AFFINITY CHROMATOGRAPHY DEVICES CONTAINING A FIBRILLATED POLYMER MEMBRANE AND MANIFOLDS CONTAINING THE SAME

FIELD

[0001] The present disclosure relates generally to affinity chromatography, and more specifically, to an affinity chromatography device that includes a fibrillated polymer membrane containing therein a blend of spherical particles, a particle size distribution that has a D90/D10 less than or equal to 3, and which enables the separation of a targeted molecule from an aqueous mixture. Manifolds containing multiple affinity chromatography devices and manifolds in a parallel configuration are also disclosed.

BACKGROUND

[0002] Chromatographic methods generally are used to separate and/or purify molecules of interest such as proteins, nucleic acids, and polysaccharides from a mixture. Affinity chromatography specifically involves passing the mixture over a matrix having a ligand specific (*i.e.*, a specific binding partner) for the molecule of interest bound to it. Upon contacting the ligand, the molecule of interest is bound to the matrix and is therefore retained from the mixture. Affinity chromatography provides certain advantages over other types of chromatography. For example, affinity chromatography provides a purification method that can isolate a target protein from a mixture of the target protein and other biomolecules in a single step in high yield.

[0003] Despite the advantages of current affinity chromatography devices, there exists a need in the art for a chromatography device that can be used at shorter residence times than conventional devices while providing the same binding capacity or better binding capacities than current offerings and that is re-useable.

SUMMARY

[0003a] In a first aspect of the present disclosure, there is provided an article comprising:

an affinity chromatography device including:

a fluid inlet;

a fluid outlet fluidly connected to the fluid inlet; and

a fibrillated polymer membrane positioned between the fluid inlet and fluid outlet and containing therein inorganic particles having a spherical shape and a nominal particle size from about 5 microns to about 20 microns; and

a housing member encompassing the fluid inlet, the fluid outlet, and the fibrillated polymer membrane,

wherein a particle size distribution has a D90/D10 less than or equal to 3, and

wherein at least one of the fibrillated polymer membrane and the inorganic particles has covalently bonded thereto an affinity ligand that reversibly binds to a targeted molecule.

[0003b] In another aspect of the present disclosure, there is provided a use of the article as disclosed herein to separate the targeted molecule from a fluid stream.

[0003c] In yet another aspect of the present disclosure, there is provided a manifold comprising at least two of the affinity chromatography devices as disclosed herein arranged in a parallel configuration.

[0003d] In a further aspect of the present disclosure, there is provided a device comprising a first manifold and a second manifold in a parallel configuration, wherein each of the first manifold and the second manifold includes at least two of the affinity chromatography devices as disclosed herein.

[0004] In one Example (“Example 1”), an affinity chromatography device includes a fluid inlet, a fluid outlet fluidly connected to the fluid inlet, a fibrillated polymer membrane positioned between the fluid inlet and fluid outlet and containing therein inorganic particles having a spherical shape and a nominal particle size from about 5

microns to about 20 microns, and a housing encompassing the fluid inlet, the fluid outlet and the fibrillated polymer membrane, where a particle size distribution has a D90/D10 less than or equal to 3, and where at least one of the fibrillated polymer membrane and the inorganic particles has covalently bonded thereto an affinity ligand that reversibly binds to a targeted molecule.

[0005] According to another Example ("Example 2") further to Example 1, where the targeted molecule is a protein, antibody, viral vector, and combinations thereof.

[0006] According to another Example ("Example 3") further to Example 1 or Example 2, including a hydraulic permeability from about 100 (X 10^{-12} cm^2) ^{to} about 500 (X 10^{-12} cm^2).

[0007] According to another Example ("Example 4") further to any one of Examples 1 to 3, where the inorganic particles having a spherical shape are selected from silica, zeolites, hydroxyapatite, metal oxides and combinations thereof.

