

aggregation behavior of the peptides are due to their high hydrophobicity. At higher pH, deamidation of peptide can occur, which results in conversion of the gross positively-charged peptide to a neutral peptide. Due to the hydrophobic nature of other amino acid residues on this peptide, the lack of charge leads to micro-collapse of the peptide chains and resultant precipitation. The formulations of the present invention address these challenges.

SUMMARY

[0006] In one ~~aspeet~~example, the present disclosure refers to a composition comprising: a therapeutically effective amount of a 1 kDa to 2 kDa peptide, a generally recognized as safe solubilizer, one or more generally recognized as safe surfactants and a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5. When boric acid and mannitol are included, boric acid can be generally from 0.05% to 1.0%, or from 0.05% to 0.2%, of the total composition, and mannitol can be generally from 0.5% to 5.0%, or from 2.0% to 4.0% of the total composition.

[0007] In another ~~aspeet~~example, the present disclosure refers to a composition comprising: a therapeutically effective amount a 1 kDa to 2 kDa adiponectin peptidomimetic, a generally recognized as safe solubilizer, one or more a generally recognized as safe surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality of is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

[0007a] In a futherone aspect, the present disclosure refers to ~~the use of~~ a composition comprising, by weight: 0.01% to 2% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1% to 2% propylene glycol, 0.08% to 0.12% Tyloxapol or Poloxamer, 0.02% to 0.20% acetic acid and 0.05% to 0.5% sodium acetate a therapeutically effective amount of a 1 kDa to 2 kDa peptide, a generally recognized as safe solubilizer, one or more generally recognized as safe surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality of the formulation is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5, in the manufacture of a medicament for treating a disease in a patient. In another aspect, the present disclosure refers to a composition comprising, by weight: 1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.20% propylene glycol, 0.10% Tyloxapol, 0.07% acetic acid, 0.06% sodium acetate, 0.09% boric acid and 3.66% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5. In another aspect, the present disclosure refers to a composition comprising, by weight: 0.401% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097% Tyloxapol, 0.014% acetic acid, 0.138% sodium acetate, 0.09% boric acid and 3.65% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5. In another aspect, the present disclosure refers to a composition comprising, by weight: 0.4% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097% Tyloxapol, 0.015% acetic acid, 0.228% sodium acetate, 0.09% boric acid and 3.53% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5. In another aspect, the present disclosure refers to a composition comprising, by weight: 0.1% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097% Tyloxapol, 0.0065% acetic acid, 0.25% sodium acetate, 0.09% boric acid and 3.6% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

[0008] In one example, there is disclosed a method for treating a disease in a patient by administering to the patient a composition comprising: a therapeutically effective amount of a 1 kDa to 2 kDa peptide, a generally recognized as safe solubilizer, one or more generally recognized as safe

surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

[0008a] In a further aspect, the present disclosure refers to a composition for use as a medicament wherein the composition comprises, by weight: 0.01% to 2% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1% to 2% propylene glycol, 0.08% to 0.12% Tyloxapol or Poloxamer, 0.02% to 0.20% acetic acid and 0.05% to 0.5% sodium acetate; wherein osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5. In a still further aspect, the present disclosure refers to use of a composition comprising, by weight: 0.20% to 1.0% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.20% to 1.90% propylene glycol, 0.10% Tyloxapol or Poloxamer, 0.04% to 0.20% acetic acid and 0.08% to 0.42% sodium acetate; wherein osmolality is between 270 to 280 mOsm/kg or wherein osmolality is adjusted to between 270 to 280 mOsm/kg and the pH is between 4.5 to 5.5, in the manufacture of a medicament for treating a disease in a patient in which the disease is an ocular disease associated with inflammation.

[0009] In another example, there is disclosed a method for treating a disease in a patient by administering to the patient a composition comprising: a therapeutically effective amount a 1 kDa to 2 kDa adiponectin peptidomimetic, a generally recognized as safe solubilizer, one or more a generally recognized as safe surfactants, a generally

CLAIMS

What is claimed is:

~~1. A composition comprising: a therapeutically effective amount of a 1 kDa to 2 kDa peptide, a generally recognized as safe solubilizer, one or more generally recognized as safe surfactants, generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.~~

~~2. A composition comprising: a therapeutically effective amount a 1 kDa to 2 kDa adiponectin peptidomimetic, a generally recognized as safe solubilizer, one or more a generally recognized as safe surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.~~

~~3. The composition of Claim 2 comprising: an adiponectin peptidomimetic, a generally recognized as safe solubilizer selected from polypropylene glycol, glycerol, PEG400 and propylene glycol, a generally recognized as safe surfactant selected from Tween 80, Tyloxapol, Poloxamer, PEG 40 Hydrogenated Caster Oil, PEG 35 Caster Oil and PEG 40 Sterate, an acetate buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.~~

~~4.1. The A~~ composition ~~of Claim 3~~ comprising, by weight: 0.01% to 2% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1% to 2% propylene glycol, 0.08% to 0.12% Tyloxapol or Poloxamer, 0.02% to 0.20% acetic acid and 0.05% to 0.5% sodium acetate; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~5.2.~~ The composition of Claim ~~4.1~~ comprising, by weight: 0.20% to 1.0% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.20% to 1.90% propylene glycol, 0.10% Tyloxapol or Poloxamer, 0.04% to 0.20% acetic acid and 0.08% to 0.42% sodium acetate; wherein the osmolality is is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~6.3.~~ The composition of Claim ~~5-2~~ selected from, by weight:

