during long term storage in a liquid state at temperatures ranging from just above freezing to ambient temperatures would be operationally advantageous as well as greatly increase convenience and flexibility for the health care provider and patient. The invention fulfills this need by providing such compositions.

SUMMARY

[0007] Disclosed is a live virus composition comprising a herpes simplex virus, a protein, at least one sugar, sodium chloride and sodium phosphate at pH 7-8. In one example, the present disclosure refers to a live virus composition comprising: a herpes simplex virus, a protein, wherein the protein is partially hydrolyzed gelatin or human serum albumin, at least one sugar, sodium chloride, and sodium phosphate or potassium phosphate, wherein the composition is at pH 7-8. Disclosed is a live virus composition comprising a herpes simplex virus, a protein, at least one sugar, and phosphate buffer at pH 7-8. In one aspect, the present disclosure refers to a live virus composition comprising a herpes simplex virus-1, a protein, wherein the protein is partially hydrolyzed gelatin or human serum albumin, at least one sugar, wherein the sugar is sorbitol, myo-inositol, trehalose or sucrose, and a buffer, wherein said buffer comprises [i] sodium chloride and sodium phosphate; or [ii] sodium chloride and potassium phosphate, wherein the composition is at pH 7.4. In still another example, the present disclosure refers to a live virus composition comprising: a herpes simplex 1 virus; partially hydrolyzed gelatin at a concentration of 3% (w/v); sorbitol at a concentration of 3% (w/v); sodium chloride at a concentration of 50 to 250 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a frozen live virus composition comprising: a herpes simplex 1 virus; partially hydrolyzed gelatin at a concentration of 3% (w/v); sorbitol at a concentration of 3% (w/v); sodium chloride at a concentration of 50 to 250 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); sorbitol at a concentration of 3% (w/v); sodium chloride at a concentration of 50 to 250 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a frozen live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); sorbitol at a concentration of 3% (w/v); sodium chloride at a concentration of 50 to 250 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a frozen live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); sorbitol at a concentration of 3% (w/v); sodium chloride at a concentration of 50 to 250 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a frozen live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); trehalose at a concentration of 15% (w/v); sodium chloride at a concentration of 137 mM; and wherein said composition is at pH 7.4. In another example, the present disclosure refers to a live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); sorbitol at a concentration of 0.5% to 3% (w/v); myo-inositol at a concentration of 4% (w/v); sodium chloride; and wherein said composition is at pH 7.4. In another example, the present disclosure

refers to a frozen live virus composition comprising: a herpes simplex 1 virus; human serum albumin at a concentration of 0.25% to 2% (w/v); sorbitol at a concentration of 0.5% to 3% (w/v); myo-inositol at a concentration of 4% (w/v); sodium chloride; and wherein said composition is at pH 7.4. In another aspect, the present disclosure refers to the use of a composition as disclosed herein in the manufacture of a medicament for killing tumor cells. In another aspect, the present disclosure refers to a composition as disclosed herein for use in therapy. In one example, disclosed herein is a live virus composition comprising a herpes simplex virus, a protein, at least one sugar, sodium chloride and sodium phosphate at pH 7.4, wherein the composition is frozen.

[0008] In one example the composition may be thawed and stored at 2°C to at least 25°C. In a related example following thawing at 2°C to at least 25°C, the live virus composition is frozen again and stored at a temperature of at least -30°C.

[0009] In another example the composition may be thawed and stored at 2°C to 8°C. In a related example following thawing at 2°C to 8°C, the live virus composition is frozen again and stored at a temperature of at least -30°C.

[0010] In another example the protein is partially hydrolyzed gelatin or human serum albumin.

[0011] In another example the concentration of partially hydrolyzed gelatin is from 0.01% to 1% (w/v).

[0012] In another example the concentration of human serum albumin is from 0.25% to 1%.

[0013] In another example at least one sugar is sorbitol, myo-inositol or sucrose. In a related example the concentration of sorbitol is 2% (w/v). In a related example the concentration of myo-inositol is 4% (w/v). In a related example the concentration of sucrose is 9% (w/v) to 15% (w/v).

[0014] In another example the concentration of sodium chloride is 145 mM.

[0015] In another example the concentration of sodium chloride is about 145 mM.

[0016] In another example the concentration of sodium phosphate is 100 mM.

[0017] In another example the concentration of sodium phosphate is about 100 mM.

