BRIEF SUMMARY OF THE INVENTION

[0017] The present disclosure relates to a pharmaceutical composition comprising plasminogen, and uses thereof.

[0018] The present disclosure relates to the following items 1 to 61:

[0019] 1. A pharmaceutical composition comprising:

[0020] - plasminogen, or a biologically active variant thereof;

[0021] - a tonicity modifier; and

[0022] - a stabilising agent;

[0023] wherein the composition has a pH of about 3.0 to about 10.0.

[0024] 2. The pharmaceutical composition of item 1, wherein the pH is from 5.0 to 8.0; or from 6.0 to 8.0; or from 6.5 to 7.5.

[0025] 3. The pharmaceutical composition of item 1, wherein the concentration of the plasminogen or biologically active variant thereof is about 0.01 mg/ml to about 80 mg/ml, or from about 5 mg/ml to about 60 mg/ml.

[0026] 4. The pharmaceutical composition of item 3, wherein the concentration of the plasminogen or biologically active variant thereof is about 40, 30, 20, 10 or 5 mg/ml.

[0027] 5. The pharmaceutical composition of any one of items 1 to 4, wherein the plasminogen or biologically active variant thereof represents at least 80% of the total protein content of the composition or more than 90% of the total protein content of the composition.

[0028] 6. The pharmaceutical composition of item 5, wherein the plasminogen or biologically active variant thereof represents more than 95 or 98% of the total protein content of the composition.

[0029] 7. The pharmaceutical composition of any one of items 1 to 6, wherein the stabilising agent comprises (i) an amino acid, (ii) an amino acid salt, (ii) an amino acid analog, or (iv) any mixture of (i), (ii) and/or (iii).

[0075] 53. The pharmaceutical composition of item 52, wherein the bulking agent is glycine, glutamic acid, alanine, mannitol, sorbitol, hydroxyethyl starch, dextran, PVP (poly vinyl pyrrolidone), mannitol, polyethylene glycol, sorbitol, maltitol, lactitol, maltotriitol, xylitol or any combination thereof.

[0076] 54. The pharmaceutical composition of item 53, wherein the bulking agent is mannitol or sorbitol.

[0077] 55. The pharmaceutical composition of item 52, 53 or 54, wherein the bulking agent is in a concentration of about 50 mM to about 300 mM.

[0078] 56. The pharmaceutical composition of any one of items 38 to 55, wherein the pharmaceutical composition has an osmolality between about 180 mOsm and about 350 mOsm.

[0079] 57. The pharmaceutical composition of any one of items 38 to 61, wherein the pharmaceutical composition has a pH of about 6.5 to about 8.0.

[0080] 58. The pharmaceutical composition of any one of items 38 to 57, wherein said plasminogen or a biologically active variant thereof is human plasminogen.

[0081] 59. The pharmaceutical composition of any one of items 38 to 58, wherein said plasminogen or a biologically active variant thereof consists of more than 80% of Glu-plasminogen.

[0082] 60. The pharmaceutical composition of any one of items 38 to 58, wherein said plasminogen or a biologically active variant thereof is Glu-plasminogen.

[0083] 61. The pharmaceutical composition of any one of items 38 to 60, for use as a medicament.

In one aspect, the present disclosure relates to a pharmaceutical composition comprising: plasminogen, or a biologically active variant thereof, in a concentration from about 0.01 mg/ml to about 80 mg/ml; a tonicity modifier, which contains sodium, wherein the tonicity modifier is in a concentration adjusted to reach an osmolality of the composition between about 180 mOsm and about 350 mOsm; and a stabilising agent, which is arginine or glycine, in a concentration from about 20 mM to about 200 mM; wherein the composition has a pH of about 3.0 to about 10.0.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising plasminogen or a biologically active variant thereof, which contains an amount of particles equal to or

greater than 10 μm that is lower than 6000 particles per 100 ml, which comprises a stabilising agent that is arginine or glycine.

In another aspect, the present disclosure relates to the pharmaceutical composition as disclosed herein for use as a medicament.

[0084] Further aspects of the present disclosure will be apparent to a person skilled in the art from the following description, claims, and generalizations herein.

