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(54) Title: SALICYLIC ACID GEL

(57) Abstract: A salicylic acid gel consisting of salicylic acid and a stabilizer compound, wherein the salicylic acid comprises at least 1 wt% of the total weight of the gel. A salicylic acid gel comprising salicylic acid and a stabilizer compound, wherein the salicylic acid comprises at least 30 wt% of the total weight of the gel. The gels may be diluted and/or incorporated into final skin care products.



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SALICYLIC ACID GEL

CROSS-REFERENCE OF RELATED APPLICATIONS

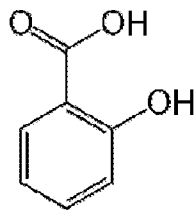
[001] This application claims priority to U.S. Application Serial No. 13/789,780 filed on March 8, 2013, hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[002] The invention relates to a gel of salicylic acid, and products produced therefrom.

BACKGROUND OF THE INVENTION

[003] Salicylic acid, also known as 2-hydroxybenzenecarboxylic acid, is a monohydroxybenzoic acid. Its salts and esters are known as salicylates. Salicylic acid has the formula:



[004] Salicylic acid is also known for providing pain relief when applied as a liniment, for example

[005] Salicylic acid is used in many skin-care products. For example, salicylic acid is well known for its use in anti-acne treatments. In addition to the treatment of acne, salicylic acid is also used in products for treatment of psoriasis, calluses, corns, keratosis pilaris, and warts. It works as a keratolytic, bactericide and comedolytic agent. Salicylic acid is also used in shampoos for treatment of dandruff and as a chemical exfoliant.

[006] Salicylic acid can cause burns if applied in high concentrations. Typically, over-the-counter limits are 2% for topical treatments (that remain on the skin) and 3% for cleansers or shampoo (products that are washed off.) Higher concentrations (e.g. up to

40 wt %) may be used for wart removal but should be applied cautiously and only to the wart and not the surrounding skin.

- [007] Salicylic acid is poorly soluble in water. It is therefore difficult to prepare solutions of salicylic acid that remain precipitate-free.

BRIEF SUMMARY OF THE INVENTION

- [008] The present invention is directed to a salicylic acid gel consisting of salicylic acid and a stabilizer compound, wherein the salicylic acid is present in at least 1 wt% based on total weight of the gel. The present invention is further directed to a salicylic acid solution comprising the salicylic acid gel and a solvent. The present invention is further directed to products prepared with the salicylic acid gel or with dilute solutions of the gel.
- [009] The present invention is further directed to a salicylic acid gel comprising salicylic acid and a stabilizer compound, wherein the salicylic acid comprises at least 30 wt%, based on total weight of the gel. The present invention is further directed to a salicylic acid solution comprising the salicylic acid gel and a solvent. The present invention is further directed to products prepared with the salicylic acid gel or with dilute solutions of the gel in solvent. The present invention is further directed to a salicylic acid gel consisting of salicylic acid and a stabilizer compound, wherein the salicylic acid comprises at least 30 wt%, based on total weight of the gel.
- [010] In further aspects, the salicylic acid gel prepared in accordance with any aspect above is combined with ingredients to form various products including body or hand lotions, anti-dandruff shampoos, wart medications, and anti-acne medications.
- [011] Further aspects are directed to making a solution or skin care product comprising mixing the salicylic acid gel in accordance with any aspect defined above with a solvent.

DETAILED DESCRIPTION OF THE INVENTION

- [012] Aspects of the invention are directed to a gel of salicylic acid and at least one stabilizer compound selected from nitrogen compounds. One aspect is particularly directed to a

concentrated gel. The concentrated gel allows relatively large amounts of salicylic acid to be shipped and stored in a safe and stable manner. A higher concentration of salicylic acid further allows smaller shipping and storage space. Another aspect is directed to gel consisting of salicylic acid and at least one stabilizer compound selected from nitrogen compounds. This gel also allows salicylic acid to be shipped and stored in a safe and stable manner. In addition, the gel is flowable so is easier to manufacture and use.

