Claims

1. A pharmaceutical composition comprising a hydrogel-linked prodrug for use in the prevention, diagnosis and/or treatment of an ocular condition.

2. A pharmaceutical composition comprising a hydrogel-linked prodrug for use for intraocular injection.

3. A pharmaceutical composition comprising a hydrogel-linked prodrug for use for intraocular injection in the prevention, diagnosis and/or treatment of an ocular condition.

4. The pharmaceutical composition for use of claim 1 or 3, wherein the ocular condition is in particular an anterior ocular condition or posterior ocular condition.

5. The pharmaceutical composition for use of claim 4, wherein the anterior ocular condition is selected from the group comprising aphakia, pseudophakia, astigmatism, blepharospasm, cataract, conjunctival diseases, conjunctivitis, corneal diseases, corneal ulcer, dry eye syndromes, eyelid diseases, lacrimal apparatus diseases, lacrimal duct obstruction, myopia, presbyopia, pupil disorders, refractive disorders, glaucoma and strabismus.

6. The pharmaceutical composition for use of claim 4, wherein the posterior ocular condition is selected from the group comprising acute macular neuroretinopathy; Behcet's disease; choroidal neovascularization; diabetic uveitis; histoplasmosis; infections, such as fungal or viral-caused infections; macular degeneration, such as acute macular degeneration, non-exudative age related macular degeneration and exudative age related macular degeneration; edema, (such as macular edema, cystoid macular edema and diabetic macular edema; multifocal choroiditis; ocular trauma which affects a posterior ocular site or location; ocular tumors; retinal disorders, such as central retinal vein occlusion, diabetic retinopathy (including proliferative diabetic retinopathy), proliferative vitreoretinopathy (PVR), retinal arterial occlusive disease, retinal detachment, uveitic retinal disease; sympathetic opthalmia; Vogt Koyanagi-Harada (VKH) syndrome; uveal diffusion; a posterior ocular condition caused by or

influenced by an ocular laser treatment; posterior ocular conditions caused by or influenced by a photodynamic therapy, photocoagulation, radiation retinopathy, epiretinal membrane disorders, branch retinal vein occlusion, anterior ischemic optic neuropathy, nonretinopathy diabetic retinal dysfunction, retinitis pigmentosa, and glaucoma.

7. The pharmaceutical composition for use of any one of claims 1 to 6 contained in a container suited for engagement with an injection device.

8. The pharmaceutical composition for use of any one of claims 1 to 7, wherein the hydrogel is a biodegradable hydrogel.

9. The pharmaceutical composition for use of claim 8, wherein the hydrogel is a PEG-based hydrogel.

10. The pharmaceutical composition for use of any one of claims 1 to 9, wherein the hydrogel-linked prodrug is bead-shaped.

11. The pharmaceutical composition for use of any one of claims 1 to 10, wherein the beads have a diameter of 1 to 1000 µm.

12. The pharmaceutical composition for use of any one of claims 1 to 11, wherein the hydrogel is a hydrogel obtainable by a process comprising the steps of:

(a) providing a mixture comprising

(a-i) at least one backbone reagent, wherein the at least one backbone reagent has a molecular weight ranging from 1 to 100 kDa, and comprises at least three amines ($-NH_2$ and/or -NH-);

(a-ii) at least one crosslinker reagent, wherein the at least one crosslinker reagent has a molecular weight ranging from 6 to 40 kDa, the at least one crosslinker reagent comprising

(i) at least two carbonyloxy groups (–(C=O)–O– or –O–(C=O)–), and additionally

(ii) at least two activated functional end groups selected from the group consisting of activated ester groups, activated carbamate groups, activated carbonate groups and activated thiocarbonate groups,

and being PEG-based comprising at least 70% PEG; and

(a-iii) a first solvent and at least a second solvent, which second solvent is immiscible in the first solvent,

in a weight ratio of the at least one backbone reagent to the at least one crosslinker reagent ranging from 1:99 to 99:1;

(b) polymerizing the mixture of step (a) in a suspension polymerization to a hydrogel; and

(c) optionally working-up the hydrogel.

13. The pharmaceutical composition for use of claim 12, wherein the mixture of step (a) further comprises a detergens.

14. The pharmaceutical composition for use of claim 12 or 13, wherein the polymerization in step (b) is initiated by adding a base.

15. The pharmaceutical composition for use of any one of claims 12 to 14, wherein the mixture of step (a) is an emulsion.

16. The pharmaceutical composition for use of any one of claims 12 to 15, wherein the at least one backbone reagent is selected from the group consisting of

a compound of formula (I)

$$B(-(A^0)_{x1}-(SP)_{x2}-A^1-P-A^2-Hyp^1)_x \quad (I),$$

wherein

B is a branching core,

SP is a spacer moiety selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl,

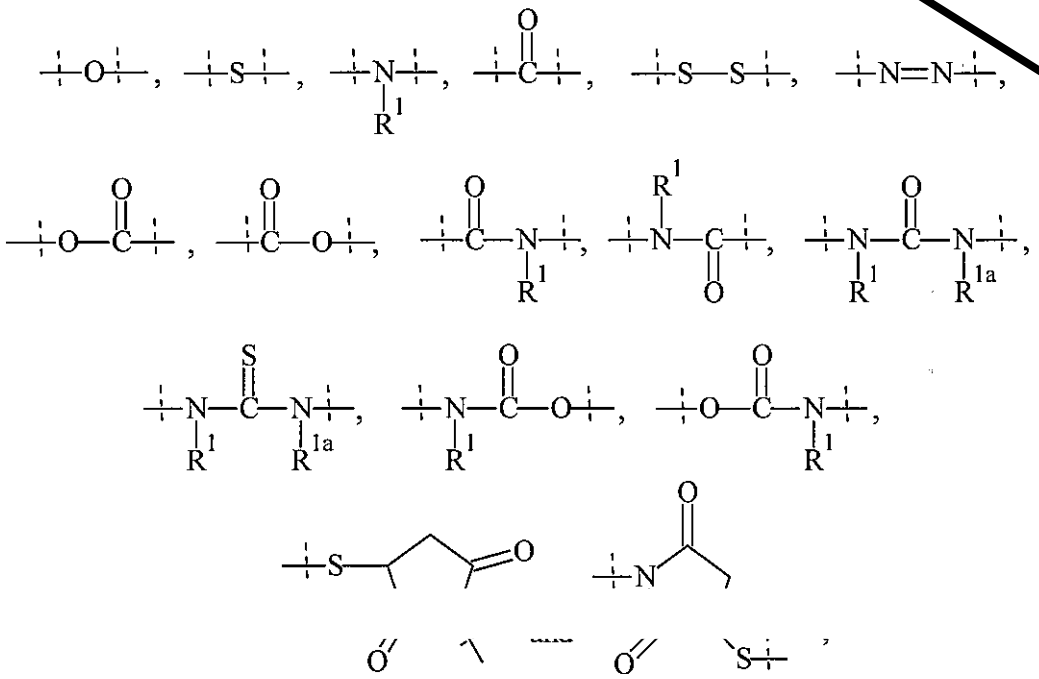
P is a PEG-based polymeric chain comprising at least 80% PEG, preferably at least 85% PEG, more preferably at least 90% PEG and most preferably at least 95% PEG,

Hyp^1 is a moiety comprising an amine ($-NH_2$ and/or -NH-) or a polyamine comprising at least two amines ($-NH_2$ and/or -NH-),

x is an integer from 3 to 16,

x1, x2 are independently of each other 0 or 1, provided that x1 is 0, if x2 is 0,

A^0, A^1, A^2 are independently of each other selected from the group consisting of



wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

a compound of formula (II)

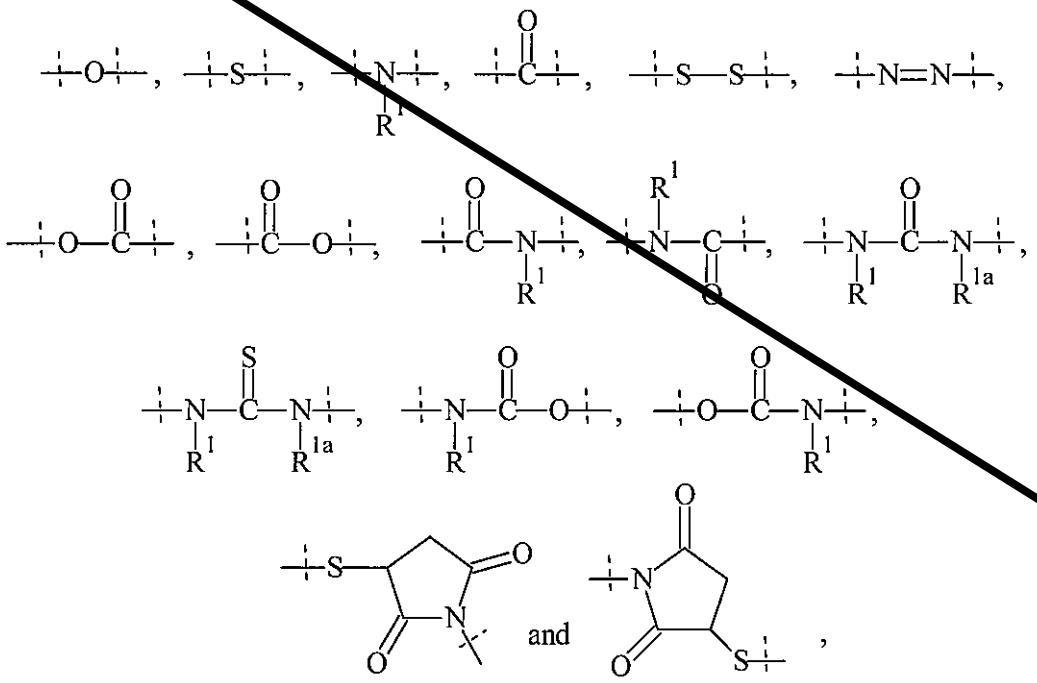
$$Hyp^2 - A^3 - P - A^4 - Hyp^3 \quad (II),$$

wherein

P is defined as above in the compound of formula (I),

Hyp^2, Hyp^3 are independently of each other a polyamine comprising at least two amines ($-NH_2$ and/or -NH-), and

A^3 and A^4 are independently selected from the group consisting of



wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

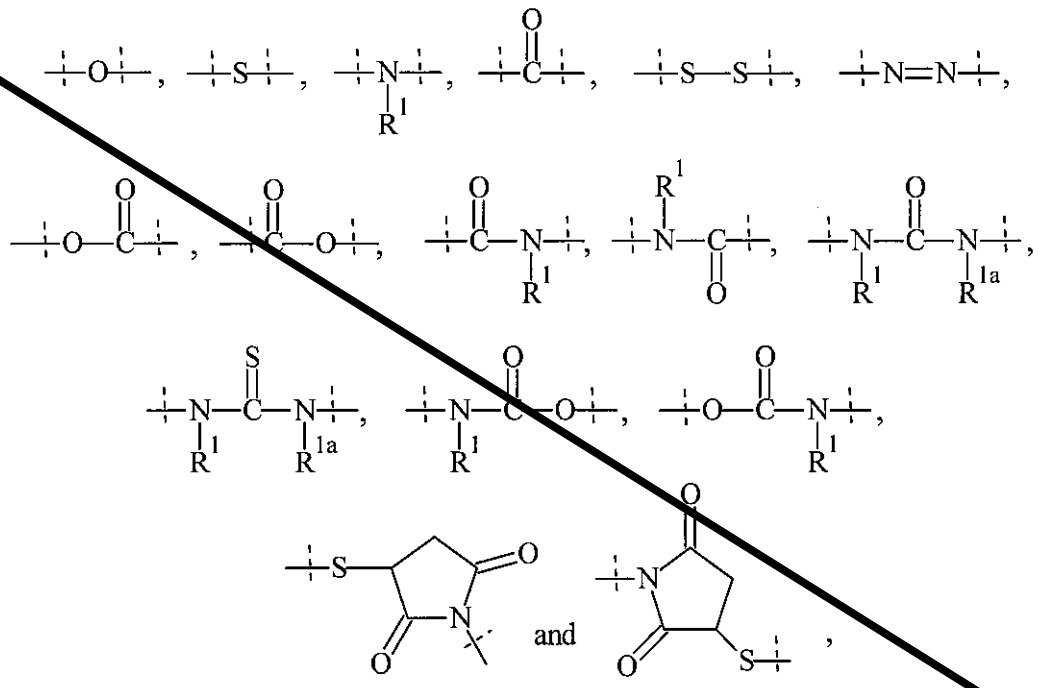
a compound of formula (III)

wherein

P^1 is a PEG-based polymeric chain comprising at least 80% PEG, preferably at least 85% PEG, more preferably at least 90% PEG and most preferably at least 95% PEG,

Hyp^4 is a polyamine comprising at least three amines ($-NH_2$ and/or -NH), and

A^5 is selected from the group consisting of



and

wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

and

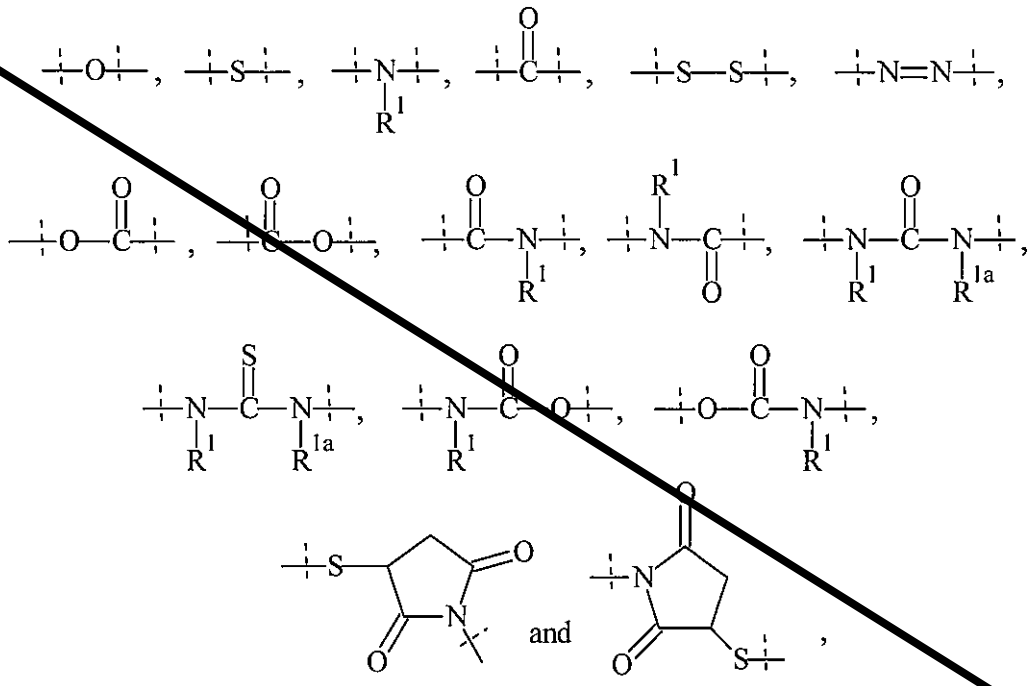
a compound of formula (IV),

$T^1 - A^6 - Hyp^5$ (IV),

wherein

Hyp is a polyamine comprising at least three amines (-NH2 and/or -NH-),

A^6 is selected from the group consisting of

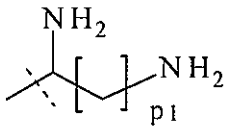


wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl; and

T^1 is selected from the group consisting of C_{1-50} alkyl, C_{2-50} alkenyl or C_{2-50} alkynyl, which fragment is optionally interrupted by one or more group(s) selected from -NH-, -N(C_{1-4} alkyl)-, -O-, -S-, -C(O)-, -C(O)NH-, -C(O)N(C_{1-4} alkyl)-, -O-C(O)-, -S(O)-, -$S(O)_2$-, 4- to 7-membered heterocyclyl, phenyl or naphthyl.

