

WHAT IS CLAIMED IS:

1. Chromatography media comprising:
porous inorganic particles having a median pore diameter of from about 600 Å to about 1600 Å; a pore size distribution relative span of at least about 0.75; and a functionalized surface comprising an average of from greater than 1 to about 3 linker molecules per square nanometer of surface area of said porous inorganic particles.
2. Chromatography media comprising:
porous inorganic particles having a median pore diameter of from about 600 Å to about 1600 Å; a pore size distribution relative span of at least about 0.75; and a functionalized surface comprising a protein covalently bonded to surface portions of said porous inorganic particles, said protein having a molecular weight ranging from about 10,000 to about 100,000 D.
3. The chromatography media of claim 2, wherein said protein is covalently bonded to surface portions of said porous inorganic particles via an average of greater than about 1 to about 3 linker molecules per square nanometer of surface area of said porous inorganic particles.
4. Chromatography media comprising:
porous inorganic particles having an average BET surface area of from about 20 m²/g to about 100 m²/g; an average pore volume of at least about 1 ml/g; a pore size distribution relative span of at least about 0.75; a functionalized surface comprising an average of from greater than about 1 to about 3 linker molecules per square nanometer of surface area of said porous inorganic particles; and a protein covalently bonded to at least some of said linker molecules, said protein having a molecular weight ranging from about 10,000 to about 100,000 D.

5. The chromatography media of any one of claims 1 to 4, wherein said porous inorganic particles have a pore size distribution relative span of at least about 0.9.
6. The chromatography media of any one of claims 1 to 5, wherein said porous inorganic particles have a pore size distribution relative span of at least about 0.99.
7. The chromatography media of any one of claims 1 to 6, wherein said porous inorganic particles have a pore size distribution relative span of from about 1.0 to about 1.3.
8. The chromatography media of any one of claims 1 to 7, wherein at least 40% of the total pore volume is in pores having a diameter between about 600 Å to about 1600 Å.
9. The chromatography media of claim 8, wherein from about 40% to about 90 % of the total pore volume is in pores having a diameter between about 600 Å to about 1600 Å.
10. The chromatography media of any one of claims 1 to 9, wherein at least 20% of the total pore volume have pores in a diameter ranging from about 1000 Å to about 1600 Å.
11. The chromatography media of claim 10, wherein from about 20% to about 60% of the total pore volume have pores in a diameter ranging from about 1000 Å to about 1600 Å.
12. The chromatography media of any one of claims 1 to 11, wherein at least 15% of the total pore volume have pores in a diameter ranging from about 1200 Å to about 1500 Å.

13. The chromatography media of claim 12, wherein from about 15% to about 30% of the total pore volume have pores in a diameter ranging from about 1200 Å to about 1500 Å.

14. The chromatography media of any one of claims 1 to 3 and 5 to 13, wherein said porous inorganic particles have an average BET surface area of greater than about 10 m²/g.

15. The chromatography media of claim 14, wherein said porous inorganic particles have an average BET surface area of from about 20 m²/g to about 200 m²/g.

16. The chromatography media of claim 15, wherein said porous inorganic particles have an average BET surface area of from about 25 m²/g to about 100 m²/g.

17. The chromatography media of any one of claims 1 to 3 and 5 to 15, wherein said porous inorganic particles have an average pore volume of at least about 1 ml/g.

18. The chromatography media of claim 17, wherein said porous inorganic particles have an average particle dimension of from about 30 µm to about 120 µm.

19. The chromatography media of claim 18, wherein said porous inorganic particles have an average particle dimension of from about 50 µm to about 90 µm.

20. The chromatography media of claim 19, wherein said porous inorganic particles have an average particle dimension of about 70 µm.

21. The chromatography media of any one of claims 1 to 20, wherein said porous inorganic particles comprise silica, alumina, zirconia, or mixtures thereof.

22. The chromatography media of claim 21, wherein said porous inorganic particles comprise silica.

23. The chromatography media of claim 22, wherein said porous inorganic particles comprise silica having at least 97% by weight SiO_2 based upon a total weight of said porous inorganic particles.

24. The chromatography media of any one of claims 1 to 23, wherein said functionalized surface comprises a reaction product resulting from a reaction between (i) hydroxyl groups on said porous inorganic particles and (ii) a silane.

25. The chromatography media of claim 24, wherein said functionalized surface comprises a reaction product resulting from a reaction between hydroxyl groups on said particles and an epoxy silane.

26. The chromatography media of claim 25, wherein said functionalized surface comprises a reaction product resulting from a reaction between hydroxyl groups on said particles and (3-glycidyloxypropyl) trimethoxysilane.