- [013] In one aspect, a (concentrated) salicylic acid gel comprises at least 30 wt% salicylic acid, at least 35 wt%, or at least 40 wt% salicylic acid gel, for example 30 wt% to 60 wt% salicylic acid, or 35 wt% to 55 wt%, or 40 to 55 wt% salicylic acid each based on total weight of the gel. Specific amounts may be 30 wt%, 35 wt%, 40 wt%, 50 wt%, and 60 wt% based on total weight of the gel based on total weight of the gel.
- [014] The concentrated salicylic acid gel comprises the stabilizer compound in an amount of at least 40 wt%, at least 45 wt%, at least 60 wt%, and up to 70 wt%, for example 40 to 70 wt%, or 45 to 60 wt%, each based on total weight of the gel which is an amount effective to provide stability to the salicylic acid in the gel. Specific amounts may be 40 wt%, 50 wt%, 60 wt%, 65 wt%, and 70 wt% based on total weight of the gel.
- [015] In one aspect, the concentrated salicylic acid gel is formed by mixing salicylic acid with the stabilizer compound until the salicylic acid is dissolved in the stabilizer compound. In a particular aspect, no water or solvent such as ethanol is included in the gel. In a further particular aspect, no other active ingredient is present in the gel. In a particular aspect, there are only two components that form the concentrated gel: the stabilizer compound (complexing agent) and the salicylic acid. That is the salicylic acid gel consists of salicylic acid and a stabilizer compound, wherein the salicylic acid comprises at least 30 wt%, based on total weight of the gel.
- [016] The mixing of the salicylic acid and the stabilizer compound may be done at room temperature. Alternatively the mixing may occur at an elevated temperature such as up to 50° C. Generally mixing takes about 30 to 120 minutes.

- [017] The concentrated gel may then be stored for future use. A benefit of the concentrated gel is that such gel contains very concentrated amounts of salicylic acid, and less storage space is required than dilute solutions of salicylic acid. The gel is storage stable for at least 2 years.
- [018] The stabilizer compound may be any suitable nitrogen compound that stabilizes the salicylic acid in the concentrated gel. Nitrogen compounds useful to form the highly concentrated salicylic gel include, but not limited to, alkoxyated amides, alkoxyated amines, alkyl-substituted amino acids, alkylamido alkylamines, amides, amine oxides, amines, and betaines. Ideally, a clear product should be produced.
- [019] In one aspect, the nitrogen compound is cocamidopropyl dimethylamine. The cocamidopropyl dimethylamine is particularly suitable for high concentrations of salicylic acid. When diluted in water, the resulting solution is stable and clear.
- [020] The concentrated gel can be diluted to any suitable level for use. Dilution of the salicylic acid gel may occur by the addition of water, a short chain alcohol such as ethanol and isopropanol, or any combination thereof. Upon dilution, the salicylic acid forms a clear, stable solution in the water or alcohols – that is, the salicylic acid does not precipitate out.
- [021] In particular the dilute solutions comprise wherein the concentration of the salicylic acid in the solution is at least 0.5 wt%, at least 1 wt%, at least 5 wt%, at least 10 wt%, at least 15 wt% or at least 20 wt% each based on total weight of the solution.
- [022] The present invention is further directed to products prepared with the salicylic acid gel or with dilute solutions of the gel in solvent wherein the concentration of the salicylic acid in the product is at least at least 0.5 wt%, at least 1 wt%, at least 5 wt%, at least 10 wt%, at least 15 wt%, at least 20 wt%, at least 30 wt%, or at least 40 wt% each based on total weight of the product.
- [023] Other aspects of the invention are directed to a gel consisting of salicylic acid and at least one stabilizer compound selected from nitrogen compounds. The gel allows salicylic acid to be shipped and stored in a safe and stable manner.

