



(51) International Patent Classification:
A61K 31/722 (2006.01)

(21) International Application Number:
PCT/IB2014/002172

(22) International Filing Date:
16 April 2014 (16.04.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/811,644 4 December 2013 (04.12.2013) US

(72) Inventor; and

(71) Applicant : MELDER, C., Patrick [US/US]; 257 Hanson Way, Marietta, GA 30064 (US).

(74) Agent: MELDER, Patrick, Charles; 257 Hanson Way, Marietta, GA, 30064 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,

DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))



WO 2015/082965 A2

(54) Title: NOVEL CHITOSAN NASAL WASH

(57) Abstract: A nasal rinse composition comprising sodium, chloride, sodium bicarbonate, and chitosan.

Novel Chitosan Nasal Wash

Description:

TECHNICAL FIELD

This invention relates to a composition for rinsing nasal passages.

BACKGROUND

The nose is a very specialized and complicated structure that serves dual functions; it is the organ for the sense of smell, and it is also an entrance to the respiratory tract. As a part of the respiratory tract, a healthy nose moisturizes and warms incoming air and filters out foreign materials.

Nasal passages and other portions of the respiratory tract are lined with specialized tissue layers. In the nose and sinus areas, this tissue is often called the nasal mucosa. Like many tissues, the nasal mucosa is composed of several cell layers and cell types. Mucous cells are located throughout the nasal mucosa and are generally clustered into small glands. These glands secrete a sticky substance called mucus. Mucus is composed of water, shed epithelial (surface) cells, dead leukocytes, mucin, and inorganic salts, among other things, that are all held in suspension. Mucus functions as a trap for airborne particles (e.g., dust, bacteria, and viruses) that enter the nasal passages. Mucus also lubricates the walls of the nose, sinuses, and throat.

In a healthy nose, the mucus is cleared from the nasal passages on a regular basis by a layer of cells in the

nasal mucosa called the ciliated columnar epithelium. These cells possess small hair-like projections called cilia that undulate and "sweep" mucus through the nasal passages allowing it to drain to the back of the throat where it can be swallowed or expelled. This line of defense protects the body against the bacteria and viruses that continually enter the nose and mouth.

Connected to the nose are sinuses or air-filled cavities located behind certain facial bones. There are four groups of sinuses, namely: frontal, sphenoidal, ethmoidal, and maxillary. The sinuses are also lined with a mucus-secreting tissue. The sinuses are normally kept clear when mucus drains through them into the nasal passages. If they are obstructed for any reason, such as from the congestion present during a cold, normal drainage may not occur and the sinuses may be subsequently infected.

Virtually all persons are occasionally stricken with acute upper respiratory infections (common colds), acute or chronic allergy flare-ups of the nose, and/or acute or chronic non-allergic rhinosinusitis. Persons afflicted by such conditions usually incur significant discomfort and inconvenience.

All of these disorders are characterized by intense inflammation of the nasal mucosa. A number of symptoms contribute to the discomfort and inconvenience associated with the common cold or sinusitis. Symptoms often include one or more of the following: nasal congestion, anosmia, post-nasal drip, decreased sense of smell, ear fullness, headache, sore throat, malaise, muscle and joint aches, fatigue, cough, chest congestion, fever, chills and gastrointestinal maladies. Considerable research has been conducted over the years aimed at reducing the incidence and duration of symptoms associated with allergies and common colds.

Perhaps the most common symptom experienced by cold and allergy sufferers is "congestion." Congestion is commonly used by the layperson and in the patent literature as catch-all term to describe a complex series of events that hinder a person's ability to breathe through the nose when they have a cold, sinusitis or an allergic reaction.

For example, congestion can include a physiological response to an irritant that involves increased blood flow to tissues lining the nose. This increased blood flow causes these tissues to swell and physically block the nasal passages. Alternatively, when a nose is irritated or injured, fluid can seep into the free spaces in the tissues of the nose or build up in individual cells thereby causing additional congestion.

Congestion can also include the overproduction of mucus or the buildup of mucus due to increased mucus viscosity or depressed cilia activity or both. Congestion may also occur when a person lies on his or her side causing receptor cells in the nose to close off one nasal airway. Changes in temperature and/or humidity can alter the tissue of the nose and cause a congested feeling.

There are various methods to treat the symptoms of or to cure sinus disease, including surgery. Saline nasal irrigations have been used for many years and have been mentioned in medical textbooks going back hundreds of years. A wide variety of techniques have been described, including swimming in salt water, which often results in some degree of inadvertent nasal salt water irrigation. Alternatively, an effective nasal rinse can significantly reduce or permanently cure the symptoms of nasal allergies and sinus disease.

