

WHAT IS CLAIMED IS:

1. A formable composition comprising from 25% to 40% by weight of demineralized bone matrix, from 6% to 15% by weight of a hyaluronic acid salt, and from 40% to 72% by weight of a biologically compatible liquid.
2. The composition of claim 1 further comprising a rheology modifier.
3. The composition of claim 1 wherein the hyaluronic acid salt has an average molecular weight of at least 500,000 Daltons.
4. The composition of claim 1 further characterized in that, when subject to the Instron Syringe Extrusion Force (ISEF) test, the composition exhibits an extrusion force of from 12.0 Newtons to 30.0 Newtons.
5. The composition of claim 1 further comprising a pharmaceutically active ingredient.
6. The composition of claim 5 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.
7. The composition of claim 5 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF- β , IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.
8. The composition of claim 5 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.
9. Use of a composition comprising from 25% to 40% by weight of demineralized bone matrix, from 6% to 15% by weight of a hyaluronic acid salt, and from 40% to 72% by

weight of a biologically compatible liquid in the manufacture of a medicament for repairing cartilage in a subject.

10. A dry blend composition comprising from 60% to 92% by weight of demineralized bone matrix, from 6-15% by weight of a hyaluronic acid salt, and from 3 % to 10% by weight of a biologically compatible liquid.
11. The composition of claim 10 wherein the hyaluronic acid salt has an average molecular weight of at least 200,000 Daltons.
12. The composition of claim 10 comprising a mixture of at least two hyaluronic acid salts.
13. The composition of claim 10 further comprising a pharmaceutically active ingredient.
14. The composition of claim 13 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.
15. The composition of claim 13 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF- β , IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.
16. The composition of claim 13 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.
17. A plug comprising from 25% to 88% by weight of demineralized bone matrix and from 6-15% by weight of a hyaluronic acid salt and from 3% to 20% by weight of a biologically compatible liquid.
18. The plug of claim 17 wherein the powders further comprise a plasticizer.

19. The plug of claim 17 wherein the hyaluronic acid salt has an average molecular weight of at least 200,000 Daltons.
20. The plug of claim 17 comprising a mixture of at least two hyaluronic acid salts.
21. The plug of claim 17 wherein the powders further comprise a pharmaceutically active ingredient.
22. The plug of claim 21 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.
23. The plug of claim 21 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF- β , IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.
24. The plug of claim 21 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.
25. The plug of claim 17 characterized in that the plug exhibits an unconfined Compression Stress of at least 1.55 MPa.
26. A method of forming a plug comprising a) providing powders of demineralized bone matrix and a hyaluronic acid salt, b) mixing the powders, c) adding a liquid component to form a putty like material, d) placing the putty in a mold, and e) drying the shaped putty to form a plug.
27. The method of claim 26 wherein the plug is further conditioned to achieve a moisture content of 3-20% by weight.

28. The method of claim 27 wherein the moisture content is from 5% to 10% by weight.
29. The method of claim 26 wherein the powders further comprise a pharmacetically active ingredient.
30. The method of claim 29 wherein the pharmaceutically active ingredient is bone morphogenic protein.

WHAT IS CLAIMED IS:

1. A formable composition comprising from about 25% to about 40% by weight of demineralized bone matrix, from about 3.5% to about 25% by weight of a hyaluronic acid salt, and from about 40% to about 72% by weight of a biologically compatible liquid.
2. The composition of claim 1 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid.
3. The composition of claim 1 wherein the biologically compatible liquid is PBS, water, saline, or LRS.
4. The composition of claim 1 wherein the biologically compatible liquid is PBS.
5. The composition of claim 1 further comprising a rheology modifier.
6. The composition of claim 5 wherein the rheology modifier is glycerol or carboxymethyl cellulose.
7. The composition of claim 1 comprising from about 25% to about 35% by weight of demineralized bone matrix.
8. The composition of claim 1 comprising from about 6% to about 15 % by weight of the hyaluronic acid salt.
9. The composition of claim 1 comprising from about 6% to about 9% by weight of the hyaluronic acid salt.

