

[54] METHOD FOR REDUCING THE DURATION OF THE COMMON COLD

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[63] Continuation-in-part of Ser. No. 288,750, Jul. 31, 1981, abandoned, which is a continuation-in-part of Ser. No. 222,620, Jan. 5, 1981, abandoned.

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[56] References Cited

U.S. PATENT DOCUMENTS

Table with 4 columns: Patent No., Date, Inventor, and Reference No. Includes entries for Loose et al., Creger, Pasternack, Sandberg, Roberts et al., Yamaga et al., Jacobson, Horrobin, Shah et al., and Eby, III.

FOREIGN PATENT DOCUMENTS

0240182 3/1967 U.S.S.R.

OTHER PUBLICATIONS

Stedman's Medical Dictionary, 23rd ed., The Williams & Wilkins Co., Baltimore, 1976, p. 807.

Handbook of Non-Prescription Drugs, 6th Edition, p. 317.

The Pharmacological Basis of Therapeutics, 5th Edition, pp. 1000-1001.

Al-Nakib et al., "Prophylaxis and Treatment of Rhinovirus Colds with Zinc Gluconate Lozenges", Jnl. Antimicrob. Chemother., 20(6):893-901, 1987.

Shields (1936), "The Ionization Treatment of Hay Fever", pp. 645-648.

Bailey, et al. (1937), Brit. Med. Jnl., Apr. 17, 1937, p. 808.

Gutman (1941) Modern Drug Encyclopedia.

Howard, Modern Drug Encyclopedia.

Marone et al. (1980), Jrn. All Clin. Immunology, 65:171.

Godfrey (1988), Antimicrob. Agents Chemother., 32:605.

Eby (1988), Antimicrob. Agents Chemother., 32:606.

Farr et al. (1988), Antimicrob. Agents Chemother., 32:607.

Martin (1988), Antimicrob. Agents Chemother., 32:600.

Farr et al. (1987), Antimicrob. Agents Chemother., 31:1183.

Al-Nakib et al. (1987), Jnl. Antimicrob. Chemother., 20:893.

Pasternak (1987), Bioscience Rep., 7(2):81.

"Zinc Zaps Common Cold" (1987), The Evening Wellington, New Zealand.

Zerial et al. (1985), Antimicrob. Agents Chemother., 27(5):846.

"Zinc vs. Colds" (1984), Austin American Statesman, Dec. 2, 1984, p. A15.

Eby et al. (1984), Antimicrob. Agents Chemother., 25(1):20.

Couch (1984), Jnl. Infect. Dis., 150(2):174.

Hayden et al. (1984), Jnl. Infect. Dis., 150(2):174.

Samo et al. (1984), Jnl. Infect. Dis., 150(2):101.

Phillpotts et al. (1983), Antimicrob. Agents Chemother., 23(5):671.

Anderson et al. (1983), "Viral Respiratory Illnesses", Medical Clinics of North America, 67(5):1009.

Levandowski et al. (1982), Antimicrob. Agents Chemother., 22(6):1004.

Andermann et al. (1982), Eur. Jnl. Drug Metab. Pharma., 7(8):233.

Hayden et al. (1982), Antimicrob. Agents Chemother., 21(6):892.

"Idoxuridine and Some Other Antiviral Agents" (1982), Martindale, The Extra Pharmacopocia, 28th Edition, pp. 820-827.

Giron (1982), Proc. Soc. Exp. Biol. Med., 170:25.

Korant (1979), "Inhibition of Viral Protein Cleavage", in Design of Inhibitor of Viral Functions, K. Gauri, ed., Academic Press.

Korant (1979), "Role of Cellular and Viral Proteases . . ." in The Molecular Biology of Picornoviruses, pp. 149-173.

Webster's New Collegiate Dictionary (1979), "lozenge" and troche.

Korant et al. (1976), Jnl. Virol., 18(1):298.

Butterworth et al. (1976), Arch. Virol., 51:109.

Harmon et al. (1976), Proc. Soc. Exp. Biol. Med., 152:598.

Primary Examiner—Ronald W. Griffin Attorney, Agent, or Firm—Arnold, White & Durkee

(List continued on next page.)

[57] ABSTRACT

The invention disclosed and claimed is a method to reduce duration of common colds in humans as evinced by reduction of duration of 10 common cold symptoms through use of zinc gluconate topically and frequently applied to the oral mucosa. The invention improves upon the prior art using zinc intranasally as an astringent and decongestant in treatment of common colds. Results of a clinical study are presented in support of disclosure and claims.

31 Claims, No Drawings

OTHER PUBLICATIONS

Korant et al. (1974), *Nature*, 248:588.

1948 Quarterly Cumulative Index Medicus, vol. 44, p. 797.

Van Voris, "Antiviral Chemotherapy", Chapter 8 in *Textbook of Human Virology*, pp. 193-229.