Hyp^2, Hyp^3, Hyp^4, and Hyp^5 are selected from the group consisting of

a moiety of formula (e-i)



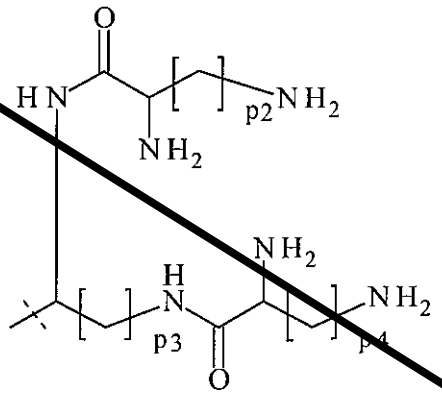
(e-i)

wherein

p1 is an integer from 1 to 5, preferably p1 is 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I) and to A^3 or A^4 if the backbone reagent has the structure of formula (II);

a moiety of formula (e-ii)



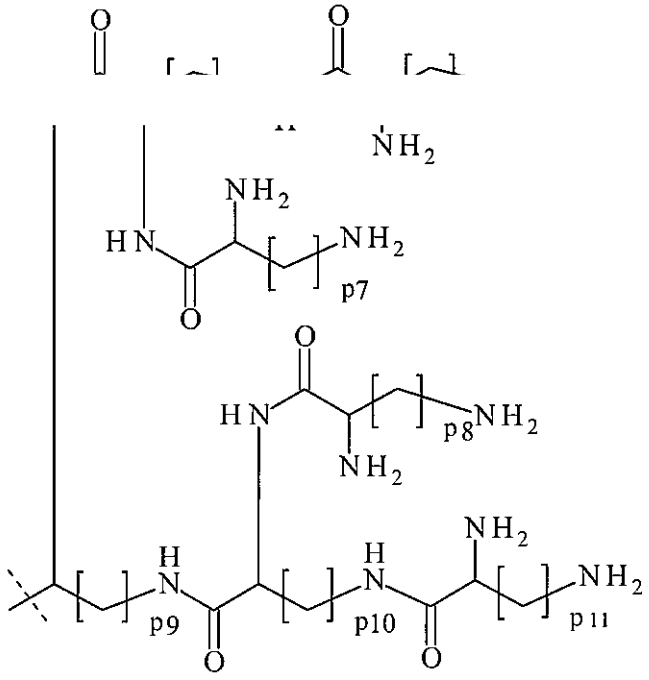
(e-ii)

wherein

p2, p3 and p4 are identical or different and each is independently of the others an integer from 1 to 5, preferably p2, p3 and p4 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-iii)



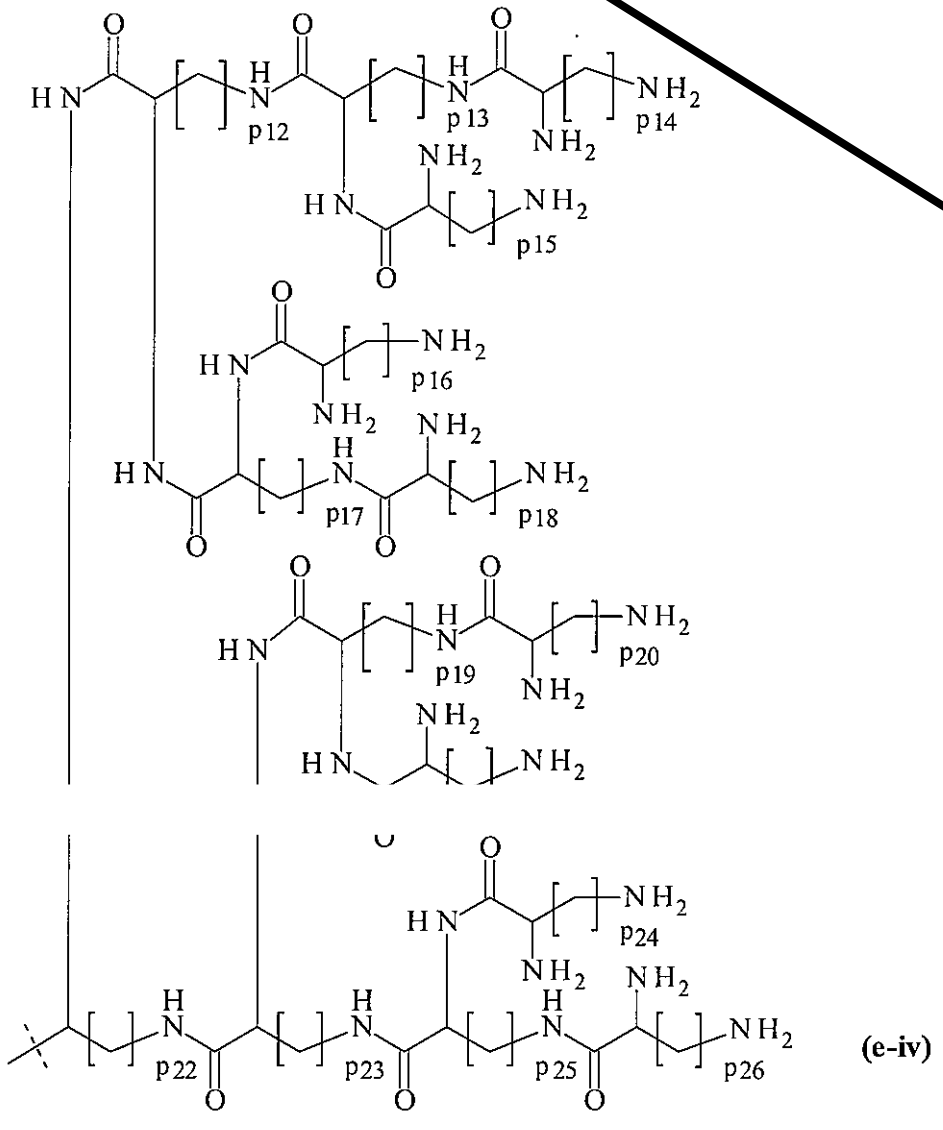
(e-iii)

wherein

p5 to p11 are identical or different and each is independently of the others an integer from 1 to 5, preferably p5 to p11 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent is of formula (I), to A^3 or A^4 if the backbone reagent is of formula (II), to A^5 if the backbone reagent is of formula (III) and to A^6 if the backbone reagent is of formula (IV);

a moiety of formula (e-iv)



(e-iv)

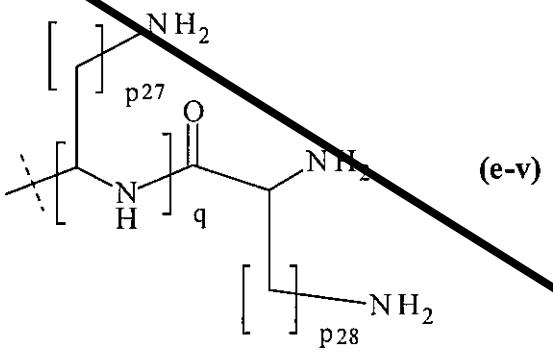
wherein

p12 to p26 are identical or different and each is independently of the others an integer from 1 to 5, preferably p12 to p26 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if

the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-v)



(e-v)

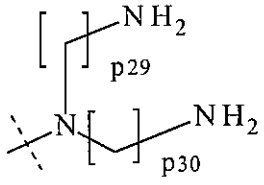
wherein

p27 and p28 are identical or different and each is independently of the other an integer from 1 to 5, preferably p27 and p28 are 4,

q is an integer from 1 to 8, preferably q is 2 or 6 and most preferably 1 is 6, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-vi)



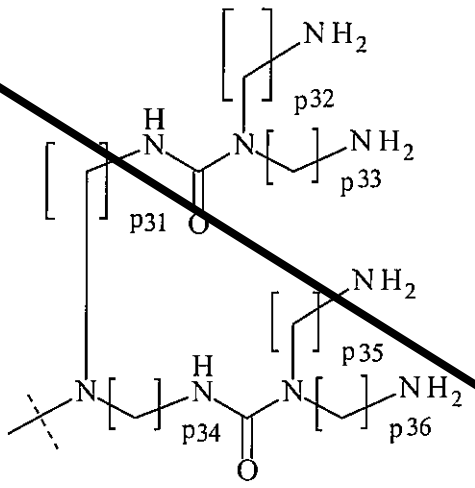
(e-vi)

wherein

p29 and p30 are identical or different and each is independently of the other an integer from 2 to 5, preferably p29 and p30 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has the structure of formula (I), to A^3 or A^4 if the backbone reagent has the structure of formula (II), to A^5 if the backbone reagent has the structure of formula (III) and to A^6 if the backbone reagent has the structure of formula (IV);

a moiety of formula (e-vii)



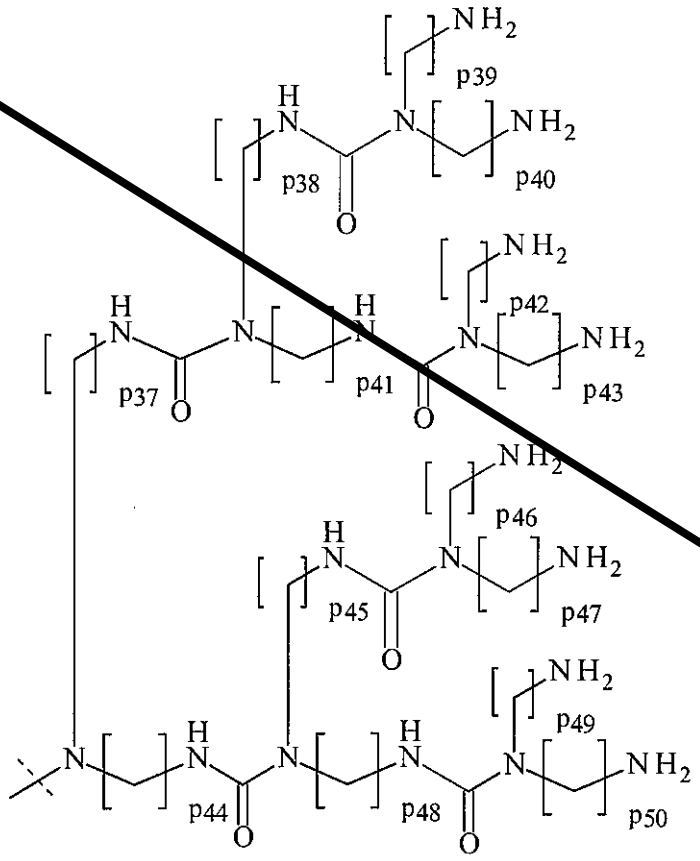
(e-vii)

wherein

p31 to p36 are identical or different and each is independently of the others an integer from 2 to 5, preferably p31 to p36 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-viii)



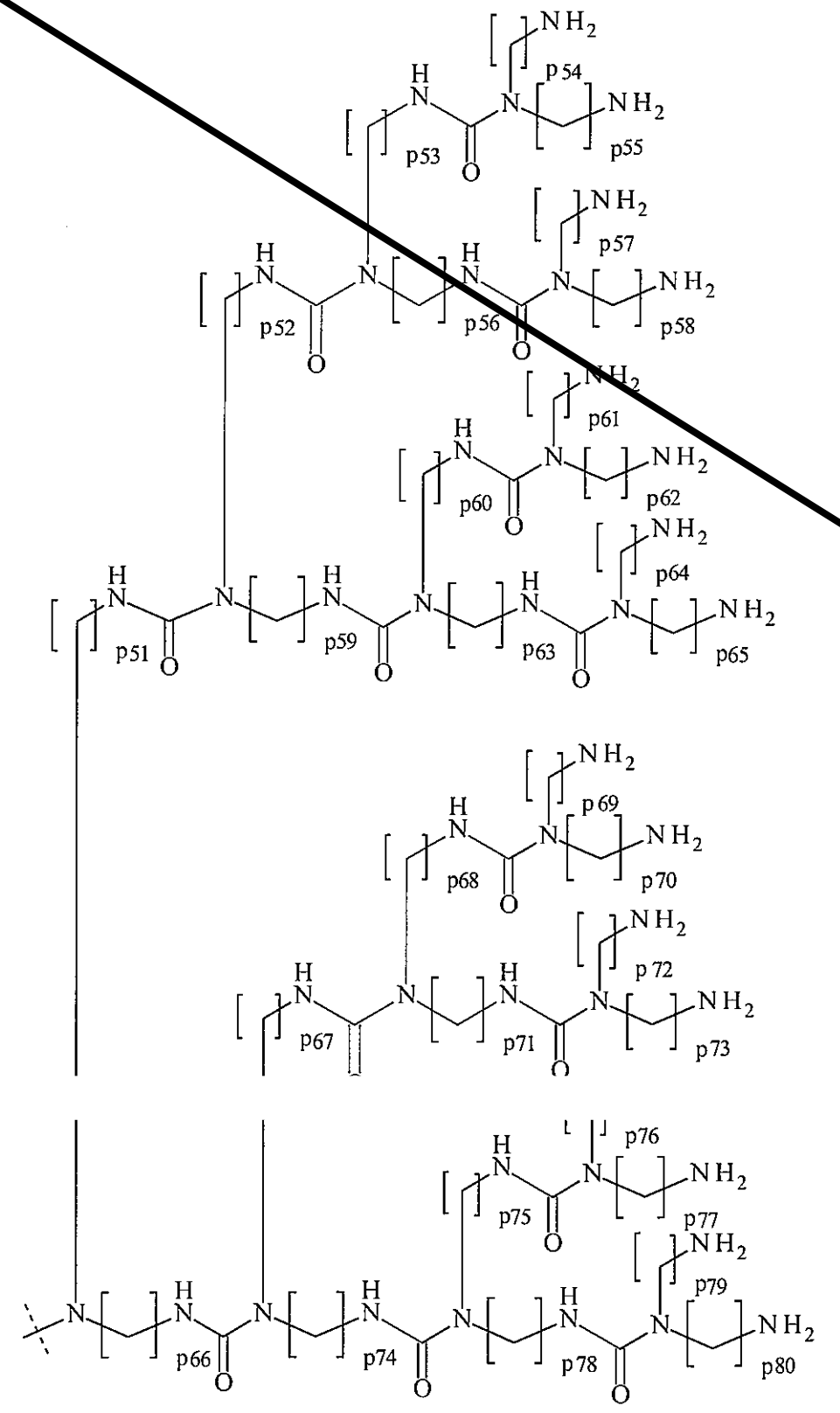
(e-viii)

wherein

p37 to p50 are identical or different and each is independently of the others an integer from 2 to 5, preferably p37 to p50 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent

a moiety of formula (e-ix):



