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(54) Title: XYLITOL COMPOSITIONS FOR TREATING UPPER RESPIRATORY CONDITIONS

(57) Abstract

Xylitol/xylose compositions and their methods of use for the treatment or prevention of nasopharyngeal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation by nasal administration of the xylitol/xylose compositions are disclosed.

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XYLITOL COMPOSITIONS FOR TREATING UPPER RESPIRATORY CONDITIONS

BACKGROUND OF THE INVENTION

(1) Field of the Invention

This invention relates to cleaning the nasopharynx and thereby reducing the number of bacteria resident there. This reduction translates into less problems with upper respiratory infections (specifically otitis and sinusitis) and reduction in the severity of asthma when the asthma is triggered by upper respiratory irritants. The invention also relates to xylitol/xylose compositions and their use in treating upper respiratory conditions.

(2) Description of the Related Art

Xylitol is the alcohol form of xylose, a pentose wood sugar. Since both forms are readily interchangeable, the term "xylitol/xylose" is used herein to mean "xylitol" or "xylose" or "xylitol and xylose". Xylitol, xylose, and mixtures of xylitol and xylose are equivalent and all equally effective in equal amounts in all therapeutic uses described herein. Xylitol is present in natural chemical cycles in the body (see *Touster*, 1974). It has about the same safety and toxicity as table sugar (*Jori*, 1984). Based on measuring the amount of xylitol in the urine of a group of southern European people who are deficient in an enzyme that assists in its metabolism *Touster* points out that the human body uses between 5 and 15 grams of xylitol daily. Xylitol is approved by the FDA as a food additive and is widely used as a sweetener especially in chewing gums. Xylitol is available at most health food stores. When ingested by mouth xylitol is about 90% absorbed, mostly in the jejunum, and rapidly metabolized; *Asano* and his group could find no detectable xylitol in the serum one and two hours after oral doses of 5 to 30 grams (*Asano*, 1973). Xylose is found in the body on the glycoprotein ligands that extend from cells and that are thought to participate in intercellular communication (*Murray*, 1996). Xylitol/xylose has been studied extensively for reducing dental caries through its effect on strep mutans, one of the bacteria responsible for cariogenic plaque. These studies have demonstrated that the action of xylitol/xylose that produces the cariogenic protection is by making this bacteria weaker and less adherent to dental plaque (*Trahan*, 1995). *Paul Naaber* found a similar decrease in adherence when he looked at Clostridium difficile in the gut in the presence of xylitol/xylose (*Naaber*, 1996). In 1998 *Kontiokari* found that a 2.5 percent solution of xylitol/xylose decreased the adherence of this bacteria when present either in the nasal mucosal cell or in the bacteria. When a five percent solution was present in both the bacteria and the mucosal cell, adherence of strep pneumonia,

the major pathogen, was reduced by two-thirds; from an average of 41 bacteria per cell to 13 (*Kontiokari*, 1998). His article concludes by stating:

> "These observations are consistent with the fact that monosaccharides are able to inhibit adherence only at the high concentrations, that are easily achieved in the oral cavity. The worldwide spread of penicillin-resistant strains of pneumocci substantiates the need for new approaches to preventing bacterial infections. Xylitol seems to be a promising agent for this purpose."

U. S. Patent 5,719,196 (Uhari, 1998) discloses the effects of oral xylitol/xylose in reducing the incidence of recurrent otitis (also see Uhari 1996). Uhari's original study studied the effect of xylitol chewing gum in reducing the incidence of otitis. The highest incidence of otitis is in infants less than two who cannot chew gum. Uhari subsequently studied the incidence of otitis in children getting an oral solution of xylitol. He found between a thirty and forty-percent reduction in the incidence of otitis using these supplements.

SUMMARY OF THE INVENTION

In accordance with the present invention, compositions for the treatment or prevention of nasopharyngeal congestion, irritation or inflammation, and associated upper respiratory infections such as otitis media, sinusitis by nasal application of xylitol/xylose in aqueous solution are provided. Also provided by the present invention are methods of treating a human subject suffering from nasopharyngeal congestion, irritation or inflammation, and associated upper respiratory infections such as otitis media and sinusitis, the methods comprising nasal administration of the new xylitol/xylose compositions. The present compositions and methods of delivering xylitol to the patient provide more efficient delivery to the nasopharynx than is possible with conventional xylitol treatments for respiratory infections, such as xylitol chewing gum. The compositions and methods of the invention are especially useful for treating infants younger than two years who cannot chew gum.

It is an object of the present invention to provide compositions and methods for reducing infections of the nasopharynx and symptoms associated with these infections.

