Claims

1. The calcium complex of 10-(2,3-Dihydroxy-1-(hydroxymethyl)propyl)-1,4,7,10-tetraazacyclodecane-1,4,7-triacetic acid with a purity of 99.0% or more.

2. The complex according to claim 1 with a purity of 99.4% or more.

3. Use of the complex according to claim 1 or 2 for preparation of galenic formulations of Gadobutrol.

4. A process for the preparation of the calcium complex of 10-(2,3-Dihydroxy-1-(hydroxymethyl)propyl)-1,4,7,10-tetraazacyclodecane-1,4,7-triacetic acid (Calcobutrol), wherein
a) the gadolinium complex of 10-(2,3-Dihydroxy-1-(hydroxymethyl)propyl)-1,4,7,10-tetraazacyclodecane-1,4,7-triacetic acid (Gadobutrol) is de-complexed with a de-complexing agent,
b) the precipitated gadolinium salt is removed,
c) the free ligand in the solution resulting from step b) is bound to an acidic ion exchange resin,
d) said resin is eluted with an aqueous alkaline solution,
e) the eluate is treated with acidic ion exchange resin, and
f) the ligand is complexed with Ca^{2+} ions and crystallised.

5. The process according to claim 4, wherein the de-complexing agent in step a) is an oxalate ion source or a phosphate ion source.

6. The process according to claim 5, wherein the de-complexing agent in step a) is oxalic acid.

7. The process according to any one of claims 4 to 6, wherein the de-complexation reaction according to step a) is carried out in water at temperatures from 75 to 100°C.

8. The process according to any one of claims 4 to 7, wherein the aqueous alkaline solution of step d) is a solution of ammonia or a volatile amine, or mixtures thereof.

9. The process according to claim 8, wherein the aqueous alkaline solution in step d) is a solution of ammonia, dimethylamine, methylamine, ethylamine, trimethylamine, iso-propylamine, or mixtures thereof.

10. The process according to claim 9, wherein the aqueous alkaline solution in step d) is a solution of ammonia.

11. The process according to any one of claims 4 to 10, wherein the product resulting from step e) is isolated by freeze-drying.

12. The process according to any one of claims 4 to 10, wherein the product resulting from step e) is reacted directly with calcium ion source without isolating it first.

13. The process according to any one of claims 4 to 12, wherein the calcium ion source in step f) is calcium carbonate, oxide, or hydroxide.

14. The process according to any one of claims 4 to 13, wherein the pH in step a) before adding the de-complexing agent is higher than 2.

Claims

1. A process for the preparation of the calcium complex of 10-(2,3-Dihydroxy-1-(hydroxymethyl)propyl)-1,4,7,10-tetraazacyclodecane-1,4,7-triacetic acid (Calcobutrol), wherein

a) the gadolinium complex of 10-(2,3-Dihydroxy-1-(hydroxymethyl)propyl)-1,4,7,10-tetraazacyclodecane-1,4,7-triacetic acid (Gadobutrol) is de-complexed with a de-complexing agent, wherein the de-complexing agent is an oxalate ion source or a phosphate ion source and the pH before adding the de-complexing agent is higher than 2

b) the precipitated gadolinium salt is removed,

c) the free ligand in the solution resulting from step b) is bound to an acidic ion exchange resin,

d) said resin is eluted with an aqueous alkaline solution,

e) the eluate is treated with acidic ion exchange resin, and

f) the ligand is complexed with Ca^{2+} ions and crystallised.

2. The process according to claim 1, wherein the de-complexing agent in step a) is oxalic acid.

3. The process according to any one of claims 1 and 2, wherein the de-complexation reaction according to step a) is carried out in water at temperatures from 75 to 100°C.

4. The process according to any one of claims 1 to 3, wherein the aqueous alkaline solution of step d) is a solution of ammonia or a volatile amine, or mixtures thereof.

5. The process according to claim 4, wherein the aqueous alkaline solution in step d) is a solution of ammonia, dimethylamine, methylamine, ethylamine, trimethylamine, iso-propylamine, or mixtures thereof.

6. The process according to claim 5, wherein the aqueous alkaline solution in step d) is a solution of ammonia.

7. The process according to any one of claims 1 to 6, wherein the product resulting from step e) is isolated by freeze-drying.

8. The process according to any one of claims 1 to 6, wherein the product resulting from step e) is reacted directly with calcium ion source without isolating it first.

9. The process according to any one of claims 1 to 8, wherein the calcium ion source in step f) is calcium carbonate, oxide, or hydroxide.