BRIEF DESCRIPTION OF THE FIGURES

[0085] **Figure 1A** is a schematic of the primary structure of plasminogen showing its kringle domains, plasmin cleavage site and streptokinase binding site.

CLAIMS:

1. A pharmaceutical composition comprising:

- plasminogen, or a biologically active variant thereof, in a concentration from about 0.01 mg/ml to about 80 mg/ml;

- a tonicity modifier, which contains sodium, wherein the tonicity modifier is in a concentration adjusted to reach an osmolality of the composition between about 180 mOsm and about 350 mOsm; and

- a stabilising agent, which is arginine or glycine, in a concentration from about 20 mM to about 200 mM;

wherein the composition has a pH of about 3.0 to about 10.0.

2. The pharmaceutical composition of claim 1, wherein the pH is from 5.0 to 8.0; or from 6.0 to 8.0; or from 6.5 to 7.5.

3. The pharmaceutical composition of claim 1 or 2, wherein the concentration of the plasminogen or biologically active variant thereof is from about 5 mg/ml to about 60 mg/ml, or is about 40, 30, 20, 10 or 5 mg/ml.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the stabilising agent is in a concentration of about 25 mM to about 75 mM.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the tonicity modifier is sodium chloride.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the tonicity modifier is present in a concentration of about 30 mM to about 250 mM, or of between about 25 mM to about 50 mM, or of about 35 mM.

7. The pharmaceutical composition of any one of claims 1 to 6, further comprising a non-reducing sugar, which is sucrose.

8. The pharmaceutical composition of any one of claims 1 to 7, wherein said plasminogen or a biologically active variant thereof is Glu-plasminogen.

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the composition contains an amount of particles equal to or greater than 10 µm that is lower than 6000 particles per 100 ml, or lower than 2000 or 1000 particles per 100 ml.

10. The pharmaceutical composition of any one of claims 1 to 9, which is suitable for intravenous, subcutaneous, topical, intradermal, ophthalmic and/or intramuscular administration.

11. The pharmaceutical composition of any one of claims 1 to 9, which is a liquid composition, a liquid composition suitable for lyophilisation, a liquid composition suitable for freezing, a lyophilised composition, a frozen composition or a reconstituted composition.

12. The pharmaceutical composition of any one of claims 1 to 11, for use as a medicament.

13. A pharmaceutical composition comprising plasminogen or a biologically active variant thereof, which contains an amount of particles equal to or greater than 10 µm that is lower than 6000 particles per 100 ml, which comprises a stabilising agent that is arginine or glycine.

14. The pharmaceutical composition of claim 13, wherein the amount of particles is lower than 2000 or 1000 particles per 100 ml.

15. The pharmaceutical composition of claim 13 or 14, wherein the stabilising agent is arginine.

16. The pharmaceutical composition of claim 13 or 14, wherein the stabilising agent is glycine.

17. The pharmaceutical composition of any one of claims 13 to 16, wherein the stabilising agent in a concentration from about 20 mM to about 200 mM, or of about 25 mM to about 75 mM.

18. The pharmaceutical composition of any one of claims 13 to 17, further comprising a non-reducing sugar, which is sucrose.

19. The pharmaceutical composition of any one of claims 13 to 18, wherein the concentration of the plasminogen or biologically active variant thereof is from about 0.01 mg/ml to about 80 mg/ml.

20. The pharmaceutical composition of any one of claims 13 to 19, which further comprises a tonicity modifier, which contains sodium.

21. The pharmaceutical composition of claim 20, wherein the tonicity modifier is sodium chloride.

22. The pharmaceutical composition of claim 20 or 21, wherein the tonicity modifier is in a concentration adjusted to reach an osmolality of the pharmaceutical composition between about 180 mOsm and about 350 mOsm.

23. The pharmaceutical composition of claim 20 or 21, wherein the tonicity modifier is present in a concentration of about 30 mM to about 250 mM, or between about 25 mM to about 50 mM, or of about 35 mM.

24. The pharmaceutical composition of any one of claims 13 to 23, wherein the pharmaceutical composition has a pH of about 6.5 to about 8.0.

25. The pharmaceutical composition of any one of claims 13 to 24, wherein said plasminogen or a biologically active variant thereof is Glu-plasminogen.

26. The pharmaceutical composition of any one of claims 13 to 25, for use as a medicament.