CLAIMS

1. A therapeutic composition (5,6) comprising an inner portion (7) and a biocompatible membrane (4, 10) fully or partially surrounding the inner portion; wherein the biocompatible membrane comprises at least two layers:

a first layer (1) of a porous, non-woven network of thermoplastic polyurethane polymer fibres formed by electrospinning and having a porosity of greater than or equal to 50%; an average pore diameter of less than 5µm; and has a thickness in the range 10 to 250µm; wherein the first layer is non-biodegradable; and

a second layer (2) of a porous, non-woven network of thermoplastic polymer fibres formed by electrospinning, the second layer (2) having a porosity which is substantially equal to or higher than the porosity of first layer (1); and/or wherein the mean average fibre diameter of the second layer (2) is greater than the mean average fibre diameter in the first layer (1); and/or wherein the average pore diameter of the second layer (2) is greater than the average pore diameter of the first layer (1); and

wherein the inner portion (7) comprises a therapeutic agent (3).

2. A therapeutic composition according to claim 1, wherein the biocompatible membrane (4, 10) is in the form a pouch or bag (5, 6, 11) which partially or fully encapsulates the inner portion (7) comprising the therapeutic agent (3).

3. A therapeutic composition according to claim 2, further comprising a carrier (8) on or in which the therapeutic agent (3) is disposed, preferably wherein the therapeutic agent (3) is:

attached to the surface of the carrier (8);

disposed in pores of the carrier (8); and/or

encapsulated within the carrier (8).

4. A therapeutic composition according to clam 2 or 3, wherein the pouch or bag (6) is arranged such that the first layer (1) faces or is in contact with the encapsulated inner portion (7) and, optionally, the therapeutic agent (3); whilst the second layer (2) faces externally.

5. A therapeutic composition according to claim 2, wherein the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7) and, optionally, the therapeutic agent (3).

6. A therapeutic composition according to claim 3, wherein the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7), the carrier (8) and, optionally, the therapeutic agent (3).

7. A therapeutic composition according to claim 2 or 3, wherein the biocompatible membrane (10) comprises three layers: a first layer (1) provided between two second layers (2), wherein the inner portion (7) is provided within an internal-facing surface of one of the second layers (2) when the biocompatible membrane (4) is in the form the pouch or bag (11); with the other of the two second layers (2) providing an external-facing surface; and wherein a carrier is optionally disposed within the inner portion (7).

8. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has a porosity in the range 50% to 90%, optionally 50 to 80%.

9. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has an average pore diameter of less than 2μm.

10. A therapeutic composition according to any one of the preceding claims, wherein the first layer (1) has a thickness in the range 10 to 150μm, preferably in the range 20 to 150μm, most preferably in the range 50 to 150μm or 50 to 200 μm.

11. A therapeutic composition according to any one of the preceding claims, wherein the mean diameter of the polymer fibres of the first layer (1) is less than 700nm, preferably less than 600nm, preferably less than 500nm and is most preferably in the range 100-500nm, even more preferably in the range 50-500nm.

12. A therapeutic composition according to any preceding claim, wherein the second layer (2) is or comprises polyurethane or any other biocompatible, thermoplastic polymer or polymer blend.

13. A therapeutic composition according to any preceding claim, wherein the first layer (1) andthe second layer (2) of the biocompatible membrane (4, 10) are non-biodegradable.

14. A therapeutic composition according to any one of the preceding claims, wherein the therapeutic agent (3) is selected from therapeutic cells, a drug, a nucleic acid, a polynucleotide, a protein, a polypeptide, an antibody, a particle such as lipid nanoparticle, an extracellular vesicle or exosome, optionally wherein the polynucleotide comprises DNA, RNA, RNAi, saRNA or siRNA.

15. A therapeutic composition according to claim 3, wherein the biocompatible membrane (4) fully or partially surrounds the carrier.

16. A therapeutic composition according to claim 3 or 15, wherein the carrier (8) comprises a porous, non-woven network of polymer fibres or a hydrogel, gelatin, collagen (optionally fibres or sponges) or decellularized tissue.

17. A therapeutic composition according to any one of the preceding claims, comprising cells (3), wherein the cells are preferably pancreatic β cells or islet cells.