Levandowski, "Rhinoviruses", Chapter 16 in *Textbook of Human Virology*, pp. 391-405.

Tyrrell et al., "Antirhinovirus Drugs" pp. 340-341.

Chapter 57, "Antiviral Chemotherapy & Prophylaxis," in *Review of Medical Pharmacology*, 7th Edition, Meyers et al. eds., pp. 589-592.

Akzo Chemie "Gluconates", pp. 5-15.

Unpublished letter of Mr Eby's.

Eby et al., "Effect of Zinc Orotate Lozenges with Zinc Gluconate Nasal Spray in Common Cold Treatment—a Double Blind Study," unpublished.

Christison, *A Dictionary*, Philadelphia; Lee and Blanchard, 1948, p. 983.

Merck Index, 9th ed., Merck and Co., Inc., 1976, p. 1310.

Carter et al., *Chemotherapy of Cancer*, 2nd ed., John Wiley & Sons, pp. 26-29.

Gutman, *Modern Drug Encyclopedia*, 1941, p. 731.

METHOD FOR REDUCING THE DURATION OF THE COMMON COLD

Matter enclosed in heavy brackets [] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.

A continuation-in-part of "A Rapid Acting Treatment for the Common Cold" Ser. No. 288,750 filed [7/31/81] July 31, 1981, now abandoned, which was a continuation-in-part of "Treatments for Viral Infections, Including the Common Cold, and Allergies" Ser. No. 222,620 filed Jan. 5, 1981, now abandoned.

FIELD OF INVENTION

This invention relates to a method for reducing the duration of the common cold in humans.

BACKGROUND

The art of managing viral upper respiratory infections commonly called common colds has not been adequate. Common colds are the most common acute illness in the United States and account for about one-half of all lost school days and lost work days. An estimated one billion colds occur in the United States each year. Thus, there can be no question as to the need for a safe, simple, inexpensive, effective and available treatment to minimize or eliminate this important and costly public health problem.

Heretofore, treatment of common colds involved use of symptomatic therapy. Such therapy did not reduce duration of common colds. For example, with or without treatment, duration of 50% of the common colds caused by rhinoviruses remained at 7 days. Primary common colds symptoms are nasal drainage and nasal congestion. Secondary symptoms often accompanying primary symptoms include: headache, fever, myalgia, sneezing, sore throat, scratchy throat, cough and hoarseness. The prior art teaches individual treatment of each symptom as needed to ameliorate symptoms during their association with a common cold, rather than teaches treatment of the common cold to reduce the duration of all symptoms associated with them.

PRIOR ART

It has been established in vitro that zinc ions can inhibit replication of a few of the many antigenically different rhinoviruses. The concentration of zinc ions required to be antirhinoviral is 10^{-4} M or greater which is 10 times or greater than the zinc ionic concentration found in human serum. But other in vitro studies have demonstrated that inhibitory effects of zinc on rhinoviruses are reversible and provide no lasting effect once the zinc ions are removed from the medium. [According to the latter studies, when zinc is removed from rhinoviruses, they resume their replication and again become fully infective.] According to the latter studies, when zinc is removed from rhinoviruses, then resume their replication and again becomes fully infective. The best use [fo] for zinc in activities involving the rhinoviruses was suggested to be as a method to temporarily or reversibly inhibit rhinovirus replication in laboratory experiments. Since the antirhinoviral effect was observed to be reversible and since the inhibitory effects had been demonstrated in only a few of the antigenically different viruses known to cause the common

cold, zinc was not considered to be a suitable antirhinoviral agent for the treatment of the common cold in humans.

It has been established that zinc can provide an astringent and decongestant effect in common cold treatment. Zinc inhibits the release of histamine from mast cells and basophils. Histamine is a mediator of two primary common cold symptoms. The effect of zinc in inhibiting the release of histamine from mast cells and basophils produces a reduction in histamine mediated nasal drainage and nasal congestion, which might be considered as astringent-like and decongestant. A technique used earlier in this century to provide astringent and decongestant effects in the treatment of common colds requires that 4 to 10 drops of a 0.2% to 2.0% zinc borate aqueous suspension be applied by spray, instillation or Dowling packing into each nostril or eye several times per day. Such an intranasal method operates only to relieve the treatment human from certain discomfort associated with the congestion symptoms. But it can now be disclosed that the low dosages of zinc and the method of application only brings temporary relief, perhaps because natural circulation removes zinc ions from the locus of the treatment more rapidly than the low application rate of zinc ions by the dosages replaces them. Because it has been established in vitro that zinc ions can inhibit replication of rhinoviruses, one may theorize that a low dosage of zinc may produce a zinc ion concentration that may or may not reach antiviral concentrations and that a method of application that does not maintain a sufficiently high level of zinc ions in the locus of treatment would not prevent continued viral replications. Regardless of a theoretical justification for a method of [decreasing.] increasing zinc ion concentration, the astringent-like and decongestant effects of the low zinc dosages under the prior art methods of application cease when the treatment is discontinued before the cold has run its normal, untreated duration.

