

PATENT SPECIFICATION

NO DRAWINGS

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COMPLETE SPECIFICATION

Antiseptic Therapeutic Compositions comprising 2:4-Dichlorobenzyl Alcohol

5 We, BOOTS PURE DRUG COMPANY LIMITED, a British Company, of Station Street, Nottingham, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

10 This invention relates to new pharmaceutical preparations which have been found to possess valuable properties.

15 In British Patent Specification No. 794,402 disinfecting compositions are described wherein the active ingredient is 3:4-dichlorobenzyl alcohol.

20 It has now been found that the compound 2:4-dichlorobenzyl alcohol possesses marked lethal activity against a wide range of bacteria and fungi and that this compound is surprisingly less toxic than the corresponding 3:4-dichlorobenzyl derivative when applied to animal or human tissue. Compositions containing this compound can be employed to combat bacterial and fungal infections of the ear, throat, scalp and skin. Accordingly the present invention comprises a pharmaceutical composition for oral or topical administration which comprises 2:4-dichlorobenzyl alcohol together with a pharmaceutically acceptable diluent or carrier.

25 Thus the compositions of the invention include mouth washes, toothpastes, pastilles, lozenges and boiled sweets for medication of the throat, ointments, jellies and lotions for the treatment of the skin, eardrops and medicated powders all of which contain 2:4-dichlorobenzyl alcohol.

30 Whilst the compound 2:4-dichlorobenzyl alcohol is found to be bactericidal and fungicidal we have also found that the value of certain of the compositions of the invention may be enhanced by the inclusion of a sub-

stance which possesses bacteriostatic and/or fungistatic properties. Hexachlorophene and amyl-*m*-cresol are both valuable substances for this purpose as they are effective as bacteriostats and fungistats at very high dilutions and are perfectly compatible with 2:4-dichlorobenzyl alcohol in the compositions of the invention. It will be understood therefore that compositions for oral or topical use which contain a mixture of either of these compounds hexachlorophene or amyl-*m*-cresol with 2:4-dichlorobenzyl alcohol form a part of the present invention.

35 The compositions of the invention which are suitable for oral use may take the form of boiled sweets, tablets, lozenges and pastilles containing 2:4-dichlorobenzyl alcohol as active ingredient and may be prepared by methods well known in the art. The diluents which may be employed in the preparation of such compositions include those solid diluents which are non-toxic and which slowly dissolve in human saliva for example, sucrose. In addition to diluents which are incorporated for flavouring purposes it is occasionally desirable but not essential that the compositions also comprise a pharmaceutically acceptable binding agent, for example gum acacia, and a minor quantity of a pharmaceutically acceptable lubricant for example stearic acid or a metal salt thereof. The concentration of 2:4-dichlorobenzyl alcohol employed in the lozenges, etc. may vary according to the requirements of the particular medication for which they are intended.

40 We have found that a boiled sweet of approximately 3 grams weight and containing 0.01 to 0.2% by weight of 2:4-dichlorobenzyl alcohol is a very convenient and valuable composition for use in medication of

the throat. If desired the compositions of the invention may also contain other pharmaceutically active ingredients. Thus it has been found that the substance saligenin (o-hydroxybenzyl alcohol) which has local anæsthetic activity can be incorporated to give oral compositions which are particularly valuable in that they possess both bactericidal properties and local anæsthetic activity.

The compositions of the invention which are suitable for topical use include ointments, lotions, jellies and eardrops containing 2:4-dichlorobenzyl alcohol as the active ingredient. Suitable ointments and creams are water-miscible or water-immiscible in character and include those of the oil-in-water emulsion and water-in-oil emulsion types which are prepared from water-miscible polyethylene glycols. Such ointments and creams may contain 2:4-dichlorobenzyl alcohol as the sole active ingredient or may contain a mixture of this compound and amyl-*m*-cresol or hexachlorophene. The ointments and creams may also comprise a small quantity of an anti-foaming agent, for example, a silicone which facilitates the application of the preparation to the skin, and a colour stabilising agent. A substance which is particularly suitable for use in the latter capacity is citric acid, which in addition to preventing discoloration of the ointments and creams on storage, can be used to adjust the pH of the preparation approximately to that of normal skin.

