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(54) Title: ORAL SPRAY TO REDUCE COLD SYMPTOMS AND DURATION OF SAME

(57) Abstract: An oral spray composition for preventing and/or reducing the symptoms of the common cold including a zinc formulation containing both zinc acetate and zinc gluconate to ensure sustained availability of increased amounts of ionizable zinc.



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**ORAL COMPOSITION TO REDUCE COLD SYMPTOMS
AND DURATION OF SAME**

Field of Invention

5 The present invention relates generally to a composition formulated to maintain a therapeutically beneficial ingredient in association with the nasal, oral, and oropharyngeal membranes to reduce cold symptoms and their duration. More specifically, the present invention relates to an oral spray having a zinc composition for absorption by the nasal, oral, and/or oropharyngeal membranes to reduce cold symptoms and their duration.

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Background of the Invention and Prior Art

 The oral and topical administration of zinc and zinc containing compounds have long been utilized in the treatment and prophylaxis of the common cold. For example, a number of patents have been issued to George A. Eby, III, which disclose zinc containing
15 compounds for treating the symptoms of, or curing, the common cold.

 Eby's U.S. Patent No. 4,503,070 issued in 1995 discloses the use of a lozenge containing zinc gluconate to reduce the duration of a cold and his U.S. Patent No. 5,409,905 discloses a composition having a highly ionizable zinc compound which provides sustained release of Zn^{2+} ions. The highly ionizable zinc compound is selected from zinc acetate, zinc
20 propionate, zinc butyrate, zinc beta-hydroxybutyrate, zinc benzoate, zinc formate, and mixtures thereof while the composition specifically excludes flavor masking amounts of anethole and strong zinc chelators.

 U.S. Patent No. 4,956,385 issued to Eby, III describes the method of applying an ionizable zinc compound other than zinc gluconate to the oral mucosa for treating the
25 common cold. Later, in 1990, Eby's U.S. Patent No. 4,503,070 was reissued as Re. 33,465 and included claims similar to Eby's '385 patent with the exception that the ionizable zinc compound was specifically identified and defined as being zinc gluconate.

 Finally, U.S. Patent Nos. 5,002,970 and 5,095,035 were issued to Eby, III in 1999 and 1992, respectively, which disclosed oral compositions for releasing zinc ions which
30 included an anethole in an amount to flavor-mask the zinc aftertaste, or a sweet pharmaceutically acceptable carrier. Zinc gluconate, zinc acetate and zinc ascorbate were all identified as individual possibilities for the ionizable zinc compound used with an anethole

while zinc acetate was identified as an ionisable zinc compound for use with a sweet pharmaceutically acceptable carrier.

Later, in 1997, two patents were issued to Bryce-Smith, namely U.S. Patent No. 5,622,724 and U.S. Patent No. 5,688,531, which disclosed nasal, oral and
5 opthalmological sprays having a dilute solution of unchelated zinc ion for treating cold and allergy symptoms. Zinc sulfate and/or zinc chloride were specifically identified as acceptable selections for the unchelated zinc ion.

Still later, U.S. Patent No. 6,139,864 was issued to Durr et al in 2000. The Durr et al patent describes foods and pharmaceuticals containing zinc and an antimicrobially
10 effective amount of a sugar alcohol mixture. The zinc was identified as being present in the form of zinc gluconate or zinc acetate.

All of these patents disclose zinc compositions that include a single zinc compound as the source of zinc ions. Such composition are thought to be deficient because the zinc compounds are generally configured to provide only slow release of
15 zinc ions. Accordingly, improved methods and compositions for treating cold symptoms are desired.

Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of
20 these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

Summary of the Invention

While the way in which the present invention addresses the deficiencies and
25 disadvantages of the prior art is described in greater detail hereinbelow, in general, according to various aspects of the present invention, a method and composition are provided for maintaining a therapeutically beneficial ingredient in association with the nasal, oral, and/or oropharyngeal membranes to reduce and prevent the common cold and its symptoms.

30 In accordance with one aspect of the invention there is provided a composition for delivering an active substance to at least one of an oral membrane, an oral pharyngeal membrane and a nasal membrane by administration through the oral cavity, said composition comprising:

- a pharmaceutically acceptable carrier;
- 35 about 2 wt% to about 4 wt% zinc gluconate; and
- zinc acetate.

In accordance with various aspects of the present invention, the zinc containing composition is formulated to both increase the concentration of zinc and its ionization potential, and to sustain the release of ionizable zinc. In accordance with various embodiments of the invention, the oral composition includes a zinc formulation
5 containing both zinc gluconate and zinc acetate.

Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

10 In accordance with various embodiments of the invention, as further described in greater detail below, the oral spray composition comprises a very low viscosity, similar to that of water, and is administered to the oral cavity via a fine spray mist in a dosage of about four squirts, each containing approximately .25 milliliters, with the dosage administered approximately every three hours.

