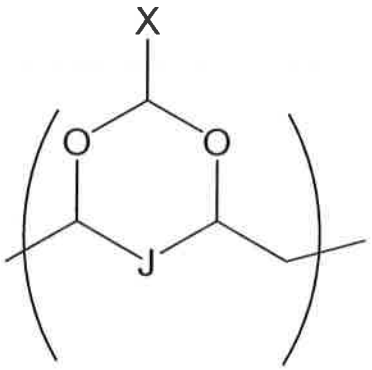
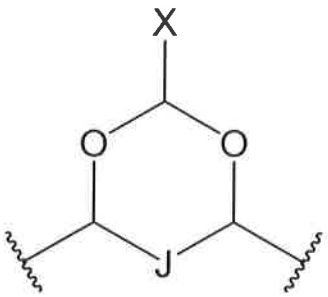
CLAIMS

1. A hydrogel comprising 1,2-diol or 1,3-diol groups acetalised with a radiopaque species, wherein the hydrogel is a cross-linked polymer network, wherein the radiopaque species is acetalised in the hydrogel in the form of a cyclic acetal and wherein the radiopaque species is iodine.

2. A hydrogel according to claim 1 wherein the structure of the 1,2-diol or 1,3-diol groups acetalised with a radiopaque species is of the general formula I or II



I



II

wherein X is a group of the formula

ZQ III

wherein Z is a linking group, or is absent, such that Q is directly bonded to the cyclic acetal;

where Z is present Z is C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{1-6} alkoxylene or C_{1-6} alkoxyalkylene and is optionally substituted by one or more halogens;

Q is C_5 to C_7 aryl, substituted by 1 or more iodines

and

J is a group $-CH_2-$ or is a bond.

3. A hydrogel according to claim 2, wherein Q is a phenyl group, substituted by 2, 3 or 4 iodines and Z is either absent or is a C_{1-6} alkylene, or a group $-(CH_2)_q-O-(CH_2)_p-$ wherein p is 0, 1 or 2 and q is 1 or 2;

and J is a bond or $-CH_2-$.

4. A hydrogel according to claim 1 wherein the radiopaque species comprises an iodinated phenyl group.

5. A hydrogel according to claim 1 wherein the hydrogel comprises polyvinyl alcohol (PVA) or copolymers of PVA.

6. A hydrogel according to any preceding claim wherein the hydrogel comprises greater than 20% iodine by dry weight.

7. A hydrogel according to any preceding claim wherein the hydrogel is in the form of microparticles or microspheres.

8. A hydrogel according to any preceding claim wherein the hydrogel is in the form of microparticles or microspheres having an iodine content of greater than 15mg/ml of fully hydrated microparticles or microspheres in normal saline.

9. A hydrogel according to either of claims 5 or 6 wherein the hydrogel is in the form of microspheres with a mean diameter size range of from 10 to 2000μm.

10. A hydrogel according to any preceding claim in the form of microspheres or microparticles having a mean radiopacity of 500HU or greater.

11. A hydrogel according to any preceding claim wherein the hydrogel has a net charge at pH 7.4.

12. A composition comprising a hydrogel according to any preceding claim and a therapeutic agent wherein the therapeutic agent is absorbed into the hydrogel matrix.

13. A composition according to claim 12 wherein the therapeutic agent is electrostatically held in the hydrogel and elutes from the hydrogel in electrolytic media.

14. A method of making a radiopaque hydrogel polymer comprising reacting a polymer comprising 1,2- diol or 1,3-diol groups with a radiopaque species capable of forming a cyclic acetal with said 1,2-diol or 1,3 diols under acidic conditions, wherein the radiopaque species is a compound of the formula IV:

X-A IV

wherein X is a group of the formula ZQ,

wherein Z is a linking group, or is absent, such that Q is directly bonded to the cyclic acetal;

where Z is present Z is C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{1-6} alkoxylene or C_{1-6} alkoxyalkylene and is optionally substituted by one or more halogens;

Q is C_5 to C_7 aryl, substituted by 1 or more iodines.

