Therefore, a need exists to provide for Lysyl-Prolyl-Threonine having an increased storage stability. In particular, a need exists to provide for Lysyl-Prolyl-Threonine in a form suitable to be administered as a medicament that remains safe and efficacious over an extended time period.

Summary

In one aspect, the present invention refers to a lyophilized formulation comprising Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, further comprising one or more bulking agents and one or more buffering agents, wherein the bulking agent is selected from the group consisting of mannitol, sucrose and trehalose and wherein the buffering agent is selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine; further comprising one or more pH adjusting agents. In one example, there is disclosed a lyophilized formulation comprising Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, further comprising one or more bulking agents and one or more buffering agents, wherein the bulking agent is selected from the group consisting of mannitol, sucrose and trehalose and wherein the buffering agent is selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine. In another aspect, the present invention refers to a process for preparing the lyophilized formulation as defined herein comprising the steps of: (a) mixing in any order the following components: (i) Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, (ii) an aqueous carrier, (iii) one or more bulking agents, selected from mannitol, sucrose and trehalose, (iv) one or more buffering agents selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine, and (v) if present, one or more pH adjusting agents; to provide for an aqueous preparation having a pH in the range of 3.0-5.0, wherein the free base of Lysyl-Prolyl-Threonine has a concentration of 0.1-175 mg/g, based on the aqueous preparation; (b) lyophilizing the aqueous preparation to provide for the lyophilized formulation in solid form. In yet another aspect, the present invention refers to non-therapeutic use of the lyophilized formulation disclosed herein as a cosmetic. In a further aspect, the present invention refers to non-therapeutic use of the lyophilized formulation disclosed herein for the cosmetic treatment of the skin and/or mucosa of a mammal. In one example, disclosed herein is a lyophilized formulation comprising Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof. In another example, there is disclosed a process for preparing the lyophilized formulation as defined herein comprising the steps of: (a) mixing in any order the following components: (i) Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, (ii) an aqueous carrier, (iii) optionally one or more bulking agents, (iv) optionally one or more buffering agents, and (v) optionally one or more pH adjusting agents; to provide for an aqueous preparation having a pH in the range of 3.0-5.0, wherein the free base of Lysyl-Prolyl-Threonine has a concentration of 0.1-175 mg/g, based on the aqueous preparation; (b) lyophilizing the aqueous preparation to provide for the lyophilized formulation in solid form. In yet another example, disclosed herein is a lyophilized

Claims

1. A lyophilized formulation comprising Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, further comprising one or more bulking agents and one or more buffering agents, wherein the bulking agent is selected from the group consisting of mannitol, sucrose and trehalose and wherein the buffering agent is selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine; further comprising one or more pH adjusting agents.

2. The lyophilized formulation according to claim 1 obtainable by lyophilizing an aqueous preparation having a pH of 3.0-5.0, wherein the aqueous preparation comprises:
(i) Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof, wherein the free base has a concentration of 0.1-175 mg/g, based on the aqueous preparation,
(ii) aqueous carrier,
(iii) one or more bulking agents, wherein the bulking agent is selected from the group consisting of mannitol, sucrose and trehalose, and
(iv) one or more buffering agents, wherein the buffering agent is selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine.

3. The lyophilized formulation according to any one of claims 1 to 2, wherein the Lysyl-Prolyl-Threonine is (L)Lys-(D)Pro-(L)Thr, (L)Lys-(L)Pro-(D)Thr, (L)Lys-(D)Pro-(D)Thr, (L)Lys-(L)Pro-(L)Thr, (D)Lys-(D)Pro-(L)Thr, (D)Lys-(D)Pro-(D)Thr, (D)Lys-(L)Pro-(L)Thr, (D)Lys-(L)Pro-(D)Thr, or mixtures thereof.

4. The lyophilized formulation according to any one of claims 1 to 3, wherein the pH adjusting agent is an acid or a base that maintains a pH value at 3.0-5.0 selected from sodium hydroxide and hydrochloric acid.

5. The lyophilized formulation according to any one of claims 1 to 4 for use as a medicament.

6. The lyophilized formulation according to any one of claims 1 to 5 for use in the therapeutic and/or prophylactic treatment of diseases chosen from the group comprising pain-related diseases, pruritus-related diseases, inflammatory diseases, and/or multiple sclerosis.

7. The lyophilized formulation for use according to any one of claims 5 to 6, wherein the lyophilized formulation is to be administered to a patient in solid form, or wherein the solid lyophilized formulation is reconstituted with an aqueous carrier to form an aqueous preparation, the aqueous preparation subsequently to be administered to a patient.

8. A process for preparing the lyophilized formulation as defined in any one of claims 1 to 7 comprising the steps of:

(a) mixing in any order the following components:

(i) Lysyl-Prolyl-Threonine or a pharmaceutically acceptable salt thereof,

(ii) an aqueous carrier,

(iii) one or more bulking agents, selected from mannitol, sucrose and trehalose

(iv) one or more buffering agents selected from the group consisting of citric acid, sodium dihydrogenphosphate, acetic acid, succinic acid, glutamate, Tris and histidine, and

(v) if present, one or more pH adjusting agents;

to provide for an aqueous preparation having a pH in the range of 3.0-5.0, wherein the free base of Lysyl-Prolyl-Threonine has a concentration of 0.1-175 mg/g, based on the aqueous preparation;

(b) lyophilizing the aqueous preparation to provide for the lyophilized formulation in solid form.

9. A pharmaceutical composition comprising the lyophilized formulation as defined in any one of claims 1 to 7 and one or more pharmaceutical excipients.

10. A cosmetic composition comprising the lyophilized formulation as defined in any one of claims 1 to 4 and one or more cosmetic excipients.

11. Non-therapeutic use of the lyophilized formulation according to any one of claims 1 to 4 as a cosmetic.

12. Non-therapeutic use of the lyophilized formulation according to claim 11 for the cosmetic treatment of the skin and/or mucosa of a mammal.