[0008] According to another Example ("Example 5") further to any one of Examples 1 to 4, where the fibrillated polymer membrane comprises an expanded polytetrafluoroethylene membrane, an expanded modified polytetrafluoroethylene membrane, an expanded tetrafluoroethylene copolymer membrane, or an expanded polyethylene membrane.

[0009] According to another Example ("Example 6") further to any one of Examples 1 to 5, where the fibrillated polymer membrane is an expanded polytetrafluoroethylene membrane.

[00010] According to another Example ("Example 7") further to any one of Examples 1 to 6, where the affinity ligand is selected from Protein A, Protein G, Protein L, human Fc receptor protein, antibodies, polysaccharides, and combinations thereof.

[00011] According to another Example ("Example 8") further to any one of Examples 1 to 7, where the inorganic particles comprise at least a first inorganic particle having a spherical shape and a first nominal particle size and a second inorganic particle having a spherical shape and a second nominal particle size, the first and second nominal particle sizes being different from each other.

[00012] According to another Example ("Example 9") further to any one of Examples 1 to 8, where the nominal particle sizes are selected from about 5 microns, about 10 microns, about 15 microns, about 20 microns, and combinations thereof.

[00013] According to another Example (“Example 10”) further to any one of Examples 1 to 9, where the inorganic particles having a spherical shape comprises a blend of 10-micron spherical particles and 20-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00014] According to another Example (“Example 11”) further to any one of Examples 1 to 9, where the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 10-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00015] According to another Example (“Example 12”) further to any one of Examples 1 to 9, where the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 20-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00016] According to another Example (“Example 13”) further to any one of Examples 1 to 12, including a dynamic binding capacity (DBC) of at least 35 mg/ml at a residence time of 20 seconds.

[00017] According to another Example (“Example 14”) further to any one of Examples 1 to 13, including a cycling durability of at least 100 cycles at an operating pressure less than 0.3 MPa.

[00018] According to another Example (“Example 15”) further to any one of Examples 1 to 14, where the fibrillated polymer membrane has a wound configuration.

[00019] According to another Example (“Example 16”) further to any one of Examples 1 to 15, where the fibrillated polymer membrane has a stacked configuration.

[00020] According to another Example (“Example 17”) further to any one of Examples 1 to 16, where the fibrillated polymer membrane has a wound configuration, a stacked configuration, and a combination thereof.

[00021] According to another Example (“Example 18”) further to any one of Examples 1 to 17, where an inner intermediate material is circumferentially positioned on an outer surface of a core and where the fibrillated polymer membrane is circumferentially positioned on the inner intermediate material.

[00022] According to another Example (“Example 19”) further to Example 18, where the outer intermediate material circumferentially positioned on the fibrillated polymer membrane.

[00023] According to another Example (“Example 20”) further to Example 18 or Example 19, where the inner intermediate material and outer intermediate material are selected from a porous fluoropolymer film, a porous non-fluoropolymer film, a porous non-woven material, and a porous woven material.

[00024] According to another Example (“Example 21”) further to any one of Examples 18 to 20, where at least one of the inner intermediate material and outer intermediate material is a polypropylene non-woven material.

[00025] According to another Example (“Example 22”), where the article of any one of Examples 18 to 21 is used to separate the targeted molecule from a fluid stream.

[00026] In one Example (“Example 23”) a manifold includes at least two of the affinity chromatography devices of any one of Examples 1 to 21 are arranged in a parallel configuration.

[00027] According to another Example (“Example 24”) further to Example 23, where the manifold is enclosed within a housing.

[00028] In one Example (“Example 25”) an article includes a first manifold and a second manifold in a parallel configuration, where each of the first manifold and the second manifold includes a plurality of the affinity chromatography devices of any one of Examples 1 to 21.

[00029] In another Example (“Example 26”) further to Example 25, where the first manifold and the second manifold are enclosed within a housing.