Nasal rinsing or lavaging is a treatment for rhinitis and sinusitis. Nasal rinsing is comprised of the dispensing of a saline solution into nasal passages, in order to cleanse and wash away mucus and allergens that create particles and irritants. Nasal rinsing allows the sinuses to drain normally and reduces the inflammation of the mucus membrane. Further, it is a common practice after sinus and nasal surgery for surgeons to recommend patients perform nasal & sinus rinsing to wash away debris and promote healing. It is also a common practice for surgeons to recommend the use of compounded medications with a large volume sinus rinse or nasal nebulization. Topical application of antibiotics in the form of nasal irrigation or nebulization is growing in importance due to the rise of bacterial resistance to antibiotics and the desire of patients to avoid the systemic side effects of oral antibiotics.

Saline solutions can be purchased, or prepared at home using household ingredients. However, there is a concern that the ready-to-use saline solutions may be contaminated, and that those solutions may not have a proper concentration of salt and acidity level. In particular, a saline solution made from only table salt is acidic in nature, and this acidity can cause burning when used to rinse nasal passages. Furthermore, there is a need to maintain the saline solution at a pH level consistent with the pH of mucous membranes of tissues, so that the saline solution will not irritate the nasal membrane and cause a stinging and burning sensation.

Numerous examples of nasal solutions, methods of use, and variations thereof have been reported. For example, topical nasal moisturizers and washes may be formulated so as to be isotonic, hypotonic, or hypertonic with respect to saline. Examples of marketed topical nasal moisturizers include NaSal™ Moisturizer, which contains sodium chloride 0.65%,

benzalkonium chloride, thimerosal 0.001% as preservatives, mono- and dibasic sodium phosphates as buffers, and purified water.

Another example is Ayr® Saline Nasal Mist and Drops, which is similarly preserved and contains a buffered isotonic saline. Ayr® Saline Nasal Mist and Drops uses monobasic potassium phosphate/sodium hydroxide buffer to adjust the pH and tonicity of the saline. It is desirable to instead provide a product in form of a dry and blended powder to extend its storage time. It is also advantageous to let the consumer to prepare the saline solution with water of a specific source and temperature at his or her choosing.

In another example, U.S. Pat. No. 6,520,384 (Mehta) discloses the use of an apparatus and a saline solution contained therein for rinsing nasal passages. Mixing water with a blend of 39 parts of sodium chloride and 1 to 2 parts of sodium bicarbonate produces the saline solution.

The currently available mixes available are generally composed of a mixture of saline and sodium bicarbonate. Some readily available mixes also contain herbal components such as aloe, while others contain citric acid. Still other readily available rinses contain xylitol with the enhanced ability to decrease bacterial counts in the nasal secretions by disrupting adherence of bacteria. However, the above referenced rinses contain no ingredients that are directly bactericidal, anti-fungal, anti-inflammatory, and naturally hemostatic.

For the foregoing reasons, there is a need for a solid blend of salt and sodium bicarbonate having a prolong storage time without preservatives with the complex carbohydrate and biopolymer, chitosan. The solid blend can be mixed with any potable water to form a pH-balanced

saline based solution, such that the solution does not cause a stinging or burning sensation upon its administration into nasal passages. Further, there is a need to provide a chitosan based mixture that can be used for nasal nebulization and surgical irrigation. Further, there is a need to provide a concentrated chitosan based nasal spray to promote healing immediately after surgery. The above mentioned chitosan formulations may be used with compounded medications for the treatment of chronic sinusitis.

SUMMARY OF THE INVENTION

The present invention is directed toward a composition of a novel saline rinse with chitosan. The known benefits of a buffered saline solution are combined with the known hemostatic, fibrinolytic, anti-bacterial, and anti-fungal properties of chitosan.

DETAILED DESCRIPTION OF THE INVENTION

The composition is comprised of a solid blend of sodium chloride, sodium bicarbonate, and chitosan. The composition is mixed with water to form a saline solution.

The Composition

The composition is comprised of a solid blend of sodium chloride, sodium bicarbonate, citric acid, and chitosan. The composition is mixed with water to form a saline solution.

The solution is subsequently administered to nasal passages. Sodium chloride (NaCl) is used in the granule form, and is presented in an amount of about 25 to 75 wt. % of the total composition, preferably about 58 to 87 wt. % of the total composition, and more preferably about 61 to 83 wt. % of the total composition.