In accordance with further embodiments, the oral spray composition includes one or more of a sweetener, flavoring, and a preservative, in addition to a pharmaceutically acceptable carrier.

5 In accordance with various other aspects of the invention, a system for delivering the composition to the oral cavity is provided. More specifically, a spray applicator is provided for administering spray into the oral cavity.

These and other advantages of the various compositions, methods and systems according to various aspects of the present invention will be apparent to those skilled in the art upon reading and understanding the detailed description below.

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Detailed Description of Exemplary Embodiments

In accordance with various aspects of the invention, an oral spray composition is provided which includes two or more zinc salts. The zinc from the zinc salts is desirably freely available, i.e. non-chelated and in an ionizable form, to ensure that it is biologically
15 available and can be readily adsorbed. When administered to the oral cavity via a fine spray mist, the oral spray composition containing the zinc salts will produce a biological electrical circuit from the mouth, through the oral membranes, the oralpharyngeal membranes, and into the nasal membranes. This positive ionic flow of readily ionizable zinc that can be adsorbed into the mucosal membranes is capable of binding to viral ICAM-1 receptors in the
20 nasal passages and inhibits rhinovirus from binding to and infecting nasal mucosal cells.

The oral spray composition of the present invention reduces the presence and/or duration of symptoms associated with the common cold including, but not limited to, headaches, sore throat, runny and/or congested nose, and coughs. More particularly, the oral spray composition of the present invention functions to treat infections associated with those
25 viruses typically recognized as causing common colds. The oral spray of the present invention is preferably used from any time when an individual first notices any signs of a cold up until when the symptoms have cleared.

In a preferred embodiment of the present invention, the composition contains a zinc salt in an amount of about 2 to 6 weight percent of the composition.

30 In another preferred embodiment of the present invention, the zinc formulation contains both zinc gluconate and zinc acetate, and preferably comprises about 2 to 6 weight percent of the oral spray composition. Moreover, in such a preferred embodiment, zinc gluconate preferably comprises about 2 to 4 weight percent of the oral spray composition

and zinc acetate preferably comprises about 0.2 to 2.0 weight percent of the oral spray composition.

In accordance with various aspects of this embodiment, zinc gluconate is present in an amount of about 32 to about 35 mg/ml, preferably about 33.4 mg/ml, and the zinc acetate is present in an amount of about 3 to about 6, preferably about 3.3 mg/ml. Additionally, the combination of the zinc salts provides about 3 to about 7 mg/ml of free ionic zinc, and preferably about 6.1 mg/ml of free ionic zinc.

In accordance with the present invention, the oral spray composition also includes a pharmaceutically acceptable carrier. The pharmaceutically acceptable carrier may include any suitable fluid or liquid such as, for example, purified water, or the like. Preferably, the pharmaceutically acceptable carrier comprises purified water in an amount of about 84.16 to 88 weight percent of the oral spray composition.

The oral spray composition may also include a stabilizer such as glycerin, or the like which functions to keep the zinc in its ionic form. In a preferred embodiment, the stabilizer includes glycerin present at a concentration of about 0.8 to 1.2 weight percent of the oral spray composition, and preferably at about 1.0 weight percent of the oral spray composition. Glycerin as the preferred stabilizer also functions to add a small amount of flavoring to the oral spray composition.

A sweetener and flavor enhancers may also be included in the oral spray composition. Sweeteners may include fructose, dextrose, sucrose or the like. Non-artificial sweeteners work best with a preferred embodiment including fructose in an amount of about 8 to 15 weight percent of the oral spray composition, and preferably at about 10 weight percent of the oral composition. A variety of flavorings may be used, preferably in the form of a stable extract. Alcohol containing forms of flavorings are not preferred. One preferred embodiment of the oral spray composition includes a flavor enhancer, such as peppermint, for example, in an amount of about 0.5 to 2.0 weight percent of the oral spray composition, and preferably at about 1 weight percent of the oral composition.

In accordance with another aspect of the present invention, a preservative may be added to the oral composition to facilitate stability of the various ingredients. Any suitable preservative may be used in accordance with the present invention such as, for example, benzalkonium chloride, benzyl alcohol, and disodium EDTA. Preferably, the preservative includes a 50% solution of benzalkonium chloride admixed into the oral composition at a

concentration of about 0.01 to 0.02 percent by weight, and preferably about 0.015 percent by weight.

5 The composition of the present invention is preferably delivered to the oral cavity through the mouth by way of a fine spray mist. The method includes the steps of obtaining an oral composition in accordance with the present invention for delivery into the oral cavity. The method further includes the step of applying the oral composition to the oral cavity with a spray applicator. Practitioners will appreciate that any suitable applicator may be used. In accordance with a preferred embodiment, the applicator is available from Pfeiffer of America, 12 Roszel Road, Suite C-104, Princeton, New Jersey 08540 as Item 10 #63922. This applicator is configured to hold about 120 metered 0.25 ml doses, of the composition.

