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DENTAL PREPARATIONS CONTAINING HIGHER ALIPHATIC ACYL SARCOSIDE COMPOUNDS

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The present invention relates to dental preparations comprising certain higher aliphatic acyl sarcoside compounds. The instant application is a continuation-in-part of co-pending applications, Serial No. 258,759 filed November 28, 1951, and Serial No. 271,864 filed February 15, 1952, now U. S. Patent No. 2,689,170 issued September 14, 1954.

Many commercial dental preparations have incorporated therein minor amounts of certain detergents such as soap to provide detersive and foaming characteristics.

According to the present invention, improved dental preparations may be prepared by the incorporation of a substantially saturated higher aliphatic acyl sarcoside compound containing 17–18 carbons in said acyl group.

Thus, these active ingredients comprise the stearoyl and heptadecanoyl amides of sarcosine compounds. These compounds may be employed in the form of the free acids or preferably as the water-soluble salts thereof. Suitable salts are the alkali metal (e. g. sodium and potassium), ammonium, amine and alkylolamine (e. g. mono-, di- and triethanolamine) salts and the like. Further specific examples are stearoyl sarcosine and its sodium and potassium salts, and heptadecanoyl sarcosine and its sodium and potassium salts. For convenience, herein, the terms "sarcoside compound" or "sarcoside" refer to such compounds having a free carboxylic group or the water-soluble salts thereof, unless further specified.

These amide compounds should be utilized in pure or substantially pure form. They should be substantially free from soap or similar higher fatty acid material which is formed in normal commercial methods of manufacture and which tends to neutralize or substantially reduce some of the special characteristics of the active ingredients. In usual practice, the amount of higher fatty acid material should be less than 15% by weight of the amide compound and insufficient to substantially adversely affect said amide, and preferably less than about 10% of said amide with optimum results at 0–5% fatty acid material.

These compounds may be produced in pure or substantially pure form by the condensation of the corresponding fatty acylating substance, such as stearic acid chloride (or equivalent substantially saturated fatty acid mixtures consisting essentially of the stearic acid chloride), with sarcosine in an alkaline medium, as described in co-pending application, S. N. 271,864, now U. S. Patent No. 2,689,170. It is believed that the heptadecanoyl sarcoside compounds are specifically novel, and therefore the process will be illustrated with particular reference thereto. Normal heptadecanoic acid is treated with phosphorus trichloride to obtain the corresponding acid chloride. The heptadecanoyl acid chloride is condensed with sarcosine (20% molar excess) at a pH of about 10.5 in presence of sodium hydroxide and at room temperature to form the corresponding sodium heptadecanoyl sarcoside. This product is acidified to a pH of 2, extracted with ethyl ether, washed with 5% sulfuric acid and water, and dried. The resulting heptadecanoyl sarcosine

is crystallized from Skellysolve E, neutralized with alcoholic sodium hydroxide and re-crystallized from alcohol. Analysis of the sodium salt shows that it has a melting point of 143.5–144° C. and a neutral equivalent of 344 with less than 1% soap content. The heptadecanoyl sarcosine compound has a melting point of 69–70° C. The other soluble salts, as indicated above, are formed similarly by neutralization with the desired base, such as potassium hydroxide or ethanolamine to form the corresponding salts.

These compounds exhibit many highly unusual and beneficial characteristics of particular desirability in dental preparations. Among the unusual properties is their anti-bacterial power on the oral flora (the complex mixture of micro-organisms normally present in the mouth). These compounds exhibit a superior inhibiting effect on bacterial growth and the production of acid from fermentable carbohydrates by these micro-organisms found in saliva. This superior inhibiting effect may be illustrated by the Snyder dilution test which is known in the art. In accordance with this test, a very small portion of these compounds may be added to Snyder tubes containing a nutrient dextrose agar with brom-cresol green indicator which had been inoculated previously with saliva. After 72 hours incubation at 37° C., the tubes containing these compounds are still green in color indicating marked inhibition of acid production with no evidence of bacterial growth. As a control, similar tubes without the addition of these compounds have turned yellow after only 24 hours incubation indicative of rapid and substantial acid formation, with the formation of bacterial colonies. For example, the minimum amount of sodium stearoyl sarcoside which is necessary to maintain a predominantly green color for 72 hours in the Snyder test is an amount corresponding to about 50 milligrams per 100 cc. of the saliva normally turning the control tubes yellow in 24 hours. As indicative of the specificity of action with respect to the chemical structure of these active ingredients, it has been found that such structurally-similar materials as sodium stearoyl glycide and sodium oleyl sarcoside are not equivalents but are markedly inferior in anti-bacterial activity against the oral flora and inhibition of acid formation.

