United States Patent Office 3,826,845 Patented July 30, 1974

3,826,845

OINTMENT BASE

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No Drawing Filed Feb. 4, 1970, Ser. No. 8,711
Claims priority, application Japan, Feb. 8, 1969, 44/9,426; Dec. 27, 1969, 45/159
Int. Cl. A61k 9/06
U.S. Cl. 424—365 5 Claims

ABSTRACT OF THE DISCLOSURE

This invention relates to a novel ointment base whose consistency is proper for an ointment base and is scarcely varied depending upon a temperature. It is useful for a preparation of ointments, cosmetics and the like, and comprises triglyceride being liquid at ordinary temperatures or a mixture of a dibasic aliphatic carboxylic acid ester and a salicyclic acid ester; silicic acid anhydride; and a nonionic surfactant or an ionic surfactant selected from the group of a fatty acid polyoxyethylene-phosphate, a fatty alcohol-polyoxyethylene-phosphate, lecithin, and alkylsulfate, a fatty acid-polypeptide condensate or an ampholytic surfactant of carboxylic acid type.

The present invention relates to a novel ointment base whose features will become apparent as this description progresses.

As an ointment base, there have been known fatty oil, lanolin, Vaseline, glycerine and blend of them.

However, these prior bases have a disadvantage that their consistency is varied depending upon a temperature. More particularly, at low temperatures the consistency of them remarkably increases so that the spreadability of them becomes worse. And at high temperatures the consistency decreases so that they become smeary.

On the other hand, it is known that various organic solvents are gelled by addition of silicic acid anhydride. However, the gel thus obtained is not proper for an ointment base because of its strong thixotropic property, change of consistency by addition of medicaments or change in a temperature, appearance of bleeding and inferiority of spreadability and brightness.

The main object of this invention is to overcome the disadvantages above described and to provide an ointment base whose consistency is proper for an ointment base and is scarcely varied depending upon a temperature. Another object of the present invention is to provide a non-irritant, smooth, easily spreadable ointment base.

As a result of earnest studies to discover such an improved ointment base, it is found that an ointment base having various excellent properties is obtained by adding silicic acid anhydride and a certain surfactant to triglyceride being liquid at ordinary temperatures or to a mixture of a dibasic aliphatic carboxylic acid ester and a salicylic acid ester. The present invention is completed based upon this knowledge and relates to an ointment base which comprises triglyceride being liquid at ordinary temperatures or a mixture of dibasic aliphatic carboxylic acid ester and a salicyclic acid ester; silicic acid anhydride; and a nonionic surfactant or an ionic surfactant selected from the group of a fatty acid polyoxyethylene-phosphate, a fatty alcohol-polyoxyethylene-phosphate, lecithin, an alkylsulfate, a fatty acid-polypeptide condensate or an ampholytic surfactant of carboxylic acid type.

In the present invention, the term "liquid at ordinary temperatures" means liquid at about 20–30° C.

The triglyceride employed as a dispersion medium in this invention means a trifatty acid glyceride having the formula



wherein R_1, R_2 and R_3 may be the same or different and each represents an aliphatic acyl group provided that at least one of them is an aliphatic acyl group having 9–19 carbon atoms.

Representative examples of the R_1, R_2 and R_3 are those acyl groups derived from acetic acid, propionic acid, caprylic acid, capric acid, oleic acid, linolenic acid, linoleic acid, ricinoleic acid, eruic acid and palmitic acid. In the present invention, said triglycerides may be employed alone or blended with each other. Most preferably, there may be employed vegetable oils which contain the triglyceride as a main ingredient. The following are examples of such vegetable oils: sesame oil, bean oil, cotton seed oil, rape seed oil, apricot oil, rice-bran oil, peanut oil, olive oil, castor oil, palm oil, Neobee oil (Drew Chem. Co.) and the like. An amount of the triglyceride employed in this invention is about 88–97.5%. In this invention, percent means weight percent based upon the total amount of the ointment base. The mixture of a dibasic aliphatic carboxylic acid ester and a salicylic acid ester which may be employed as dispersion medium in this invention must be liquid at ordinary temperatures. Examples of the dibasic acid ester include methyl-, ethyl-, propyl- and isopropyl mono (or di-) ester of glutaric acid, adipic acid, pimelic acid, suberic acid, azelaic acid, sebacic acid or undecanedioic acid.