The composition may be delivered to an individual in any suitable dosage. In accordance with one embodiment of the invention, the oral spray applicator is configured to supply a unit dose of about .25 mls of composition to the individual each time a pump 15 associated with the spray applicator is activated (.25 mls/spray). Preferably, the composition is delivered by applying about 4 sprays in the mouth approximately every 3 hours during waking hours until the cold symptoms have subsided.

EXAMPLES

20 The Examples set forth below are illustrative of various aspects of certain preferred embodiments of the present invention. The compositions, methods and various parameters reflected therein are intended only to exemplify various aspects and embodiments of the invention, and are not intended to limit the scope of the claimed invention.

EXAMPLE 1

An exemplary oral spray composition for delivering an active zinc compound to the oral cavity to reduce the presence and duration of cold symptoms is prepared by admixing
5 the following ingredients:

<u>Component</u>	<u>Function</u>	<u>Amount % w/w</u>
Zinc Gluconate, USP	Active Substance	3.34
Zinc Acetate Dihydrate, USP	Active Substance	0.44
Glycerin Oral Solution, USP	Stabilizer	1.00%
Fructose, USP	Sweetener	10.00%
Peppermint Flavor, GRAS	Flavor Enhancer	1.00%
Benzalkonium Chloride (50% solution), NF	Preservative	0.015%
Purified Water, USP	Diluent/Carrier	84.2%

EXAMPLE 2

Another exemplary oral spray composition for delivering an active zinc compound to the oral cavity is prepared by admixing the following ingredients:

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<u>Component</u>	<u>Function</u>	<u>Amount % w/w</u>
Zinc Gluconate, USP	Active Substance	3.34
Zinc Acetate Dihydrate, USP	Active Substance	0.44
Glycerin Oral Solution, USP	Stabilizer	1.00%
Fructose, USP	Sweetener	10.00%
Mint Flavor	Flavor Enhancer	1.00%
Benzalkonium Chloride (50% solution), NF	Preservative	0.015%
Purified Water, USP	Diluent/ Carrier	84.2%

The above compositions include about 33.40 mg/ml of zinc gluconate and about 4.40 mg/ml of zinc acetate to provide approximately 6.10 mg/ml of free ionic zinc for adsorption.

10 An oral spray composition for reducing the severity and duration of symptoms of the common cold has been presented. The oral spray is delivered by way of a fine spray mist through the use of a spray applicator. The zinc formulation included in the oral spray contains zinc or a zinc combination which functions to increase the zinc concentration and the ionization potential of zinc, and to sustain the availability of ionizable zinc for adsorption into the oral, oropharyngeal, and/or nasal membranes.

15 The present invention has been described above with reference to exemplary embodiments and examples. It should be appreciated that the particular embodiments shown and described herein are illustrative of the invention and its best mode and are not intended to limit in any way the scope of the invention as set forth in the claims. Those skilled in the art having read this disclosure will recognize changes and modifications may
20 be made to the exemplary embodiments without departing from the scope of the present invention. For example, artisans will recognize that reference to oral, oropharyngeal, and nasal membranes includes any interior surface of the oral and nasal cavities permitting delivery of an active substance, such as the zinc formulation, to the body, including the epithelial layer of the membranes or mucous of the epithelial layer of the membranes.

Further, though reference is made both to “substances” and “ingredients”, skilled artisans will further appreciate that the two terms can be used interchangeably. Additionally, although certain components were described herein as being included in the oral composition in addition to the zinc formulation and the pharmaceutically acceptable carrier, 5 it should be understood that carrier may be referred to as also including those certain components and that any suitable carrier may be achieved through any number of combination of additives now known or hereinafter devised. Accordingly, these and other changes or modifications are intended to be included to be within the scope of the present invention, as expressed in the following claims.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A composition for delivering an active substance to at least one of an oral membrane, an oral pharyngeal membrane and a nasal membrane by administration through the oral cavity, said composition comprising:
 - 5 a pharmaceutically acceptable carrier;
greater than 2 wt% to about 4 wt% zinc gluconate; and
zinc acetate.
2. The composition of claim 1, wherein said composition comprises zinc gluconate in an amount of about 32 to 35 mg/ml, such as about 33.4 mg/ml and zinc acetate in an
10 amount of about 3 to 6 mg/ml, such as about 4.4 mg/ml.
3. The composition of claim 1 or claim 2, wherein said composition comprises free ionic zinc in an amount of about 5 to 7 mg/ml, such as about 6.10 mg/ml.
4. The composition of any one of claims 1 to 3, wherein said composition comprises an oral spray.
- 15 5. The composition of any one of claims 1 to 4, wherein said pharmaceutically acceptable carrier comprises about 84 to 88 weight percent of said composition, and said carrier optionally comprises purified water.
6. The composition of any one of claims 1 to 5, wherein said zinc gluconate and zinc acetate comprise about 2 to 6 weight percent of said composition.
- 20 7. The composition of any one of claims 1 to 6 further comprising a stabilizer, wherein said stabilizer comprises glycerine optionally in an amount of about 0.8 to about 1.2 weight percent.
8. The composition of any one of claims 1 to 7 further comprising a sweetener wherein said sweetener comprises at least one of the following: fructose and dextrose.
- 25 9. The composition of claim 8 wherein said sweetener comprises fructose in an amount of about 8 to about 15 weight percent.
10. The composition of any one of claims 1 to 9 further comprising a preservative wherein said preservative comprises at least one of the following: benzalkonium chloride and benzyl alcohol.
- 30 11. The composition of claim 10, wherein said preservative comprises benzalkonium chloride in an amount of about 0.01 to about 0.02 weight percent.
12. The composition of any one of claims 1 to 11 further comprising a flavour enhancer optionally in an amount of about 0.5 to about 2 weight percent of said composition.