[00030] In one Example (“Example 27”) an article includes a centrally located core, a fibrillated polymer membrane containing therein spherical inorganic particles having a spherical shape and a nominal particle size from about 5 microns to about 20 microns wound around the core, a housing member surrounding both the core and the fibrillated polymer membrane, a first end cap positioned at a first end of the housing member, and a second end cap positioned at a second end of the housing member, where a particle size distribution has a D90/D10 less than 3, and at least one of the fibrillated polymer membrane and the spherical inorganic particles has covalently bonded thereto an affinity ligand that reversibly binds to a targeted molecule.

[00031] According to another Example (“Example 28”) further to Example 27, where the targeted molecule is a protein, antibody, viral vector, and combinations thereof.

[00032] According to another Example (“Example 29”) further to Example 27 or Example 28, including a hydraulic permeability from about 100 (X 10^{-12} cm^2) to about 500 (X 10^{-12} cm^2).

[00033] According to another Example (“Example 30”) further to any one of Examples 27 to 29, where the inorganic particles having a spherical shape are selected from silica, zeolites, hydroxyapatite, metal oxides and combinations thereof.

[00034] According to another Example (“Example 31”) further to any one of Examples 27 to 30, where the fibrillated polymer membrane includes at least one of an expanded polytetrafluoroethylene membrane, an expanded modified polytetrafluoroethylene membrane, an expanded tetrafluoroethylene copolymer membrane, or an expanded polyethylene membrane.

[00035] According to another Example (“Example 32”) further to any one of Examples 27 to 31, where the fibrillated polymer membrane is an expanded polytetrafluoroethylene membrane.

[00036] According to another Example (“Example 33”) further to any one of Examples 27 to 32, where the affinity ligand is selected from Protein A, Protein G, Protein L, human Fc receptor protein, antibodies, polysaccharides, and combinations thereof.

[00037] According to another Example (“Example 34”) further to any one of Examples 27 to 33, where the inorganic particles include at least a first inorganic particle having a spherical shape and a first nominal particle size and a second inorganic particle having a spherical shape and a second nominal particle size, and where the first and second nominal particle sizes are different from each other.

[00038] According to another Example (“Example 35”) further to any one of Examples 37 to 34, where the nominal particle size is selected from about 5 microns, about 10 microns, about 15 microns, about 20 microns, and combinations thereof.

[00039] According to another Example (“Example 36”) further to any one of Examples 27 to 34, where the inorganic particles having a spherical shape include a blend of 10-micron spherical particles and 20-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00040] According to another Example (“Example 37”) further to any one of Examples 27 to 34, where the inorganic particles having a spherical shape include a

blend of 5-micron spherical particles and 10-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00041] According to another Example ("Example 38") further to any one of Examples 27 to 34, where the inorganic particles having a spherical shape comprise a blend of 5-micron spherical particles and 20-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00042] According to another Example ("Example 39") further to any one of Examples 27 to 38, including a dynamic binding capacity (DBC) of at least 35 mg/ml at a residence time of 20 seconds.

[00043] According to another Example ("Example 40") further to any one of Examples 27 to 39, including a cycling durability of at least 100 cycles and an operating pressure less than 0.3 MPa.

[00044] According to another Example ("Example 41") further to any one of Examples 27 to 40, where an inner intermediate material is circumferentially positioned on an outer surface of a core and the fibrillated polymer membrane is circumferentially positioned on the inner intermediate material.

[00045] According to another Example ("Example 42") further to any one of Examples 27 to 41, including an outer intermediate material circumferentially positioned on the fibrillated polymer membrane.

[00046] According to another Example ("Example 43") further to Example 42, where the inner intermediate material and the outer intermediate material are selected from a porous fluoropolymer film, a porous non-fluoropolymer film, a porous non-woven material, and a porous woven material.

[00047] According to another Example ("Example 44") further to Example 43, where at least one of the inner intermediate material and outer intermediate material is a polypropylene non-woven material.

[00048] According to one Example ("Example 45") a manifold includes at least two of the affinity chromatography devices of any one of claims 27 to 44 arranged in a parallel configuration.

[00049] According to another Example ("Example 46") further to Example 45 where the manifold is enclosed within a housing.