[0018] In another example the concentration of sodium phosphate is 102 mM.

Claims

1. A live virus composition comprising:

a herpes simplex virus-1,

a protein, wherein the protein is partially hydrolyzed gelatin or human serum albumin,

at least one sugar, wherein the sugar is sorbitol, myo-inositol, trehalose or sucrose, and

a buffer, wherein said buffer comprises [i] sodium chloride and sodium phosphate; or [ii] sodium chloride and potassium phosphate,

wherein the composition is at pH 7.4.

2. The live virus composition according to claim 1, wherein the composition is frozen.

3. The live virus composition according to claim 1 or 2, wherein the herpes simplex virus-1 is selected from the group consisting of talimogene laherparepvec, Seprehvir™, G207, OrienX010, NV1020, M032, ImmunoVEX and OncoVEX$^{GALV/CD}$.

4. The live virus composition according to any one of claims 1-3, wherein the herpes simplex virus-1 is talimogene laherparepvec.

5. The live virus composition according to any one of claims 1-4, wherein said composition comprises partially hydrolyzed gelatin at a concentration of 0.1% to 3% (w/v).

6. The live virus composition according to any one of claims 1-4, wherein said composition comprises partially hydrolyzed gelatin at a concentration of 0.01% to 1% (w/v).

7. The live virus composition according to any one of claims 1-4, wherein said composition comprises partially hydrolyzed gelatin at a concentration of 3% (w/v).

8. The live virus composition according to any one of claims 1-4, wherein said composition comprises human serum albumin at a concentration of 0.25% to 2.5%.

9. The live virus composition according to any one of claims 1-4, wherein said composition comprises human serum albumin at a concentration of 0.25% to 2% (w/v).

10. The live virus composition according to any one of claims 1-4, wherein said composition comprises human serum albumin at a concentration of 0.25% to 1% (w/v).

11. The live virus composition according to any one of claims 1-10, wherein said composition comprises sorbitol at a concentration of 0.5% to 4% (w/v).

12. The live virus composition according to any one of claims 1-10, wherein said composition comprises sorbitol at a concentration of 0.5% to 3% (w/v).

13. The live virus composition according to any one of claims 1-10, wherein said composition comprises sorbitol at a concentration of 3% (w/v).

14. The live virus composition according to any one of claims 1-10, wherein said composition comprises sorbitol at a concentration of 2% (w/v).

15. The live virus composition according to any one of claims 1-14, wherein said composition comprises sucrose at a concentration of 9% (w/v) to 15% (w/v).

16. The live virus composition according to any one of claims 1-15, wherein said composition comprises sodium chloride at a concentration of 130 to 160 mM.

17. The live virus composition according to any one of claims 1-15, wherein said composition comprises sodium chloride at a concentration of 50 to 250 mM.

18. The live virus composition according to any one of claims 1-15, wherein said composition comprises sodium chloride at a concentration of 137 mM.

19. The live virus composition according to any one of claims 1-15, wherein said composition comprises sodium chloride at a concentration of 145 mM.

20. The live virus composition according to any one of claims 1-19, wherein said composition comprises sodium phosphate at a concentration of 10 to 300 mM.

21. The live virus composition according to any one of claims 1-19, wherein said composition comprises sodium phosphate at a concentration of 70 to 130 mM.

22. The live virus composition according to any one of claims 1-19, wherein said composition comprises sodium phosphate at a concentration of 80 to 120 mM.

23. The live virus composition according to any one of claims 1-19, wherein said composition comprises sodium phosphate at a concentration of 102 mM.

24. The live virus composition according to any one of claims 1-7 and 11-23, wherein the partially hydrolyzed gelatin is porcine.

25. Use of a composition according to any one of claims 1-24 in the manufacture of a medicament for killing tumor cells.

26. The use according to claim 25, wherein said composition further comprises a check point inhibitor.

27. The use according to claim 25 or 26, wherein said tumor cells are astrocytoma, oligodendroglioma, meningioma, neurofibroma, glioblastoma, ependymoma, Schwannoma, neurofibrosarcoma, medulloblastoma, melanoma cells, pancreatic cancer cells, prostate carcinoma cells, breast cancer cells, lung cancer cells, colon cancer cells, hepatoma cells, mesothelioma, bladder cancer cells, or epidermoid carcinoma cells.

28. A composition according to any one of claims 1-27 for use in therapy.