of about 50 to 85 mol%. As above, the percentages recited herein relate to the composition of the final polymer and not the feed amounts utilised when forming the polymer. A representative polymer of PPHO (Formula (II)) is shown above.

[0025] It is an object of the present invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

[0026] There is a general need in the art for effective intranasal delivery vehicles that may stabilise mRNA and/or LNPs for a sufficient period prior to their administration or to retain the formulation throughout the upper respiratory region to enable their intranasal administration.

[0027] It is against this background that the present invention has been developed. Various embodiments of the present invention may find utility relating to one or more of the general needs identified above.

[0028] In particular, the present invention is useful in providing a physical and commercial alternative to intramuscular injectable delivery of certain pharmaceutical substances such as COVID-19 vaccines.

[0029] Although the invention will be described with reference to specific examples it will be appreciated by those skilled in the art that the invention may be embodied in many other forms.

Summary

[0030] In a broad form, the present disclosure relates to an effective concentration of a polymer to encapsulate and stabilise one or more active pharmaceutical agents within a vaccine or medicament to increase the stability and shelf life of the active/s and if needed, to encapsulate and retain one or more active pharmaceutical agents within a vaccine or medicament otherwise restricted mainly to intramuscular injectable delivery. It is surprisingly found that the polymer enables stabilisation of one or more active pharmaceutical agents to increase their shelf life and/or to allow their storage in a less restricted condition.

[0031] Applicant's polymer/s in solution or hydrogel form prior to administration can stabilise the active/s within a vaccine by preventing their agglomeration, *etc.*, so the shelf life of such vaccines can be extended and/or enhanced under relatively mild conditions (*e.g.*, ambient temperature). If then administered intranasally, it can adhere/retain the active agents throughout the upper respiratory region (nasal cavity) for better biological activity.

[0032] There is provided a polymer for forming a solution and/or hydrogel to stabilise one or more pharmaceutically active agents prior to, during or post-administration, the polymer comprising:

[0033] a first monomer for binding water;

[0034] a second monomer for imparting mechanical properties to the scaffold;

[0035] optionally, a third monomer for binding to a natural or synthetic peptide or protein (NSPP); and

[0036] a fourth monomer for imparting phase-transition behaviour.

[0036a] According to a first aspect of the present disclosure, there is provided a polymer for forming a solution and/or hydrogel to stabilise one or more pharmaceutically active agents prior to, during or post-administration, the polymer comprising:

a first monomer for binding water;

a second monomer for imparting mechanical properties to the scaffold;

optionally, a third monomer for binding to a natural or synthetic peptide or protein (NSPP); and

a fourth monomer for imparting phase-transition behaviour,

wherein the first monomer is oligo (ethylene) glycol monomethyl ether methacrylate (OEGMA); the second monomer is hydroxyethyl methacrylate poly(lactic acid) (PLA/HEMA); the third monomer is N-acryloxysuccinimide (NAS); and the fourth monomer is (N-isopropylacrylamide) (NIPAAm);

wherein the polymer comprises: OEGMA in an amount of from about 1 to about 15 mol%; PLA/HEMA in an amount of from 5 to about 50 mol%; NAS in an amount of from 0 to about 15 mol%; and NIPAAm in an amount of up to about 85 mol%;

wherein the one or more pharmaceutically active agents comprise an mRNA vaccine; and

wherein the polymer preserves the integrity of the mRNA at 37 °C for up to 4 days.

[0037] In an example, the stabilising of one or more pharmaceutically active agents prior to administration is to prevent their degradation, denaturation, sheering or any chemical or physical changes that can impact their biological activity.

[0038] In an example, the administration is by way of intravascular, intramuscular, subcutaneous, inhalable lung, oral inhaled or intranasal administration.

[0039] In an example, the administration is intranasal.

[0040] In an example, the first monomer is selected from: polyethers, polyvinyl alcohol (PVA); poly(vinyl pyrrolidone) (PVP); poly(amino acids) and dextran.

[0041] In an example, the polyethers are selected from: polyethylene glycol (PEG), oligo(ethylene glycol) (OEG), polyethylene oxide (PEO), polyethylene oxide-co-propylene oxide (PPO), co-polyethylene oxide block or random copolymers thereof.

[0042] In an example, the first monomer is oligo (ethylene) glycol monomethyl ether methacrylate (OEGMA).

[0043] In an example, the second monomer is a methacrylate, or a random co-

polymer comprising a methacrylate.