10. The composition of claim 1 wherein the hyaluronic acid salt has an average molecular weight of at least about 500,000 Daltons.
11. The composition of claim 1 comprising a mixture of at least two hyaluronic acid salts.
12. The composition of claim 11 comprising a mixture of two hyaluronic acid salts, comprising a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.
13. The composition of claim 12 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.
14. The composition of claim 12 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.
15. The composition of claim 12 wherein the average molecular weight ratio of the hyaluronic acid salt of the first average molecular weight to the hyaluronic acid salt of the second average molecular weight ranges from 1:5 to 5:1.
16. The composition of claim 12 wherein the average molecular weight difference between the hyaluronic acid salt of the first average molecular weight and the hyaluronic acid salt of the second average molecular weight is at least about 0.5 million Daltons.
17. The composition of claim 1 further characterized in that, when subject to the Instron Syringe Extrusion Force (ISEF) test, the composition exhibits an extrusion force of from about 12.0 Newtons to about 30.0 Newtons.
18. The composition of claim 17 wherein the extrusion force is from about 18.0 Newtons to about 26.0 Newtons.

~~19. The composition of claim 17 wherein the extrusion force is measured in a 3 mL syringe with a diameter of 8.6 mm and 15 gauge 1-1/1 needle.~~

20. The composition of claim 1 further comprising a pharmaceutically active ingredient.

21. The composition of claim 20 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

22. The composition of claim 20 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF-B, IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

23. The composition of claim 20 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

24. Use of demineralized bone matrix and a hyaluronic acid salt in the manufacture of a composition for repairing cartilage in a subject, wherein the composition is to be administered at a site of a defect in cartilaginous tissue.

25. The use of claim 24 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid.

26. The use of claim 24 wherein the composition further comprises a biologically compatible liquid.

27. The use of claim 26 wherein the biologically compatible liquid is PBS, water, saline, or LRS.

- ~~28. The use of claim 26 wherein the biologically compatible liquid is PBS.~~
29. The use of claim 26 wherein the biologically compatible liquid is water.
30. The use of claim 24 wherein the composition further comprises a rheology modifier.
31. The use of claim 30 wherein the rheology modifier is glycerol or carboxymethyl cellulose.
32. The use of claim 24 wherein the composition is a formable composition, comprising from about 25% to about 40% by weight of demineralized bone matrix.
33. The use of claim 32 wherein the composition comprises at least from about 3.5% to about 25% by weight of the hyaluronic acid salt.
34. The use of claim 32 wherein the composition comprises from about 6% to about 15% by weight of the hyaluronic acid salt.
35. The use of claim 32 wherein the composition comprises from about 6% to about 9% by weight of the hyaluronic acid salt.
36. The use of claim 32 wherein the composition comprises from about 40% to about 72% by weight of a biologically compatible liquid.

~~37. The use of claim 24 wherein the composition is a dry blend composition, comprising from about 60% to about 92% by weight of demineralized bone matrix.~~

38. The use of claim 37 wherein the composition comprises at least from about 3.5% to about 38% by weight of the hyaluronic acid salt.

39. The use of claim 37 wherein the composition comprises from about 3% to about 10% by weight of a biologically compatible liquid.

40. The use of claim 24 wherein the composition is a plug, comprising from about 25% to about 88% by weight of demineralized bone matrix.

41. The use of claim 40 wherein the composition comprises at least from about 3.5% to about 38% by weight of the hyaluronic acid salt.

42. The use of claim 40 wherein the composition further comprises from about 3% to about 20% by weight of a biologically compatible liquid.

43. The use of claim 40 wherein the composition further comprises from about 5% to about 10% by weight of a biologically compatible liquid.

44. The use of claim 24 wherein the composition comprises a mixture of at least two hyaluronic acid salts.

45. The use of claim 44 wherein the composition comprises a mixture of two hyaluronic acid salts, comprising a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.

46. The use of claim 45 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.

47. The use of claim 45 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.

48. The use of claim 45 wherein the average molecular weight ratio of the hyaluronic acid salt of the first average molecular weight to the hyaluronic acid salt of the second average molecular weight ranges from 1 :5 to 5:1.

49. The use of claim 45 wherein the average molecular weight difference between the hyaluronic acid salt of the first average molecular weight and the hyaluronic acid salt of the second average molecular weight is at least about 0.5 million Daltons.