[00050] According to one Example ("Example 47") a device includes a first manifold and a second manifold in a parallel configuration, where each of the first

manifold and the second manifold includes at least two of the affinity chromatography devices of any one of claims 27 to 44.

[00051] According to another Example (“Example 48”) further to Example 47, where the first manifold and the second manifold are enclosed within a housing.

[00052] In one Example (“Example 49”), an affinity chromatography device includes a housing, an inlet to permit fluid flow into the housing, first and second flow distributors, the first flow distributor and the second flow distributor positioned at opposing ends of the housing, an outlet to permit fluid flow out of the housing, and a stacked membrane assembly disposed within the housing between the fluid inlet and fluid outlet, the stacked membrane assembly that includes two or more fibrillated polymer membranes in a stacked configuration, the fibrillated polymer membrane containing therein a blend of inorganic particles having a spherical shape and a nominal particle size from about 5 microns to about 20 microns, a particle size distribution has a D90/D10 less than 3, and at least one of the fibrillated polymer membrane and the spherical inorganic particles has covalently bonded thereto an affinity ligand that reversibly binds to a targeted molecule.

[00053] According to another Example (“Example 50”) further to Example 49, including first and second flow distributors, the first flow distributor and the second flow distributor positioned at opposing ends of the housing member.

[00054] According to another Example (“Example 51”) further to Example 49 or Example 50, where the targeted molecule is a protein, antibody, viral vector, and combinations thereof.

[00055] According to another Example (“Example 52”) further to any one of Examples 49 to 51, including a hydraulic permeability from about 100 (X 10^{-12} cm^2) to about 500 (X 10^{-12} cm^2).

[00056] According to another Example (“Example 53”) further to any one of Examples 49 to 52, where the inorganic particles having a spherical shape are selected from silica, zeolites, hydroxyapatite, metal oxides and combinations thereof.

[00057] According to another Example (“Example 54”) further to any one of Examples 49 to 53, where the fibrillated polymer membrane includes an expanded polytetrafluoroethylene membrane, an expanded modified polytetrafluoroethylene membrane, an expanded tetrafluoroethylene copolymer membrane, or an expanded polyethylene membrane.

[00058] According to another Example (“Example 55”) further to any one of Examples 49 to 54, where the fibrillated polymer membrane is an expanded polytetrafluoroethylene membrane.

[00059] According to another Example (“Example 56”) further to any one of Examples 49 to 55, where the affinity ligand is selected from Protein A, Protein G, Protein L, human Fc receptor protein, antibodies, polysaccharides, and combinations thereof.

[00060] According to another Example (“Example 57”) further to any one of Examples 49 to 56, where the inorganic particles include at least a first inorganic particle having a spherical shape and a first nominal particle size and a second inorganic particle having a spherical shape and a second nominal particle size, where the first and second nominal particle sizes are different from each other.

[00061] According to another Example (“Example 58”) further to any one of Examples 49 to 57, where the nominal particle size is selected from about 5 microns, about 10 microns, about 15 microns, about 20 microns, and combinations thereof.

[00062] According to another Example (“Example 59”) further to any one of Examples 49 to 58, where the inorganic particles having a spherical shape comprises a blend of 10-micron spherical particles and 20-micron spherical particles, and where the blend is from 90:10 to 10:90.

[00063] According to another Example (“Example 60”) further to any one of Examples 49 to 58, where the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 10-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00064] According to another Example (“Example 61”) further to any one of Examples 49 to 58, where the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 20-micron spherical particles, and where the blend is from 10:90 to 90:10.

[00065] According to another Example (“Example 62”) further to any one of Examples 49 to 61, including a dynamic binding capacity (DBC) of at least 35 mg/ml at a residence time of 20 seconds.

[00066] According to another Example (“Example 63”) further to any one of Examples 49 to 62, including a cycling durability of at least 100 cycles and an operating pressure less than 0.3 MPa.