18. A therapeutic composition according to claim 4 or 7, wherein the externally-facing second layer further comprises a hydrogel, gelatin or collagen (optionally fibres or sponges), or decellularized tissue.

19. A therapeutic composition according to any one of the preceding claims, wherein the second layer (2) is formed from electrospun fibres, and

(i) the porosity is in the range 70 to 98%, preferably in the range 80 to 95%; and/or

(ii) the average pore diameter is in the range 5 to 80μm, preferably in the range 10 to 50μm; and/or

(iii) the mean diameter of the polymer fibres is in the range 1 to 10μm, preferably in the range 2 to 8μm, most preferably in the range 3 to 7μm.

20. A therapeutic composition according to any one of the preceding claims, wherein

(i) the porosity of the second layer (2) is within at least 120%, 110%, 100% of the porosity of the first layer (1), optionally 100% to 110%, 100% to 150%, 100% to 175%, or 100% to 190%, or 100% up to 199% or 200% compared to the porosity of the first layer (1); and/or

(ii) the average pore size/diameter of the second layer (2) is at least 2 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the pore size/diameter of the first layer (1); and/or

(iii) the mean diameter of the polymer fibres of the second layer (2) is at least 2 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the diameter of the first layer (1).

21. A therapeutic composition according to any one of the preceding claims, which further comprises one or more additives, wherein the additives are preferable disposed within the carrier (8) or one or both of the first layer (1) or the second layer (2), further wherein the additives are selected from growth factors such as VEGF, crosslinking agents, Growth factors, Catalase and other enzymes; or an oxygen- releasing material such as CaO_2 or Haemoglobin, Peroxides (for instance, H_2O_2, CaO_2, MgO_2, Li_2O_2, Na_2O_2), Sodium Percarbonate (Na_2CO_3), Perfluorocarbons, Hydroxyapatite, Tricalcium phosphate (bone growth promoting materials), most preferably CaO_2 and/or MgO_2.

22. A membrane comprising at least two layers, wherein

(i) the first layer (1) is a biocompatible, non-biodegradable membrane comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres formed by electrospinning, wherein the biocompatible membrane has a porosity of greater than or equal to 50%; an average pore diameter of less than 5μm; and has a thickness in the range 10 to 250μm; and

(ii) the second layer (2) is disposed on the first layer and wherein the second layer (2) is of a porous, non-woven network of thermoplastic polymer fibres formed by electrospinning;

which fibres of the second layer (2) may or may not be polyurethane,

the second layer (2) having a porosity which is substantially equal to or higher than the porosity of the first layer (1); and/or wherein the second layer (2) having a mean

average fibre diameter of the second layer (2) greater than the mean average fibre diameter in the first layer (1);

and/or wherein the average pore diameter of the second layer (2) is greater than the average pore diameter of the first layer (1).

23. A membrane according to claim 22, wherein the first layer (1) and/or the second layer (2) is as defined in any of claims 1 to 21.

24. A membrane or a therapeutic composition according to any one of the preceding claims for use in a method for treatment of the human or animal body by therapy.

25. A membrane or a therapeutic composition according to claim 24 for use in a method of immunoprotecting therapeutic cells or in a method of treating (preferably type I) diabetes.

26. A method of treatment of the human or animal body in need thereof comprising administering to the human or animal body a therapeutically effective amount of a therapeutic composition or membrane according to any one of the preceding claims.

27. A device comprising a therapeutic composition according to any one of claims 1 to 21, wherein the inner portion (7) comprises pancreatic beta or islet cells, with or without the carrier material (8).

28. A device comprising a therapeutic composition according to any one of claims 1 to 21, wherein the inner portion (7) comprises hepatocytes.

29. A device comprising a therapeutic composition according to any one of claims 1 to 21, wherein the inner portion comprises erythrocytes and/or leukocytes, preferably engineered leukocytes such as CAR-T cells.

30. A process for producing a therapeutic composition according to any one of claims 1 to 21 comprising

(i) an electrospinning process to produce a biocompatible membrane (4) comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres; and

(ii) shaping the biocompatible membrane to produce a therapeutic composition in which an inner portion (7) is fully or partially surrounded; the shaping being optionally by welding edges.