[0044] In an example, the second monomer is selected from: hydroxyethyl methacrylate (HEMA), a hydroxyethyl methacrylate poly(lactic acid) copolymer (PLA/HEMA), poly(lactic acid), poly(caprolactone), poly(glycolide), poly(glycolide-colactide) or poly(glycolide-co-caprolactone).

[0045] In an example, the second monomer is hydroxyethyl methacrylate poly(lactic acid) (PLA/HEMA).

[0046] In an example, the third monomer has electrophilic functional groups for binding to the NSPP.

[0047] In an example, the third monomer is selected from: N-hydroxysulfosuccinimide (SNHS), N-hydroxyethoxylated succinimide (ENHS), and N-acryloxysuccinimide (NAS).

[0048] In an example, the third monomer is N-acryloxysuccinimide (NAS).

[0049] In an example, the fourth monomer has a lower critical solution temperature (LCST) less than about 37 °C.

[0050] In an example, the fourth monomer is selected from: poly(ethylene oxide)/poly(propylene oxide) and poly(N-isopropylacrylamide) (PNIPAAm) homopolymers

and copolymers.

[0051] In an example, the fourth monomer is (N-isopropylacrylamide) (NIPAAm).

[0052] In an example, the polymer comprises the first monomer in an amount of from about 1 to about 15 mol%.

[0053] In an example, the polymer comprises the second monomer in an amount of from about 5 to about 50 mol%.

[0054] In an example, the polymer comprises the third monomer in an amount of from about 0 to about 15 mol%.

[0055] In an example, the polymer comprises the fourth monomer in an amount of from about 50 to about 85 mol%.

[0056] In an example, the polymer comprises: the first monomer in an amount of from about 1 to about 15 mol%; the second monomer in an amount of from about 5 to about 50 mol%; the third monomer in an amount of 0 to about 15 mol%; and the fourth monomer in an amount which makes up the remainder to 100% of the polymer.

[0057] In an example, the first monomer is OEGMA; the second monomer is PLA/HEMA; the third monomer is NAS; and the fourth monomer is NIPAAm,

[0058] wherein the polymer comprises: OEGMA in an amount of from about 1 to about 15 mol%; PLA/HEMA in an amount of from 5 to about 50 mol%; NAS in an amount of from 0 to about 15 mol%; and NIPAAm in an amount of up to about 85 mol%.

[0059] In an example, the one or more pharmaceutically-active agents comprise a therapeutic active, and/or vaccine otherwise restricted to delivery via intramuscular injection. Non-limiting examples include mRNA and siRNA vaccines and the like.

[0060] In an example, the vaccine otherwise restricted to delivery via intramuscular injection is a COVID-19 (SARS-CoV-2) vaccine.

[0061] In an example, the COVID-19 vaccine is the Pfizer-BioNTech (Comirnaty/Tozinameran) vaccine.

[0062] In an example, the polymer is present in a concentration greater than or equal to about 15 mg/mL.

[0063] In an example, the polymer is present in a concentration between about 25 and about 35 mg/mL.

[0064] In an example, the polymer is present in a concentration of about 35 mg/mL.

[0065] In an example, the first monomer is OEGMA; the second monomer is PLA/HEMA; the third monomer is NAS; and the fourth monomer is NIPAAm;

[0066] wherein the polymer comprises: OEGMA in an amount of from about 1 to about 15

mol%; PLA/HEMA in an amount of from 5 to about 50 mol%; NAS in an amount of from 0 to about 15 mol%; and NIPAAm in an amount of up to about 85 mol%;

[0067] wherein the vaccine is an mRNA vaccine, preferably the Pfizer-BioNTech (Comirnaty/Tozinameran) COVID-19 vaccine;

[0068] wherein the polymer is present in a concentration of about 35 mg/mL; and

[0069] wherein the polymer preserves the integrity of the mRNA at 37 ^{o}C for up to 4 days.

[0070] Preferably, the polymer the polymer comprises:

[0071] a first monomer for binding water;

[0072] a second monomer for imparting mechanical properties to the polymer;

[0073] optionally, a third monomer for binding to a natural or synthetic peptide or protein (NSPP); and

[0074] a fourth monomer for imparting phase-transition behaviour.

[0075] In an example, the first monomer is selected from: polyethers, polyvinyl alcohol (PVA); poly(vinyl pyrrolidone) (PVP); poly(amino acids) and dextran.

[0076] In an example, the polyethers are selected from: polyethylene glycol (PEG), oligo(ethylene glycol) (OEG), polyethylene oxide (PEO), polyethylene oxide-co-propylene oxide (PPO), co-polyethylene oxide block or random copolymers thereof.

[0077] In an example, the first monomer is oligo (ethylene) glycol monomethyl ether methacrylate (OEGMA).