[00067] According to another Example (“Example 64”) further to any one of Examples 49 to 63, where at least one first intermediate material is positioned on a first side of the stacked membrane assembly and a second intermediate material is positioned on a second side of the stacked membrane assembly, the second side opposing the first side.

[00068] According to another Example (“Example 65”) further to Example 64, where the first intermediate material and the second intermediate material are selected from a porous fluoropolymer film, a porous non-fluoropolymer film, a porous non-woven material, and a porous woven material.

[00069] According to another Example (“Example 66”) further to Example 65, where at least one of the first intermediate material and the second intermediate material is a polypropylene non-woven material.

[00070] In one Example (“Example 67”) a manifold includes at least two of the affinity chromatography devices of any one of claims 49 to 66 arranged in a parallel configuration.

[00071] According to another Example (“Example 68”) further to Example 67, where the manifold is enclosed within a housing.

[00072] In one Example (“Example 69”) a device includes a first manifold and a second manifold in a parallel configuration where each of the first manifold and the second manifold includes at least two of the affinity chromatography devices of any one of claims 49 to 66.

[00073] According to another Example (“Example 70”) further to Example 69, where the first manifold and the second manifold are enclosed within a housing.

[00074] In another Example (“Example 71”), a diagnostic article includes a fibrillated polymer membrane containing therein inorganic particles having a spherical shape and a nominal particle size from about 5 microns to about 20 microns where a particle size distribution has a D90/D10 less than or equal to 3 and where at least one of the fibrillated polymer membrane and the inorganic particles has covalently bonded thereto a ligand that reversibly binds to a targeted substance in a biological fluid.

[00075] According to another Example (“Example 72”) further to Example 71, including a fluid inlet and a fluid outlet fluidly connected to the fluid inlet.

[00076] According to another Example (“Example 73”) further to Example 71 or Example 72 including a housing member encompassing the fluid inlet, the fluid outlet, and the fibrillated polymer membrane.

BRIEF DESCRIPTION OF THE DRAWINGS

[00077] The accompanying drawings are included to provide a further understanding of the disclosure and are incorporated in and constitute a part of this specification, illustrate embodiments, and together with the description serve to explain the principles of the disclosure.

[00078] FIG. 1 is an exploded view of a chromatography device containing a wound membrane assembly including a fibrillated polymer membrane containing therein spherical inorganic polymer particles according to at least one embodiment;

[00079] FIG. 2 is a cross section of a chromatography device depicting the outer flow channel and inner flow channel according to at least one embodiment in accordance with at least one embodiment;

[00080] FIG. 3 is a schematic cross-section of another spiral wound, normal flow chromatography device in accordance with at least one embodiment;

[00081] FIG. 4 is an exploded view of a chromatography device containing a stacked membrane assembly including a fibrillated polymer membrane containing therein spherical inorganic particles in accordance with at least one embodiment;

[00082] FIG. 5 is a graphical illustration depicting the relationship between dynamic binding capacity (DBC) and liquid permeability from the affinity chromatography devices described in Examples 1 and 2;

[00083] FIG. 6 is a graphical illustration depicting the relationship of devices S and T with spiral wound membrane to affinity chromatography devices C through R with stacked membranes in accordance with at least one embodiment;

[00084] FIG. 7 is a schematic illustration of a front view of a manifold containing two chromatography devices arranged in a parallel configuration;

[00085] FIG. 8 is a schematic illustration of a top view of the manifold of FIG. 7;

[00086] FIG. 9 is a schematic illustration of a perspective view of a manifold containing four chromatography devices arranged in a parallel configuration;

[00087] FIG. 10 is a schematic illustration of a top view of the manifold of FIG. 9.

WHAT IS CLAIMED IS:

1. An article comprising:

an affinity chromatography device including:

a fluid inlet;

a fluid outlet fluidly connected to the fluid inlet; and

a fibrillated polymer membrane positioned between the fluid inlet and fluid outlet and containing therein inorganic particles having a spherical shape and a nominal particle size from about 5 microns to about 20 microns; and

a housing member encompassing the fluid inlet, the fluid outlet, and the fibrillated polymer membrane,

wherein a particle size distribution has a D90/D10 less than or equal to 3, and

wherein at least one of the fibrillated polymer membrane and the inorganic particles has covalently bonded thereto an affinity ligand that reversibly binds to a targeted molecule.