(e-ix)

wherein

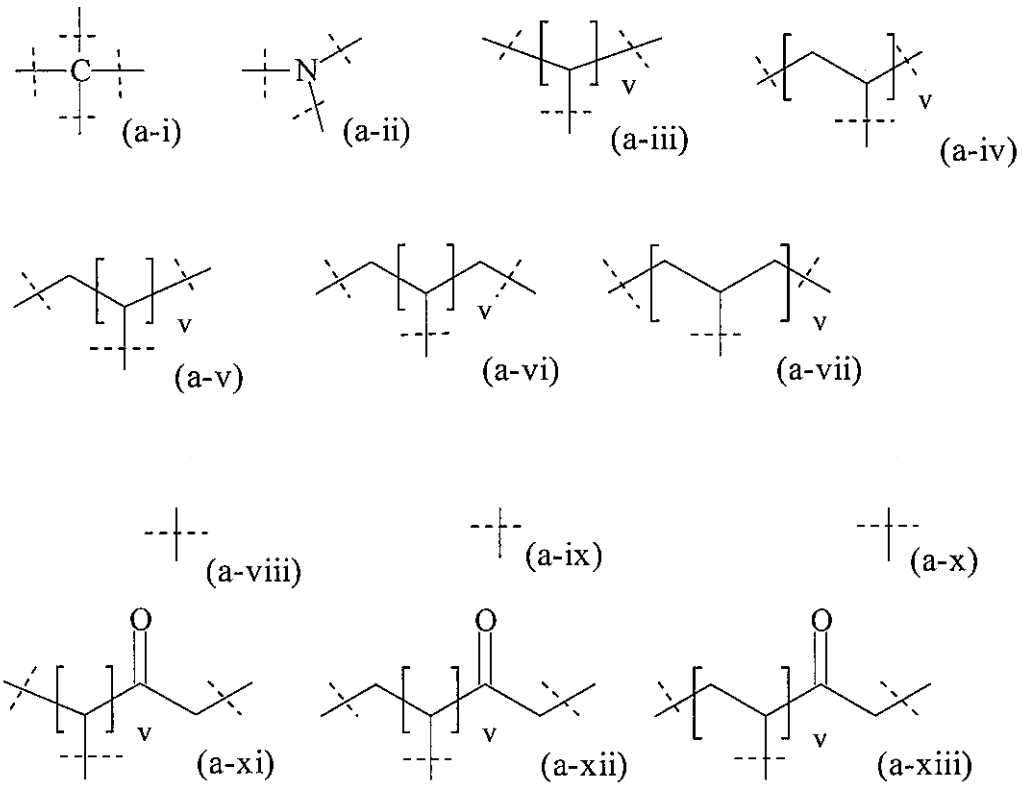
p51 to p80 are identical or different and each is independently of the others an integer from 2 to 5, preferably p51 to p80 are 3, and

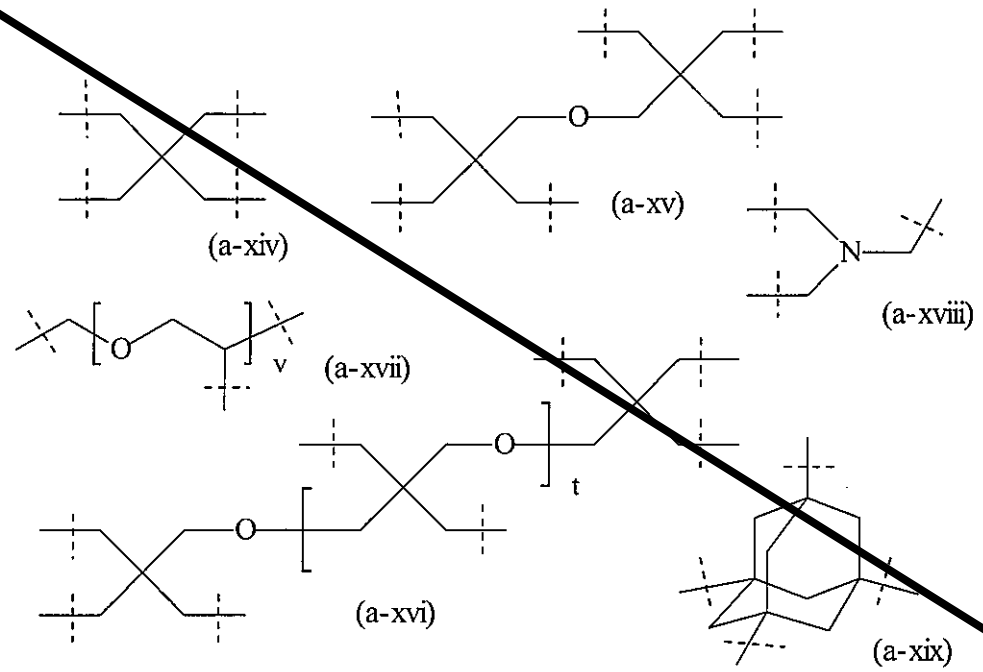
the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV); and

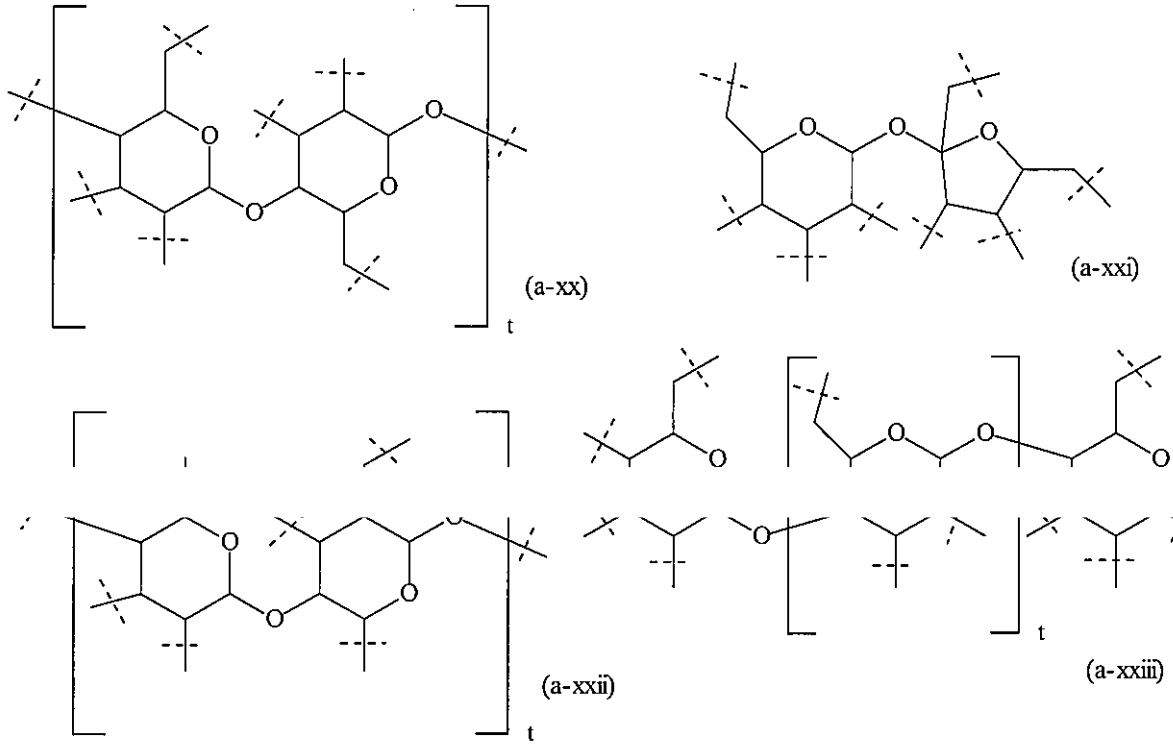
wherein the moieties (e-i) to (e-v) may at each chiral center be in either R- or S-configuration, preferably, all chiral centers of a moiety (e-i) to (e-v) are in the same configuration.

18. The pharmaceutical composition for use of any one of claims 12 to 17, wherein the backbone reagent is a compound of formula (I).

19. The pharmaceutical composition for use of any one of claims 12 to 18, wherein the branching core B is selected from the following structures:







wherein

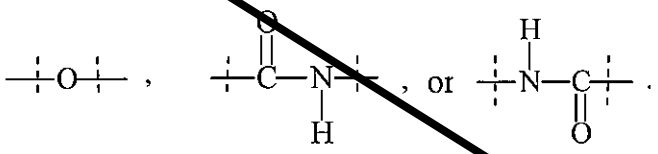
dashed lines indicate attachment to A^0 or, if x1 and x2 are both 0, to A^1,

t is 1 or 2; preferably t is 1,

v is 1, 2, 3, 4, 5, ,6 ,7 ,8 , 9, 10, 11, 12, 13 or 14; preferably, v is 2, 3, 4, 5, 6; more preferably, v is 2, 4 or 6; most preferably, v is 2.

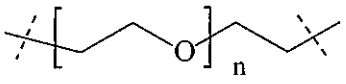
20. The pharmaceutical composition for use of any one of claims 12 to 19, wherein B is of formula (a-xiv).

21. The pharmaceutical composition for use of any one of claims 12 to 20, wherein A^0 is



22. The pharmaceutical composition for use of any one of claims 12 to 21, wherein x1 and x2 are 0.

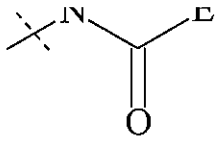
23. The pharmaceutical composition for use of any one of claims 12 to 22, wherein P has the structure of formula (c-i):



(c-i),

wherein n ranges from 6 to 900, more preferably n ranges from 20 to 700 and most preferably n ranges from 20 to 250.

24. The pharmaceutical composition for use of any one of claims 12 to 23, wherein the moiety – A^2 – Hyp^1 is a moiety of the formula



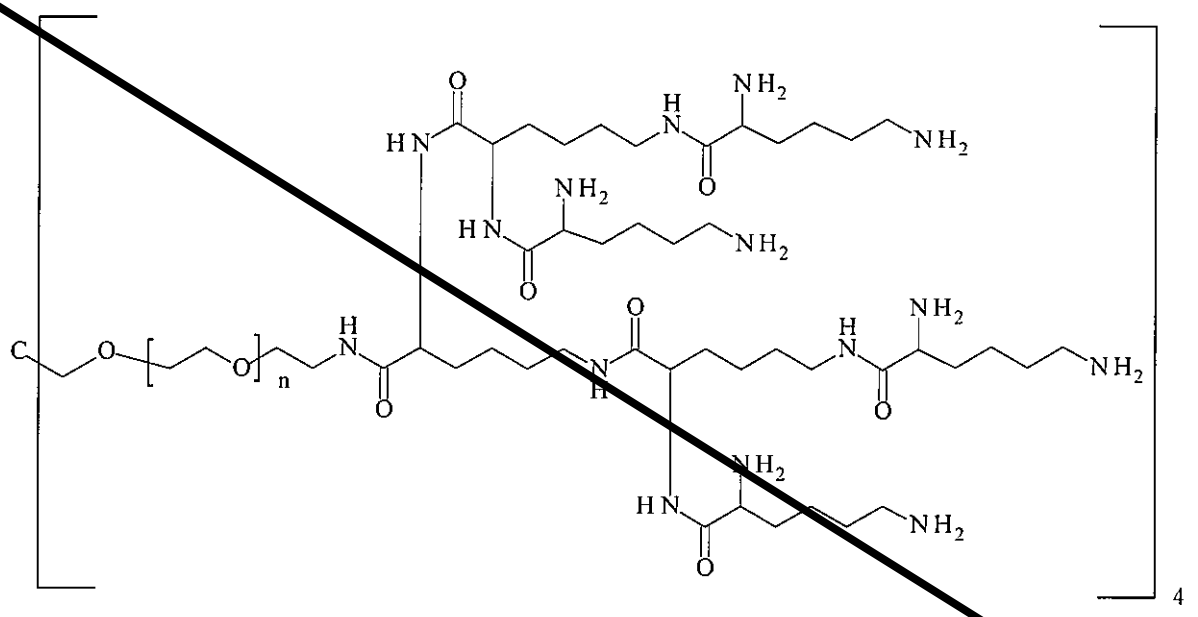
,

wherein

the dashed line indicates attachment to P; and

E^1 is selected from formulas (e-i) to (e-ix).

25. The pharmaceutical composition for use of any one of claims 12 to 24, wherein the backbone reagent has the following formula:

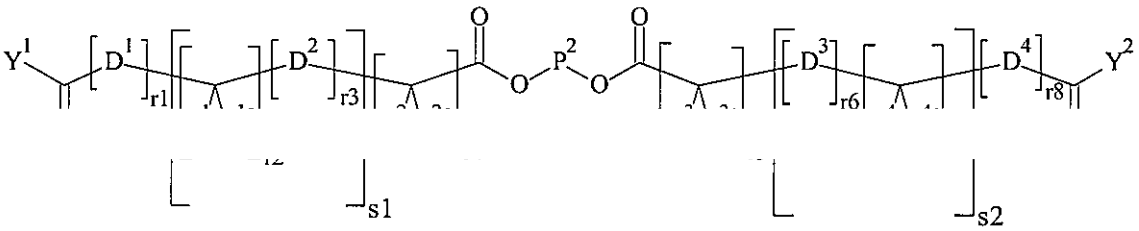


wherein

n ranges from 10 to 40, preferably from 10 to 30, more preferably from 10 to 20.

26. The pharmaceutical composition for use of any one of claims 12 to 25, wherein the backbone reagent is present in the form of its acidic salt.