27. The chromatography media of claim 1, wherein each of said linker molecules comprises a diol.

28. The chromatography media of claim 1 or 27, wherein said functionalized surface comprises (i) a diol group and (ii) unreacted hydroxyl groups on said porous inorganic particles.

29. The chromatography media of claim 27 or 28, wherein said diol is present in an amount ranging from about 30 to about 150 $\mu\text{mol/g}$ of said porous inorganic particles.

30. The chromatography media of any one of claims 27 to 29, wherein said diol is present in an amount ranging from about 50 to about 100 $\mu\text{mol/g}$ of said porous inorganic particles.

31. The chromatography media of claim 1, wherein each of said linker molecules comprises an aldehyde.

32. The chromatography media of any one of claims 1 and 5 to 31, wherein said functionalized surface comprises a protein covalently linked to surfaces of said porous inorganic particles via at least some of said linker molecules.

33. The chromatography media of any one of claims 2 to 32, wherein said functionalized surface comprises (i) said protein covalently linked to surface portions of said porous inorganic particles and (ii) unreacted hydroxyl groups on said porous inorganic particles.

34. The chromatography media of any one of claims 2 to 26 and 32 to 33, wherein said protein comprises Protein A.

35. The chromatography media of any one of claims 2 to 26 and 32 to 34, wherein said said proten is a recombinant Protein A (rProA).

36. The chromatography media of any one of claims 2 to 29 and 32 to 35, wherein said protein is present in an amount ranging from about 4.0 to about 16 mg/ml of said porous inorganic particles.

37. The chromatography media of any one of claims 2 to 26 and 32 to 36, wherein said protein is present in an amount ranging from about 5.0 to about 12 mg/ml of said porous inorganic particles.

38. The chromatography media of any one of claims 1 to 37, wherein said chromatography media, when used in an affinity column, has a non-specific protein binding level of less than about 20.0 ng/ml.

39. The chromatography media of any one of claims 1 to 38, wherein said chromatography media, when used in an affinity column, has a non-specific protein binding level of less than about 5.0 ng/ml.

40. The chromatography media of any one of claims 1 to 39, wherein said chromatography media, when used in an affinity column, has a dynamic binding capacity of at least 30 mg/ml.

41. The chromatography media of any one of claims 1 to 40, wherein said chromatography media, when used in an affinity column, has a dynamic binding capacity of from about 30 to about 90 mg/ml.

42. A method for making the chromatography media of any one of claims 1 to 41, said method comprising:

forming the porous inorganic particles; and

reacting surface portions of the porous inorganic particles with at least one reactant so as to form the functionalized surface.

43. The method of claim 42, wherein said forming step comprises forming porous inorganic particles via a particle-forming process selected from the group consisting of gelation, precipitation, aggregation, or combinations thereof.

44. The method of claim 42 or 43, wherein said forming step comprises forming porous inorganic particles via a gelation process.

45. The method of any one of claims 42 to 44, wherein the at least one reactant comprises a silane.

46. The method of any one of claims 42 to 45, wherein the at least one reactant comprises an epoxy silane.

47. The method of claim 48, wherein the epoxy silane comprises (3-glycidyloxypropyl) trimethoxysilane.

48. The method of any one of claims 45 to 47, further comprising:
converting at least one functional group on the silane to a hydroxyl group so as to form a diol.
49. The method of any one of claims 42 to 48, wherein the functionalized surface comprises (i) a diol and (ii) unreacted hydroxyl groups on the porous inorganic particles.
50. The method of claim 48 or 49, wherein the diol is present on the surface in an amount ranging from about 30 to about 150 $\mu\text{mol/g}$ of the porous inorganic particles.
51. The method of any one of claims 48 to 50, wherein the diol is present in an amount ranging from about 50 to about 100 $\mu\text{mol/g}$ of the porous inorganic particles.
52. The method of any one of claims 48 to 51, further comprising:
converting at least one diol to an aldehyde group.
53. The method of claim 52, further comprising reacting at least one aldehyde group with at least one free amino group on the desired protein to form an imine group and, optionally, reducing the imine group to an amine.
54. The method of claim 53, further comprising covalently bonding a protein to the functionalized surface via the an imino or amino group.
55. The method of any one of claims 42 to 54, wherein the functionalized surface comprises a protein covalently linked to surfaces of the porous inorganic particles.
56. The method of any one of claims 42 to 55, wherein the functionalized surface comprises (i) a protein covalently linked to surfaces of the porous inorganic particles and (ii) unreacted hydroxyl groups on the porous inorganic particles.

57. The method of any one of claims 42 to 56, wherein the functionalized surface comprises recombinant Protein A (rProA) covalently linked to surfaces of said porous inorganic particles.

58. The method of any one of claims 54 to 57, wherein the protein is present in an amount ranging from about 4.0 to about 16 mg/ml of the porous inorganic particles.