- [024] The salicylic acid gel consists of at least 1 wt%, at least 5 wt%, at least 10 wt%, at least 15 wt%, or at least 20 wt%, salicylic acid based on total weight of the gel. Specific amounts may be, but not limited to, 1wt%, 5 wt% 10 wt%, or 20 wt%.
- [025] The salicylic acid gel consists of the stabilizer compound in an amount of at least 30 wt%, at least 80 wt%, at least 90 wt%, at least 95 wt%, at least 99 wt%, and up to 99 wt%, for example between 70 wt% and 99 wt%.
- [026] In one aspect, the salicylic acid gel is formed by mixing salicylic acid with the stabilizer compound until the salicylic acid is dissolved in the stabilizer compound. No water or solvent such as ethanol is included in the gel. The mixing of the salicylic acid and the stabilizer compound may be done at room temperature. Alternatively the mixing may occur at an elevated temperature such as up to 50° C. Generally mixing takes about 3 to 120 minutes. The gel may be stored.
- [027] The stabilizer compound may be any suitable nitrogen compound that stabilizes the salicylic acid in the gel as discussed above and incorporated by reference herein.
- [028] As discussed above, the gel can be diluted to any suitable level for use such as by the addition of water, a short chain alcohol such as ethanol and isopropanol, or any combination thereof. In particular the dilute solutions comprise wherein the concentration of the salicylic acid in the solution is at least 0.5 wt%, at least 1 wt%, at least 5 wt%, at least 10 wt%, at least 15 wt% or at least 20 wt% each based on total weight of the solution. Upon dilution, the salicylic acid forms a clear, stable solution in the water or alcohols.
- [029] The present invention is further directed to products prepared with the salicylic acid gel or with dilute solutions of the gel in solvent wherein the concentration of the salicylic acid in the product is at least at least 0.5 wt%, at least 1 wt%, at least 5 wt%, at least 10 wt%, at least 15 wt% or at least 20 wt% each based on total weight of the product.
- [030] For pH evaluation, 95 wt% water was added to 5 wt% of the concentrated gel (40 wt% salicylic acid, 60 wt% cocamidopropyl dimethylamine) resulting in a 2 wt% salicylic acid

concentration; the maximum allowed for anti-acne products. The same evaluation was run using 92.5 wt% water and 7.5 wt% of the gel (resulting in 3 wt% active salicylic acid; the maximum allowed for anti-dandruff products) and 40 wt% water and 60 wt% of the gel (resulting in 24 wt% active salicylic acid) to evaluate for the wart remover monograph. All of these studies resulted in clear, stable solutions with pH levels between 3 and 4.

- [031] The pH of the dilute system is generally less than 5, such as 2 to 5, 2.5 to 4.5, typically 3 to 4.
- [032] For topical purposes, the dilute system must pass the USP Monograph for a Salicylic Gel which includes an assay for salicylic acid.
- [033] The diluted product may be combined with other suitable ingredients to form the final products such as creams, lotions, make-ups, toners, astringents, skin cleansing compositions, shampoos, and conditioners. These compositions contain about 0.1-40 wt% of salicylic acid. The amount of salicylic acid in the final product depends on the intended purpose of the product.
- [034] Creams typically contain about 10-90 wt% water and 10-90 wt% oil. Creams may also contain humectants, emollients, surfactants, emulsifiers, preservatives and fragrances. Creams would generally contain from 0.1 to 5 wt% salicylic acid.
- [035] Lotions typically contain 20-80 wt% oil and 10-80 wt% water in an emulsion form. In addition, lotions may contain humectants, emollients, surfactants, fragrances, preservatives and so forth. Creams would generally contain from 0.2 to 5 wt% salicylic acid.
- [036] Make-ups typically contain about 5-70 wt% oil, 10-95 wt% water, and about 5-40 wt% pigment. In addition, the makeup may contain surfactants, silicones as part of the oil phase, humectants, emollients, preservatives, fragrances, etc. Make-up would generally contain from 0.1 to 3 wt% salicylic acid.

- [037] Anti-dandruff shampoos typically contain 1-40 wt% of a cleansing surfactant and 10-90 wt% water. The shampoo may also contain any one of ingredients such as surfactants, colorants, preservatives, fragrance, emulsifiers, viscosity adjusters, and conditioning agents. Anti-dandruff shampoos would generally contain from 0.18 to 3 wt% salicylic acid.
- [038] Hair conditioners typically contain include 10-95 wt% water, 0.5-30 wt% conditioning ingredients such as quaternary ammonium compounds or amphoteric polymers, proteins, etc., and 1-40% surfactants. Hair conditioners may also contain volatile or nonvolatile silicones. Hair conditioners would generally contain from 0.1 to 4 wt% salicylic acid.
- [039] Toners typically contain about 0-85 wt% alcohol, 0.01-5 wt% surfactant, and 0.1-5 wt% humectants, 0.1-85% water.
- [040] The salicylic acid may also be used in ointments, gels, or solutions. Suitable ointments are hydrophilic ointments (USP) or petroleum.
- [041] The amount of salicylic acid present in the final product depends on the product. For example, acne treatment products generally contain 0.5 to 2 wt% salicylic acid, dandruff and seborrheic dermatitis, and psoriasis treatment products generally contain 3 wt% salicylic acid, and wart treatments generally contain up to 40 wt% salicylic acid, typically 5 wt% to 40 wt% or 17 wt% to 25 wt%.
- [042] Example 1
- [043] A 40% salicylic acid was blended with 60% cocamidopropyl dimethylamine. The resulting concentrated gel was slightly viscous, clear, and yellow.
- [044] The concentrated gel was diluted to 2 wt% active salicylic acid in water and separately in ethanol. The resulting solutions were clear and colorless. No precipitate was formed either in water or in ethanol. The pH of the water solution was approximately 3.2.
- [045] Stability tests were then performed on the water solution. The concentrated gel and the diluted 2 wt % active salicylic acid solution were prepared and subjected to accelerated