27. The pharmaceutical composition for use of any one of claims 12 to 26, wherein the crosslinker reagent is a compound of formula (V):



(V),

wherein

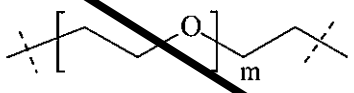
D^1, D^2, D^3 and D^4 are identical or different and each is independently of the others selected from the group comprising O, NR^5,S and CR^5R^{5a};

R^1, R^{1a}, R^2, R^2, R^3, R^{3a}, R^4, R^{4a}, R^5 and R^{5a} are identical or different and each is independently of the others selected from the group comprising H and C_{1-6} alkyl; optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^3/R^{3a}, R^4/R^{4a}, R^1/R^2, R^3/R^4, R^{1a}/R^{2a}, and R^{3a}/R^{4a} form a chemical bond or are joined together with the atom to which they are attached to form a C_{3-8} cycloalkyl or to form a ring A or are joined together

with the atom to which they are attached to form a 4- to 7-membered heterocyclyl or 8- to 11-membered heterobicyclyl or adamantyl;

A is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl and tetralinyl;

P^2 is



m ranges from 120 to 920, preferably from 120 to 460 and more preferably from 120 to 230;

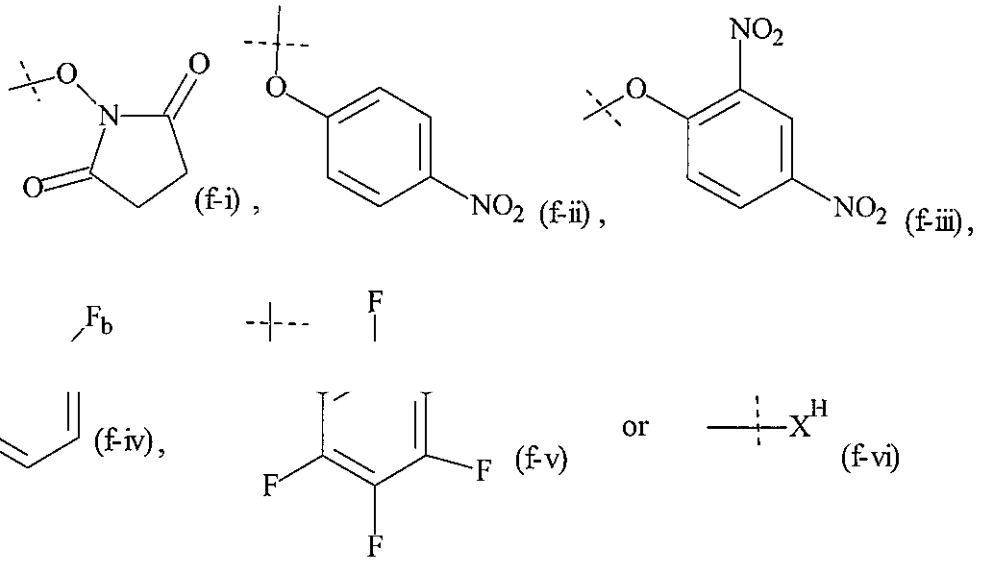
r1, r2, r7, r8 are independently 0 or 1;

r3, r6 are independently 0, 1, 2, 3, or 4;

r4, r5 are independently 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

s1, s2 are independently 1, 2, 3, 4, 5 or 6;

Y^1, Y^2 are identical or different and each is independently of the other selected from formulas (f-i) to (f-vi):



(f-i), (f-ii), (f-iii), (f-iv), (f-v) or (f-vi)

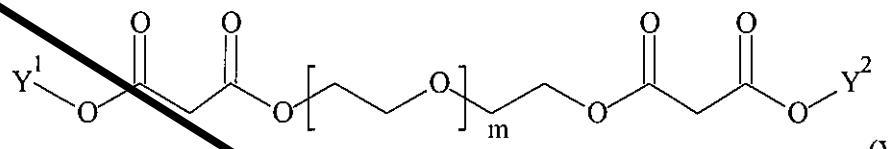
wherein

the dashed lines indicate attachment to the rest of the molecule,

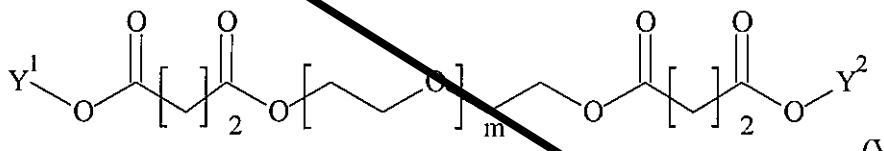
b is 1, 2, 3 or 4

X^H is Cl, Br, I, or F.

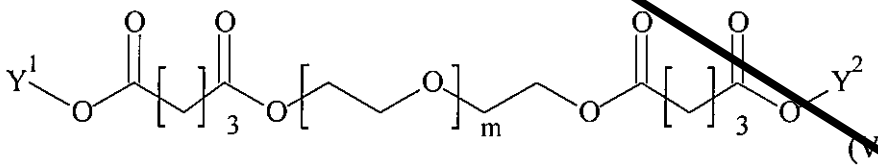
28. The pharmaceutical composition for use of any one of claims 12 to 27, wherein the crosslinker reagent is of formula (V-1) to (V-53):



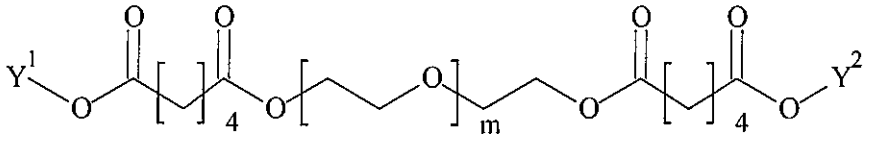
(V-1),



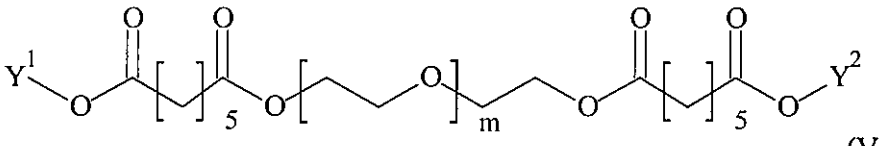
(V-2),



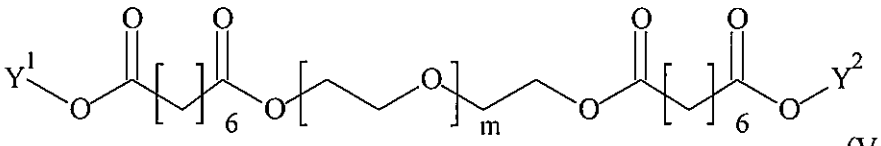
(V-3),



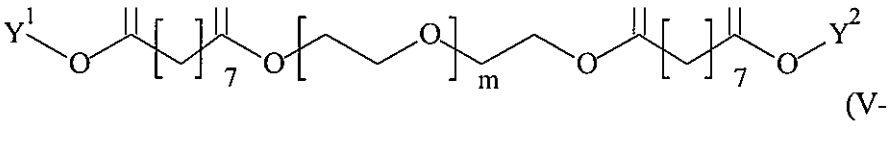
(V-4),



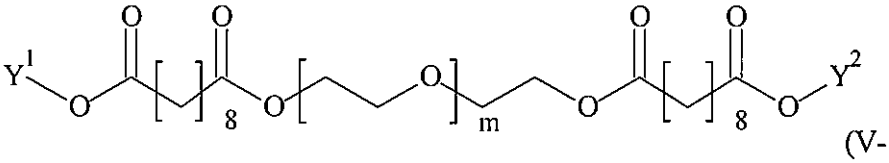
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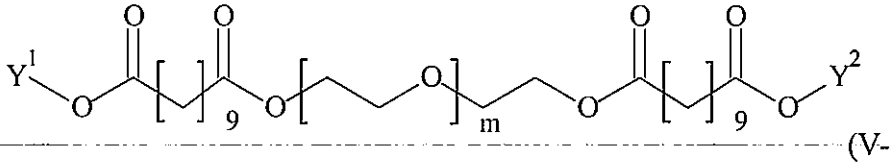
(V-6),



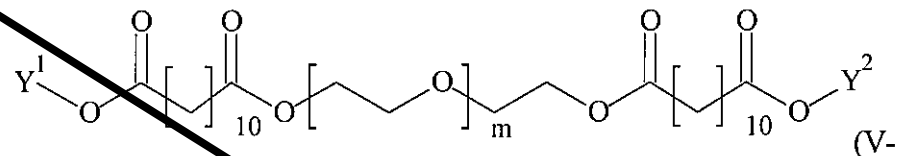
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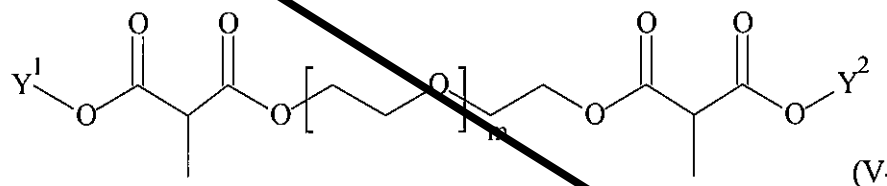
(V-8),



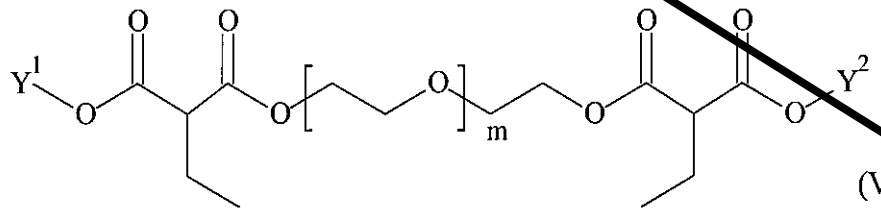
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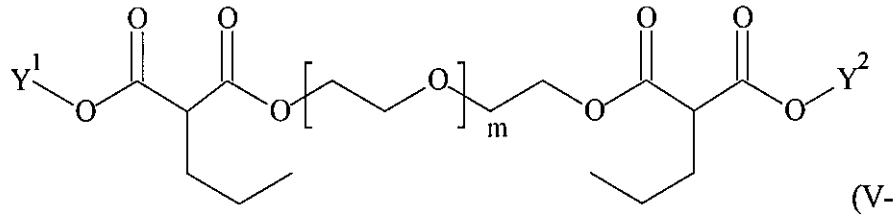
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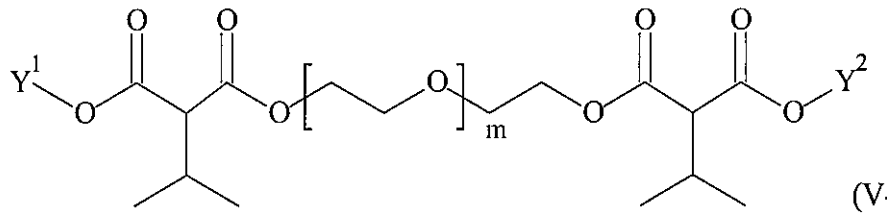
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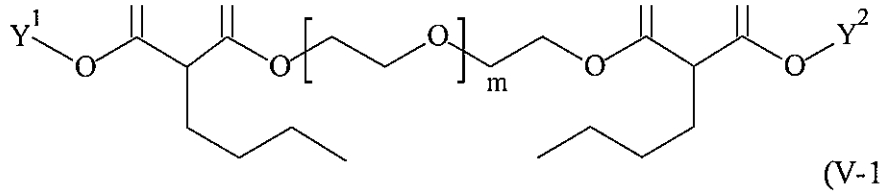
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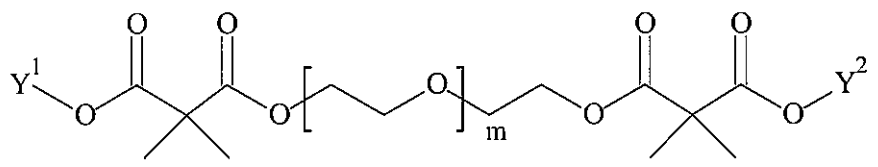
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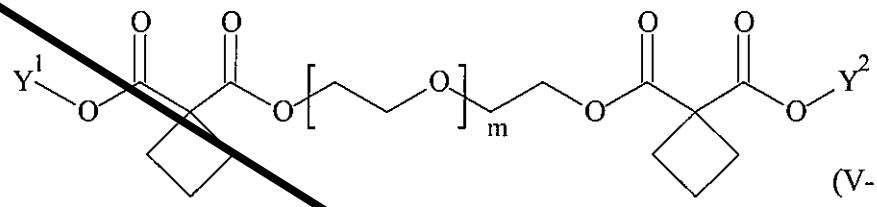
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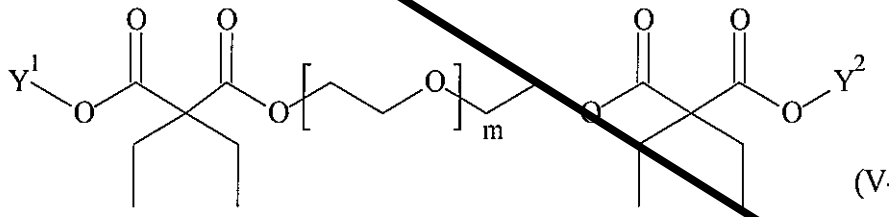
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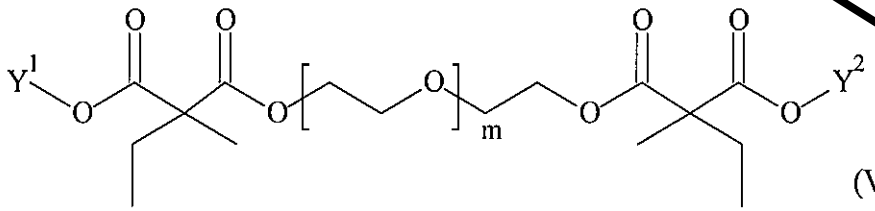
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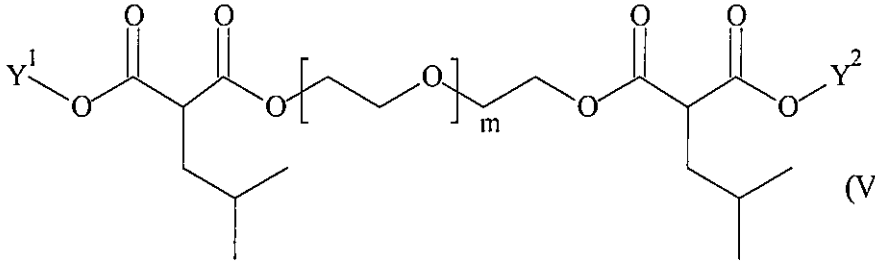
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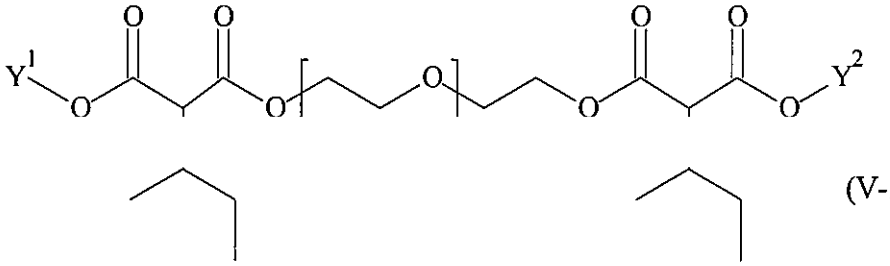
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(V-19)

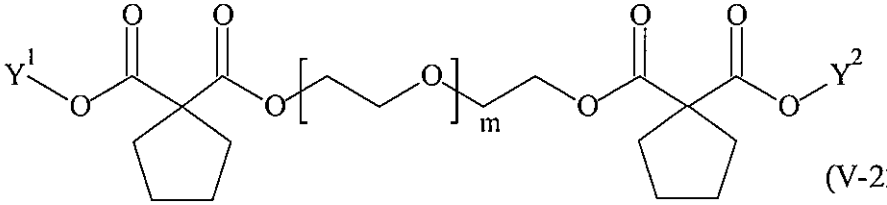


(V20)

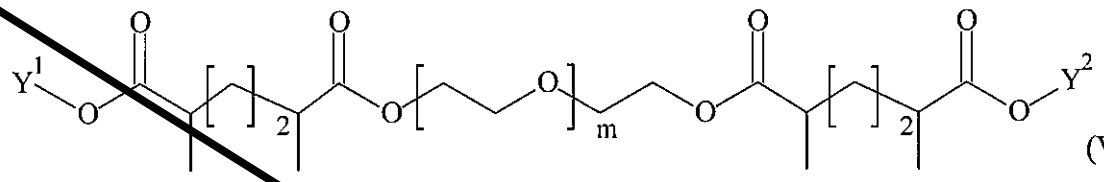


(V-21)

