The preparation disclosed herein successfully combines these benefits as will be set out in more detail hereinafter. In particular, the newly developed formulation acts as an antiviral treatment with all its associated benefits and, in addition, exerts an immediate effect on a blocked nose. In case of patients suffering from an allergic reaction in the nasal cavity the newly developed formulation provides additional relief due to its antiviral activity. It is known in the art that respiratory viral infections can lead to substantial worsening of an existing allergic disease. For example, it is accepted medical knowledge that patients suffering from hay fever have an increased risk of developing allergic asthma if they are hit by recurrent viral infections of the respiratory tract.

The use of carrageenans in nasal sprays is known in the art. Especially iota- and kappa-carrageenans are well tolerated and unlike lambda-carrageenan they do not promote any inflammatory processes. In addition, carrageenans are widely used as excipients and viscosifiers in the pharmaceutical, cosmetic, and food industries.

SUMMARY

In one aspect, the present invention refers to use of a hyperosmolar aqueous solution comprising iota carrageenan, optionally in combination with kappa carrageenan, in the manufacture of a pharmaceutical composition for immediate deblocking of a stuffy nose, wherein the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality djusting agent; the hyperosmolar aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0; the hyperosmolar aqueous solution comprises EDTA at a concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml; the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride; the osmolality of the hyperosmolar aqueous solution is adjusted to a value within a range of from 500 to 1000 mOs; the composition in its ready-for-use formulation contains no more than 1.5% w/v of a said ionic osmolality adjusting agent; and wherein the composition has antiviral activity and contains iota carrageenan, optionally in combination with kappa carrageenan, in an antiviral effective amount ranging from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use formulation.

In another aspect, the present invention refers to use of a hyperosmolar aqueous solution comprising iota carrageenan, optionally in combination with kappa carrageenan, in the manufacture of a pharmaceutical composition for a combined prophylactic or therapeutic treatment of a viral infection of the upper respiratory tract and an immediate deblocking of a stuffy nose, wherein the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality adjusting agent; the hyperosmolar aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0; the hyperosmolar aqueous solution comprises EDTA at a

concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml; the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride; the osmolality of the hyperosmolar aqueous solution is adjusted to a value within a range of from 500 to 1000 mOs; the composition in its ready-for-use formulation contains no more than 1.5% w/v of a said ionic osmolality adjusting agent; and wherein the composition has antiviral activity and contains iota carrageenan, optionally in combination with kappa carrageenan, in an antiviral effective amount ranging from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use formulation.

In yet another aspect, the present invention refers to a pharmaceutical composition as described comprising a hyperosmolar aqueous solution which has an immediate stuffy nose deblocking activity and which is active against viral infections of the respiratory tract, wherein the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality adjusting agent, and a carrageenan component as an active antiviral ingredient, and wherein the aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0; the aqueous solution comprises EDTA at a concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml; the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride; the non-ionic osmolality adjusting agent is selected from the group consisting of monosacchar ides, disaccharides, oligosaccharides, and low molecular weight polyols; the aqueous solution is adjusted to a hyperosmolar value of from 500 mOs to 1000 mOs, preferably to a value of from 650 to 900 mOs; the carrageenan component is the sole antiviral active ingredient and is selected from iota-carrageenan, kappa-carrageenan, and a mixture of iota- and kappa carrageenan; the concentration of the carrageenan component ranges from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use preparation; with the proviso that the aqueous solution in its ready-for-use formulation contains no more than 1.5% (w/v) or no more than 1.2% (w/v) or no more than 0.9% (w/v), and preferably less than 0.9% (w/v) of the ionic osmolality adjusting agent.

BRIEF DESCRIPTION OF THE INVENTION

The term "hyperosmolar" as used herein refers to any solution exerting an osmotic pressure higher than the one generated by a physiological, i.e. 0.9% wt, sodium chloride solution.

Hyperosmolar solutions of nasal sprays usually contain sodium chloride in concentrations of up to 3% by weight. It has been found that carrageenans are

responsive to the presence of various cations, such as sodium, potassium, calcium or magnesium ions, in that they may change their polymeric secondary structure from a random structure to a more helical parallel structure. This change in structure effects both the viscosity of aqueous solutions containing the carrageenan polymer and the activity of the polymer against particular viruses, such as human rhinoviruses. It has further been recognized that higher cationic salt concentrations lead to more viscous solutions and to significant losses in antiviral activity of the carrageenans, particularly against human rhinoviruses, as evidenced by substantially increased IC_{50} values of iota-carrageenan in the treatment of HRV1a and HRV8 infections. Similarly, the minimal inhibitory concentration required for the inhibition of human coronavirus OC43 has been found to be increased up to 10-fold in carrageenan preparations containing hyperosmolar concentrations of sodium chloride relative to isoosmolar preparations. It can therefore be concluded that an attempt to provide an antivirally active, nose deblocking preparation comprising a hyperosmolar sodium chloride solution together with carrageenan will most likely fail.

