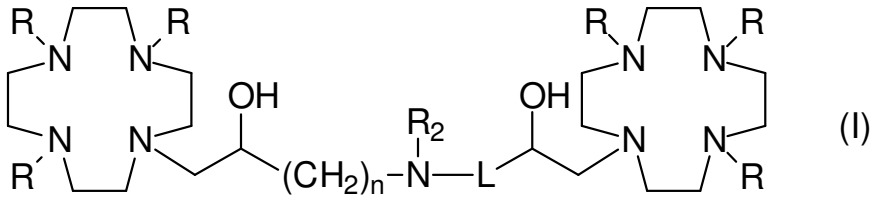
Claims

1. A compound of formula (I)



(I)

where:

R is -CH(R_1)-COOH, where:

R_1 is H or a C_1-C_3 alkyl chain that is optionally substituted by a C_1-C_3 alkoxy or C_1-C_3 hydroxyalkoxy group;

n is 1 or 2;

R_2 is selected from the group consisting of: an aryl ring; a cyclohexyl ring; a C_1-C_5 alkyl substituted by a cycloalkyl ring; a group of formula -$(CH_2)_s$CH(R_3)-G; and a C_5-C_{12} hydroxyalkyl comprising at least 2 hydroxyl groups;

in which

s is 0, 1 or 2;

R_3 is H, or an arylalkylene or cycloalkyl-alkylene having from 1 up to 3 carbon atoms in the alkylene chain;

G is a group selected from -PO(OR_4)$_2$, -PO(R_5)(OR_4) and –COOH; in which

R_4 independently of one another is H or C_1-C_5 alkyl;

R_5 is an aryl or a cyclohexyl ring, or C_1-C_5 alkyl which is optionally substituted by an aryl or cyclohexyl ring; and

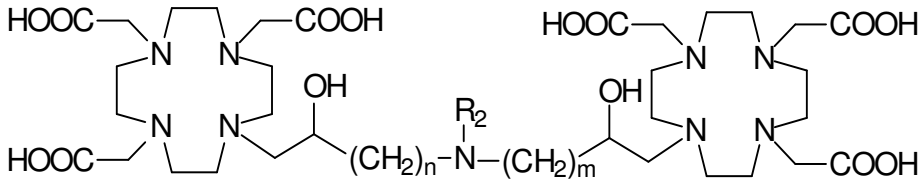
L is a C_1-C_6 alkylene, optionally interrupted by one or more –N(R'$_2$)– groups, and optionally substituted by one or more substituent groups selected from hydroxyl, C_1-C_3 alkoxy and C_1-C_3 hydroxyalkoxy, where

R'$_2$ is, independently, as defined for R_2.

as well as individual diastereoisomers and their racemic mixtures, geometric isomers and solved enantiomers of the same, and the physiologically acceptable salt thereof.

2. The compound according to claim 1 in which R_1 is H.

3. The compound according to claims 1 or 2 in which L is C_1-C_6 alkylene, having the following formula (II)



(II)

in which:

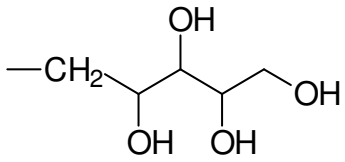
m is 1, 2, 3, 4, 5, or 6; and

n and R_2 are as defined in claim 1.

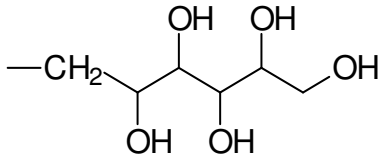
4. The compound according to claim 3 in which, in the formula (II), R_2 is a C_5-C_{12} polyol.

5. The compound according to claim 4 in which the polyol is selected from the group consisting of pentyl-polyols comprising from 2 to 4 hydroxyl groups on the C_5 alkyl chain; hexyl-polyols comprising from 2 to 5 hydroxyl groups on the C_6 alkyl chain; and heptyl-polyols comprising from 3 to 6 hydroxyl groups on the C_7 alkyl chain.