Another object of this invention is to provide a means to clean the nasopharynx and reduce the population of the pathogenic bacteria resident there.

A further object of this invention is to provide compositions and methods for reducing otitis, sinusitis and, where asthma is triggered by inflammation of the upper airway, reducing in the severity of asthma.

Another object of this invention is to provide methods of efficiently delivering xylitol/xylose for the adjunctive treatment of nasopharyngeal infections.

Other objects are to achieve the above objectives with methods that are rapid, effective, efficient, natural, safe, and inexpensive, and do not require highly skilled people to formulate and administer.

Further objects are to achieve the above with a product that has a long storage life, is safe, versatile, efficient, stable and reliable, yet is inexpensive and easy to formulate and administer.

The specific nature of the invention, as well as other objects, uses, and advantages thereof, will clearly appear from the following description.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The first level of response of the immune system is to try and wash out the irritated area. In upper respiratory infections this usually translates into nasal congestion because the immune system gets the fluid it needs for this washing by dilating blood vessels in the area. The traditional response to these symptoms is to turn off the immune response by a decongestant or antihistamine. A treatment much more respectful of the wisdom of the immune system is to facilitate it in the attempt to wash the irritated area. Consistent with this goal, the inventor has discovered that the use of certain xylitol solutions, preferably in the form of a nasal spray containing saline, is a beneficial means for delivering xylitol more efficiently to the nasopharynx than is possible with other xylitol treatments for respiratory infections. The mode of delivery encompassed by the present invention avoids the dilution associated with ingestion, absorption, metabolism and circulation to the nose where it is active, that is necessary with conventional oral delivery of xylitol.

Xylitol's effect, even when given orally, is in the nasopharynx. The exemplary compositions described in more detail below make possible the delivery of a pleasant nasal spray containing almost three orders of magnitude less xylitol/xylose than is typically given orally, and they also provide better results. Use of this spray results in cleaning of the nasopharynx, reduction of the bacteria count in the nasopharynx and a reduction in infections associated with those bacteria. Because the bacteria are not killed, resistance is not as big a problem. The use of this spray as adjunctive treatment of appropriate infections reduces the need for second and third generation antibiotics. "Resistant" strains of strep mutans that recognize and do not ingest xylitol have been isolated in the mouth, but they are more friendly and less cariogenic (Trahan, 1995). Use of the cleansing solutions of the present

invention translates into less otitis and sinusitis. Where asthma is triggered by upper respiratory inflammation, an amelioration of the severity of the asthma is accomplished. The addition of xylitol/xylose to conventional nasal sprays is an efficient method of administration which is particularly useful with infants younger than two years who cannot chew gum.

An exemplary nasal spray is formulated having approximately 10% xylitol/xylose in an aqueous solution. The spray is administered by a conventional spray bottle. As little as 1% xylitol/xylose in solution appears to be the effective minimum strength, the maximum strength is a saturated solution of 64 grams of xylitol/xylose per 100 cc.s of solution.

Mixing in a saline aqueous solution to facilitate the washing effect of the saline, the saline solution should be slightly hypotonic. The preferred saline solution is a 0.65% sodium chloride solution. The saline solution can be in the range from 0.45% sodium salt to 0.95% sodium salt. More than 0.95% sodium salt results in a burning sensation in the nasal passages. Sodium chloride is the preferred salt to make the saline solution, although other compatible sodium compounds may be used.

One formulation is 5 grams of xylitol/xylose mixed with 45 cubic centimeters of "Ocean" nasal spray manufactured by the Fleming Company of Fenton, MO. The "Ocean" spray contains 0.65% sodium chloride in water with benzalkonium chloride and phenylcarbinol as preservatives.

The recommended dosage for infants under two is a spray in each nostril with each diaper change. This, also, could be expressed as administering two sprays of the solution about seven times a day. Each spray will deliver approximately five (5) milligrams per spray. With two sprays, seven times a day this would be approximately 70 milligrams per day.

An alternate of application is that the xylitol/xylose solution could be administered as drops from a dropper. If the solution were administered by drops, there would be approximately five (5) milligrams per drop, therefore, a recommended dosage by drops would be two drops in each nostril seven times a day would result in about 140 milligrams per day. About 0.1 gram a day is normally sufficient. Basically, an excess amount is not harmful.

Another form of delivery is by swab, such as cotton wound around a small stick. The swab might be dipped into a xylitol/xylose solution as described above. A stronger solution such as a 25% xylitol/xylose solution is desirable. Also, the xyliol/xylose may be mixed in a carrier other than a solution, such as a suitable gel.

