of a crosslinking agent such as for example polyallyl sucrose or polyallyl pentaerythritol. Examples include Carbopol 934, Carbopol 940, Carbopol 950, Carbopol 954, Carbopol 980, Carbopol 951 and Carbopol 981. Carbopol 934 is a water-soluble polymer of acrylic acid crosslinked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. A most preferred polymer is Carbopol 954. Also suitable for use herein are hydrophobically-modified cross-linked polymers of acrylic acid having amphipathic properties available under the Trade Name Carbopol 1382, Carbopol 1342 and Pemulen TR-1 (CTFA Designation: Acrylates/10-30 Alkyl Acrylate Crosspolymer). A combination of the polyalkenyl polyether cross-linked acrylic acid polymer and the hydrophobically modified cross-linked acrylic acid polymer is also suitable and is preferred for use herein. The gelling agents herein are particularly valuable for providing excellent stability characteristics over both normal and elevated temperatures.

Neutralizing agents suitable for use in neutralizing acidic group containing hydrophilic gelling agents herein include sodium hydroxide, potassium hydroxide, ammonium hydroxide, monoethanolamine, diethanolamine and triethanolamine.

Other optional materials include keratolytic agents/desquamation agents such as salicylic acid; proteins and polypeptides and derivatives thereof; water-soluble or solubilizable preservatives preferably at a level of from about 0.1% to about 5%, such as Germall 115, methyl, ethyl, propyl and butyl esters of hydroxybenzoic acid, benzyl alcohol, EDTA, Euxyl (RTM) K400, Bronopol (2-bromo-2-nitropropane-1,3-diol) and phenoxypropanol; anti-bacterials such as Irgasan (RTM) and phenoxyethanol (preferably at levels of from 0.1% to about 5%); soluble or colloiddally-soluble moisturising agents such as hylaronic acid and starch-grafted sodium polyacrylates such as Sanwet (RTM) IM-1000, IM-1500 and IM-2500 available from Celanese Superabsorbent Materials, Portsmouth, VA, USA and described in USA-A-4,076,663; vitamins such as vitamin A, vitamin C, vitamin E and vitamin K; alpha and beta hydroxyacids; aloe vera; sphingosines and phytosphingosines, cholesterol; skin whitening agents; N-acetyl cysteine; colouring agents; perfumes and perfume solubilizers and additional surfactants/emulsifiers such as fatty alcohol ethoxylates, ethoxylated polyol fatty acid esters, wherein the polyol can be selected from glycerine, propyleneglycol, ethyleneglycol, sorbitol, sorbitan,

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polypropyleneglycol, glucose and sucrose. Examples include glyceryl monohydroxy stearate and stearyl alcohol ethoxylated with an average of from 10 to 200 moles of ethylene oxide per mole of alcohol and PEG-6 caprylic/capric glycerides.

The compositions of the present invention can also comprise a safe and effective amount of vitamins, such as vitamin E, B, preferably vitamin B₃ vitamin a or retinoid. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1% to about 10%, even more preferably from about 0.5% to about 10%, and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the vitamin.

The pH of the compositions is preferably from about 4 to about 9, more preferably from about 6 to about 8.0.

The balance of the composition is water or an aqueous carrier suitable for topical application to the skin. The water content of the compositions herein is generally from about 30% to about 98.89%, preferably from about 50% to about 95% and especially from about 60% to about 90% by weight.

The compositions of the invention are preferably in the form of a moisturising cream or lotion, which can be applied to the skin as a leave-on product.

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Claims

1. A composition for the reduction of the enzyme activity, comprising ethylene diamine disuccinic acid or salts thereof (EDDS) complexing agent.
2. An aqueous composition for the reduction of the enzyme activity which comprises a complexing agent, and which in use comprises calcium ions and one or more metal ions, selected from the group consisting of Cu, Fe, Zn, Ni, Co, whereby the $-\log_{10}C_T$ is equal to or greater than the smallest value of A or B, wherein

$$A \text{ is } -\log_{10}(L_T - M_T) \text{ and } B \text{ is } K_1(1 - K_2\sqrt{I})(1 - K_3.\exp(-K_4.P)),$$

C_T is the total concentration of calcium ions, L_T is the total concentration of complexing agent, M_T is the total concentration of the metal ions, selected from the group consisting of Cu, Fe, Zn, Ni and Co; P is the pH of the composition, I is the ionic strength of the composition in moles/ litre, where K_1 , K_2 , K_3 and K_4 are the following constants for the metals ions:

	Cu ⁺⁺	Fe ⁺⁺⁺	Zn ⁺⁺	Ni ⁺⁺	Co ⁺⁺
K1	11.062	5.754	7.963	13.098	7.642
K2	0.496	0.479	0.619	0.535	0.652
K3	2.479	9385.0	24.202	1.473	32.069
K4	0.227	1.092	0.506	0.126	0.532

3. A composition according to claim 1 or 2, for the reduction of the enzyme activity of enzymes in contact with the human or animal body.
4. Use of ethylene diamine disuccinic acid or salts thereof (EDDS) for preparation of a composition for reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body.

5. Use of a complexing agent for preparation of an aqueous composition for reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body, which in use comprises calcium ions and one or more metal ions, selected from the group consisting of Cu, Fe, Zn, Ni, Co, whereby the $-\log_{10}C_T$ is equal to or greater than the smallest value of A or B, wherein

$$A \text{ is } -\log_{10}(L_T - M_T) \text{ and } B \text{ is } K_1(1 - K_2\sqrt{I})(1 - K_3.\exp(-K_4.P)),$$

C_T is the total concentration of calcium ions, L_T is the total concentration of complexing agent, M_T is the total concentration of the metal ions, selected from the group consisting of Cu, Fe, Zn, Ni and Co; P is the pH of the composition, I is the ionic strength of the composition, wherein all concentrations are in moles/ litre, where K_1 , K_2 , K_3 and K_4 are the following constants for the metals ions:

	Cu	Fe	Zn	Ni	Co
K1	11.062	5.754	7.963	13.098	7.642
K2	0.496	0.479	0.619	0.535	0.652
K3	2.479	9385.0	24.202	1.473	32.069
K4	0.227	1.092	0.506	0.126	0.532

6. A composition according to any of claims 2, being an aqueous composition, obtainable by a process comprising the step of addition of the complexing agent to an aqueous solution, comprising calcium ions and the metal ions selected from the group consisting of Cu, Fe, Zn, Ni, Co.
7. A composition according to any of claims 1 to 4, wherein the complexing agent is EDDS, present at a level of from 0.001% to 30% by weight of the composition.
8. A composition according to any preceding claim for reduction of the enzyme activity of enzymes present in the body exudates.

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9. A composition according to any preceding claim for reduction of the activity of lipase enzymes.
10. A composition according to any of claim 1, 2 or 3, comprising in use calcium ions and metal ions selected from Fe, Cu, Co, Zn and Ni.
11. A composition according to any preceding claim in the form of a spray, cream, spray, foam, lotion, gel, oil, ointment or powder.
12. An absorbent article, preferably a wipe or a diaper, comprising the composition according to any preceding claim.
13. A deodorant comprising the composition according to any preceding claim.
14. Use of a composition according to any preceding claim in the preparation of a medicament useful in reduction of the enzyme activity, preferably of enzymes in contact with the human or animal body.
15. Use of a composition according to any of claims 1 to 13 in the preparation of a medicament for the treatment of enzymatic dermatitis.
16. Use of a composition according to any of claims 1 to 13 in the preparation of a medicament for the treatment of malodour of the body.