2. The article of claim 1, wherein the targeted molecule is a protein, antibody, viral vector, and combinations thereof.

3. The article of claim 1 or claim 2, comprising a hydraulic permeability from about 100 (X 10^{-12} cm^2) to about 500 (X 10^{-12} cm^2).

4. The article of any one of claims 1 to 3, wherein the inorganic particles having a spherical shape are selected from silica, zeolites, hydroxyapatite, metal oxides and combinations thereof.

5. The article of any one of claims 1 to 4, wherein the fibrillated polymer membrane comprises an expanded polytetrafluoroethylene membrane, an expanded modified polytetrafluoroethylene membrane, an expanded tetrafluoroethylene copolymer membrane, or an expanded polyethylene membrane, optionally wherein the fibrillated polymer membrane is an expanded polytetrafluoroethylene membrane.

6. The article of any one of claims 1 to 5, wherein the affinity ligand is selected from Protein A, Protein G, Protein L, human Fc receptor protein, antibodies, polysaccharides, and combinations thereof.

7. The article of any one of claims 1 to 6, wherein the inorganic particles comprise at least a first inorganic particle having a spherical shape and a first nominal particle size and a second inorganic particle having a spherical shape and a second nominal particle size, the first and second nominal particle sizes being different from each other, optionally wherein the nominal particle sizes are selected from about 5 microns, about 10 microns, about 15 microns, about 20 microns, and combinations thereof.

8. The article of any one of claims 1 to 7, wherein the inorganic particles having a spherical shape comprises a blend of 10-micron spherical particles and 20-micron spherical particles, and wherein the blend is from 10:90 to 90:10, or

wherein the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 10-micron spherical particles, and wherein the blend is from 10:90 to 90:10, or

wherein the inorganic particles having a spherical shape comprises a blend of 5-micron spherical particles and 20-micron spherical particles, and wherein the blend is from 10:90 to 90:10.

9. The article of any one of claims 1 to 8, comprising at least one of: a dynamic binding capacity (DBC) of at least 35 mg/ml at a residence time of 20 seconds; a cycling durability of at least 100 cycles at an operating pressure less than 0.3 MPa.

10. The article of any one of claims 1 to 9, wherein the fibrillated polymer membrane has a wound configuration.

11. The article of any one of claims 1 to 10, wherein the fibrillated polymer membrane has a stacked configuration.

12. The article of any one of claims 1 to 11, wherein the fibrillated polymer membrane has a wound configuration, a stacked configuration, and a combination thereof.

13. The article of any one of claims 1 to 12, wherein an inner intermediate material is circumferentially positioned on an outer surface of a core, and wherein the fibrillated polymer membrane is circumferentially positioned around the inner intermediate material, optionally wherein an outer intermediate material is circumferentially positioned on the fibrillated polymer membrane.

14. The article of claim 13, wherein the inner intermediate material and the outer intermediate material are selected from a porous fluoropolymer film, a porous non-fluoropolymer film, a porous non-woven material, and a porous woven material.

15. The article of any one of claims 13 or 14, wherein at least one of the inner intermediate material and the outer intermediate material is a polypropylene non-woven material.

16. Use of the article of any one of claims 1 to 15 to separate the targeted molecule from a fluid stream.

17. A manifold comprising at least two of the affinity chromatography devices of any one of claims 1 to 15 arranged in a parallel configuration.

18. The manifold of claim 17, wherein the manifold is enclosed within a housing.

19. A device comprising a first manifold and a second manifold in a parallel configuration, wherein each of the first manifold and the second manifold includes at least two of the affinity chromatography devices of any one of claims 1 to 15.

20. The device of claim 19, wherein the first manifold and the second manifold are enclosed within a housing.