The compositions of the invention which may be employed as eardrops comprise 2:4-dichlorobenzyl alcohol in association with a liquid diluent of low volatility which is innocuous when instilled into the ear. A diluent which has been found to be particularly suitable is propylene glycol in which 2:4-dichlorobenzyl alcohol is soluble. The eardrop compositions may include a stabilising agent, for example, citric acid to inhibit discoloration.

The compositions of the invention which may be employed as fungicidal and bactericidal mouth washes and lotions comprise 2:4-dichlorobenzyl alcohol and, if desired, amyl-*m*-cresol or hexachlorophene in association with a liquid diluent in which 2:4-dichlorobenzyl alcohol is soluble. In the case of lotions, in particular lotions intended for application to the scalp for the treatment of dandruff, the bulk of the liquid diluent in which the active ingredient is soluble is preferably a lower aliphatic alcohol containing from 1 to 8 carbon atoms inclusive, for example ethyl alcohol, which may also contain a minor proportion of water. Where the lotion is intended for use as a scalp lotion by regular application to the hair, the composition may also comprise an oil of the type normally employed in dressings for the hair. Such an oil may

be a fixed oil of animal or vegetable origin comprising glyceryl or other esters of fatty acids for example isopropyl myristate or it may be an oil of the hydrocarbon class. The compositions may also comprise other active ingredients which are commonly employed in scalp lotions, for example, hexachlorophene, salicylic acid or cetrimide. The concentration of 2:4-dichlorobenzyl alcohol which is employed in lotions is not critical but it has been found that a lotion containing 0.5% by weight of this substance is efficacious in the treatment of the scalp.

The following non-limitative examples illustrate the invention:—

EXAMPLE 1.

An intimate mixture of the following ingredients is compounded into lozenges each of which weighs one gram and contains 25 mg. of 2:4-dichlorobenzyl alcohol.

	Parts by Weight	
2:4-dichlorobenzyl alcohol - -	25	
Acacia gum - - - - -	58	
Magnesium stearate - - -	5	
Sucrose to make - - - - -	1000	90

EXAMPLE 2.

Lozenges each of weight 1.3 grams and of the following compositions are prepared as described below.

2:4-dichlorobenzyl alcohol -	5 milligrams	95
Saligenin - - - - -	50 milligrams	
Carbowax 6000 [a proprietary form of polyethylene glycol]	40 milligrams	
Magnesium stearate - - -	7 milligrams	
Tragacanth - - - - -	58 milligrams	100
Tartaric acid - - - - -	13 milligrams	
Flavouring essence - - -	0.004 ml.	
Icing sugar to make - - -	1.3 grams	

The icing sugar and tartaric acid are thoroughly mixed and treated with a solution of the 2:4-dichlorobenzyl alcohol, saligenin and Carbowax 6000 in a small quantity of industrial methylated spirit. The product is thoroughly mixed and allowed to dry. The dried mixture is passed through a sieve of mesh 40, the tragacanth is added and mixed thoroughly before the mixture is granulated by treatment with a dilute syrup followed by drying at a temperature not exceeding 110° F. The granulated material is treated with the flavouring essence and the mixture is allowed to stand overnight in a closed container before being treated with magnesium stearate and compressed into lozenges on the appropriate machine.

EXAMPLE 3.

A batch of throat sweets of approximately 60 pounds weight is prepared from the following ingredients by the method described below.

125

5	Sugar - - - - - 42 pounds Liquid glucose B.P. - - - - - 21 pounds Tartaric acid B.P. - - - - - 9 ounces 262 grains 2:4-dichlorobenzyl alcohol - - - - - 252 grains Amyl- <i>m</i> -cresol - - - - - 210 grains Flavour - - - - - A sufficient quantity Colour solution - - - - - A sufficient quantity Water - - - - - A sufficient quantity
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10 A syrup is prepared by adding the sugar and the liquid glucose B.P. to a sufficient quantity of water and then boiling until a temperature of 275° C. is attained. The tartaric acid is added to the hot syrup followed by sufficient colour solution to give the required colour and finally the 2:4-dichlorobenzyl alcohol is added together with amy-*m*-cresol and the required flavouring matter. The composition is thoroughly mixed and passed through a drop forming machine so that ten of the resulting boiled sweets weigh approximately one ounce.