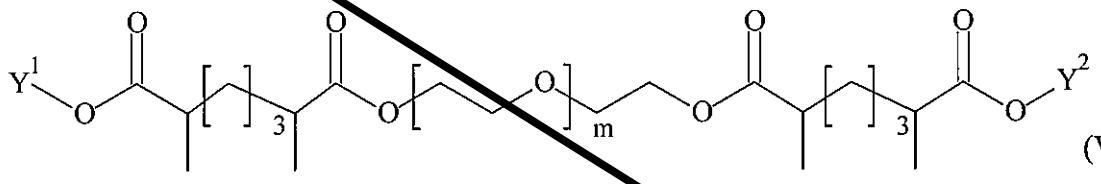
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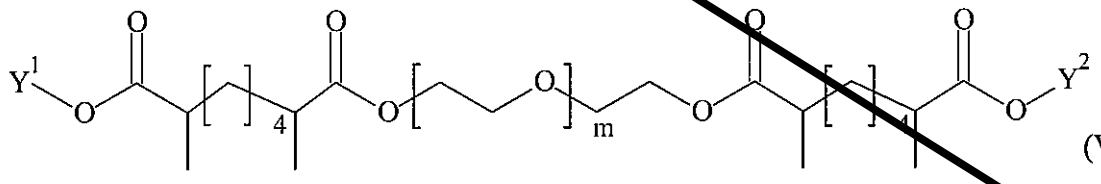
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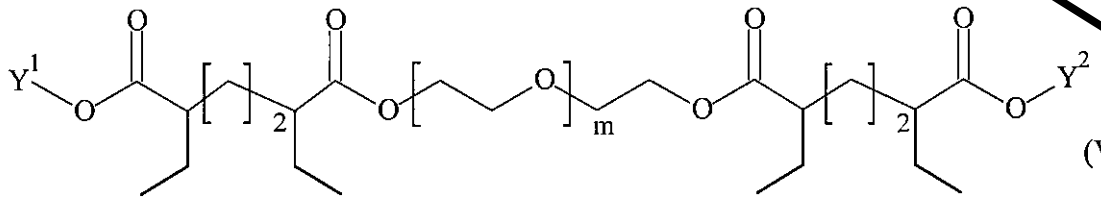
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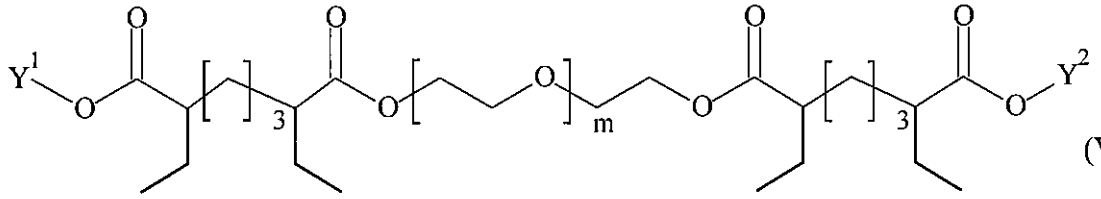
(V-24)



(V-25)



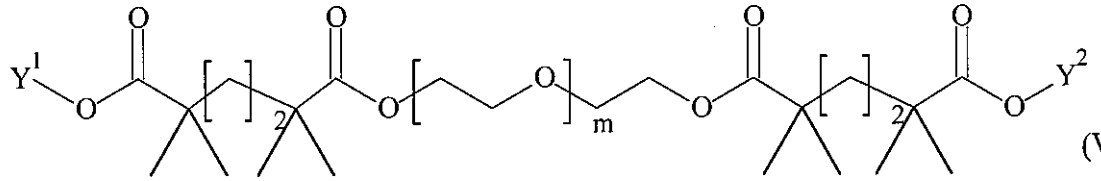
(V-26)



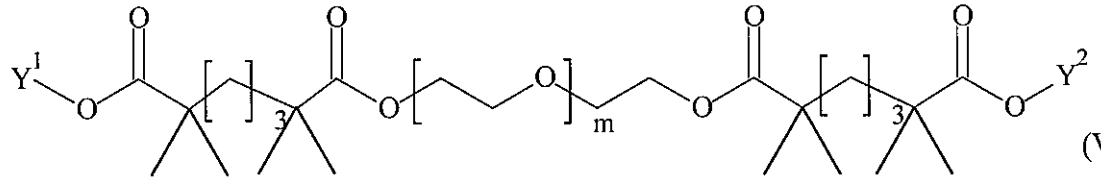
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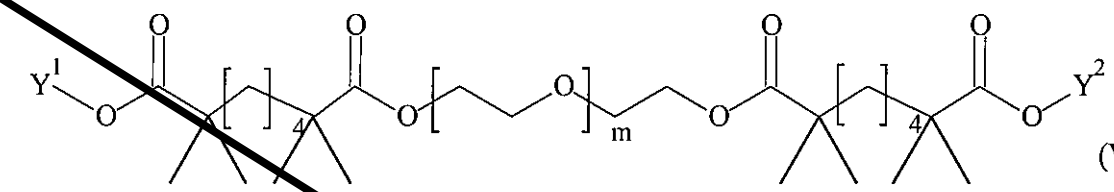
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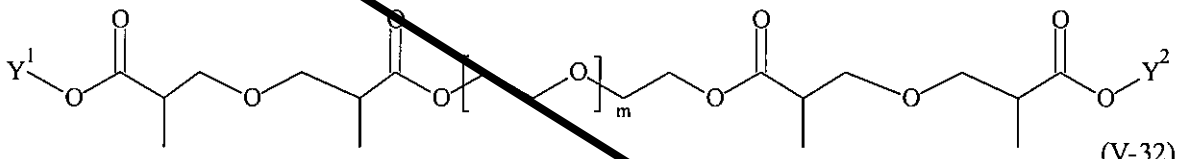
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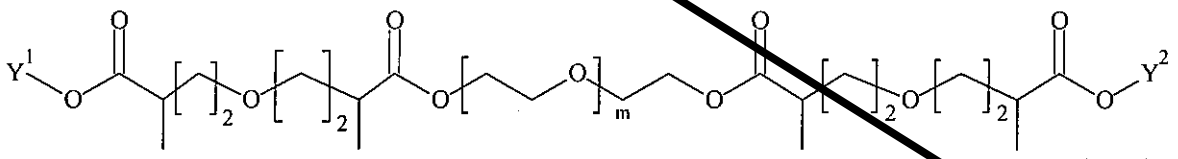
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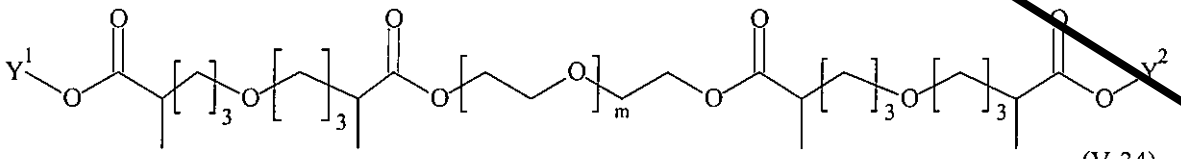
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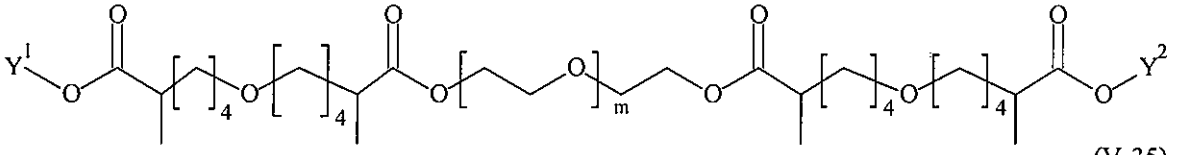
(V-32)



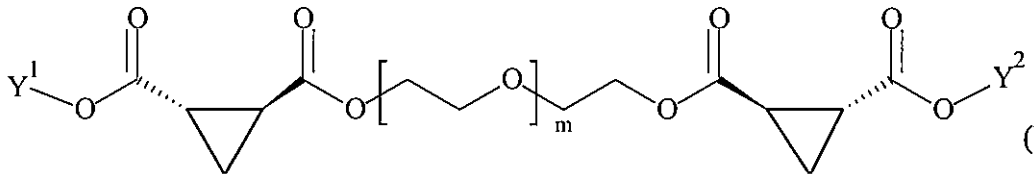
(V-33)



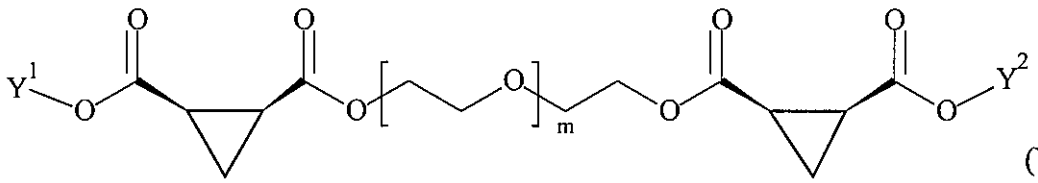
(V-34)



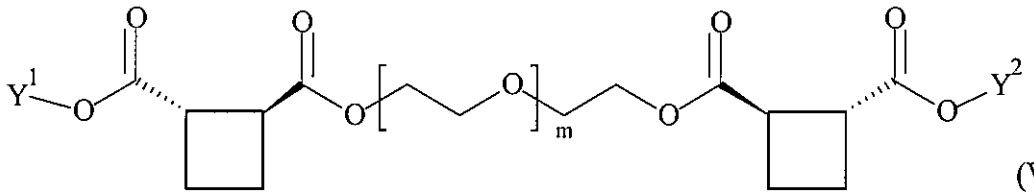
(V-35)



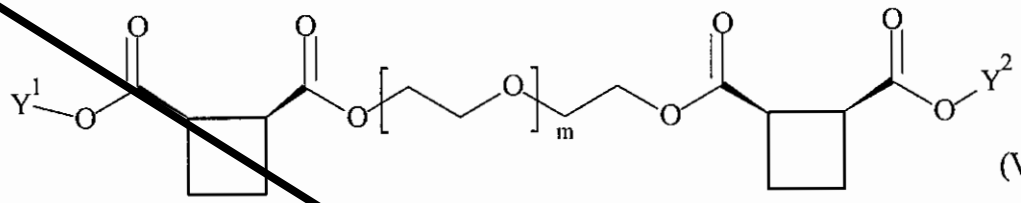
(V-36)



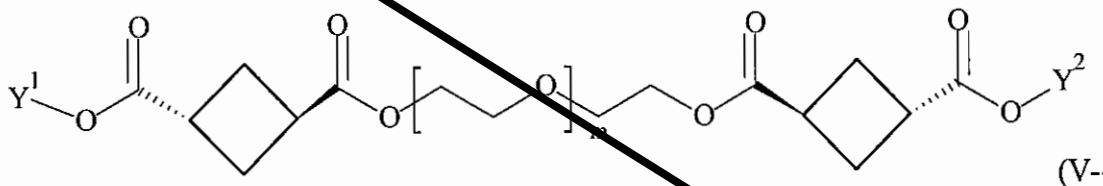
(V-37)



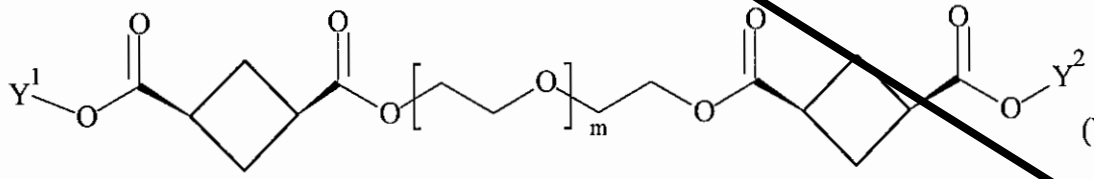
(V-38)



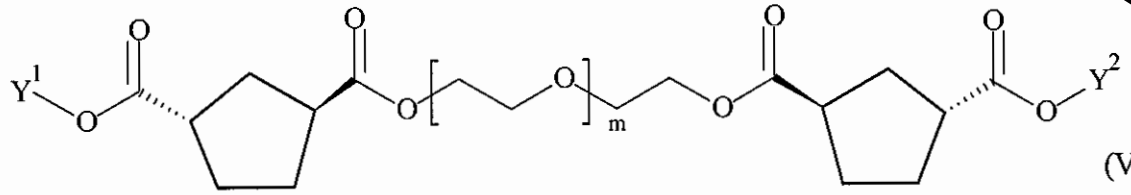
(V-39)



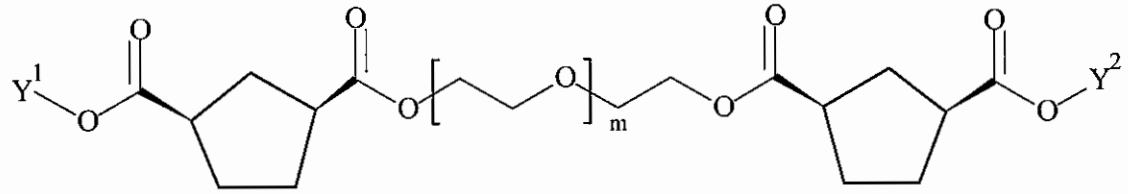
(V-40)



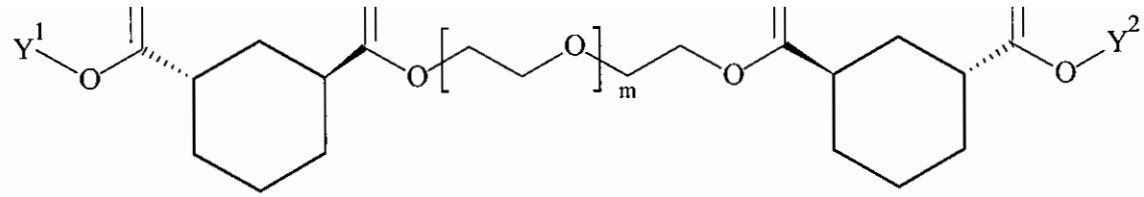
(V-41)



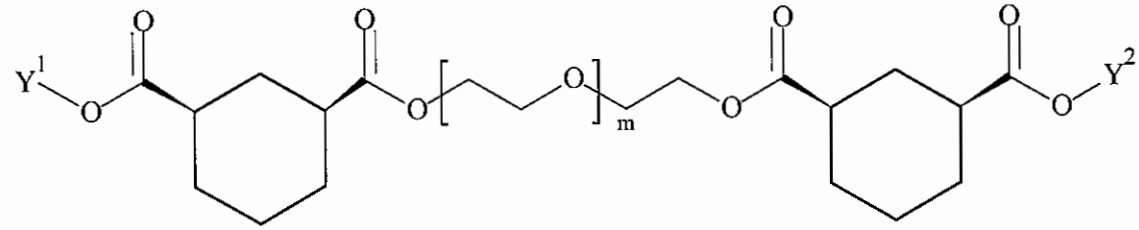
(V-42)



