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(72) Inventeurs/Inventors:
KAY, MARTHA FRANCINE, US;
RATNARAJ, TERESA RITA, US;
SANDLER, PATRICIA LYNN, US

(73) Propriétaire/Owner:
WYETH, US

(74) Agent: RIDOUT & MAYBEE LLP

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(54) Title: ORAL ANALGESIC COMPOSITIONS

(57) Abrégé/Abstract:
Alkanol free glycol based oral analgesic compositions are provided, protected against microbiological degradation by a preservative agent which is a combination of methylparaben and benzyl alcohol.

ABSTRACT

Alkanol free glycol based oral analgesic compositions are provided, protected against microbiological degradation by a preservative agent which is a combination of methylparaben and benzyl alcohol.

AHP-94185 Patent

ORAL ANALGESIC COMPOSITIONS

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to oral alkanol free glycol based analgesic compositions containing high concentrations of benzocaine. More particularly, this invention relates to oral analgesic compositions in liquid and gel form having high potency and protected from microbiological degradation by a preservative agent which is a combination of methylparaben and benzyl alcohol.

2. Description of Related Art

An anesthetic composition comprising high concentrations of benzocaine is described in U.S. Patent No. 5,446,063. The benzocaine is dispersed or suspended in an admixture of water and emollient vehicle and is not completely dissolved. Another benzocaine composition comprising high concentrations of benzocaine is described in U.S. Patent No. 4,241,048. That patent discloses a composition containing benzocaine suspended in an essentially anhydrous carrier also containing a crystal growth suppressing agent. These prior art patents disclose the use of preservatives including methylparaben and propylparaben.

SUMMARY OF THE INVENTION

According to this invention, an oral analgesic glycol based composition which is anhydrous and alkanol free, containing high concentrations of benzocaine is provided in liquid or gel form and which is protected from bacterial degradation by a preservative agent which is a combination of methylparaben and benzyl alcohol. The benzocaine compositions of the invention contain about 5 to about 20% by weight of benzocaine, based on the weight of the total composition, and the glycol based solvent system contains about 40% to about 80% by weight of polyethylene glycol, based on the weight of the total composition, and about 10% to about 20% by weight of propylene glycol, based on the weight of the total composition. The methylparaben component of the preservative agent can be about 0.05 to about 0.2% by weight of the total composition and the benzyl alcohol component of the preservative agent can be about 0.25 to about 0.5% by weight of the total composition.

DETAILED DESCRIPTION OF THE INVENTION

The invention includes analgesic compositions in liquid form and in gel form and in regular strength and maximum strength. The regular strength forms contain about 7.5% to about 10% by weight of benzocaine and the maximum strength forms contain about 10% to about 18% by weight of benzocaine.

The liquid form of the invention can contain in addition to the benzocaine, the glycol based solvent system, the preservative agent, sweeteners such as saccharin, flavoring agents such as spearmint and coloring agents.

The gel form of the invention contains in addition to the benzocaine, the glycol based solvent system, the preservative agent, a thickening agent such as Carbomer 934 P brand of carboxy-vinyl polymer, and a co-solvent for the thickening agent such as glycerin. The thickening agent can range from about 2% to about 2.5% by weight and the co-solvent for the thickening agent can range from about 16% to about 24% by weight of the total composition. Other suitable thickening agents include xanthan gum, sodium carboxymethyl cellulose and carrageenin.

The benzocaine, preservative agents and glycol solvent agents are commercially available in NF or USP grades. The glycerin is commercially available in NF grades containing up to 4% water and the taste of the final gel product is better using the 96% glycerin.

The polyethylene glycol component of the glycol solvent system can range from PEG 400 to PEG 600. Below about PEG 400, the polyethylene glycol may possibly be toxic and does not dissolve the benzocaine with ease, and above about PEG 600, the polyethylene glycol is a solid and difficult to work with.

The preparation of the formulation of the invention is illustrated in the following examples. In the examples, the polyethylene glycol PEG 400 was the commercial NF grade and the Carbomer 934 P brand of carboxy-vinyl polymer was that of BF Goodrich.