Examples of the salicylic acid ester include methyl salicylate, ethyl salicylate and ethyleneglycol monosalicylate.

The ratio of the dibasic acid ester to the salicylic acid ester is not limited but ordinarily from 1:3 to 3:1, preferably 1:1 by weight. An amount of the mixture employed in this invention is about 85–96.5%.

As the silicic acid anhydride employed in the present invention, there may be preferably used an amorphous colloidal silicic acid, usually Aerosil (Der firma Degussa A.G.) and Carbosil (Der firma G. L. Cabot Inc.). An amount of the silicic acid anhydride employed in this invention depends upon a kind of the dispersion medium. In case of using the triglyceride, an amount of the silicic acid anhydride is about 2–7% preferably about 3–5% and in case of using the mixture of the dibasic acid ester and the salicylic acid ester, it is about 3–10%, preferably about 5–7%.

A kind of the surfactant is an important factor in this invention. As a result of earnest investigations, it is found that only the surfactants used in this invention give proper consistency for an ointment base. The following are examples of the surfactant which may be used either alone or blended with each other;

Nonionic surfactant

(1) polyoxyethylene sorbitan fatty acid ester, e.g.

Tween 20 [polyoxyethylene (20) sorbitan monolaurate]
Tween 60 [polyoxyethylene (20) sorbitan monostearate]
(Atlas Chem. Ind. Inc.)

(2) sorbitan fatty acid ester, e.g.

Span 60 [sorbitan monostearate]
Span 80 [sorbitan monooleate]
Aracel 83 [sorbitan sesquioleate]
Span 85 [sorbitan trioleate]
(Atlas Chem. Ind. Inc.)

(3) sucrose fatty acid ester, e.g.

Nitto Ester
(Dainippon Sugar Mfg. Ltd.)

(4) polyoxyethylene fatty acid ester, e.g.

Myrj 51 [polyoxyethylene (20) monostearate]
Myrj 53 [polyoxyethylene (50) monostearate]
Myrj 45 [polyethylene glycol (400) monostearate]
(Atlas Chem. Ind. Inc.)

(5) polyoxyethylene fatty alcohol ether, e.g.

Brij 30 [polyoxyethylene (4) lauryl alcohol ether]
Brij 35 [polyoxyethylene (23) lauryl alcohol ether]
(Atlas Chem. Ind. Inc.)
P.O.E. hexadecyl alcohol ether [polyoxyethylene hexadecyl alcohol ether]
(Nikko Chem. Co. Ltd.)

(6) polyoxyethylene lanolin derivative, e.g.

Lanopol 300 [polyoxyethylene (48) lanolin derivative]
(Takasago Perfumery Co. Ltd.)

(7) polyoxyethylene hydrogenated lanolin derivative, e.g.

Lanopol H 200 [polyoxyethylene (16) hydrogenated lanolin derivative]
(Takasago Perfumery Co. Ltd.)

(8) polyoxyethylene lanolin alcohol derivative, e.g.

Lanopol A 170 [polyoxyethylene (17) lanolin alcohol ether]
Takasago Perfumery Co. Ltd.)

(9) polyoxyethylene castor oil derivative, e.g.

CO–10 [polyoxyethylene (10) castor oil ether, Nikkol CO–10]
(Nikko Chem. Co. Ltd.)

(10) polyoxyethylene hydrogenated castor oil derivative, e.g.

HCO–20 [polyoxyethylene (20) hydrogenated castor oil ether, Nikkol HCO–20]
HCO–60 [polyoxyethylene (60) hydrogenated castor oil ether, Nikkol HCO–60]
(Nikko Chem. Co. Ltd.)