stability protocol which consisted of five freeze/thaw cycles and two weeks in a 50°C oven. Under both of these conditions there were no significant changes to either sample. The samples that were frozen were obviously solid when removed from the freezer and the 50°C samples were less viscous. In both cases, when the samples returned to room temperature, they were essentially identical to the control samples. There was no color or viscosity change and no precipitate was formed.

[046] The gel was also diluted to 25 wt% active salicylic acid in water. The resulting solution was a slightly viscous, yellow, clear solution. No precipitate was formed. A physical accelerated stability test was run on this prototype consisting of samples be held at 50°C for two weeks and another sample run through five freeze/thaw cycles. Under both of these conditions there were no physical changes to the product include pH, viscosity, color and appearance.

[047] Example 2

[048] A lotion was prepared with 5% of the gel of example 1 in 91% water with 4% Egel 305 [Polyacrylamide (&) C12-13 isoparaffin (&) Laureth-7]. The result was a white lotion that would be applicable for an anti-acne product. It underwent the same accelerated stability testing as mentioned above (50°C for 2 weeks and 5 freeze/thaw cycles); there were no significant physical changes to the product during the stability testing.

[049] Example 3

[050] An anti-dandruff shampoo was prepared containing 3 wt% salicylic acid.

		Percent
	Water	36.50
Active ingredient	Cocamidopropyl Dimethylamine (&) Salicylic Acid (Curcyl [®] 40)	7.50
Surfactant blend	PEG-80 Sorbitan Laurate (&) Cocamidopropyl Betaine (&) Sodium Trideceth Sulfate (&) Glycerin (&) Disodium Lauroamphodiacetate (&) PEG-150 Distearate (&) Sodium Laureth-13	50.00

	Carboxylate (Sulfochem™ B-NBB)	
Thickener	PEG-120 Methyl Glucose Trioleate (& Propylene Glycol (&) Water (Glucamate™ LT)	5.00
Preservative	Propylene Glycol (&) Diazolidinyl Urea (& Methylparaben (&) Propylparaben (Nipaguard PDU)	1.00
	Citric Acid	qs to pH 4
		100.00%

[051] In an appropriate container, water, and Curcylic® 40 were mixed until uniform. Sulfochem B-NBB, Glucamate LT and Nipaguard PDU were added and mixed until homogenous. Then citric acid was added, with continued mixing, until the batch reached pH of approximately 4.0. Viscosity: >1300cp. Stability: Passed 2 weeks 50°C; 5 Freeze/ Thaw cycles.

[052] Example 4

[053] A wart remover was prepared containing ____ % salicylic acid.

		Percent
	Water	46.5
Active Ingredient	Cocamidopropyl Dimethylamine (& Salicylic Acid (Curcylic® 40)	42.5
	Propanediol (Zemea®)	5.0
	Hydrogenated Methyl Abeitate (Meristant® 101L)	1.0
	Alcohol	4.0
Surfactant Blend	Phenoxyethanol (&) Methylparaben (& Ethylparaben (&) Butylparaben (& Propylparaben (&) Isobutylparaben (Phenonip)	1.0
	Citric Acid	Qs
		100.0%

[054] In an appropriate container, water and Curcylic® 40 were blended until homogenous. In a separate container, alcohol and Meristant® 101L were mixed until homogenous and then

added to and mixed with the Curcyclic[®]/Water blend. Zemea[®] and Phenonip were then added to the blend and mixed until clear. The pH was adjusted with citric acid to 4-4.5 if necessary.