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13. A composition for delivering an active substance to at least one of an oral, an oralpharyngeal, and a nasal membrane by administration through the mouth, said composition comprising:
 - about 84 to 97.8 weight percent of a pharmaceutically acceptable carrier;
 - greater than 2 to about 4 weight percent of zinc gluconate; and
 - about 0.2 to about 2.0 weight percent of zinc acetate.
14. The composition of claim 13, wherein said composition comprises free ionic zinc in an amount of about 5 to 7 mg/ml, such as about 6.10 mg/ml.
15. The composition of claim 13, wherein said composition comprises an oral spray.
16. The composition of claim 13 or 14 wherein said pharmaceutically acceptable carrier comprises about 84 to 88 weight percent of said composition, and said carrier optionally comprises purified water.
17. The composition of any one of claims 13 to 16 wherein the viscosity of the composition is approximately the viscosity of water.
18. The composition of any one of claims 13 to 17, wherein said stabilizer comprises glycerin, optionally in an amount of about 0.8 to about 1.2 weight percent.
19. The composition of any one of claims 13 to 18 further comprising a sweetener wherein said sweetener comprises at least one of the following: fructose and dextrose.
20. The composition of claim 19, wherein said sweetener comprises fructose in an amount of about 8 to about 15 weight percent.
21. The composition of any one of claims 13 to 20 further comprising a preservative wherein said preservative comprise at least one of the following: benzalkonium chloride and benzyl alcohol.
22. The composition of claim 21, wherein said preservative comprises benzalkonium chloride in an amount of about 0.01 to about 0.02 weight percent.
23. The composition of any one of claims 13 to 22, wherein said flavour enhancer comprises about 0.5 to about 2 weight percent of said composition.
24. A method for delivering an active substance to at least one of an oral, an oralpharyngeal, and a nasal membrane by administration through the mouth, the method comprising the steps of:
 - providing a composition having a pharmaceutically acceptable carrier and a zinc formulation comprising both zinc gluconate and zinc acetate; and
 - applying the composition to the oral cavity by way of an oral spray.
25. A method for delivering an active substance to at least one of an oral, an oralpharyngeal, and a nasal membrane by administration through the mouth, the method comprising the steps of:

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providing a composition having a pharmaceutically acceptable carrier, zinc gluconate in an amount of about 32 to 35 mg/ml, and zinc acetate in an amount of about 3 to 6 mg/ml; and

applying the composition to the oral cavity by way of an oral spray.

- 5 26. A system for delivering an active substance to at least one of an oral, an oropharyngeal, and a nasal membrane by administration through the mouth, the system comprising:
- 10 a composition having a pharmaceutically acceptable carrier and a zinc formulation comprising both zinc gluconate and zinc acetate; and
- an oral spray applicator,
- wherein the composition is contained within the oral applicator for dispensing an effective dosage into the oral cavity.
27. The system of claim 26, wherein the applicator is configured to deliver a metered dosage to the oral cavity and optionally wherein the metered dosage delivered
- 15 to the oral cavity is about .25 mls.
28. The system of claim 26, wherein the composition has a viscosity approximately equal to the viscosity of water.
29. A system for reducing cold symptoms and their duration comprising:
- a composition having about 84 to about 97.8 weight percent of a
- 20 pharmaceutically acceptable carrier, greater than 2 to about 6 weight percent of zinc gluconate and about 0.2 to about 2.0 weight percent zinc acetate; and
- an oral applicator,
- wherein the composition is contained within the oral applicator for dispensing an effective dosage into the oral cavity.

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