EXAMPLE 4.

25 A water miscible cream is prepared by dissolving 2 parts by weight of 2:4-dichlorobenzyl alcohol in 98 parts by weight of a polyethylene glycol 1500 available under the proprietary name of "Carbowax 1500".

EXAMPLE 5.

30 An ear drop composition is prepared by dissolving 1.5 parts by weight of 2:4-dichlorobenzyl alcohol in propylene glycol using a high speed stirrer and making up to 100 parts by volume with propylene glycol.

EXAMPLE 6.

35 A formulation suitable for use as a scalp

65	2:4-dichlorobenzyl alcohol - - - 2.5 parts by weight Carbopol (Registered Trade Mark) 934 (a proprietary name for a synthetic gum) - - - - - 1.5 parts by weight Triethanolamine - - - - - 0.5 parts by weight Propylene glycol - - - - - 74.0 parts by weight Perfume - - - - - A sufficient quantity Water to make - - - - - 100 parts by weight
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The Carbopol 934 is dispersed in 64 parts of propylene glycol and the triethanolamine is dissolved in sufficient water and added with stirring.

75 A solution of the 2:4-dichlorobenzyl alcohol in 10 parts of propylene glycol is added followed by a sufficient quantity of the required perfume and the whole is thoroughly mixed until uniform.

EXAMPLE 9.

80 An ear canker powder for veterinary purposes is prepared by thoroughly mixing the following ingredients in a powder mixer.

lotion and of the following composition is prepared by stirring all the ingredients with the industrial methylated spirit until a clear solution is obtained.

	Parts by Weight	40
2:4-dichlorobenzyl alcohol - - - - -	0.5	
Hexachlorophene - - - - -	0.2	
Salicylic acid - - - - -	1.0	
Cholesterol - - - - -	0.2	45
Cetrimide B.P. - - - - -	0.5	
Isopropyl myristate - - - - -	8.0	
Quassia 5% aqueous solution - - - - -	0.22	
Colour - - - - -	0.0015	
Perfume - - - - -	0.3	50
Industrial methylated spirit to make - - - - -	100	

EXAMPLE 7.

An oily formulation suitable for use as a scalp lotion is prepared according to the method described in Example 6, the proportion of isopropyl myristate being increased to 18.0 parts by weight.

EXAMPLE 8.

60 An antiseptic jelly is prepared from the following ingredients by the method described below.

	Parts by Weight	85
2:4-dichlorobenzyl alcohol - - - - -	0.5	
Hexachlorophene - - - - -	1.0	
γ-benzene hexachloride - - - - -	0.2	
Boric acid B.P. - - - - -	10.0	
Zinc oxide B.P. - - - - -	5.0	90
Benzocaine B.P. - - - - -	2.5	
Magnesium stearate - - - - -	2.0	
Purified talc - - - - -	20.0	
Light kaolin B.P. - - - - -	58.8	

EXAMPLE 10.

95 A wound and strike powder for veterinary purposes is prepared by thoroughly mixing the following ingredients in a powder mixer,