This treatment is beneficial for nasal congestion. Usage as described results in a reduction of the population of resident pathogenic strep pneumonia and other bacteria with similar reduction in infections and inflammatory problems associated with these bacteria. This usage will result in a reduced incident of ear infections. Also, the dosage is recommended to lessen the frequency and severity of recurrent sinus infections.

Also, use of xylitol/xylose, as described above, in combination with a first line antibiotic is usually sufficient for treatment of most upper respiratory conditions where strep pneumonia is the agent involved with the infection.

The embodiment shown and described above is only exemplary. Various modifications can be made in the construction, material, arrangement, and operation, and still be within the scope of my invention. For example, the compositions and methods of treatment is beneficial to many people over two years of age.

The restrictive description of the specific examples above do not point out what an infringement of this patent would be, but are to point out the advantages and the progressive contribution to the healing arts and to enable one skilled in the art to make and use the invention. The limits of the invention and the bounds of the patent protection are measured by and defined in the following claims.

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Uhari, Matti and Tero Kontiokari. Patent No. 5,719,196. February 15, 1998. Method of treating respiratory infections or complications derived therefrom in humans which includes oral administration of xylitol.

U.S. Provisional Patent Application, Serial No. 60/079,184 filed March 24, 1998 entitled "Xylitol Delivery".

U.S. Patent Application Serial No. 09/220,283 filed December 23, 1998 entitled "Xylitol Delivery".

All of the above references are incorporated herein by reference.

CLAIMS

What is claimed is:

1. A composition for nasal administration to a person in need thereof for treating or preventing nasal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation, the composition comprising a xylitol/xylose solution.

2. The composition of claim 1 in the form of a nasal spray containing an aqueous xylitol/xylose solution.

3. The composition of claim 2 wherein the concentration of xylitol/xylose is suitable for administering an effective amount by spraying once in each nostril of an infant about seven times a day.

4. The composition of claim 2 wherein the concentration of xylitol/xylose is suitable for administering an effective amount by spraying once in each nostril of an infant at each diaper change.

5. The composition of claim 1 in the form of nose drops comprising an aqueous xylitol/xylose solution.

6. The composition of claim 5 wherein the concentration of xylitol/xylose is suitable for administering an effective amount by delivering two drops in each nostril of an infant about seven times a day.

7. The composition of claim 1 wherein said solution comprises 1-64 grams of xylitol/xylose in 100 cc of water.

8. The composition of claim 7 further comprising 0.45-0.85% sodium chloride.

9. The composition of claim 8 wherein said solution comprises 5 grams xylitol/xylose in 45 cc water containing 0.65% sodium, benzalkonium chloride and phenylcarbinol.

10. The composition of claim 1 comprising by weight 100 parts water, 1-65 parts xylitol/xylose, and 0.45-0.95 parts sodium chloride.

11. The composition of claim 10 further comprising an effective amount of a preservative.

12. The composition of claim 11 wherein said preservative is chosen from the group consisting of benzalkonium chloride and phenylcarbinol.

13. The composition of claim 10 wherein said composition is hypotonic and comprises 10 parts xylitol/xylose, 0.65 parts sodium chloride and 100 parts water.

14. The composition of claim 13 further comprising a preservative chosen from the group consisting of benzalkonium chloride and phenylcarbinol.

15. A pharmaceutical preparation for nasal administration in treating or preventing nasal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation, the preparation comprising an effective amount of xylitol/xylose in a suitable gel.

16. A nasal spray for treatment of a person suffering from nasal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation, the nasal spray comprising xylitol/xylose and water.

17. The nasal spray of claim 16 comprising by weight 1-65 parts xylitol/xylose, 0.45-0.95 parts sodium chloride and 100 parts water.

18. A medicated swab for nasal administration of an aqueous xylitol/xylose solution to a person in need thereof for the treatment or prevention of nasal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation, the swab containing an aqueous xylitol/xylose solution.

19. The medicated swab of claim 18 wherein said aqueous solution is 25% xylitol/xylose in a suitable gel.

20. A method of treating or preventing nasal congestion, recurrent sinus infections, infection or inflammation associated with bacteria, or asthma triggered by upper respiratory inflammation in a person suffering therefrom, the method comprising nasally administering the composition of claim 1 to said person.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/06436

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A01N 31/00, 43/04; A61K 31/70, 31/045
US CL : 514/23, 738

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)

U.S. : 514/23, 738

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,820,506 A (KLEINBERG et al) 11 April 1989.	1-20
X -- Y	GB 1,424,843 A (ONO PHAMACEUTICAL CO) 11 February 1976, Example 6.	1-6, 15-16, 18 ------ 7-14, 17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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