EXAMPLE 1

The following ingredients were incorporated into the analgesic maximum strength liquid composition of this invention.

Ingredient	Weight %	Grams Per 500 Grams
PEG-400	10.0	50.0
Propylene Glycol	10.0	50.0
Saccharin	0.177	0.885
PEG-400	50.8	254
Benzocaine	17.7	88.5
Methylparaben	0.177	0.885
Benzyl Alcohol	0.442	2.21
N & A Spearmint Flavor	0.708	3.54
PEG-400	10.0	50.0
Yellow #10	0.0106	0.0530
Red #40	0.0106	0.0530
Blue #1	0.000221	0.0011
Total	100	500

The ingredients were mixed in accordance with the following procedure:

Into a 150ml. beaker were placed 50 grams each of PEG-400 and propylene glycol and the mixture was stirred and heated to 70-75°C. The saccharin was added to the heated solution which was then cooled to 25-30°C. Into a second container were placed 254 grams of PEG 400 with stirring until the benzocaine had dissolved. Into a third container were placed 100 grams of PEG 400 and the dyes were added with stirring until dissolved.

To the benzocaine solution in the second container was added the saccharin solution from the first container and mixed well. The methyl paraben was then added to the second container with stirring until dissolved. The benzyl alcohol was then added to the second container and stirred until dissolved. Next, the flavors were added and then the dye solution from the third container.

The product was a uniform liquid at room temperature with no crystallization and no precipitation. The product is bitter but does not have a bitter after taste.

The following ingredients were incorporated into the analgesic regular strength liquid composition of this invention.

Ingredient	Weight %	Grams Per 10Kg
Polyethylene Glycol 400 NF	70.6	7060.
Propylene Glycol USP	8.93	893.0
Saccharin NF	0.223	22.3
Benzocaine USP	8.93	893.
Methylparaben NF	0.179	17.9
Benzyl Alcohol NF	0.446	44.6
N&A Spearmint Flavor	0.714	71.4
Polyethylene Glycol 400 NF	10.0	1000.0
D&C Red #33	0.000446	0.0446
FD&C Blue #1	0.0000621	0.00621
FD&C Yellow #6	0.00104	0.104
D&C Yellow 10	0.00402	0.402
Total	100	1003

The ingredients were mixed in accordance with the following procedure.

Into a 15 kilogram stainless steel kettle fitted with a Lightnin' mixer were added 7060g of PEG 400 and 893g of propylene glycol. The mixer was turned on to form a vortex. The saccharin was added and mixed for 25 minutes. The benzocaine was slowly sprinkled into the vortex and stirred for 50 minutes until completely dissolved. Concurrently, 1000g of PEG 400 were placed into a 1200 ml stainless steel beaker fitted with a Lightnin'* mixer which was turned on to form a vortex. The dyes were sequentially added and mixed until dissolved.

When benzocaine is completely dissolved in the first container, add the methylparaben and when dissolved add the benzyl alcohol and then the flavorings. The dye solution is then added to the first container with mixing.

The product was a clear amber, slightly viscous liquid with a flavor and odor characteristic of spearmint.

* Trade-mark

The following ingredients were incorporated into the analgesic maximum strength gel formulation of the invention.

Ingredients	**Weight %**	**Grams Per 2Kg**
Part 1		
Polyethylene Glycol 400, USP	42.8	400.O
Glycerin 96% USP	8.62	400.0
Propylene Glycol	17.2	200.0
Saccharin	9.216	5.0
Carbomer 934P	1.94	45.0
Benzocaine, USP	17.2	400.0
Part II		
Methylparaben, USP	0.172	4.0
Benzyl Alcohol	0.431	10.0
Spearmint Flavor	1.72	40.0
Part III		
Polyethylene Glycol 400, USP	10.0	200.0
FD&C Blue #1	0.000086	0.0020
D&C Yellow #10	0.00414	0.0960
FD&C Red #40	0.00414	0.0960
Part IV		
Polyethylene Glycol 400, USP	QS to 2000ml	

The ingredients were mixed in accordance with the following procedure in a 2 kilogram jacketed Hobart* bowl with a T-Line mixer with a 2 inch blade and a stir bar plate.