50. The use of claim 24 wherein the composition further comprises a pharmaceutically active ingredient.

51. The use of claim 50 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

52. The use of claim 50 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF-B, IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

53. The use of claim 50 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

54. A method of preparing a formable composition comprising from about 25% to about 40% by weight of demineralized bone matrix, from about 3.5% to about 25% by weight of a hyaluronic acid salt, and from about 40% to about 72% by weight of

a biologically compatible liquid, the method comprising mixing solid components, followed by the addition of a liquid component.

55. The method of claim 54 wherein the solid components comprises the demineralized bone matrix and the hyaluronic acid salt.

56. The method of claim 54 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid.

57. The method of claim 54 wherein the liquid component is a biologically compatible liquid.

58. The method of claim 57 wherein the biologically compatible liquid is PBS, water, saline, or LRS.

59. The method of claim 57 wherein the biologically compatible liquid is water.

60. The method of claim 54 wherein the liquid component is added before the intended use.

61. The method of claim 54 wherein the composition further comprises a rheology modifier.

62. The method of claim 61 wherein the rheology modifier is glycerol or carboxymethyl cellulose.

63. The method of claim 54 wherein the hyaluronic acid salt has an average molecular weight of at least about 200,000 Daltons.

64. The method of claim 54 wherein the composition comprises a mixture of at least two hyaluronic acid salts.

65. The method of claim 64 wherein the composition comprises a mixture of two hyaluronic acid salts, comprising a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.

66. The method of claim 65 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.

67. The method of claim 65 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.

68. The method of claim 65 wherein the average molecular weight ratio of the hyaluronic acid salt of the first average molecular weight to the hyaluronic acid salt of the second average molecular weight range from 1:5 to 5:1.

69. The method of claim 65 wherein the average molecular weight difference between the hyaluronic acid salt of the first average molecular weight and the hyaluronic acid salt of the second average molecular weight is at least about 0.5 million Daltons.

70. The method of claim 54 wherein the composition further comprises a pharmaceutically active ingredient.

71. The method of claim 70 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

72. The method of claim 70 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF-B, IGF-1, ascorbate, pyruvate,

BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

73. The method of claim 70 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

74. The method of claim 70 wherein the pharmaceutically active ingredient is mixed with the demineralized bone matrix and the hyaluronic acid salt.

75. The method of claim 70 wherein the pharmaceutically active ingredient is mixed with the liquid component.

76. A dry blend composition comprising from about 60% to about 92% by weight of demineralized bone matrix, from about 3.5% to about 38% by weight of a hyaluronic acid salt, and from about 3% to about 10% by weight of a biologically compatible liquid.

77. The composition of claim 76 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid.

78. The composition of claim 76 wherein the hyaluronic acid salt has an average molecular weight of at least about 200,000 Daltons.

79. The composition of claim 76 comprising a mixture of at least two hyaluroinc acid salts.

80. The composition of claim 76 comprising a mixture of two hyaluronic acid salts, a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.

81. The composition of claim 80 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.

82. The composition of claim 80 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.

83. The composition of claim 76 further comprising a pharmaceutically active ingredient.

84. The composition of claim 83 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

85. The composition of claim 83 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF- β , IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

86. The composition of claim 83 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

87. A plug comprising from about 25% to about 88% by weight of demineralized bone matrix and from about 3.5% to about 38% by weight of a hyaluronic acid salt and from about 3% to about 20% by weight of a biologically compatible liquid.

88. The plug of claim 87 wherein the biologically compatible liquid is at about 5-10% by weight.

89. The plug of claim 87 wherein the biologically compatible liquid is water.

90. The plug of claim 87 wherein the powders further comprise a plasticizer.

91. The plug of claim 90 wherein the plasticizer is glycerol or PEG.
92. The plug of claim 87 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid salt.
93. The plug of claim 87 comprising at least about 6% by weight of the hyaluronic acid salt.
94. The plug of claim 87 comprising from about 6% to about 24% by weight of the hyaluronic acid salt.
95. The plug of claim 87 comprising from about 6% to about 18% by weight of the hyaluronic acid salt.
96. The plug of claim 87 wherein the hyaluronic acid salt has an average molecular weight of at least about 200,000 Daltons.
97. The plug of claim 87 comprising a mixture of at least two hyaluronic acid salts.
98. The plug of claim 97 comprising a mixture of two hyaluronic acid salts, comprising a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.
99. The plug of claim 98 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.
100. The plug of claim 98 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.