(11) glyceryl monofatty acid ester, e.g.

glyceryl monostearate (G.M.S.)

(12) propylene glycol mono fatty acid ester, e.g.

propylene glycol monostearate (P.M.S.)

(13) polyoxyethylene alkyl aryl ether, e.g.

NP–10 [polyoxyethylene nonyl phenol ether, Nikkol NP–10]
(Nikko Chem. Co. Ltd.)

(14) polyoxyethylene - polyoxypropylene copolymer, e.g.

Pluronic L 61, L 64, F 38
(Wyandotte Chem. Corp.)

(15) ethylenediamine derivative of polyoxyethylene-polyoxypropylene copolymer, e.g.

Tetronic 702
(Wyandotte Chem. Corp.)

Ionic surfactant

(16) fatty acid polyoxyethylene-phosphate, e.g.
Hostaphat KS–340 [tri-stearic acid-tetra-glycol-phosphate]
(Hoechst A.G. Farbwerke)

(17) fatty alcohol-polyoxyethylene-phosphate, e.g.

Hostaphat KO–280 [sodium dioleyloctaglycol phosphate]
(Hoechst A.G. Farbwerke)

(18) lecithin, e.g.

soybean lecithin

(19) fatty acid-polypeptide condensate or salt thereof, e.g.

Maypon UD [potassium salt of an undecylenyl-polypeptide condensate]
Mayon 4C [potassium salt of a cocoyl-polypeptide condensate]
(Stepan Chemical Co.)

(20) alkylsulfuric acid or salt thereof, e.g.

sodium dodecylsulfate

(21) ampholytic surfactant of carboxylic acid type, e.g. sodium lauroyl sarcosinate

Miranol C 2M conc. [sodium lauroyl imidazoline dicarboxylate]

(Miranol Chemical Co.)

The surfactant which is most preferably used in this invention depends upon a kind of the dispersion medium. In case of using the triglyceride, there may be preferably used a polyoxyethylene lanolin alcohol derivative, a polyoxyethylene lanolin derivative, a polyoxyethylene castor oil derivative, a polyoxyethylene hydrogenated castor oil derivative, a fatty acid polyoxyethylene-phosphate and a fatty alcohol-polyoxyethylene-phosphate. In case of using the mixture of the dibasic acid ester and the salicylic acid ester, there may be preferably used a polyoxyethylene sorbitan fatty acid ester, a polyoxyethylene fatty acid ester, a polyoxyethylene fatty alcohol ether, a polyoxyethylene lanolin derivative, a polyoxyethylene hydrogenated lanolin derivative, a polyoxy-ethylene lanolin alcohol derivative, a polyoxyethylene castor oil derivative, a polyoxyethylene alkyl aryl ether, a polyoxyethylene-polypropylene copolymer, an ethylenediamine derivative of polyoxyethylene-polyoxypropylene copolymer and a fatty acid-polypeptide condensate.

The amounts of the surfactant employed in this invention is about 0.5–5%, preferably about 1–3%. The ointment base of this invention is produced by heating the dispersion medium at 60–70° C., adding silicic acid anhydride into the dispersion medium step by step with stirring, treating the resulting mixture with a homogenizer to complete dispersion and dissolving or dispersing the surfactant into the mixture by heating. To control consistency, spreadability, solubility of medicament, etc., other additives i.e. water, liquid paraffin, squalene and fatty acid ester, e.g. isopropyl myristate may be incorporated in the ointment base. For example, when the mixture of the dibasic acid ester and the salicylic acid ester is employed, about 1–5% water may be added into the dispersion medium for the purpose of increasing of consistency.

The ointment base of this invention has such a remarkably advantageous property that its consistency measured with curd meter (10–35 g. at 25° C.) is proper for an ointment base as shown below and is scarcely varied depending upon a temperature.

Furthermore, it has various preferable properties as an ointment base such as good spreadability, scarceness of appearance of bleeding, good solubility of medicaments.