Into the bowl were placed 400 grams of PEG 400, the glycerin (96%) and the propylene glycol and mixed at low speed until uniform. The mixture was heated to 75°-80°C with steam, the saccharin was added as dissolved, and the mixture cooled to 55°C. The benzocaine and the carbomer were dry blended in a plastic bag and then added to the bowl with mixer at high speed to pull powders into the vortex. The sides were scraped regularly and a temperature of 60°-65°C was

* Trade-mark

maintained. After 3.5 hours, the carbomer was completely dissolved and the methyparaben was added and dissolved.

Into 400ml beaker equipped with a bar/plate were added the coloring dyes and the resulting solution was added to the main batch with mixing until uniform then PEG 400 was added QS to 2000ml in the main batch.

The product was a clear reddish-brown gel with an odor and taste characteristic of spearmint.

EXAMPLE 4

The following ingredients were incorporated into the analgesic regular strength gel formulation of the invention.

Ingredients	Weight %	Grams Per 2Kg.
Part 1		
Polyethylene Glycol 400 NF	50.6	1012.
Propylene Glycol	8.62	172.4
Glycerin	17.2	344.
Saccharin NF Powder	0.216	4.32
Carbomer 934 P	1.94	38.8
Benzocaine	9.08	181.6
Part II		
Methylparaben	0.172	3.44
Benzyl Alcohol	0.431	8.62
Spearmint Flavor	1.72	34.4
Part III		
Polyethylene Glycol 400 NF	10.0	200.0
D&C Red #33	0.000950	0.0190
FD&C Yellow #6	0.00100	0.0200
FD&C Blue #1	0.0000600	0.0012
D&C Yellow #10	0.00250	0.0500
	100%	2000

The ingredients were mixed essentially in accordance with the procedure of Example 3. The product was a clear orangish brown soft gel with a mint odor and taste.

The alkanol free glycol based oral analgesic compositions of the invention are surprisingly resistant to microbiological degradation due to the unique preservative agent combination of mehtylparaben and benzyl alcohol. For example, the preservative agent was efficacious in testing in accordance with an adaptation of the USP methods for inoculating test organisms showing no growth for 28 days.

The five organisms used as test organisms were those listed in the USP as follows:

Escherichia coli	ATCC #8739
Staphylococcus aurens	ATCC #6538
Pseudomonas aeruginosa	ATCC #9027
Candida albicans	ATCC #10231
Aspergillus niger	ATCC #16404

CLAIMS:

1. An alkanol free blycol based oral analgesic composition comprising benzocaine, a glycol solvent system for the benzocaine comprising polyethylene glycol having a molecular weight of about 400 to 600 and propylene glycol, and a preservative agent consisting essentially of methyl paraben and benzyl alcohol.

2. The alkanol free glycol based oral analgesic composition of claim 1 wherein, based on the weight of the total composition, the amount of benzocaine is about 5 to about 20% by weight, the glycol solvent system is composed of about 40% to about 80% by weight polyethylene glycol and about 10% to about 20% by weight of propylene glycol, and the preservative agent is composed of about 0.05% to about 0.2% by weight of methylparaben and about 0.25 to about 0.5% by weight of benzyl alcohol.

3. The alcohol free glycol based oral analgesic composition of claim 1 in gel form additionally containing a thickening agent and a solvent for the thickening agent.

4. The alkanol free glycol based oral analgesic composition of claim 2 in gel form additionally containing a thickening agent in the amount of about 2% to about 2.5% by weight and a solvent for the thickening agent in the amount of about 16% to about 24% by weight.

5. The alkanol free glycol based oral analgesic composition of claim 3 wherein the polyethylene glycol has a molecular weight of about 400 to about 600, the thickening agent is a carboxy-vinyl polymer and the solvent for the thickening agent is glycerin.