59. The method of any one of claims 54 to 58, wherein the protein is present in an amount ranging from about 5.0 to about 12 mg/ml of the porous inorganic particles.

60. A chromatography device comprising:
a device housing; and
chromatography media positioned within said device housing,
said chromatography media comprising the chromatography media of any one of claims 1 to 41.

61. The chromatography device of claim 60, wherein said device housing comprises a tubular housing member, and at least one separate and attachable tubular housing member end cap.

62. The chromatography device of claim 60 or 61, wherein said device housing comprises a polymeric material, a metal material, a glass material, a ceramic material, or a composite thereof.

63. The chromatography device of any one of claims 60 to 62, wherein said device housing comprises a biodegradable polymeric material.

64. The chromatography device of any one of claims 60 to 63, wherein said device housing comprises a metal material.

65. The chromatography device of any one of claims 60 to 62 or 64, wherein said device housing comprises stainless steel.

66. The chromatography device of any one of claims 60 to 64, wherein said chromatography device comprises a pre-packed disposable column.

67. The chromatography device of any one of claims 60 to 66, wherein said chromatography media has a non-specific protein binding level of less than about 20.0 ng/ml.

68. The chromatography device of any one of claims 60 to 67, wherein said chromatography media has a non-specific protein binding level of less than about 5.0 ng/ml.

69. The chromatography device of any one of claims 60 to 68, wherein said chromatography media has a dynamic binding capacity of at least 30 mg/ml.

70. The chromatography device of any one of claims 60 to 69, wherein said chromatography media has a dynamic binding capacity from about 30 to about 90 mg/ml.

71. The chromatography device of any one of claims 60 to 70, wherein said chromatography device comprises an affinity column.

72. The chromatography device of any one of claims 60 to 71, wherein said chromatography device has a device back pressure of less than 5.0 bar when said chromatography media is run at a linear velocity of about 1000 cm/h.

73. A method of making the chromatography device of any one of claims 60 to 72, said method comprising the steps of:

incorporating the chromatography media of any one of claims 1 to 41 into the device housing.

74. The method of claim 73, further comprising:
forming the device housing via a thermoforming step.
75. The method of claim 74, wherein said thermoforming step comprises thermoforming a tubular housing member, and at least one separate and attachable tubular housing member end cap.
76. The method of any one of claims 73 to 75, further comprising:
validating the chromatography device via one or more validation tests.
77. A method of using the chromatography media of any one of claims 1 to 41, said method comprising the step of:
incorporating the chromatography media into an affinity column.
78. A method of using the chromatography device of any one of claims 60 to 72, said method comprising the step of:
positioning the chromatography device within an operating position of a chromatography system.
79. A method of claim 77 or 78, further comprising:
processing a fluid through the affinity column or the chromatography device.
80. The method of claim 79, wherein the fluid comprises one or more biomolecules.
81. The method of claim 79 or 80, wherein the fluid comprises a protein, a peptide, an oligonucleotide, an antibody, a virus, a vaccine or any combination thereof.
82. The method of any one of claims 79 to 81, wherein the fluid comprises a monoclonal antibody.

83. The method of any one of claims 77 to 82, wherein said method does not comprise a clean-in-place step within the chromatography system.

84. A method of any one of claims 77 to 83, said method comprising:
providing the affinity column or the chromatography device to a user, said providing step comprising providing a pre-packed and validated affinity column or chromatography device to the user.

85. Chromatography media comprising:
porous inorganic particles having a median pore diameter of from about 600 Å to about 1600 Å; a pore size distribution relative span of at least about 0.75 and a pore size distribution such that at least about 20% of the total pore volume have pores in a diameter ranging from about 1000 Å to about 1600 Å.

86. The chromatography media of claim 85 wherein the porous inorganic particles have a functionalized surface comprising an average of from greater than 1 to about 3 linker molecules per square nanometer of surface area of said porous inorganic particles.

87. The chromatography media of any one of claims 85 to 86, wherein at least 40% of the total pore volume is in pores having a diameter between about 600 Å to about 1600 Å.

88. The chromatography media of any one of claims 85 to 87, wherein from about 40% to about 90 % of the total pore volume is in pores having a diameter between about 600 Å to about 1600 Å.

89. The chromatography media of any one of claims 85 to 88, wherein at least 20% to about 60% of the total pore volume have pores in a diameter ranging from about 1000 Å to about 1600 Å.

90. The chromatography media of any one of claims 85 to 89, wherein at least 15% of the total pore volume have pores in a diameter ranging from about 1200 Å to about 1500 Å.

91. The chromatography media of any one of claims 85 to 90, wherein from about 15% to about 30% of the total pore volume have pores in a diameter ranging from about 1200 Å to about 1500 Å.