The ointment base of this invention is smooth and homogeneous while having a desirable consistency over a temperature range of from about 0° C. to about 50° C. and useful for a preparation of ointments, cosmetics and the like. In dermatologic practice, the ointment base of this invention may be usefully combined with known medicaments which are readily compatible therewith such as, for example, chrysarobin, methanol, penicillin, chloramphenicol, griseofulvin, variotin, sulfathiazol, zinc oxide, hydrocortisone acetate, camphor and the like. Especially, when the mixture of the dibasic acid ester and the salicylic acid ester is employed as the dispersion medium, the ointment base is proper for such ointments that a high absorption of medicaments contained therein are required. Examples of such ointments are water-eczema ointment containing siccanine, griseofulvin, variotin, etc., corticosteroid ointment containing triamcinolone acetonide, predni-

sone, prednisolone, dexamethasone, etc. and antihistamine ointment containing chlorpheniramine, promethazine, etc.

Those medicaments may be admixed with the ointment base after or on the way of the step of preparing the present ointment base by a conventional procedure. An amount of the admixed medicaments is not limited and varied depending upon a kind of the medicaments. Usually an amount of antihistamines, hormones or antibiotics is about 0.1–5%. The ointment using the present ointment base can be administered to a skin of animals or human in the same manner as known ointments.

The following examples show that the ointment base of this invention has a proper consistency for an ointment base.

EXAMPLE 1

To 93 g. of castor oil, olive oil, diacetyl oleyl glyceride or monoacetyl oleyl glyceride are added 5 g. of Aerosil and 2 g. of one of the various surfactants shown Table 1 and the resulting mixture is homogenized to give an ointment base.

The consistency of the ointment base thus obtained is measured with a curd meter at 25° C. The result is shown in Table 1. It will be evident from the Table 1 that the ointment base of this invention has proper consistency for an ointment base.

TABLE 1

Consistency of the ointment base at 25° C. (g.)

Surfactant	Dispersion medium: Castor oil	Olive oil	Diacetyl oleyl glyceride	Monoacetyl oleyl glyceride
None	3	0	2	3
Span 20	19	17	19	19
Tween 60	18	16	18	17
Myrj 51	14	16	16	14
Brij 30	17	17	17	18
Lanopol 300	21	20	21	21
Lanopol H 200	21	19	20	21
Lanopol A 170	19	19	22	21
Nikkol HCO-60	19	19	19	22
G.M.S.	24	24	25	25
P.M.S.	21	21	22	22
NP-10	17	17	18	18
Hostaphat KS 340	19	18	20	21
Hostaphat KW 200	19	18	19	19
Lecithin	15	14	15	15
Pluronic L 64	14	13	13	14
Tetronic 702	14	13	14	13
Maypon 4C	12	11	11	11
Sodium lauroyl sarcosinate	27	25	24	24
Sodium lauryl sulfate	10	9	9	9
Miranol C 2 M conc	14	16	13	12

EXAMPLE 2

To 93 g. of castor oil, olive oil, diacetyl oleyl glyceride or monoacetyl oleyl glyceride are added 5 g. of Aerosil and 2 g. of one of the various surfactants shown in Table 2 and the resulting mixture is homogenized to give an ointment base.

The consistency of the ointment base thus obtained is measured with a curd meter at 2° C., 15° C., 25° C. and 40° C. The result is shown in Table 2. It will be evident from the Table 2 that the consistency of the ointment base of this invention is scarcely affected by the change of temperatures.

TABLE 2

Consistency of the ointment base at various temperatures (g.)