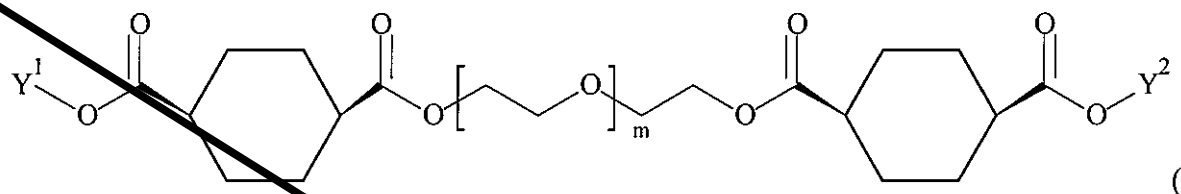
(V-43)



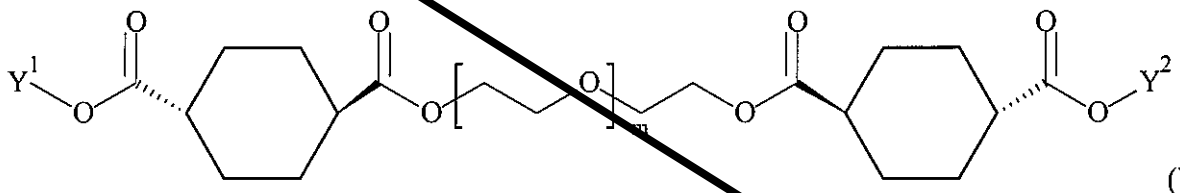
(V-43)



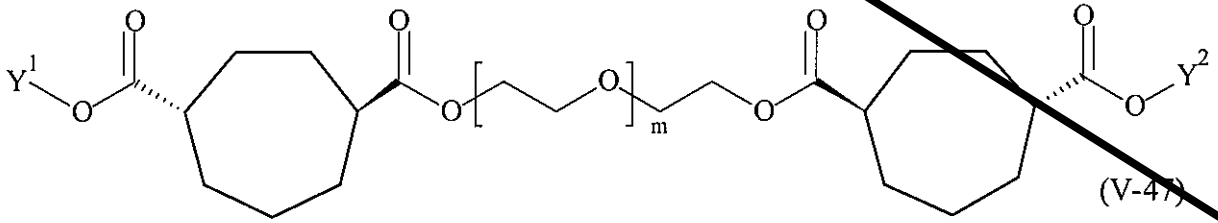
(V-44)



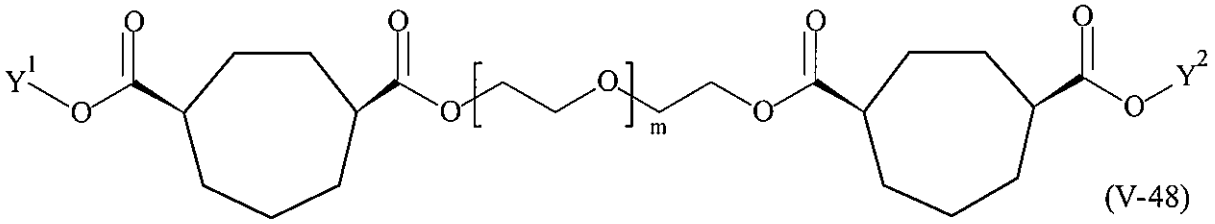
(V-45)



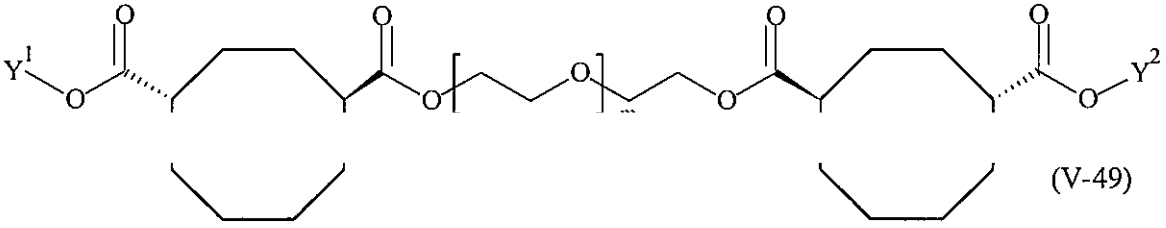
(V-46)



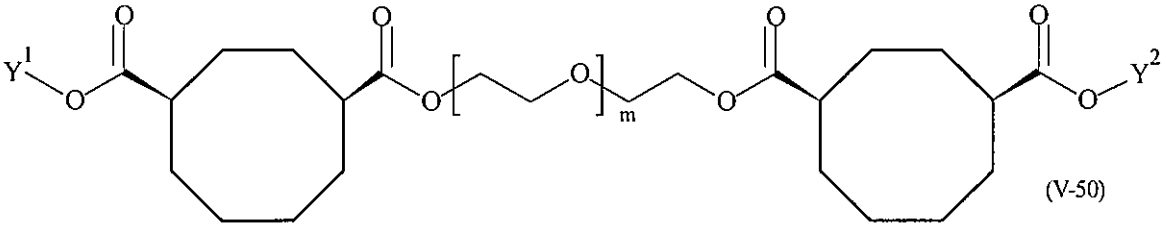
(V-47)



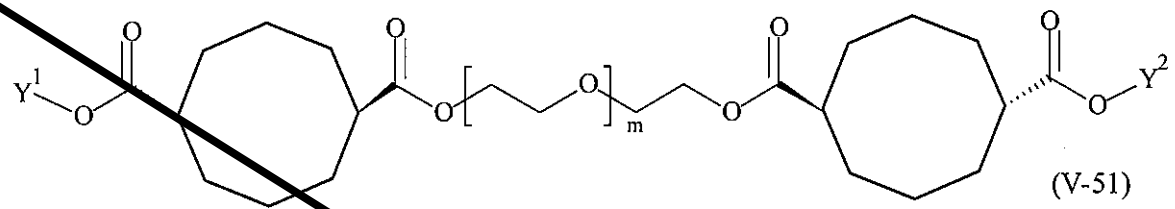
(V-48)



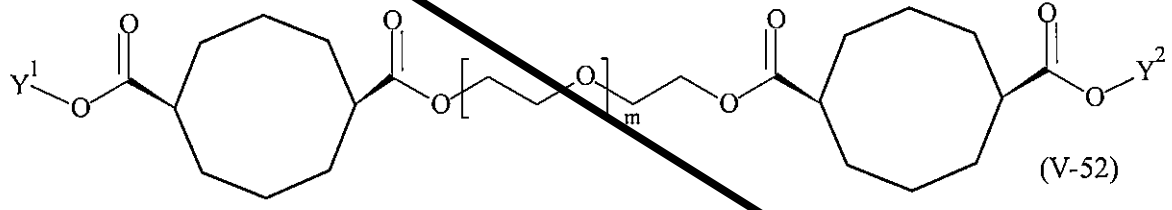
(V-49)



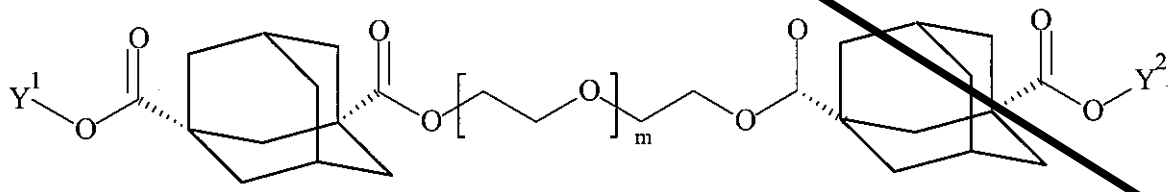
(V-50)



(V-51)



(V-52)



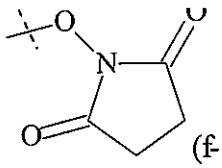
(V-53)

wherein

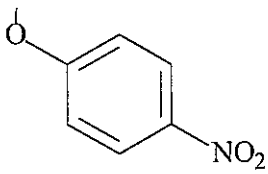
each crosslinker reagent may be in the form of its racemic mixture, where applicable; and

m ranges from 120 to 920, preferably from 120 to 460 and more preferably from 120 to 230;

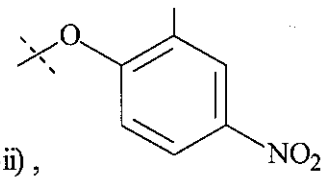
Y^1, Y^2 are identical or different and each is independently of the other selected from formulas (f-i) to (f-vi):



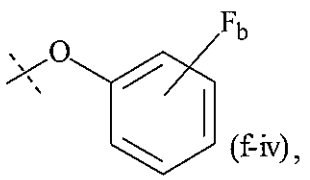
(f-i),



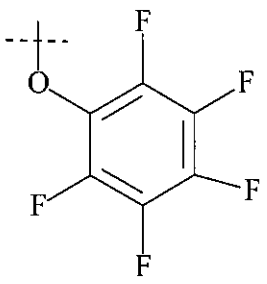
(f-ii),



(f-iii),

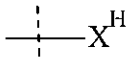


(f-iv),



(f-v)

or



(f-vi)

wherein

the dashed lines indicate attachment to the rest of the molecule,

b is 1, 2, 3 or 4

X^H is Cl, Br, J, or F.

29. The pharmaceutical composition for use of any one of claims 12 to 28, wherein the hydrogel obtained from the polymerization is a shaped article.

30. The pharmaceutical composition for use of any one of claims 12 to 29, wherein the hydrogel is in the form of microparticular beads having a diameter of 1 to 500 micrometer.

31. The pharmaceutical composition for use of any one of claims 1 to 30, wherein the hydrogel-linked prodrug comprises a biologically active moiety selected from the group consisting of anesthetics and analgesics, antiallergenics, antihistamines, anti-inflammatory agents, anti-cancer agents, antibiotics, antiinfectives, antibacterials, anti-fungal agents, anti-viral agents, cell transport/mobility impending agents, antiglaucoma drugs, antihypertensives, decongestants, immunological response modifiers, immunosuppresive agents, peptides and proteins, steroidal compounds (steroids), low solubility steroids, carbonic anhydrize inhibitors, diagnostic agents, antiapoptosis agents, gene therapy agents, sequestering agents, reductants, antipermeability agents, antisense compounds, antiproliferative agents, antibodies and antibody conjugates, bloodflow enhancers, antiparasitic agents, non-steroidal anti inflammatory agents, nutrients and vitamins, enzyme inhibitors, antioxidants, anticataract drugs, aldose reductase inhibitors, cytoprotectants, cytokines, cytokine inhibitors, and cytokine protectants, UV blockers, mast cell stabilizers, and anti neovascular agents such as antiangiogenic agents like matrix metalloprotease inhibitors and Vascular endothelial growth factor (VEGF) modulators, neuroprotectants, miotics and anti-cholinesterase, mydriatics, artificial tear/dry eye therapies, anti-TNFα, IL-1 receptor antagonists, protein kinase C-β inhibitors, somatostatin analogs and sympathomimetics.

32. An ophthalmic delivery device comprising the pharmaceutical composition of any one of claims 1 to 31.

Claims

1. Use of a pharmaceutical composition comprising a hydrogel-linked prodrug in the manufacture of a medicament for the prevention, diagnosis and/or treatment of an ocular condition, wherein the hydrogel-linked prodrug comprises a biologically active moiety which is connected to a reversible prodrug linker moiety from which the biologically active moiety is released in the form of its corresponding drug, and which reversible prodrug moiety is connected to a hydrogel carrier and the hydrogel is a hydrogel obtainable by a process comprising the steps of:

(a) providing a mixture comprising

(a-i) at least one backbone reagent, wherein the at least one backbone reagent has a molecular weight ranging from 1 to 100 kDa, and comprises at least three amines (-NH_2 and/or -NH-);

(a-ii) at least one crosslinker reagent, wherein the at least one crosslinker reagent has a molecular weight ranging from 6 to 40 kDa, the at least one crosslinker reagent comprising

(i) at least two carbonyloxy groups (–(C=O)–O– or –O–(C=O)–), and additionally

(ii) at least two activated functional end groups selected from the group consisting of activated ester groups, activated carbamate groups, activated carbonate groups and activated thiocarbonate groups,

and being PEG-based comprising at least 70% PEG; and

(a-iii) a first solvent and at least a second solvent, which second solvent is immiscible in the first solvent,

in a weight ratio of the at least one backbone reagent to the at least one crosslinker reagent ranging from 1:99 to 99:1;

(b) polymerizing the mixture of step (a) in a suspension polymerization to a hydrogel; and

(c) optionally working-up the hydrogel..

2. The use of claim 1, wherein the medicament for use for intraocular injection.

3. The use of claim 1 or 2, wherein the ocular condition is an anterior ocular condition or posterior ocular condition.

4. The use of claim 3, wherein the anterior ocular condition is selected from the group comprising aphakia, pseudophakia, astigmatism, blepharospasm, cataract, conjunctival diseases, conjunctivitis, corneal diseases, corneal ulcer, dry eye syndromes, eyelid diseases, lacrimal apparatus diseases, lacrimal duct obstruction, myopia, presbyopia, pupil disorders, refractive disorders, glaucoma and strabismus.

5. The use of claim 3, wherein the posterior ocular condition is selected from the group comprising acute macular neuroretinopathy; Behcet's disease; choroidal neovascularization; diabetic uveitis; histoplasmosis; infections, such as fungal or viral-caused infections; macular degeneration, such as acute macular degeneration, non-exudative age related macular degeneration and exudative age related macular degeneration; edema, (such as macular edema, cystoid macular edema and diabetic macular edema; multifocal choroiditis; ocular trauma which affects a posterior ocular site or location; ocular tumors; retinal disorders, such as central retinal vein occlusion, diabetic retinopathy (including proliferative diabetic retinopathy), proliferative vitreoretinopathy (PVR), retinal arterial occlusive disease, retinal detachment, uveitic retinal disease; sympathetic opthalmia; Vogt Koyanagi-Harada (VKH) syndrome; uveal diffusion; a posterior ocular condition caused by or influenced by an ocular laser treatment; posterior ocular conditions caused by or influenced by a photodynamic therapy, photocoagulation, radiation retinopathy, epiretinal membrane disorders, branch retinal vein occlusion, anterior ischemic optic neuropathy, nonretinopathy diabetic retinal dysfunction, retinitis pigmentosa, and glaucoma.

6. The use of any one of claims 1 to 5, wherein the medicament is contained in a container suited for engagement with an injection device.