15. A method according to claim 14, wherein Q is a phenyl group, substituted by 2, 3 or 4 iodines and Z is either absent or is a C_{1-6} alkylene, or a group $-(CH_2)_q-O-(CH_2)_p-$ wherein p is 0, 1 or 2 and q is 1 or 2; and
A is an aldehyde, acetal or hemiacetal.

16. A method according to claim 14 wherein the radiopaque species is an iodinated benzyl aldehyde, iodinated phenyl aldehyde or an iodinated phenoxyaldehyde.

17. A method according to any one of claims 14 to 16 wherein the polymer is cross-linked.

18. A method according to any one of claims 14 to 17 wherein the polymer comprises polyvinyl alcohol (PVA) or copolymers of PVA.

19. A method according to any of claims 14 to 18 wherein the radiopaque species is an organic molecule or organometallic complex, with radiopacity >1 HU, and which comprises a reactive moiety selected from the group consisting of aldehydes, acetals hemiacetals thioacetals and dithioacetals.

20. A method according to claim 19 wherein the radiopaque species is an iodinated benzyl aldehyde, iodinated phenyl aldehyde or an iodinated phenoxyaldehyde.

21. A method of making a radiopaque hydrogel microsphere comprising the steps of:

(a) swelling a pre-formed hydrogel microsphere comprising a polymer with 1,2-diol or 1,3-diol groups in a solvent capable of swelling said microsphere; and

(b) mixing the swollen beads with a solution of a radiopaque species capable of forming a cyclic acetal with said 1,2 or 1,3 diols under acidic conditions; and

(c) extracting the microspheres.

22. A method according to claim 21 wherein the radiopaque species is a compound of the formula:

X-A IV

wherein X is a group of the formula ZQ,

wherein Z is a linking group, or is absent, such that Q is directly bonded to the cyclic acetal;

where Z is present Z is C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{1-6} alkoxylene or C_{1-6} alkoxyalkylene and is optionally substituted by one or more halogens;

Q is a C_{1-6} alkyl group or a C_5 to C_7 aryl, C_5 to C_7 heteroaryl or C_5 to C_7 cycloalkyl group substituted by 1 or more halogens; and

A is an aldehyde, acetal or hemiacetal.

23. A method according to claim 22 wherein Q is C_5 to C_7 aryl, substituted by 1 or more iodines.

24. A method according to claim 22, wherein Q is a phenyl group, substituted by 1, 2, 3 or 4 iodines and Z is either absent or is a C_{1-6} alkylene, or a group $-(CH_2)_q-O-(CH_2)_p-$ wherein p is 0, 1 or 2 and q is 1 or 2; and
A is an aldehyde, acetal or hemiacetal.

25. A method according to any one of claims 22 to 24, wherein A is selected from –CHO, -$CHOR^1OR^2$ –$CHOR^1OH$; wherein R^1 and R^2 are independently selected from C_{1-4} alkyl.

26. A method according to claim 22 wherein the radiopaque species is an iodinated benzyl aldehyde, iodinated phenyl aldehyde or an iodinated phenoxyaldehyde.

27. A method according to any one of claims 21 to 26 which further comprises the step of drying the extracted microspheres.

28. A method according to any of claims 21 or 27 in which the reaction is conducted in polar aprotic solvent and at a temperature above 25°C.

29. A method according to claim 21 in which the radiopaque species comprises a functional group selected from the group consisting of aldehydes, acetals, hemiacetals thioacetals and dithioacetals.

30. A method according to claim 21 wherein the radiopaque species is an iodinated aldehyde.

31. A method according to claim 21 wherein the radiopaque species is an iodinated benzyl aldehyde, an iodinated phenyl aldehyde or an iodinated phenoxyaldehyde.

32. A method according to claim 21 wherein the radiopaque species is 2,3,5-triiodobenzaldehyde, 2,3,4,6-tetraiodobenzyaldehyde or 2-(2,4,6-triiodophenoxy)acetaldehyde.

33. A hydrogel according to any of claims 1 to 11 for use in embolization of a blood vessel.

34. A composition according to either of claim 12 or 13 for use in embolization of a blood vessel.