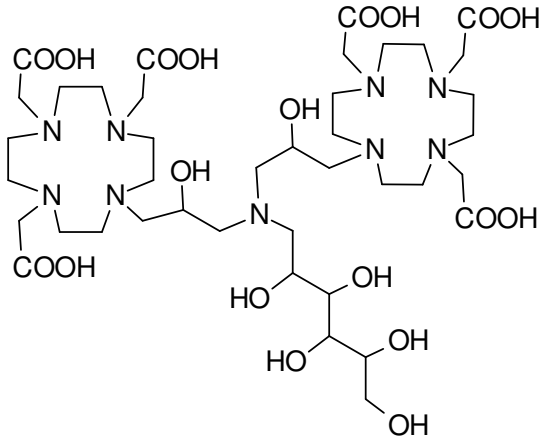
6. The compound according to claim 4 or 5 in which the polyol is selected from a pentyl-tetraol of formula



and a hexyl-pentaol of formula



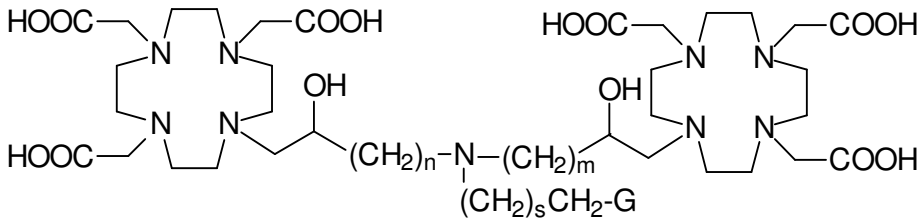
7. The compound according to any one of claims 4-6 of formula



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8. The compound according to claim 3 in which, in the formula (II), R_2 is a group of formula $-(CH_2)_sCH(R_3)-G$.

9. The compound according to claim 8 in which R_3 is H, having the formula (II B)



(II B)

in which:

s is 0, 1 or 2;

n and m, independently to one another, are 1 or 2; and

G is a group selected from -PO(OR_4)$_2$, -PO(R_5)(OR_4) and –COOH, in which

R_4 is H or a *tert*-butyl; and

R_5 is an optionally substituted phenyl or cyclohexyl ring, or a C_1-C_3 alkyl substituted or not by a phenyl or cyclohexyl ring.

10. The compound according to claim 9 in which in the formula (II B)

s is 0 or 1;

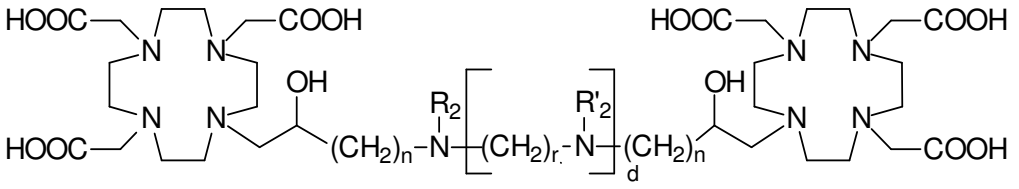
n and m are both 1; and,

G is selected from -PO(OH)$_2$ and –COOH.

11. The compound according to claim 3 in which R_2 is a C_1-C_5 alkyl substituted by a saturated C_5-C_7 cycloalkyl ring.

12. The compound according to claim 11 in which R_2 is a C_1-C_5 alkyl substituted by a cyclohexyl ring or by a piperidine, or a piperidine derivative having from 1 to 8 substituents groups linked to the carbon atom(s) of the heterocyclic ring.

13. The compound according to claims 1 or 2 in which in the formula (I) L is a C_1-C_6 alkylene chain interrupted by one or two –N(R'_2)– groups, having the formula (III)



(III)

in which:

each n, r and d is, independently, 1 or 2; and

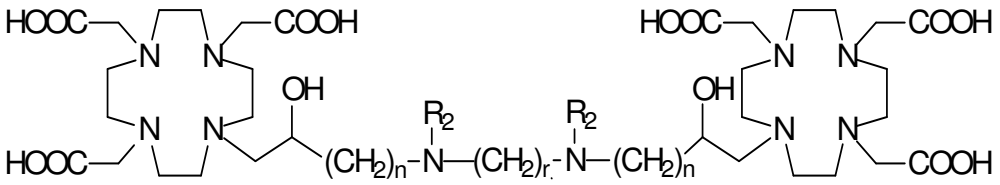
R_2 and R'_2, equal or different, are as defined in claim 1.

14. The compound according to claims 13 in which:

d is 1; and

$R'_2 = R_2$,

having the formula

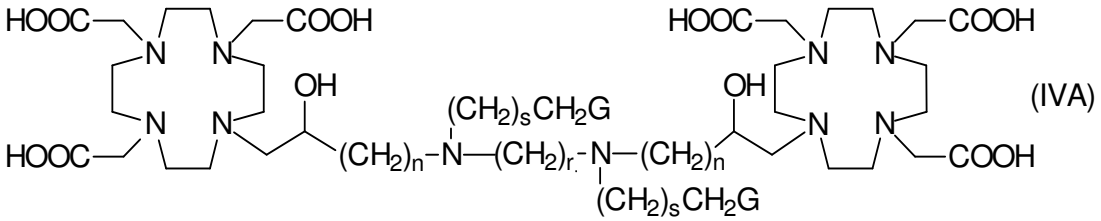


(IV)

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15. The compound according to claim 14 in which, in the formula (IV), R_2 is a group of formula $-(CH_2)_sCH(R_3)-G$ where s, R_3 and G are as defined in claim 1.