101. The plug of claim 98 wherein the average molecular weight ratio of the hyaluronic acid salt of the first average molecular weight to the hyaluronic acid salt of the second average molecular weight ranges from 1:5 to 5:1.

102. The plug of claim 98 wherein the average molecular weight difference between the hyaluronic acid salt of the first average molecular weight and the hyaluronic acid salt of the second average molecular weight is at least about 0.5 million Daltons.

103. The plug of claim 87 wherein the powders further comprise a pharmaceutically active ingredient.

104. The plug of claim 103 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

105. The plug of claim 103 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF- β , IGF-1, ascorbate, pyruvate, BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

106. The plug of claim 103 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

107. The plug of claim 87 characterized in that the plug exhibits an unconfined Compression Stress of at least about 1.55 MPa.

108. A method of forming a plug comprising

- a) providing powders of demineralized bone matrix and a hyaluronic acid salt,
- b) mixing the powders,
- c) adding a liquid component to form a putty like material,
- d) placing the putty in a mold, and

e) drying the shaped putty to form a plug.

109. The method of claim 108 wherein the hyaluronic acid salt is a sodium salt, potassium salt, or calcium salt of hyaluronic acid salt.

110. The method of claim 108 wherein the plug comprises less than about 20% by weight of a biologically compatible liquid.

111. The method of claim 110 wherein the plug comprises less than about 10% by weight of a biologically compatible liquid.

112. The method of claim 110 wherein the biologically compatible liquid is water.

113. The method of claim 108 wherein the powders further comprise a plasticizer.

114. The method of claim 113 wherein the plasticizer is glycerol or PEG.

115. The method of claim 108 wherein the plug comprises at least about 6% by weight of the hyaluronic acid salt.

116. The method of claim 108 wherein the plug comprises from about 6% to about 24% by weight of the hyaluronic acid salt.

117. The method of claim 108 wherein the plug comprises from about 6% to about 18% by weight of the hyaluronic acid salt.

118. The method of claim 108 wherein the hyaluronic acid salt has an average molecular weight of at least about 200,000 Daltons.

119. The method of claim 108 wherein the plug comprises a mixture of at least two hyaluronic acid salts.

120. The method of claim 119 wherein the composition comprises a mixture of two hyaluronic acid salts, comprising a hyaluronic acid salt of a first average molecular weight and a hyaluronic acid salt of a second average molecular weight.

121. The method of claim 120 wherein the hyaluronic acid salt of the first average molecular weight is about 0.05-1.0 million Daltons.

122. The method of claim 120 wherein the hyaluronic acid salt of the second average molecular weight is about 1.0-5.0 million Daltons.

123. The method of claim 120 wherein the average molecular weight ratio of the hyaluronic acid salt of the first average molecular weight to the hyaluronic acid salt of the second average molecular weight ranges from 1:5 to 5:1.

124. The method of claim 120 wherein the average molecular weight difference between the hyaluronic acid salt of the first average molecular weight and the hyaluronic acid salt of the second average molecular weight is at least about 0.5 million Daltons.

125. The method of claim 108 wherein the powders further comprise a pharmaceutically active ingredient.

126. The method of claim 125 wherein the pharmaceutically active ingredient is bone morphogenic protein, tissue growth factors, insulin growth factors, antioxidants, antibiotics, or combinations of growth factors.

127. The method of claim 125 wherein the pharmaceutically active ingredient is selected from BMP-2, BMP-4, BMP-6, BMP-7, TGF-B, IGF-1, ascorbate, pyruvate,

BHT, gentamycin, vancomycin, the combination of TGF- β and BMP-2, and the combination of TGF- β and IGF-1.

128. The method of claim 125 wherein the pharmaceutically active ingredient is conjugated with the hyaluronic acid salt.

129. The method of claim 108 wherein the drying is lyophilizing, air drying, or oven or vacuum drying.

130. The method of claim 108 wherein the plug is further conditioned to achieve a moisture content of about 3-20% by weight.

131. The method of claim 130 wherein the moisture content is from about 5% to about 10% by weight.