		Parts by Weight	EXAMPLE 11. A tooth paste is prepared containing the following ingredients by the method described below:—	
	2:4-dichlorobenzyl alcohol	0.5		
	Dieldrin - - - - -	0.4		
5	Boric acid - - - - -	5.0		
	Starch (pre-cooked) - - - - -	94.1		10
	Glycerin - - - - -		20 parts by weight	
	Water - - - - -		28 parts by volume	
	Tragacanth - - - - -		1 part by weight	
	Oil of peppermint - - - - -		1 part by volume	
15	Soluble saccharin - - - - -		0.1 parts by weight	
	Heavy calcium carbonate - - - - -		2.4 parts by weight	
	Light calcium carbonate - - - - -		2.4 parts by weight	
	Sodium lauryl sulphate - - - - -		0.2 parts by weight	
	2:4-dichlorobenzyl alcohol - - - - -		0.2 parts by weight	
20	A mucilage is prepared by adding traga-			and comprising also an antifoaming agent
	canth to a stirred solution of the soluble			and a colour stabilising agent.
	saccharin and glycerin in water. The cal-			13. A composition as claimed in Claim 12
	cium carbonate is incorporated in a kneading			wherein a silicone is used as the antifoaming
	machine and the 2:4-dichlorobenzyl alcohol			agent and citric acid as the colour stabilising
25	dissolved in the oil of peppermint is added.			agent. 70
	The sodium lauryl sulphate is then added, it			
	is thoroughly mixed and finally the paste is			
	milled.			
	WHAT WE CLAIM IS:—			
30	1. A pharmaceutical composition for oral			
	or topical administration comprising 2:4-di-			
	chlorobenzyl alcohol together with a pharma-			
	ceutically acceptable diluent or carrier.			
35	2. A composition as claimed in Claim 1 and			
	comprising also a bacteriostatic and/or fungi-			
	static agent.			
	3. A composition as claimed in Claim 2			
	wherein the bacteriostatic and/or fungistatic			
	agent is hexachlorophene or amyl- <i>m</i> -cresol.			
40	4. A pharmaceutical composition for oral			
	use comprising 2:4-dichlorobenzyl alcohol			
	and a non-toxic solid diluent.			
45	5. A composition as claimed in Claim 4			
	and comprising also a pharmaceutically			
	acceptable binding agent and a pharma-			
	ceutically acceptable lubricant.			
50	6. A composition as claimed in Claim 5			
	wherein gum acacia is used as the binding			
	agent and stearic acid or a salt thereof as the			
	lubricant.			
	7. A composition as claimed in Claim 5			
	or 6 and comprising also an additional pharma-			
	ceutically active ingredient.			
55	8. A composition as claimed in Claim 7			
	wherein the additional active ingredient has			
	local anaesthetic activity.			
	9. A composition as claimed in Claim 8			
	wherein the ingredient used is saligenin.			
60	10. A pharmaceutical composition for topical			
	use as an ointment or cream comprising 2:4-			
	dichlorobenzyl alcohol, an emulsifying wax,			
	or oil or a water-miscible polyethylene glycol.			
65	11. A composition as claimed in Claim 10			
	and comprising also amyl- <i>m</i> -cresol or hexa-			
	chlorophene.			
	12. A composition as claimed in Claim 11			
			15. A composition as claimed in Claim 14	
			wherein the liquid diluent which is used is	
			propylene glycol. 80	
			16. A composition as claimed in Claims	
			14 and 15 and comprising also a colour	
			stabilising agent.	
			17. A composition as claimed in Claim 16	
			in which the colour stabilising agent used is	
			citric acid. 85	
			18. A pharmaceutical mouth wash or lotion	
			comprising 2:4-dichlorobenzyl alcohol and a	
			liquid diluent in which it is soluble.	
			19. A mouth wash or lotion as claimed in	
			Claim 18 and comprising also amyl- <i>m</i> -cresol	
			or hexachlorophene. 90	
			20. A lotion as claimed in Claim 18 or 19	
			wherein the liquid solvent diluent is a lower	
			aliphatic alcohol containing from 1 to 8 carbon	
			atoms inclusive. 95	
			21. A lotion as claimed in Claim 20 wherein	
			ethyl alcohol is the liquid diluent.	
			22. A lotion as claimed in Claim 20 or 21	
			and comprising also water. 100	
			23. A lotion as claimed in any of Claims 18	
			to 22 and comprising also an oil as herein-	
			before defined.	
			24. A lotion as claimed in Claim 23 wherein	
			the oil used is isopropyl myristate. 105	
			25. A lotion as claimed in Claim 23 or 24	
			and comprising also hexachlorophene, salicylic	
			acid or cetrimide.	
			26. A pharmaceutical composition sub-	
			stantially as herein described with reference	
			to any of the examples. 110	
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