Dispersion medium	Surfactant	Temperature (° C.): 2	15	25	40
Castor oil	None		5	3	1
	Nikkol HCO-60		21	19	21
	Lanopol 300		23	21	22
	Hostaphat KW 200		21	19	20
	Myrj 51		59	14	15
Olive oil	None	2.5		0	0
	Nikkol HCO-60	22		19	21
	Lanopol 300	22		20	22
	Hostaphat KW 200	19		18	20
	Myrj 51	19		16	9
Diacetyl oleic acid glyceride.	None	2.5		0	0
	Nikkol HCO-60	22		19	20
	Lanopol 300	23		21	22
	Hostaphat KW 200	21		19	21
	Myrj 51	19		16	12
Monoacetyl oleyl glyceride.	None	2.5		1.0	0
	Nikkol HCO-60	22		19	21
	Lanopol 300	22		20	22
	Hostaphat	21		19	20
	Myrj 51	21		17	9

EXAMPLE 3

To 91 g. of the mixture of diisopropyl adipate and monoethyleneglycol salicylate each at an equal weight or the mixture of diethylsebacate and monoethyleneglycol salicylate each at an equal weight are added 6 g. of Aerosil and 3 g. of one of the various surfactants shown in Table 3 and the resulting mixture is homogenized to give an ointment base. The consistency of the ointment base thus obtained is measured with a curd meter at 25° C. The result is shown in Table 3.

It will be evident from the Table 3 that the ointment base of this invention has proper consistency for an ointment base.

TABLE 3

Consistency of the ointment base at 25° C. (g.)

Surfactant	Dispersion medium: diisopropyl adipate plus monoethylene-glycol salicylate	Diethyl sebacate plus mono-ethyleneglycol salicylate
None	5	5
Tween 60	20	18
Tween 60 plus water (2g.)	40	35
Lanopol H 200	21	19
Lanopol A 170	25	23
Nikkol HCO 60	22	21
Hostaphat KW 340	21	19
Hostaphat KS 340	20	17
Maypon 4C	27	23
Sodium lauroyl sarcosinate	16	16
Lecithin	10	9
Sodium lauryl sulfate	12	10

EXAMPLE 4

To 91 g. of the mixture of diisopropyl adipate and monoethyleneglycol salicylate each at an equal weight or the mixture of diethyl sebacate and monoethyleneglycol salicylate each at an equal weight are added 6 g. of Aerosil and 3 g. of one of the various surfactants shown in Table 4 and the resulting mixture is homogenized to give an ointment base.

The consistency of the ointment base thus obtained is measured with a curd meter at 15° C., 20° C. and 40° C. The result is shown in Table 4. It will be evident from the Table 4 that the consistency of the ointment base of this invention is scarcely affected by the change of temperatures.

TABLE 4

Consistency of the ointment base at various temperatures (g.)

Dispersion medium	Surfactant	Temperature (° C.): 15	20	40
Diisopropyl adipate plus monoethylene glycol salicylate.	None	7	5	0
	Tween 60	18	20	27
	Nikkol HCO-60	20	22	29
	Maypon 4C	22	27	35
Diethyl sebacate plus monoethyleneglycol salicylate.	None	7	5	0
	Tween 60	17	19	24
	Nikkol HCO-60	18	21	24
	Maypon 4C	20	23	30

EXAMPLE 5

To 92 g. of castor oil are added 1 g. of microcrystallines of chloramphenicol and 5 g. of Aerosil and homogeneously dispersed therein. To the resulting mixture are dissolved 2 g. of Tween 60 to give a chloramphenicol ointment.

EXAMPLE 6

	G.
Olive oil	93
Aerosil	5
Myrj 51	2
Triamcinolone acetonide	0.1

The process similar to Example 5 is repeated to give a triamcinolone acetonide ointment.

EXAMPLE 7

	G.
Diacetyl oleyl glyceride	90
Aerosil	5
Lanopol H200	2
Lidocain	3

The process similar to Example 5 is repeated to give a lidocain ointment.

EXAMPLE 8

	G.
Monoacetyl oleyl glyceride	91
Aerosil	5
Nikkol HCO–60	3
Chlorpheniramine	1

The process similar to Example 5 is repeated to give a chlorpheniramine ointment.