OBJECTIVE OF INVENTION

Accordingly, the objective of this invention is to correct deficiencies of the prior art in treatment of common colds through use of a method that significantly reduces duration of common colds in humans.

SUMMARY OF INVENTION

This invention relates to a new treatment that shortens duration of common colds through use of zinc compounds applied in a manner and at a frequency so as to cause a sustained, above normal concentration of zinc ions in the virally infected tissues until no common cold symptoms remain and without relapse of any common cold symptom.

DETAILED DESCRIPTION OF INVENTION

The invention disclosed and claimed is a method to reduce duration of common colds in humans as evinced by reduction of duration of 10 common cold symptoms defined as being: nasal drainage, nasal obstruction, headache, fever, myalgia, sneezing, sore throat, scratchy throat, cough and hoarseness with each symptom, when present, being a result of a viral upper respiratory infection. Such method involves administration of pharmaceutically acceptable zinc compounds topically applied to oral, pharyngeal and/or nasal mucosal membranes by a manner that raises the concentration of zinc ions in virally infected areas. Those concentrations

are maintained for a period of time until all common cold symptoms are eliminated without [release] relapse. Means of application include, but are not limited to the following direct, indirect, carrier, and special means or any combination of means. Direct application of zinc compounds may be by nasal sprays, nasal drops, nasal ointments, nasal washes, nasal injections, packings, or indirectly through use of throat troches or lozenges, or through use of mouth washes or gargles, or through the use of inhalants or ointments applied to the nasal nares, the bridge of the nose, or the face or any combination of these and similar methods of application. Carriers such as dimethyl sulfoxide and other special methods such as oral ingestion or parenteral introduction of zinc compounds where such treatment allows elevation of zinc ionic concentration in virally infected areas may be used as needed and given by any means of administration. The forms in which the zinc compounds may be administered include but are not limited to lozenges, troches, candies, injectants, chewing gums, tablets, powders, sprays, liquids, ointments, and aerosols. Pharmaceutically acceptable zinc compounds in dosages from 2 to 200 milligrams of zinc include but are not limited to zinc gluconate, zinc ascorbate, zinc citrate, zinc oxide, zinc acetate, zinc picolinate, zinc transferrin, zinc orotate and zinc aspartate.

AN OPERATIONAL METHOD TO DEMONSTRATE INVENTION

The following Treatment Instructions, prepared by the applicant, represent one way of using zinc compounds to reduce duration of common colds. The instruction were used in a random, double-blind, clinically controlled study in the office of Dr. William W. Halcomb, M.D., D.O. during the autumn of 1981 in Austin, Tex. Each tablet used in the double-blind study contained either 23 milligrams of zinc from zinc gluconate or 50 milligrams of calcium lactate as the placebo.

TREATMENT INSTRUCTIONS

At the office visit, patients are each given a bottle of tablets to use to treat the common cold. The patient dissolves the first tablet in the mouth so as to saturate the oral mucosa (lining of the mouth, tongue and throat) and then a second tablet immediately thereafter. Continue treatment after leaving the office during wakeful hours by dissolving in the mouth the appropriate number of tablets following the treatment schedule for age group of patient:

Age Group	Tablets/Treatment	Schedule for Treatment	Maximum Daily Dosage
Adult	1	Each 2 hours	12 tablets
Youth	1	Each 2 hours	9 tablets
Child	1/2	Each 2 hours	6 tablets

Patients should not wash down medication with either food, drink or mouthwashes. Patients should be treated immediately prior to bedtime and during the night when awake. After all symptoms have been absent for six hours, the patient may stop treatment.

RESULTS OF STUDY USING TREATMENT INSTRUCTIONS TO DEMONSTRATE INVENTION SO DESCRIBED

Data collected during the study indicate that the group treated with zinc gluconate lozenges recovered faster than did the group treated with placebo. The

placebo-treated group responded at a rate identical to untreated rhinovirus common cold patients described in medical literature. The following paragraph is the abstract from a manuscript entitled "Reduction in Duration of Common Colds by Zinc Gluconate Lozenges in a Double-Blind Study" which was prepared from data obtained during the study and was published in Antimicrobial Agents and Chemotherapy, volume 25, pages 20-24, 1984.