16. The compound according to claim 15, of formula (IV A)



(IVA)

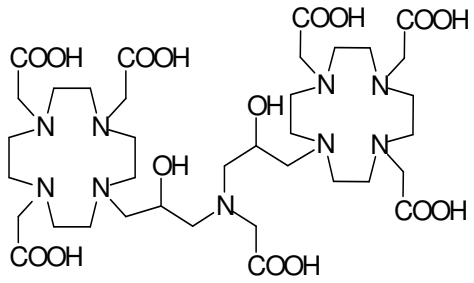
in which n is 1;

r is 1 or 2;

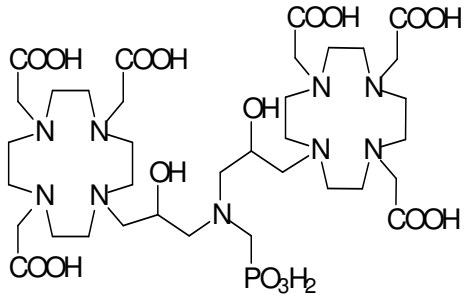
s is 0, 1 or 2; and

G a group selected from $-PO(OH)_2$ and –COOH.

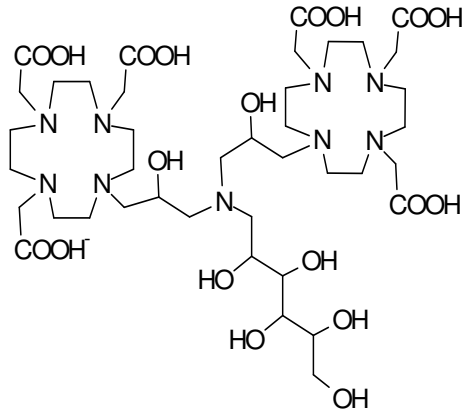
17. The compound according to claim 1 or 2 of formula:



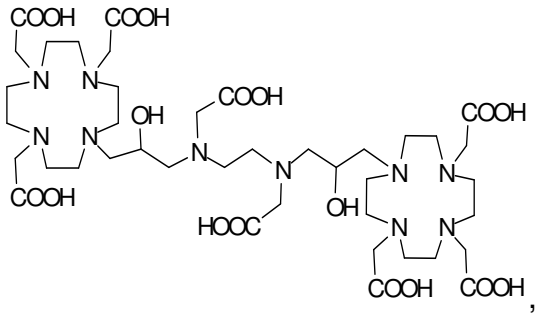
Compound 1



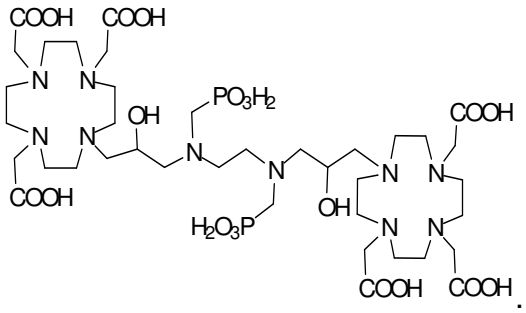
Compound 2



Compound 3



Compound 5



Compound 6

18. A chelated complex of a compound according to any one of claims 1-17 with two paramagnetic metal ions selected from the group consisting of Fe^{2+}, Fe^{3+}, Cu^{2+}, Cr^{3+}, Gd^{3+}, Eu^{3+}, Dy^{3+}, La^{3+}, Yb^{3+} or Mn^{2+}, and a physiologically acceptable salt thereof.

19. The chelated complex according to claim 18, wherein the paramagnetic metal ions are Gd^{3+} ions.

20. The compound according to any one of claims 1-17, or the chelated complex according to claims 18 - 19 wherein the physiologically acceptable salt is with a cation of (i) an inorganic base selected from an alkali or alkaline-earth metal, (ii) an organic base selected from ethanolamine, diethanolamine, morpholine, glucamine, N-methylglucamine, N,N-dimethylglucamine or (iii) an amino acid selected from lysine, arginine and ornithine.

21. A chelated complex as defined in any one of claims 18 - 20, for use as a MRI contrast agent.

22. A pharmaceutical composition comprising a chelated complex of claims 18-20 in combination with one or more pharmaceutically acceptable carriers, diluents or excipients.

23. A compound as defined in any one of claims 1-17 in which each of the carboxylic groups R linked to the nitrogen atoms of the macrocycle is in a protected form as *tert*-butyl ester.