CLAIMS

What is claimed is:

1. Use of a hyperosmolar aqueous solution comprising iota carrageenan, optionally in combination with kappa carrageenan, in the manufacture of a pharmaceutical composition for immediate deblocking of a stuffy nose, wherein
- the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality adjusting agent;
- the hyperosmolar aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0;
- the hyperosmolar aqueous solution comprises EDTA at a concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml;
- the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride;
- the osmolality of the hyperosmolar aqueous solution is adjusted to a value within a range of from 500 to 1000 mOs;
- the composition in its ready-for-use formulation contains no more than 1.5% w/v of a said ionic osmolality adjusting agent; and wherein
- the composition has antiviral activity and contains iota carrageenan, optionally in combination with kappa carrageenan, in an antiviral effective amount ranging from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use formulation.

2. Use of a hyperosmolar aqueous solution comprising iota carrageenan, optionally in combination with kappa carrageenan, in the manufacture of a pharmaceutical composition for a combined prophylactic or therapeutic treatment of a viral infection of the upper respiratory tract and an immediate deblocking of a stuffy nose, wherein
- the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality adjusting agent;
- the hyperosmolar aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0;
- the hyperosmolar aqueous solution comprises EDTA at a concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml;
- the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride;
- the osmolality of the hyperosmolar aqueous solution is adjusted to a value within a range of from 500 to 1000 mOs;
- the composition in its ready-for-use formulation contains no more than 1.5% w/v of a said ionic osmolality adjusting agent; and wherein
- the composition has antiviral activity and contains iota carrageenan, optionally in combination with kappa carrageenan, in an antiviral effective amount

ranging from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use formulation.

3. Use according to claim 1 or 2, wherein the non-ionic osmolality adjusting agent is selected from the group consisting of monosaccharides, disaccharides, oligosaccharides, and low molecular weight polyols.

4. Use according to claim 3, wherein the mono- and disaccharides are selected from the group consisting of glucose, fructose, sucrose, and mannose, and wherein the polylols are selected from the group consisting of glycerol, erythritol, mannitol, sorbitol, inositol, xylitol, threitol, and maltitol.

5. Use according to claim 1 or 2, wherein the composition further comprises at least one physiologically acceptable additive selected from the group consisting of a pH adjusting agent, a preservative, an anti-oxidant, a humectant, an emollient, a moisturizer, and a flavor.

6. Use according to claim 1 or 2, wherein the hyperosmolar aqueous solution comprises the non-ionic osmolality adjusting agent at a concentration of from 1 to 15% w/v, or of from 5 to 10% w/v, of the total composition.

7. Use according to claim 1 or 2, wherein the hyperosmolar aqueous solution comprises the ionic osmolality adjusting agent at a concentration of from 0.1 to 1.3% w/v, or of from 0.5 to 1.2% w/v, of the total composition.

8. Use according to claim 2, wherein the viral infection is caused by at least one of a human rhinovirus, human coronavirus, parainfluenza virus, metapneumovirus, respiratory syncytial virus, influenza A virus, influenza B virus, and adenovirus subtype B.

9. Use according to claim 1 or 2, wherein the composition is prepared as a nasal spray.

10. The pharmaceutical composition referred to in any of claims 1 to 9 comprising a hyperosmolar aqueous solution which has an immediate stuffy nose deblocking activity and which is active against viral infections of the respiratory tract, wherein the hyperosmolar aqueous solution comprises a non-ionic osmolality adjusting agent in combination with an ionic osmolality adjusting agent, and a carrageenan component as an active antiviral ingredient, and wherein

- the aqueous solution comprises a nasally compatible buffer and is adjusted to a pH value within a range of from 4.0 to 8.0;
- the aqueous solution comprises EDTA at a concentration of up to 2 mg/ml, preferably of 1 - 2 mg/ml;
- the ionic osmolality adjusting agent is selected from the group consisting of sodium chloride, potassium chloride, and a mixture of sodium and potassium chloride;

- the non-ionic osmolality adjusting agent is selected from the group consisting of monosaccharides, disaccharides, oligosaccharides, and low molecular weight polyols;
- the aqueous solution is adjusted to a hyperosmolar value of from 500 mOs to 1000 mOs, preferably to a value of from 650 to 900 mOs;
- the carrageenan component is the sole antiviral active ingredient and is selected from iota-carrageenan, kappa-carrageenan, and a mixture of iota- and kappa carrageenan;
- the concentration of the carrageenan component ranges from 0.05% to 1% (w/v), or from 0.1 to 0.5% (w/v), or from 0.1 to 0.3 % (w/v), of the ready-for-use preparation;

with the proviso that the aqueous solution in its ready-for-use formulation contains no more than 1.5% (w/v) or no more than 1.2% (w/v) or no more than 0.9% (w/v), and preferably less than 0.9% (w/v) of the ionic osmolality adjusting agent.

11. The pharmaceutical composition of claim 10, wherein the mono- and disaccharides are selected from the group consisting of glucose, fructose, sucrose, and mannose, and wherein the polylols are selected from the group consisting of glycerol, erythritol, mannitol, sorbitol, inositol, xylitol, threitol, and maltitol.

12. The pharmaceutical composition of claim 10 or 11, wherein the hyperosmolar aqueous solution comprises the non-ionic osmolality adjusting agent at a concentration of from 1 to 15% w/v, or of from 5 to 10% w/v.

13. The pharmaceutical composition of any of claims 10 to 12, wherein the hyperosmolar aqueous solution comprises the ionic osmolality adjusting agent at a concentration of from 0.1 to 1.3% w/v, or of from 0.5 to 1.2% w/v.

14. The pharmaceutical composition of any of claims 10 to 13, prepared as a nasal spray.