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.77% propylene glycol, 0.10% Tyloxapol, 0.14% acetic acid and 0.08% sodium acetate;

0.5% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.58% propylene glycol, 0.10% Tyloxapol, 0.09% acetic acid and 0.24% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.57% propylene glycol, 0.10% Tyloxapol, 0.09% acetic acid and 0.24% sodium acetate;

0.5% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.43% propylene glycol, 0.10% Tyloxapol, 0.04% acetic acid and 0.34% sodium acetate;

0.5% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.44% propylene glycol, 0.10% Tyloxapol, 0.04% acetic acid and 0.34% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.72% propylene glycol, 0.10% Poloxamer 188, 0.11% acetic acid and 0.09% sodium acetate;

0.51% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.73% propylene glycol, 0.10% Poloxamer 188, 0.11% acetic acid and 0.09% sodium acetate;

0.25% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.74% propylene glycol, 0.10% Poloxamer 188, 0.11% acetic acid and 0.09% sodium acetate;

0.50% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.55% propylene glycol, 0.10% Poloxamer 188, 0.10% acetic acid and 0.24% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.55% propylene glycol, 0.10% Poloxamer 188, 0.10% acetic acid and 0.24% sodium acetate;

~~1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.40% propylene glycol, 0.20% Poloxamer 188, 0.19% acetic acid and 0.30% sodium acetate;~~

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.38% propylene glycol, 0.10% Tyloxapol, 0.19% acetic acid and 0.30% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.25% propylene glycol, 0.10% Tyloxapol, 0.17% acetic acid and 0.41% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.54% propylene glycol, 0.10% Tyloxapol, 0.19% acetic acid and 0.14% sodium acetate;

0.80% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.54% propylene glycol, 0.10% Tyloxapol, 0.19% acetic acid and 0.14% sodium acetate;

0.50% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.55% propylene glycol, 0.10% Tyloxapol, 0.19% acetic acid and 0.14% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.53% propylene glycol, 0.10% Tyloxapol, 0.19% acetic acid and 0.14% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.86% propylene glycol, 0.10% Tyloxapol, 0.13% acetic acid and 0.10% sodium acetate;

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.67% propylene glycol, 0.10% Tyloxapol, 0.15% acetic acid and 0.11% sodium acetate; and

1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.62% propylene glycol, 0.10% Tyloxapol, 0.17% acetic acid and 0.13% sodium acetate;

wherein the osmolality for each composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~7.4. The A~~ composition ~~of Claim 3~~ comprising, by weight: 1.00% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.20% propylene glycol, 0.10% Tyloxapol, 0.07% acetic acid, 0.06% sodium acetate, 0.09% boric acid and 3.66% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~8.5. The A~~ composition ~~of Claim 3~~ comprising, by weight: 0.401% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097% Tyloxapol, 0.014% acetic acid, 0.138% sodium acetate, 0.09% boric acid and 3.65% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~9.6. The A~~ composition ~~of Claim 3~~ comprising, by weight: 0.4% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097%

Tyloxapol, 0.015% acetic acid, 0.228% sodium acetate, 0.09% boric acid and 3.53% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~10.7.~~ The A composition of Claim 3 comprising, by weight: 0.1% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 0.193% propylene glycol, 0.097% Tyloxapol, 0.0065% acetic acid, 0.25% sodium acetate, 0.09% boric acid and 3.6% mannitol; wherein the osmolality for the composition is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~11. Use of a composition comprising: a therapeutically effective amount of a 1 kDa to 2 kDa peptide, a generally recognized as safe solubilizer, one or more generally recognized as safe surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality of the formulation is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5, in the manufacture of a medicament for treating a disease in a patient.~~

~~12. The use of Claim 11 in which the composition comprises: a therapeutically effective amount a 1 kDa to 2 kDa adiponectin peptidomimetic, a generally recognized as safe solubilizer, one or more a generally recognized as safe surfactants, a generally recognized as safe buffer, optionally boric acid and optionally mannitol; wherein the osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.~~

~~13.8.~~ The use of Claim 12 in which the A composition for use as a medicament wherein the composition comprises, by weight: 0.01% to 2% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1% to 2% propylene glycol, 0.08% to 0.12% Tyloxapol or Poloxamer, 0.02% to 0.20% acetic acid and 0.05% to 0.5% sodium acetate; wherein osmolality is between 260 to 330 mOsm/kg and the pH is between 4.5 to 5.5.

~~14.9.~~ The use composition for use as a medicament of Claim 13-8 in which the composition comprises, by weight: 0.20% to 1.0% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.20% to 1.90% propylene glycol, 0.10% Tyloxapol

or Poloxamer, 0.04% to 0.20% acetic acid and 0.08% to 0.42% sodium acetate; wherein osmolality is between 270 to 280 mOsm/kg or wherein osmolality is adjusted to between 270 to 280 mOsm/kg.

15.10. Use of a composition comprising, by weight: 0.20% to 1.0% D-Asn-Ile-Pro-Nva-Leu-Tyr-D-Ser-Phe-Ala-D-Ser-NH₂, 1.20% to 1.90% propylene glycol, 0.10% Tyloxapol or Poloxamer, 0.04% to 0.20% acetic acid and 0.08% to 0.42% sodium acetate; wherein osmolality is between 270 to 280 mOsm/kg or wherein osmolality is adjusted to between 270 to 280 mOsm/kg and the pH is between 4.5 to 5.5, in the manufacture of a medicament for treating a disease in a patient ~~The use of Claim 14~~ in which the disease is an ocular disease associated with inflammation.