CLAIMS

1. A therapeutic composition (5,6) comprising an inner portion (7) and a biocompatible membrane (4, 10) fully or partially surrounding the inner portion; in which the biocompatible membrane comprises at least two layers:

a first layer (1) of a porous, non-woven network of thermoplastic polyurethane polymer fibres formed by electrospinning and having a porosity of greater than or equal to 50%; an average pore diameter of less than 5μm; and has a thickness in the range 10 to 250μm; in which the first layer is non-biodegradable; and

a second layer (2) of a porous, non-woven network of thermoplastic polymer fibres formed by electrospinning, the second layer (2) having a porosity which is substantially equal to or higher than the porosity of first layer (1); and/or in which the mean average fibre diameter of the second layer (2) is greater than the mean average fibre diameter in the first layer (1); and/or in which the average pore diameter of the second layer (2) is greater than the average pore diameter of the first layer (1); and

in which the inner portion (7) comprises a therapeutic agent (3).

2. A therapeutic composition according to Claim 1, in which the biocompatible membrane (4, 10) is in the form a pouch or bag (5, 6, 11) which partially or fully encapsulates the inner portion (7) comprising the therapeutic agent (3).

3. A therapeutic composition according to Claim 2, further comprising a carrier (8) on or in which the therapeutic agent (3) is disposed, preferably in which the therapeutic agent (3) is:

attached to the surface of the carrier (8);

disposed in pores of the carrier (8); and/or

encapsulated within the carrier (8).

4. A therapeutic composition according to Claim 2 or 3, in which the pouch or bag (6) is arranged such that the first layer (1) faces or is in contact with the encapsulated inner portion (7) and, optionally, the therapeutic agent (3); whilst the second layer (2) faces externally.

5. A therapeutic composition according to Claim 2, in which the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7) and, optionally, the therapeutic agent (3).

6. A therapeutic composition according to Claim 3, in which the pouch or bag (5) is arranged such that the first layer (1) faces externally; whilst the second layer (2) faces or is in contact with the encapsulated inner portion (7), the carrier (8) and, optionally, the therapeutic agent (3).

7. A therapeutic composition according to Claim 2 or 3, in which the biocompatible membrane (10) comprises three layers: a first layer (1) provided between two second layers (2), in which the inner portion (7) is provided within an internal-facing surface of one of the second layers (2) when the biocompatible membrane (4) is in the form the pouch or bag (11); with the other of the two second layers (2) providing an external-facing surface; and in which a carrier is optionally disposed within the inner portion (7).

8. A therapeutic composition according to any preceding claim, in which the first layer (1) has a porosity in the range 50% to 90%, optionally 50 to 80%.

9. A therapeutic composition according to any preceding claim, in which the first layer (1) has an average pore diameter of less than 2μm.

10. A therapeutic composition according to any preceding claim, in which the first layer (1) has a thickness in the range 10 to 150μm, preferably in the range 20 to 150μm, most preferably in the range 50 to 150μm or 50 to 200 μm.

11. A therapeutic composition according to any preceding claim, in which the mean diameter of the polymer fibres of the first layer (1) is less than 700nm, preferably less than 600nm, preferably less than 500nm and is most preferably in the range 100-500nm, even more preferably in the range 50-500nm.

12. A therapeutic composition according to any preceding claim, in which the second layer (2) is or comprises polyurethane or any other biocompatible, thermoplastic polymer or polymer blend.

13. A therapeutic composition according to any preceding claim, in which the first layer (1) and the second layer (2) of the biocompatible membrane (4, 10) are non-biodegradable.

14. A therapeutic composition according to any preceding claim, in which the therapeutic agent (3) is selected from therapeutic cells, a drug, a nucleic acid, a polynucleotide, a protein, a polypeptide, an antibody, a particle such as lipid nanoparticle, an extracellular vesicle or

exosome, optionally in which the polynucleotide comprises DNA, RNA, RNAi, saRNA or siRNA.

15. A therapeutic composition according to Claim 3, in which the biocompatible membrane (4) fully or partially surrounds the carrier.

16. A therapeutic composition according to Claim 3 or 15, in which the carrier (8) comprises a porous, non-woven network of polymer fibres or a hydrogel, gelatin, collagen (optionally fibres or sponges) or decellularized tissue.

17. A therapeutic composition according to any preceding claim, comprising cells (3), in which the cells are preferably pancreatic β cells or islet cells.