Sodium bicarbonate (NaCOH_3) is used in either a granule or powder form, but preferably in the same form as sodium chloride. By having the same physical form during the manufacturing process, the separation of the two components can be minimized, and the uniformity of the blend can be maximized. The sodium bicarbonate can be one of the various USP grades selected from 1, 2, 3, 4, 5, MP, or micronized. Grade MP is preferred. The particle size of the sodium bicarbonate powder is between 149 and 250 microns. A coarser particle size is possible. The amount of sodium bicarbonate used is about 10 to 46 wt. % of the total composition, more preferably about 13 to 42 wt. % of the total composition. The particle size of the granulated sodium chloride is substantially different from the particle size of the sodium bicarbonate. The amount of chitosan used is about 0 to 5 wt. % of the total composition, more preferably 0 to 2 wt. % of the total composition.

The packet or pouch can be of any conventional size, for example, 1.5×2.5 in. Typically, the packet has an appropriate size to accommodate about 1.5 to 4.0 g of the mixture. The packet must have a low moisture permeability and be sealed completely upon filling with the mixture. An aluminum lining may be used inside the packets to protect the contents from moisture, which can adversely affect the ease with which the $\text{NaCl}/\text{NaHCO}_3/\text{Chitosan}$ dissolves in the water. A dotted line can be marked on the exterior of the packet to provide a guide for cutting open the packet.

For those familiar with the prior art, the saline mixture described above may have various other compositions to include herbal extracts, xylitol, alcohol, and essential oils.

Further, described above is dry powder composition for nasal irrigation. Said composition may also be manufactured and sold as a solution in a commonly available nasal spray bottle. Further embodiments may include placing the chitosan in a saline gel for use in the nose. Another embodiment may be to use a dry, sterile chitosan powder placed in a sterile saline (or other sterile solution - Lactated Ringers, D5W) bag to use intra-operatively during nasal and sinus surgery for irrigation purposes. Another embodiment may include using the chitosan mixture for nasal nebulization. Another embodiment may include using the chitosan mixture for nasal nebulization with compounded medication. Another embodiment may include using a concentrated form of chitosan after surgery in the form of a rinse or spray to promote healing.

The Saline Solution

Each packet contains a solid blend of approximately 25 to 75 wt. % of sodium chloride, about 10 to 15wt. % of sodium bicarbonate, and 0 to 5 wt. % chitosan. The blend is dissolved with a sufficient amount of water to produce an isotonic saline solution, which has a concentration of approximately 0.5 to 2% of sodium, preferably 0.7 to 1.5% of sodium, and more preferably 0.9% to 1% of sodium. The water is selected from distilled water, tap water, boiled water and filtered water.

The isotonic saline solution is pH-balanced and compatible with the human nasal and sinus mucosa to prevent burning or stinging during nasal lavaging. Burning or stinging are negative sensations that are often caused by plain water, or by saline solution prepared from either home ingredients, (i.e. table salt) or an ill-proportioned blend of sodium chloride and sodium bicarbonate.

CLAIMS

- 1.1 A nasal rinse composition comprising a buffered saline solution and water soluble chitosan.
2. A nasal rinse composition of claim number 1 comprising a buffered saline solution and water soluble methylcarboxylated chitosan.
3. A nasal rinse composition of claim number 1 comprising a buffered saline solution and water soluble oligosaccharide chitosan.
4. A nasal saline rinse composition of claim number 1 comprising a buffered saline solution and a blend of methylcarboxylated chitosan and oligosaccharide chitosan.
5. A nasal rinse composition of claim number 1 comprising about 25 to 75 wt. % of sodium chloride, about 10 to 15wt. % of sodium bicarbonate, 0 to 5 wt. % of citric acid, and 0 to 5 wt. % chitosan.
6. A nasal rinse composition of claim number 1 comprising about 61 to 83 wt. % of sodium chloride, about 10 to 40 wt. % of sodium bicarbonate, 0 to 5 wt. % of citric acid, and 0 to 5 wt. % methylcarboxylated chitosan.
7. A nasal rinse composition of claim number 1 comprising a solid blend of sodium chloride, sodium bicarbonate, and water soluble chitosan.
8. A nasal rinse composition of claim number 2 comprising a solid blend of sodium chloride, sodium bicarbonate, and water soluble methylcarboxylated chitosan.
9. A nasal rinse composition of claim number 3 comprising a solid blend of sodium chloride, sodium bicarbonate, and water soluble oligosaccharide chitosan.
10. A nasal rinse composition of claim number 2 comprising a solid blend of sodium chloride, sodium bicarbonate, and a blend of water soluble methylcarboxyl and oligosaccharide chitosan.
11. A nasal rinse composition of claim number 2 comprising a solid blend of sodium chloride, sodium bicarbonate, citric acid, and water soluble chitosan.

12. A method for rinsing nasal passages with a chitosan infused buffered saline solution comprising 1) pouring a solid buffered saline blend from a package comprising sodium chloride, sodium bicarbonate, water soluble chitosan, 2) mixing said blend with water in a dispenser to form a saline solution.