7. The use of any one of claims 1 to 6, wherein the hydrogel-linked prodrug is a shaped article.

8. The use of claim 7, wherein the hydrogel-linked prodrug is bead-shaped.

9. The use of claim 8, wherein the beads have a diameter of 1 to 1000 µm.

10. The use of claim 8 or 9, wherein the beads have a diameter of 1 to 500 micrometer.

11. The use of any one of claims 1 to 10, wherein the mixture of step (a) further comprises a detergent.

12. The use of any one of claims 1 to 11, wherein the polymerization in step (b) is initiated by adding a base.

13. The use of any one of claims 1 to 12, wherein the mixture of step (a) is an emulsion.

14. The use of any one of claims 1 to 13, wherein the at least one backbone reagent is selected from the group consisting of

a compound of formula (I)

$$B(-(A^0)_{x1}-(SP)_{x2}-A^1-P-A^2-Hyp^1)_x \quad (I),$$

wherein

B is a branching core,

SP is a spacer moiety selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl,

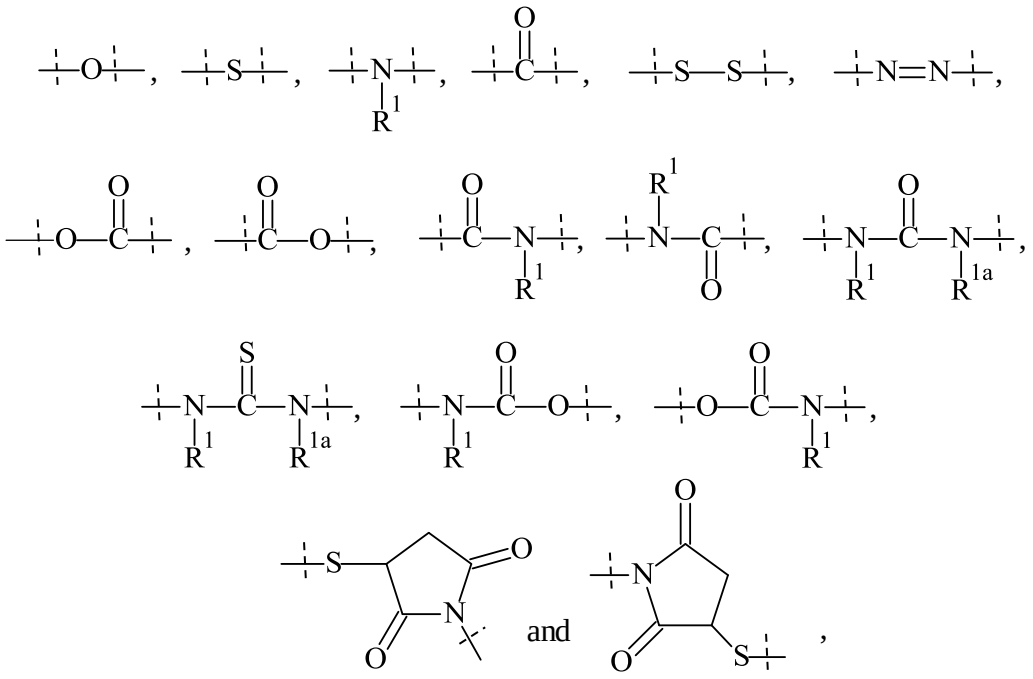
P is a PEG-based polymeric chain comprising at least 80% PEG, preferably at least 85% PEG, more preferably at least 90% PEG and most preferably at least 95% PEG,

Hyp^1 is a moiety comprising an amine ($-NH_2$ and/or -NH-) or a polyamine comprising at least two amines ($-NH_2$ and/or -NH-),

x is an integer from 3 to 16,

x1, x2 are independently of each other 0 or 1, provided that x1 is 0, if x2 is 0,

A^0, A^1, A^2 are independently of each other selected from the group consisting of



wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

a compound of formula (II)

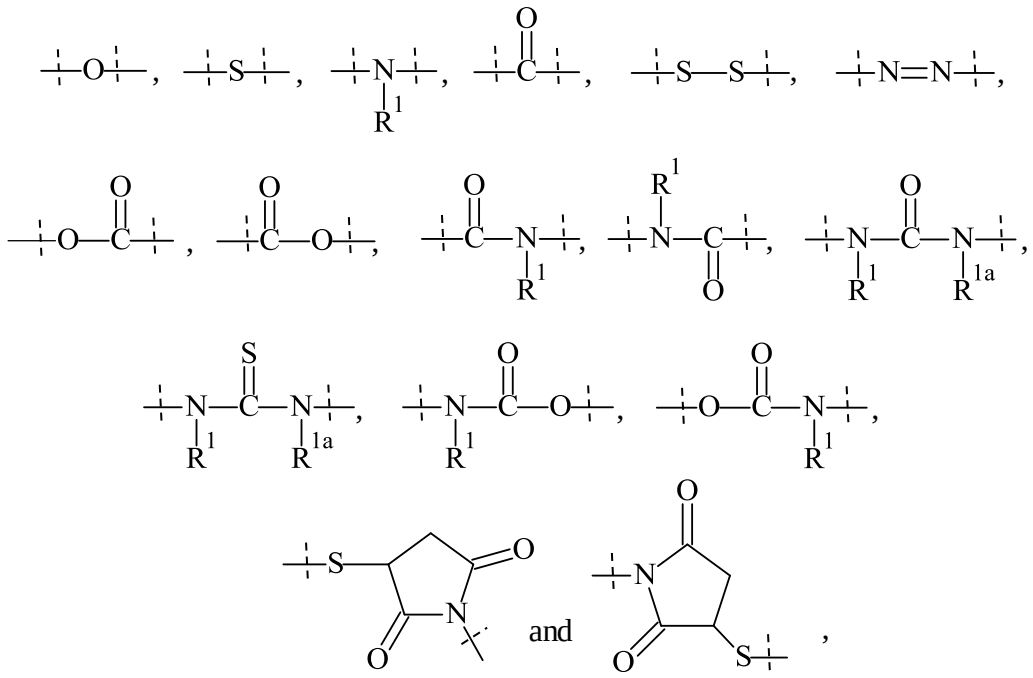
$$Hyp^2 – A^3 – P – A^4 – Hyp^3 \quad (II),$$

wherein

P is defined as above in the compound of formula (I),

Hyp^2, Hyp^3 are independently of each other a polyamine comprising at least two amines ($-NH_2$ and/or -NH-), and

A^3 and A^4 are independently selected from the group consisting of



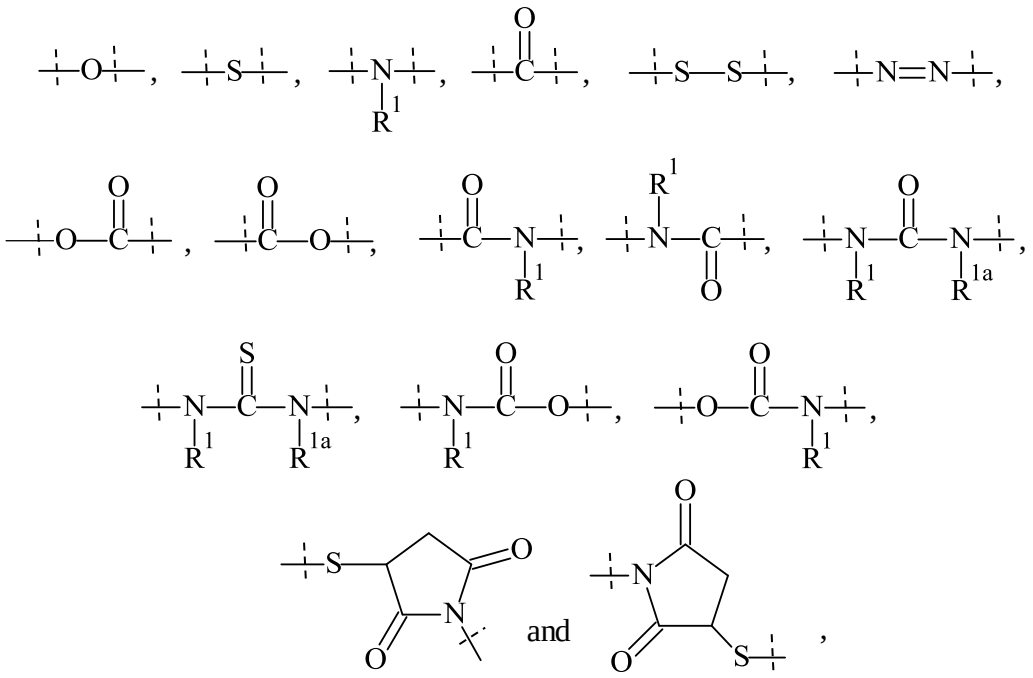
wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

a compound of formula (III)

$$P^1 – A^5 – Hyp^4 \qquad \text{(III)},$$

wherein

P^1	is a PEG-based polymeric chain comprising at least 80% PEG, preferably at least 85% PEG, more preferably at least 90% PEG and most preferably at least 95% PEG,
Hyp^4	is a polyamine comprising at least three amines ($-NH_2$ and/or -NH), and
A^5	is selected from the group consisting of



wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl;

and

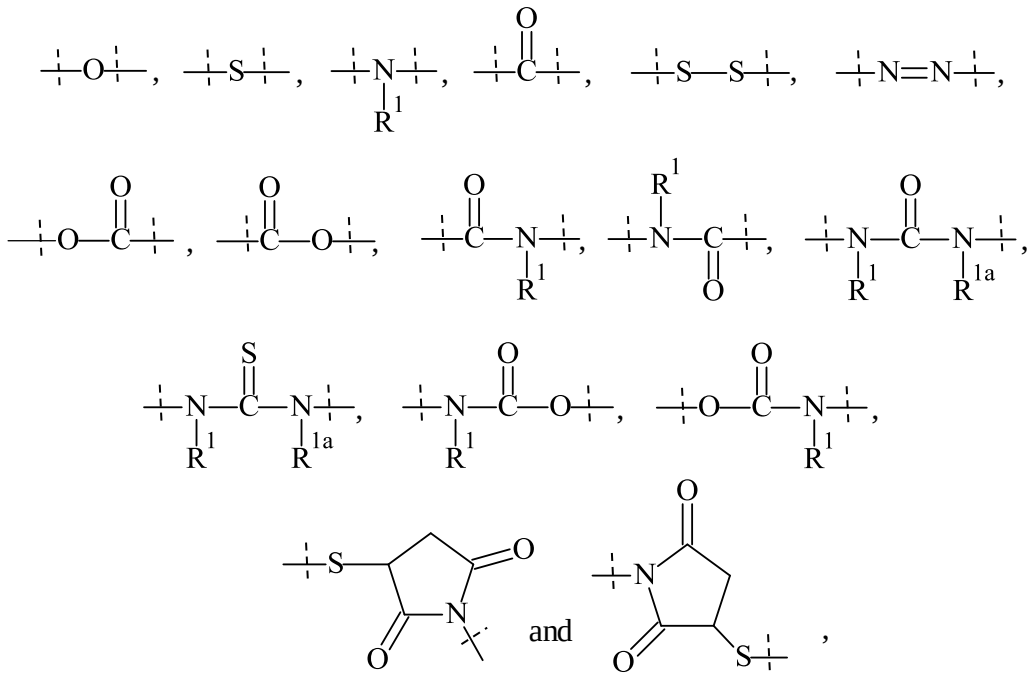
a compound of formula (IV),

$T^1 – A^6 – Hyp^5$ (IV),

wherein

Hyp^5 is a polyamine comprising at least three amines ($-NH_2$ and/or -NH), and

A^6 is selected from the group consisting of

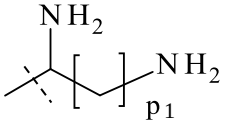


wherein R^1 and R^{1a} are independently of each other selected from H and C_{1-6} alkyl; and

T^1 is selected from the group consisting of C_{1-50} alkyl, C_{2-50} alkenyl or C_{2-50} alkynyl, which fragment is optionally interrupted by one or more group(s) selected from -NH-, -N(C_{1-4} alkyl)-, -O-, -S-, -C(O)-, -C(O)NH-, -C(O)N(C_{1-4} alkyl)-, -O-C(O)-, -S(O)-, -$S(O)_2$-, 4- to 7-membered heterocyclyl, phenyl or naphthyl.

15. The use of claim 14, wherein Hyp^1, Hyp^2, Hyp^3, Hyp^4, and Hyp^5 are selected from the group consisting of

a moiety of formula (e-i)



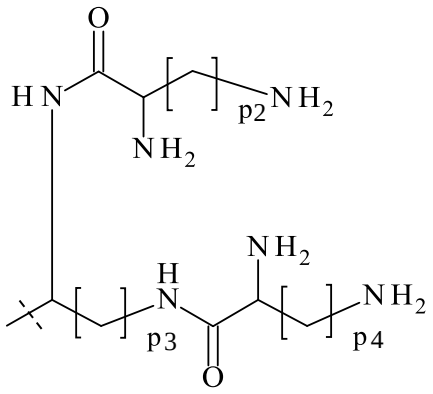
(e-i)

wherein

p1 is an integer from 1 to 5, preferably p1 is 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I) and to A^3 or A^4 if the backbone reagent has the structure of formula (II);

a moiety of formula (e-ii)



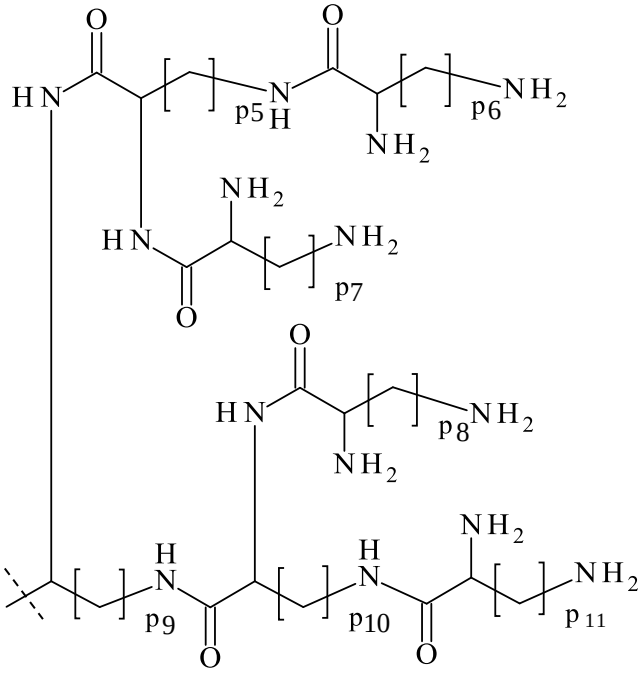
(e-ii)

wherein

p2, p3 and p4 are identical or different and each is independently of the others an integer from 1 to 5, preferably p2, p3 and p4 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-iii)