[0078] In an example, the second monomer is a methacrylate, or a random co-polymer comprising a methacrylate.

[0079] In an example, the second monomer is selected from: hydroxyethyl methacrylate (HEMA), a hydroxyethyl methacrylate poly(lactic acid) copolymer (PLA/HEMA), poly(lactic acid), poly(caprolactone), poly(glycolide), poly(glycolide-colactide) or poly(glycolide-co-caprolactone).

[0080] In an example, the second monomer is hydroxyethyl methacrylate poly(lactic acid) (PLA/HEMA).

[0081] In an example, the third monomer has electrophilic functional groups for binding to the NSPP.

[0082] In an example, the third monomer is selected from: N-hydroxysulfosuccinimide (SNHS), N-hydroxyethoxylated succinimide (ENHS), and N-acryloxysuccinimide (NAS).

[0083] In an example, the third monomer is N-acryloxysuccinimide (NAS).

[0084] In an example, the fourth monomer has a lower critical solution temperature (LCST) less than about 37 °C.

[0085] In an example, the fourth monomer is selected from: poly(ethylene oxide)/poly(propylene oxide) and poly(N-isopropylacrylamide) (PNIPAAm) homopolymers and copolymers.

[0086] In an example, the fourth monomer is (N-isopropylacrylamide) (NIPAAm).

[0087] In an example, the polymer comprises the first monomer in an amount of from about 1 to about 15 mol%.

[0088] In an example, the polymer comprises the second monomer in an amount of from about 5 to about 50 mol%.

[0089] In an example, the polymer comprises the third monomer in an amount of from about 0 to about 15 mol%.

[0090] In an example, the polymer comprises the fourth monomer in an amount of from about 50 to about 85 mol%.

[0091] In an example, the polymer comprises: the first monomer in an amount of from about 1 to about 15 mol%; the second monomer in an amount of from about 5 to about 50 mol%; the third monomer in an amount of 0 to about 15 mol%; and the fourth monomer in an amount which makes up the remainder to 100% of the polymer.

[0092] In an example, the first monomer is OEGMA; the second monomer is PLA/HEMA; the third monomer is NAS; and the fourth monomer is NIPAAm, wherein the polymer comprises: OEGMA in an amount of from about 1 to about 15 mol%; PLA/HEMA in an amount of from 5 to about 50 mol%; NAS in an amount of from 0 to about 15 mol%; and NIPAAm in an amount of up to about 85 mol%.

[0093] In an example, the polymer comprises: OEGMA in an amount of about 5 mol%, HEMA-PLA in an amount of about 7 mol%, NAS in an amount of greater than about 7 mol% and NIPAAm in an amount about 81 mol%.

[0094] According to a second aspect of the present disclosure there is provided a method for the delivery of one or more pharmaceutically active agents, the method comprising administration to a subject in need thereof an effective concentration of the one or more pharmaceutically active agents dispersed within a polymer as defined herein.

[0095] In an example, the administration is performed at ambient temperature, with the polymer transitioning to its hydrogel form at higher (*e.g.*, body) temperatures.

[0096] In an example, the administration is performed via intranasal spray or deposition.

[0097] In an example, the one or more pharmaceutically active ingredients may be dispersed within the polymer *in situ*, or pre-formulated and stored under conditions supporting

viability of the active/s.

[0098] In an example, the conditions supporting viability of the active/s comprise freeze-drying the formulation prior to reconstitution of it.

[0099] According to a third aspect of the present disclosure there is provided use of a polymer as defined herein in the manufacture of a medicament for delivery of one or more pharmaceutically active agents.

[00100] In an example, the administration is performed under ambient or substantially ambient conditions, and thereafter reaches body temperature whereupon the transition to hydrogel occurs.

[00101] In an example, the administration is performed, via intravascular, intramuscular injection or intranasal delivery or any other routes of administration.

[00102] In an example, the one or more pharmaceutically active ingredients may be dispersed within the polymer *in situ*, or pre-formulated and stored under conditions supporting viability of the active/s.

[00103] In an example, the conditions supporting viability of the active/s comprise freeze-drying the formulation prior to reconstitution of it.

[00104] According to a fourth aspect of the present disclosure there is provided a kit for enabling delivery of one or more pharmaceutically active agents, the kit comprising a polymer as defined herein; an effective concentration of the one or more pharmaceutically active agents stored under appropriate conditions; and optionally instructions for adding an effective concentration of the polymer to the one or more pharmaceutically active agents.