It has been found also that these active ingredients have the property of reducing the solubility of tooth enamel in acid to a marked degree. Such laboratory tests for evaluating the reduction in enamel solubility are known. Data obtained in such tests indicate that both sodium stearoyl and heptadecanoyl sarcosides exhibit significant effects in this respect whereas unsaturated compounds such as sodium oleyl and elaidyl sarcosides are markedly inferior.

These active ingredients may be utilized in any preparation designed for application to the oral cavity which are referred to herein as dental preparations. Such dental preparations include suitable toothpaste and dental creams, tooth powders, liquid dentifrices, mouth washes or rinses, lozenges, tablets, chewing gum, dental floss and the like. These preparations may contain various adjuvant materials in suitable amounts provided the same do not substantially adversely affect the desired results.

Any suitable amount of these compounds may be incorporated in the dental preparation. The specific amount will vary, naturally, depending upon the specific type of preparation and the specific effects desired, but will generally be a minor amount of the composition, such as usually at least about 0.05 and up to about 10% by weight. In the case of dentifrices such as dental creams, it is preferred to use an amount from about 0.25 to about 5% by weight.

Any suitable practically water-insoluble polishing agent may be admixed with these active ingredients in the prep-

aration of various dentifice compositions. There is a relatively large number of such materials known in the art including, for example, calcium carbonate, dicalcium phosphate, tricalcium phosphate, insoluble sodium metaphosphate, aluminum hydroxide, magnesium carbonate and bentonite. It is preferred to use the water-insoluble calcium and magnesium salts, and more particularly calcium carbonate and/or a calcium phosphate. In general, these polishing agents comprise a major proportion by weight of the solid ingredients and aid in cleansing the mouth.

In the preparation of tooth powders, it is usually sufficient to mechanically admix the various ingredients.

In dental cream formulations, the liquids and solids should necessarily be proportioned to form a creamy mass of desired consistency which is extrudible from a collapsible aluminum or lead tube. In general, the liquids in the dental cream will comprise chiefly water, glycerine, sorbitol, propylene glycol and the like, including suitable mixtures thereof. It is usually advantageous to use a mixture of both water and a humectant or binder such as glycerine, sorbitol, and the like. The total liquid content will generally be about 20–75% by weight of the formulation.

Other types of compositions will be formulated in known manner also.

It is advantageous to incorporate a stabilizing agent in the dentifrice compositions. Such materials are the calcium and magnesium ion suppression agents which aid in maintenance of the active ingredients in their active forms, particularly in dentifrices containing calcium- and magnesium-containing polishing agents. These agents provide improved stability of the dental cream such that the active ingredients maintain their effectiveness even after aging for long periods of time.

Various suitable stabilizing agents are calcium and magnesium sequestering agents such as the water-soluble inorganic polyphosphate salts. Examples thereof are the alkali metal salts of pyrophosphoric, tripolyphosphoric or tetraphosphoric acids. Specific materials are tetrasodium pyrophosphate, disodium diacid pyrophosphate, sodium and potassium tripolyphosphate, hexasodium tetraphosphate and sodium hexametaphosphate salts, with the pyrophosphates preferred. Soluble sodium and potassium metaphosphate may be used also. Other suitable stabilizing agents are chelating agents such as the alkali metal and preferably sodium salts of ethylene diamine tetraacetic acid and citric acid. These stabilizing agents may be employed in any suitable amount depending upon the specific formulation but will usually be up to 5% and preferably from 0.1–3% by weight of the composition.