EXAMPLE 9

Into 90 g. of a mixture of diisopropyl adiphate and monoethyleneglycol salicylate each at an equal weight are dissolved 1 g. of siccanine by heating. To the resulting mixture are added 6 g. of Aerosil and 3 g. of Tween 60 and homogeneously dispersed therein to give siccanine ointment.

When, in the procedure of Example 9, the siccanine is replaced by 3 g. of griseofulvin or 3×10^6 I.U. of variotin, there is also obtained a water-eczema ointment.

EXAMPLE 10

Into 91 g. of a mixture of diethyl sebacate and monoethyleneglycol salicylate each at an equal weight are dissolved 0.1 g. of triamcinolone acetonide by heating. To the resulting mixture are added 6 g. of Aerosil and 3 g. of Lanopol H 200 and homogeneously dispersed therein to give a triamcinolone acetonide ointment.

When, in the procedure of Example 10, the triamcinolone acetonide is replaced by an equal amount of dexamethasone or 0.5 g. of prednisolone, there is also obtained a corticosteroid ointment.

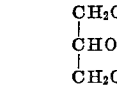
EXAMPLE 11

Into 90 g. of a mixture of diisopropyl adipate and monoethyleneglycol salicylate each at an equal weight are dissolved 1 g. of chlorpheniramine. To the resulting mixture are added 6 g. of Aerosil and 3 g. of polyoxyethylene hydrogenated castor oil (Nikkol HCO–60) and homogeneously dispersed therein to give a chlorpheniramine ointment.

What is claimed is:

1. An ointment base comprising

(A) a material selected from the group consisting of (a) from 88 to 97.5 percent by weight of a triglyceride liquid at a temperature of from 20° C. to 30° C. and having the formula



wherein R_1, R_2 and R_3 are the same or different and each represents an aliphatic acyl group at least one of which has from 9 to 19 carbon atoms, and (b) from 85 to 96.5 percent by weight of a mixture of a dibasic aliphatic carboxylic acid ester liquid at a temperature of from 20° C. to 30° C. and a salicylic acid ester;

(B) from 2 to 7 percent by weight with (a) of a silicic acid anhydride or from 3 to 10 percent by weight with (b) of said silicic acid anhydride; and

(C) from 0.5 to 5 percent by weight of a surfactant selected from the group consisting of a nonionic surfactant, tristearic acid tetraglycol phosphate, sodium dioleyl octaglycol phosphate, lecithin, an alkyl sulfate, a fatty acid-polypeptide condensate, sodium lauroyl sarcosinate, and sodium lauroyl imidazoline dicarboxylate.

2. The ointment base of Claim 1, comprising

(A) said triglyceride;

(B) said silicic acid anhydride; and

(C) a surfactant selected from the group consisting of a nonionic surfactant, tristearic acid tetraglycolphosphate, sodium dioleyl octaglycol phosphate, and lecithin.

3. The ointment base of Claim 1, comprising

(A) said mixture;

(B) said silicic acid anhydride; and

(C) said surfactant.

4. The ointment base of Claim 1, wherein said surfactant is a polyoxyethylene lanolin alcohol ether having 17 oxyethylene units, a polyoxyethylene lanolin derivative having 48 oxyethylene units, a polyoxyethylene castor oil ether having 10 oxyethylene units or a polyoxyethylene hydrogenated castor oil ether having 60 oxyethylene units.

5. The ointment base of Claim 1, wherein (A) is said mixture and (C) is selected from the group consisting of a polyoxyethylene sorbitan fatty acid ester having 60 oxyethylene units, a polyoxyethylene lanolin derivative having 48 oxyethylene units, a polyoxyethylene hydrogenated lanolin ether having 16 oxyethylene units, a polyoxyethylene lanolin alcohol ether having 17 oxyethylene units, a polyoxyethylene castor oil ether having 10 oxyethylene units and a fatty acid-polypeptide condensate.

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U.S. Cl. X.R.

424—145, 181, 230, 238, 243, 247, 263, 270, 271, 274, 278, 320, 332, 343