[00105] In an example, the kit further comprises means for effecting the intranasal delivery of the one or more pharmaceutically active agents and the effective concentration of the polymer.

[00106] In an example, the kit comprises the polymer and the one or more pharmaceutically active agents in pre-mixed form.

Definitions and Nomenclature

[00107] In describing and claiming the present invention, the following terminology will be used in accordance with the definitions set out below. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only and is not intended to be limiting. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one having

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A polymer for forming a solution and/or hydrogel to stabilise one or more pharmaceutically active agents prior to, during or post-administration, the polymer comprising:

    a first monomer for binding water;

    a second monomer for imparting mechanical properties to the scaffold;

    optionally, a third monomer for binding to a natural or synthetic peptide or protein (NSPP); and

    a fourth monomer for imparting phase-transition behaviour,

    wherein the first monomer is oligo (ethylene) glycol monomethyl ether methacrylate (OEGMA); the second monomer is hydroxyethyl methacrylate poly(lactic acid) (PLA/HEMA); the third monomer is N-acryloxysuccinimide (NAS); and the fourth monomer is (N-isopropylacrylamide) (NIPAAm);

    wherein the polymer comprises: OEGMA in an amount of from about 1 to about 15 mol%; PLA/HEMA in an amount of from 5 to about 50 mol%; NAS in an amount of from 0 to about 15 mol%; and NIPAAm in an amount of up to about 85 mol%;

    wherein the one or more pharmaceutically active agents comprise an mRNA vaccine; and

    wherein the polymer preserves the integrity of the mRNA at 37 ^{o}C for up to 4 days.

2. A polymer according to claim 1, wherein the administration is by way of intravascular, intramuscular, subcutaneous, inhalable respiratory, oral inhaled or intranasal administration.

3. A polymer according to claim 2, wherein the administration is intranasal.

4. A polymer according to any one of the preceding claims, wherein the mRNA vaccine is a vaccine otherwise restricted to delivery via intramuscular injection.

5. A polymer according to any one of the preceding claims, wherein the vaccine otherwise restricted to delivery via intramuscular injection is a COVID-19 (SARS-CoV-2) vaccine.

6. A polymer according to claim 5, wherein the COVID-19 vaccine is the Pfizer-BioNTech (Comirnaty/Tozinameran) vaccine.

7. A polymer according to any one of the preceding claims, wherein the polymer is present in a concentration greater than or equal to about 15 mg/mL.

8. A polymer according to any one of claims 1 to 6, wherein the polymer is present in a concentration between about 25 and about 35 mg/mL.

9. A polymer according to any one of claims 1 to 6, wherein the polymer is present in a concentration of about 35 mg/mL.

10. A method for the delivery of one or more pharmaceutically active agents, the method comprising administration to a subject in need thereof an effective concentration of the one or more pharmaceutically active agents dispersed within a polymer as defined according to any one of claims 1 to 9.

11. A method according to claim 10, wherein the administration is performed at ambient temperature, with the polymer transitioning to its hydrogel form at higher (*e.g.*, body) temperatures.

12. A method according to claim 10 or claim 11, wherein the administration is performed intranasally, by intranasal spray or deposition.

13. A method according to any one of claims 10 to 12, wherein the one or more pharmaceutically active ingredients may be dispersed within the polymer *in situ*, or pre-formulated and stored under conditions supporting viability of the active/s.

14. A method according to claim 13, wherein the conditions supporting viability of the active/s comprise freeze-drying the formulation prior to reconstitution of it.

15. Use of a polymer as defined according to any one of claims 1 to 9 in the manufacture of a medicament for the delivery of one or more pharmaceutically active agents.

16. Use according to claim 15, wherein the administration is performed at ambient temperature, with the polymer transitioning to its hydrogel form at higher (*e.g.*, body) temperatures.

17. Use according to claim 15 or claim 16, wherein the administration is performed via intranasal spray or deposition.

18. Use according to any one of claims 15 to 17, wherein the one or more pharmaceutically active ingredients may be dispersed within the polymer *in situ*, or pre-formulated and stored under conditions supporting viability of the active/s.

19. Use according to claim 18, wherein the conditions supporting viability of the active/s comprise freeze-drying the formulation prior to reconstitution of it.

20. A kit for enabling delivery of one or more pharmaceutically active agents, the kit comprising a polymer as defined according to any one of claim 1 to 9; an effective concentration of the one or more pharmaceutically active agents stored under appropriate conditions; and optionally instructions for adding an effective concentration of the polymer to the one or more pharmaceutically active agents.

21. A kit according to claim 20, wherein the polymer and the one or more pharmaceutically active agents in pre-mixed form.