Other adjuvant materials are usually incorporated in suitable amounts, particularly in dental creams. It is preferred to use a gelling agent such as the natural and synthetic gums and gum-like materials, e. g. Irish moss, gum tragacanth, sodium carboxymethylcellulose, and starch. Furthermore, such materials as soluble saccharin, coloring agents, flavoring oils, preservatives, alcohol, and the like, may be used as desired in proper amount.

Mouth washes or rinses are also within the scope of the present invention. Such products are usually an effective amount of the active ingredients dissolved or dispersed in a suitably flavored liquid vehicle, preferably aqueous alcoholic vehicle. The alcohol concentration may vary depending on the mouth effect desired, such as about 5–70% alcohol, and preferably 5–40% by weight. Liquid dentifrices are also included, such products usually containing in addition a mucilaginous material and optionally combined with small amounts of polishing agent, glycerine and the like. Another embodiment is chewing gum which will contain minor but effective amounts of these active ingredients incorporated in the gum base such as chicle or other natural or synthetic rubber and gum-like materials.

The pH of the final formulations of the present invention is variable and, therefore, the products may have any suitable pH value in solution compatible with the stability of the materials. Where reference is made to pH values it has reference to the pH as determined on a liquid product per se, and in the case of a dental cream or powder or similar product as determined on a 20% aqueous slurry or mixture of said cream or powder. Thus it is generally desired that the pH of the product under the testing conditions indicated be from about 5 up to about 10, and preferably from about 5.5 to 9, with optimum desired effects at a substantially neutral pH value in solution, e. g., about 6 to 8.

The following specific examples are further illustrative of the nature of the present invention, but it is to be understood that the invention is not limited thereto. The preparations may be prepared in the usual manner and all amounts of the various ingredients are by weight unless otherwise specified.

Example I.—Dental cream

	Percent
Sodium stearoyl sarcoside	2.8
Calcium carbonate	12.1
Dicalcium phosphate dihydrate	36.2
Glycerine	30.6
Water	15.3
Irish moss gum	1.0
	98.0

the balance consisting essentially of soluble saccharin, flavor and preservatives.

Example II.—Tooth powder

	Percent
Sodium heptadecanoly sarcoside	3.0
Calcium carbonate	25.0
Dicalcium phosphate dihydrate	70.0
Saccharin, soluble	0.2
Flavor	1.8
	100.0

Example III.—Mouth wash

	Percent
Potassium stearoyl sarcoside	0.1–0.2
Ethyl alcohol	10.0
Flavor	0.15
Saccharin, soluble	0.01
Distilled water	Balance

Example IV.—Chewing gum

	Percent
Sodium stearoyl sarcoside	0.5
Gum base, e. g. chicle	20.0
Sucrose	60.0
Corn syrup	18.5
Flavor	1.0
	100.0

Example V.—Liquid dentirifice

	Percent
Sodium stearoyl sarcoside	2.0
Sodium carboxymethylcellulose	2.0
Flavor	0.5
Distilled water	Balance

Although the present invention has been described with reference to particular embodiments and examples, it will be apparent to those skilled in that art that variations and modifications of this invention can be made and that equivalents can be substituted therefor without departing from the principles and true spirit of the invention.

Having thus described the invention, what is claimed is:

1. A dental preparation comprising a sarcoside com-

pound selected from the group consisting of N-heptadecanoyl and N-strearoyl sarcoside compounds having less than about 15% based on the weight of said sarcoside of higher fatty acid material, the amount of said material being insufficient to adversely affect said sarcoside.

2. A dentifrice comprising a polishing material and a minor amount of sodium N-heptadecanoyl sarcoside having less than about 10% of higher fatty acid material based on the weight of sarcoside.

3. A dentifrice comprising a polishing material and a minor amount of sodium N-stearoyl sarcoside having less than about 10% of higher fatty acid material based on the weight of sarcoside.

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