As a possible treatment for common colds, we tested zinc gluconate lozenges in a double-blind, placebo-controlled, clinical trial. One 23-mg zinc lozenge or matched placebo was dissolved in the mouth every 2 wakeful hours after an initial double dose. After 7 days 86% of 37 zinc-treated subjects were asymptomatic, compared with only 46% of 28 placebo-treated subjects (P=0.0005). Side effects or complaints were usually minor and consisted mainly of objectionable taste and mouth irritation. Zinc lozenges shortened the average duration of common colds by about 7 days.

Not only was duration of common colds treated with zinc significantly shorter, but duration of 10 common cold symptoms was shorter and severity of symptoms was also reduced. Duration of common colds is defined as the longest period of time in which any one, or more, of the 10 common cold symptoms remained.

CONTRAINDICATIONS TO TREATMENT

There are no known contraindications to the treatment.

What is claimed is:

1. The method of administering an agent to reduce duration of common cold symptoms in humans, which includes reducing the duration of nasal drainage, nasal congestion, headache, fever, myalgia, sneezing, sore throat, scratchy throat, cough, and [hoarseness] hoarseness when such symptoms evince existence of a common cold, comprising:

- 40 applying, in the form of a lozenge, zinc gluconate to the oral mucosa of a human in need of treatment; permitting zinc to remain in contact with the mucosa for a period of time necessary for lozenges to dissolve;
- 45 and applying additional dosages of zinc until the symptoms have disappeared.

2. The method according to claim 1 wherein dosages of zinc gluconate each contain 2 to 50 milligrams of zinc.

3. The method according to claim 1 wherein the first dosage of zinc gluconate is double that of additional dosages, additional dosages each consists of a single lozenge given two hours after a previously applied dosage, and all dosages are applied during the waking hours of the human in need of treatment.

- 4. A method for treating the common cold comprising:
 - (a) applying an effective dosage of zinc gluconate to the oral mucosa of a human in need of treatment;
 - (b) permitting the zinc thereof to remain in contact with the oral mucosa for a period of time necessary for it to saturate the oral mucosa; and
 - (c) applying additional dosages to zinc gluconate in like fashion until the cold has been treated.

65 5. The according to claim 4 wherein a first dosage of zinc gluconate is double that of additional dosages, additional dosages each consisting of a single dosage given approximately two hours after a previously applied dosage.

6. The method according to claim 4 wherein dosages of zinc gluconate each contain between about 2 and about 200 milligrams of zinc.

7. The method according to claim 6 wherein dosages of zinc gluconate each contain between about 2 and about 50 milligrams of zinc.

8. The method of claim 4 wherein the dosage form is a solid dosage form, and the zinc is permitted to remain in contact with the oral mucosa for a period of time necessary for it to dissolve.

9. The method of claim 8 wherein the dosage form is a candy.

10. The method of claim 8 wherein the dosage form is a chewing gum.

11. The method of claim 8 wherein the dosage form is a lozenge.

12. The method of claim 8 wherein the dosage form is a troche.

13. The method of claim 8 wherein the dosage form is a tablet.

14. The method of claim 8 wherein the dosage form is a powder.

15. The method of claim 4 wherein the dosage form is an aerosol.

16. The method of claim 4 wherein the dosage form is a liquid.

17. The method of claim 16 wherein the liquid is a liquid spray.

18. A method for treating symptoms commonly associated with the common cold, the symptoms including nasal drainage, nasal congestion, headache, fever, myalgia, sneezing, sore throat, scratchy throat, cough or hoarseness to reduce the duration or severity thereof comprising:

(a) applying an effective dosage of zinc gluconate to the oral mucosa of a human in need of treatment;

(b) permitting the zinc thereof to remain in contact with the oral mucosa for a period of time necessary for it to saturate the oral mucosa; and

(c) applying additional dosages of zinc gluconate in like fashion until the severity or duration of the symptom has been reduced.

19. The method according to claim 18 wherein a first dosage of zinc gluconate is double that of additional dosages, additional dosages each consisting of a single dosage given approximately two hours after a previously applied dosage.

20. The method according to claim 18 wherein dosages of zinc gluconate each contain between about 2 and about 200 milligrams of zinc.

21. The method according to claim 20 wherein dosages of zinc gluconate each contain between about 2 and about 50 milligrams of zinc.

22. The method of claim 18 wherein the dosage form is a solid dosage form, and the zinc is permitted to remain in contact with the oral mucosa for a period of time necessary for it to dissolve.

23. The method of claim 22 wherein the dosage form is a candy.

24. The method of claim 22 wherein the dosage form is a chewing gum.

25. The method of claim 22 wherein the dosage form is a lozenge.

26. The method of claim 22 wherein the dosage form is a troche.

27. The method of claim 22 wherein the dosage form is a tablet.

28. The method of claim 22 wherein the dosage form is a powder.

29. The method of claim 18 wherein the dosage form is an aerosol.

30. The method of claim 18 wherein the dosage form is a liquid.

31. The method of claim 30 wherein the dosage form is a liquid spray.

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