18. A therapeutic composition according to Claim 4 or 7, in which the externally-facing second layer further comprises a hydrogel, gelatin or collagen (optionally fibres or sponges), or decellularized tissue.

19. A therapeutic composition according to any preceding claim, in which the second layer (2) is formed from electrospun fibres, and:

(i) the porosity is in the range 70 to 98%, preferably in the range 80 to 95%; and/or

(ii) the average pore diameter is in the range 5 to 80μm, preferably in the range 10 to 50μm; and/or

(iii) the mean diameter of the polymer fibres is in the range 1 to 10μm, preferably in the range 2 to 8μm, most preferably in the range 3 to 7μm.

20. A therapeutic composition according to any preceding claim, in which:

(i) the porosity of the second layer (2) is within at least 120%, 110%, 100% of the porosity of the first layer (1), optionally 100% to 110%, 100% to 150%, 100% to 175%, or 100% to 190%, or 100% up to 199% or 200% compared to the porosity of the first layer (1); and/or

(ii) the average pore size/diameter of the second layer (2) is at least 2 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the pore size/diameter of the first layer (1); and/or

(iii) the mean diameter of the polymer fibres of the second layer (2) is at least 2 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times or at least 100 times the diameter of the first layer (1).

21. A therapeutic composition according to any preceding claim, which further comprises one or more additives, in which the additives are preferable disposed within the carrier (8) or one or both of the first layer (1) or the second layer (2), further in which the additives are selected from growth factors such as VEGF, crosslinking agents, Growth factors, Catalase and other enzymes; or an oxygen- releasing material such as CaO_2 or Haemoglobin, Peroxides (for instance, H_2O_2, CaO_2, MgO_2, Li_2O_2, Na_2O_2), Sodium Percarbonate (Na_2CO_3), Perfluorocarbons, Hydroxyapatite, Tricalcium phosphate (bone growth promoting materials), most preferably CaO_2 and/or MgO_2.

22. A membrane comprising at least two layers, in which

(i) the first layer (1) is a biocompatible, non-biodegradable membrane comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres formed by electrospinning, in which the biocompatible membrane has a porosity of greater than or equal to 50%; an average pore diameter of less than 5µm; and has a thickness in the range 10 to 250µm; and

(ii) the second layer (2) is disposed on the first layer and in which the second layer (2) is of a porous, non-woven network of thermoplastic polymer fibres formed by electrospinning;

which fibres of the second layer (2) may or may not be polyurethane,

the second layer (2) having a porosity which is substantially equal to or higher than the porosity of the first layer (1); and/or in which the second layer (2) having a mean average fibre diameter of the second layer (2) greater than the mean average fibre diameter in the first layer (1);

and/or in which the average pore diameter of the second layer (2) is greater than the average pore diameter of the first layer (1).

23. A membrane according to Claim 22, in which the first layer (1) and/or the second layer (2) is as defined in any of Claims 1 to 21.

24. A therapeutic composition according to any of Claims 1 to 21 or a membrane according to Claim 22 or 23 for use in a method for treatment of the human or animal body by therapy.

25. A therapeutic composition or membrane according to Claim 24 for use in a method of immunoprotecting therapeutic cells or in a method of treating (preferably type I) diabetes.

26. Use of a therapeutic composition according to any of Claims 1 to 21 or a membrane according to Claim 22 or 23 in the preparation of a medicament for the treatment of diabetes, preferably type I diabetes.

27. A device comprising a therapeutic composition according to any of Claims 1 to 21, in which the inner portion (7) comprises pancreatic beta or islet cells, with or without the carrier material (8).

28. A device comprising a therapeutic composition according to any of Claims 1 to 21, in which the inner portion (7) comprises hepatocytes.

29. A device comprising a therapeutic composition according to any of Claims 1 to 21, in which the inner portion comprises erythrocytes and/or leukocytes, preferably engineered leukocytes such as CAR-T cells.

30. A process for producing a therapeutic composition according to any of Claims 1 to 21 comprising:

(i) an electrospinning process to produce a biocompatible membrane (4) comprising a porous, non-woven network of thermoplastic polyurethane polymer fibres; and

(ii) shaping the biocompatible membrane to produce a therapeutic composition in which an inner portion (7) is fully or partially surrounded; the shaping being optionally by welding edges.