[055] While the invention has been described with respect to specific examples including presently preferred modes of carrying out the invention, those skilled in the art will appreciate that there are numerous variations and permutations of the above described systems and techniques that fall within the spirit and scope of the invention as set forth in the appended claims.

We Claim:

1. A salicylic acid gel consisting of salicylic acid and a stabilizing amount of at least one nitrogen compound, wherein the salicylic acid comprises at least 1 wt% of the total weight of the gel.
2. The salicylic acid gel of claim 1 consisting of at least 5 wt%, at least 10 wt%, at least 15 wt%, or at least 20 wt% salicylic acid based on total weight of the gel.
3. A salicylic acid gel comprising salicylic acid and a stabilizing amount of at least one nitrogen compound, wherein the salicylic acid comprises at least 30 wt% salicylic acid based on total weight of the gel.
4. The salicylic acid gel of claim 3 comprising at least 35 wt% salicylic acid based on total weight of the gel.
5. The salicylic acid gel of claim 3 comprising at least 40 wt% stabilizer compound based on total weight of the gel.
6. The salicylic acid gel of claim 3 comprising 40 to 55 wt% salicylic acid based on total weight of the gel.
7. The salicylic acid gel according to any one of claims 1-6 wherein the nitrogen compound is selected from the group consisting of alkoxyated amides, alkoxyated amines, alkyl-substituted amino acids, alkylamido alkylamines, amides, amine oxides, amines, and betaines.
8. The salicylic acid gel of claim 7 wherein the nitrogen compound is cocamidopropyl dimethylamine.
9. A salicylic acid gel according to any one of claims 3-8 wherein no solvent is present in the gel.

10. A salicylic acid gel according to any one of claims 3-9 consisting of salicylic acid and nitrogen compound selected from the group consisting of alkoxyated amides, alkoxyated amines, alkyl-substituted amino acids, alkylamido alkylamines, amides, amine oxides, amines, and betaines.
11. A salicylic acid gel according to any one of claims 1-10 consisting of salicylic acid and cocamidopropyl dimethylamine.
12. A salicylic acid solution comprising the salicylic acid gel according to any one of claims 1-11 and a solvent.
13. The salicylic acid solution of claim 12 comprising at least 0.5 wt% salicylic acid based on total weight of the solution.
14. The salicylic acid solution of claim 12 wherein the pH is 2 to 5, or 3 to 4.
15. The salicylic acid solution of claim 12 wherein the solvent is water, ethanol, or isopropylalcohol.
16. An acne treatment product comprising the salicylic acid gel according to any one of claims 1-11 and a solvent wherein the concentration of the salicylic acid is 0.5 to 2 wt% based on total weight of the acne treatment product.
17. A wart treatment product comprising the salicylic acid gel according to any one of claims 1-11 and a solvent wherein the concentration of the salicylic acid is 5 to 40 wt%, or 17 to 25 wt%, based on total weight of the wart treatment product.
18. A lotion comprising the salicylic acid gel according to any one of claims 1-11 and a solvent wherein the concentration of the salicylic acid is 0.2 to 5 wt% based on total weight of the lotion.
19. An anti-dandruff shampoo comprising the salicylic acid gel according to any one of claims 1-11 and a solvent wherein the concentration of the salicylic acid is 1.8 to 3 wt% based on total weight of the shampoo.

20. A method of making a salicylic acid solution comprising combining the salicylic acid gel according to any one of claims 1-11 with a solvent and mixing.
21. A method of making a skin care product comprising combining the salicylic acid gel according to any one of claims 1-11 with a solvent and mixing.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER INV. A61K9/00 A61K9/06 A61K31/60 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/02593 A2 (BENAC SA [FR]; PEYROT JACQUES [FR]; LEFEVRE JEAN MARIE [FR]; ALLART JE) 20 January 2000 (2000-01-20) claims 4-9 -----	1-21
X	EP 0 052 705 A1 (BERNSTEIN JOEL E) 2 June 1982 (1982-06-02) claims 1-5 -----	1-21
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X	WO 98/52927 A1 (SCIVOLETTO ROSEMARIE [US]) 26 November 1998 (1998-11-26) claims 10,11,16 -----	1-21
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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