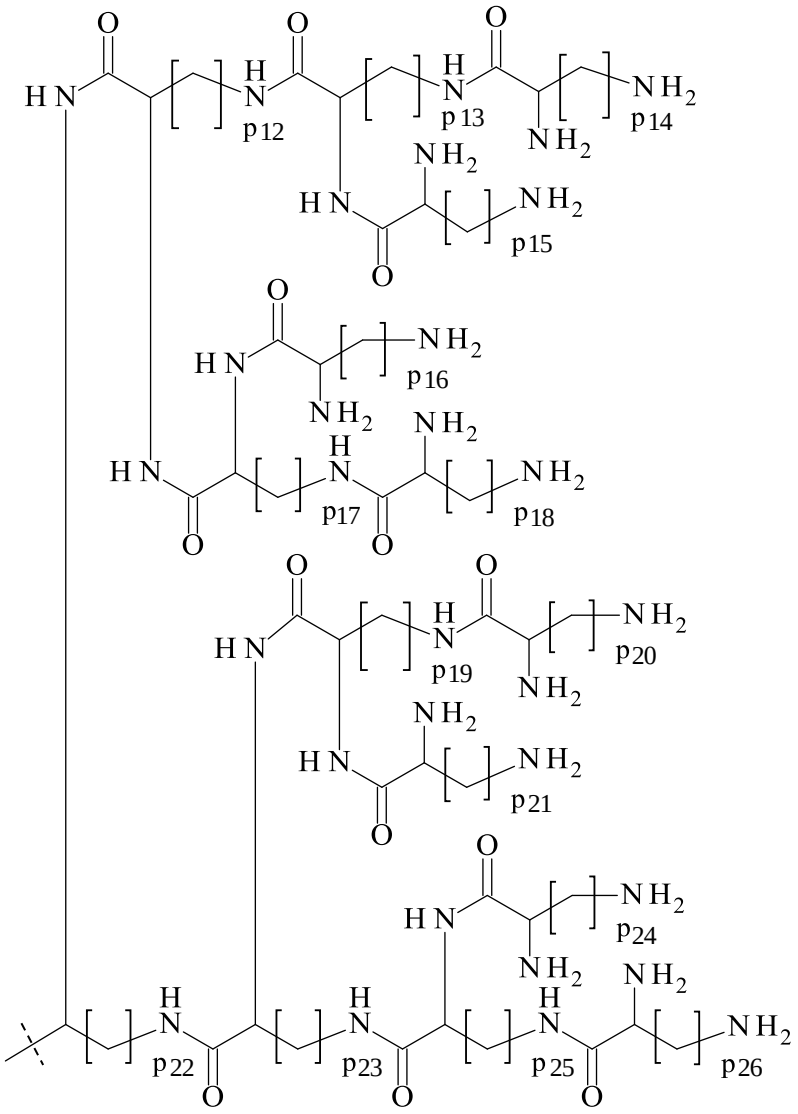
(e-iii)

wherein

p5 to p11 are identical or different and each is independently of the others an integer from 1 to 5, preferably p5 to p11 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent is of formula (I), to A^3 or A^4 if the backbone reagent is of formula (II), to A^5 if the backbone reagent is of formula (III) and to A^6 if the backbone reagent is of formula (IV);

a moiety of formula (e-iv)



(e-iv)

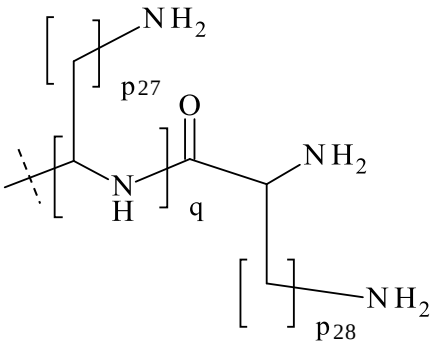
wherein

p12 to p26 are identical or different and each is independently of the others an integer from 1 to 5, preferably p12 to p26 are 4, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if

the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-v)



(e-v)

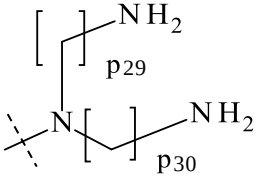
wherein

p27 and p28 are identical or different and each is independently of the other an integer from 1 to 5, preferably p27 and p28 are 4,

q is an integer from 1 to 8, preferably q is 2 or 6 and most preferably 1 is 6, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-vi)



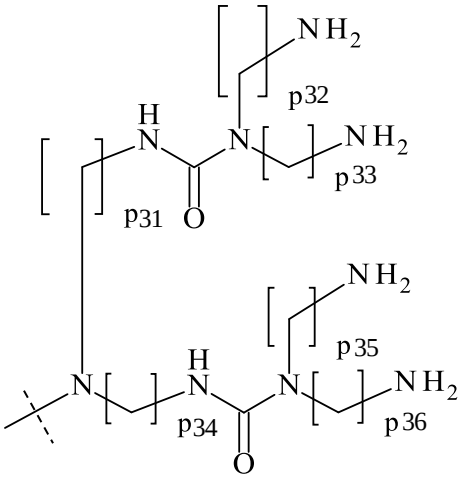
(e-vi)

wherein

p29 and p30 are identical or different and each is independently of the other an integer from 2 to 5, preferably p29 and p30 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has the structure of formula (I), to A^3 or A^4 if the backbone reagent has the structure of formula (II), to A^5 if the backbone reagent has the structure of formula (III) and to A^6 if the backbone reagent has the structure of formula (IV);

a moiety of formula (e-vii)



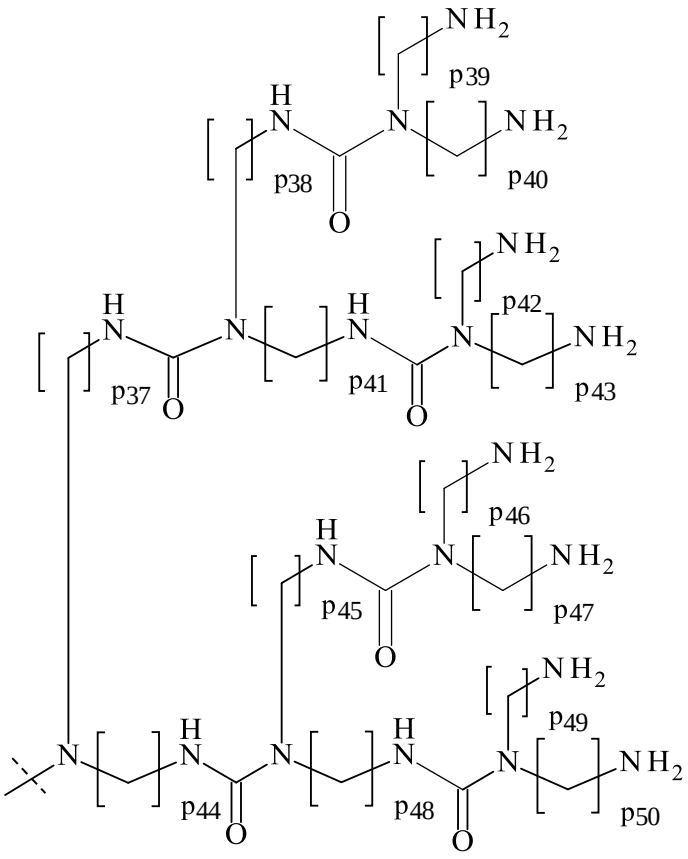
(e-vii)

wherein

p31 to p36 are identical or different and each is independently of the others an integer from 2 to 5, preferably p31 to p36 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV);

a moiety of formula (e-viii)



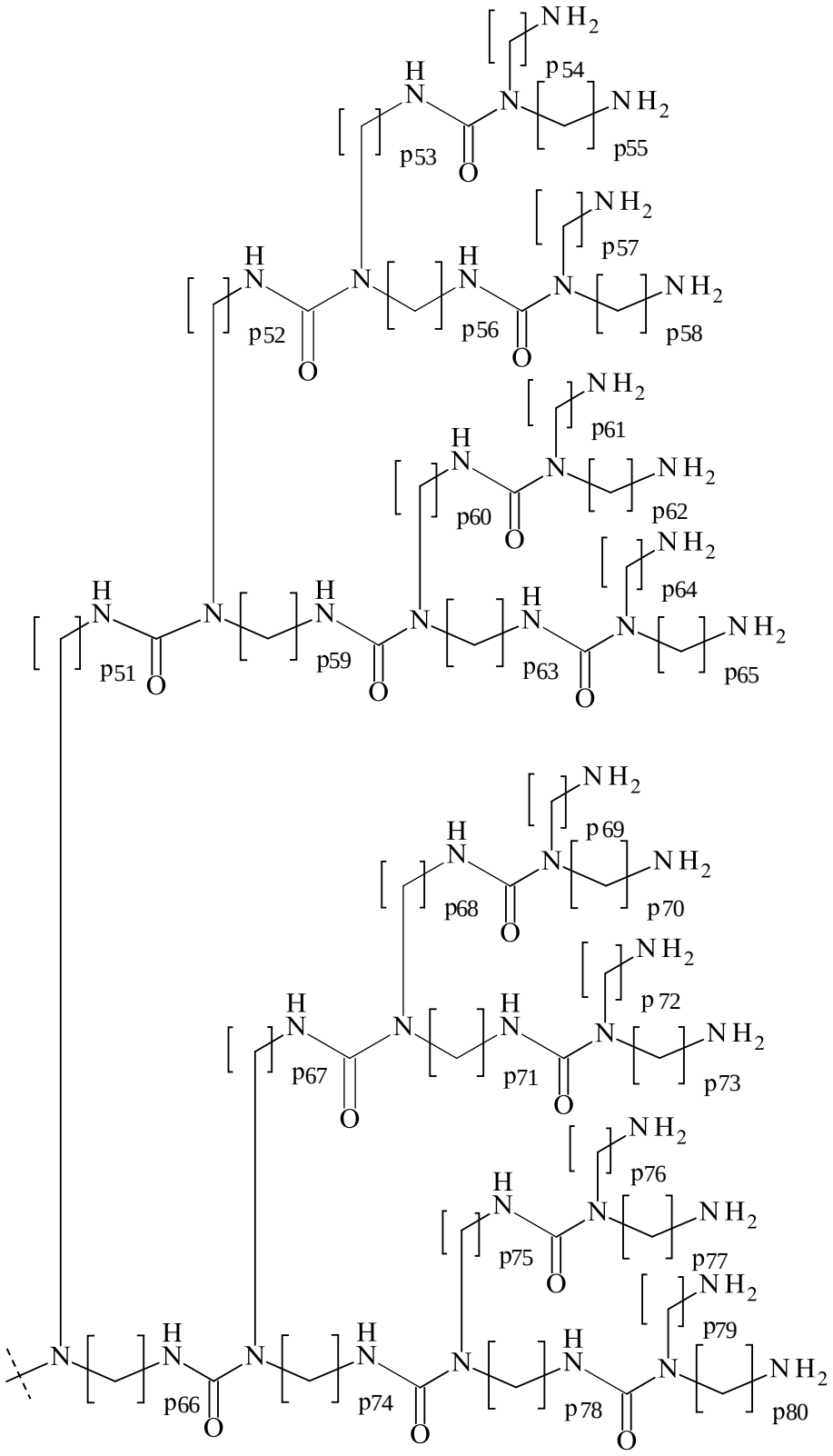
(e-viii)

wherein

p37 to p50 are identical or different and each is independently of the others an integer from 2 to 5, preferably p37 to p50 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV); and

a moiety of formula (e-ix):



(e-ix)

wherein

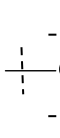
p51 to p80 are identical or different and each is independently of the others an integer from 2 to 5, preferably p51 to p80 are 3, and

the dashed line indicates attachment to A^2 if the backbone reagent has a structure of formula (I), to A^3 or A^4 if the backbone reagent has a structure of formula (II), to A^5 if the backbone reagent has a structure of formula (III) and to A^6 if the backbone reagent has a structure of formula (IV); and

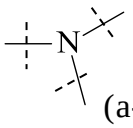
wherein the moieties (e-i) to (e-v) may at each chiral center be in either R- or S-configuration, preferably, all chiral centers of a moiety (e-i) to (e-v) are in the same configuration.

16. The use of claims 14 or 15, wherein the backbone reagent is a compound of formula (I).

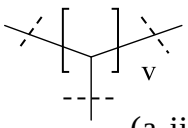
17. The use of any one of claims 14 to 16, wherein the branching core B is selected from the following structures:



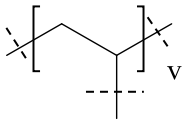
(a-i)



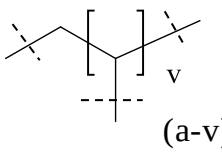
(a-ii)



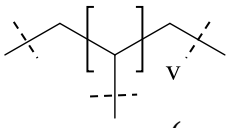
(a-iii)



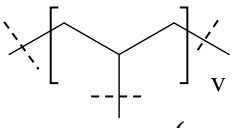
(a-iv)



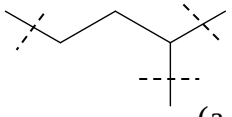
(a-v)

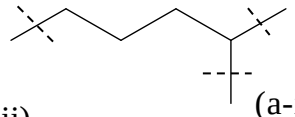


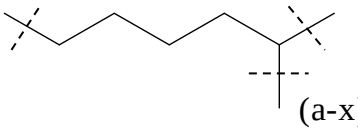
(a-vi)

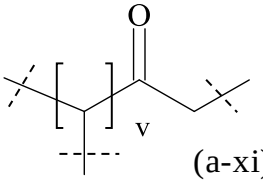


(a-vii)

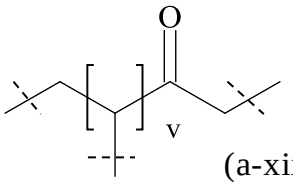

(a-viii)


(a-ix)

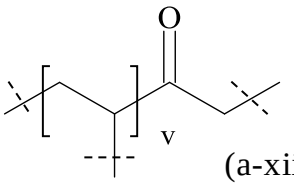

(a-x)



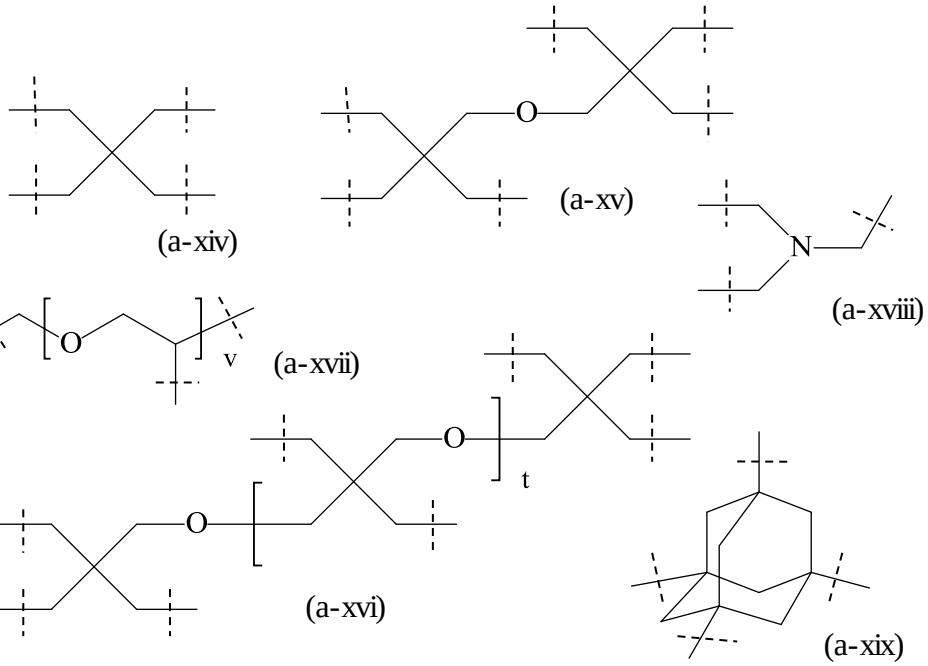
(a-xi)

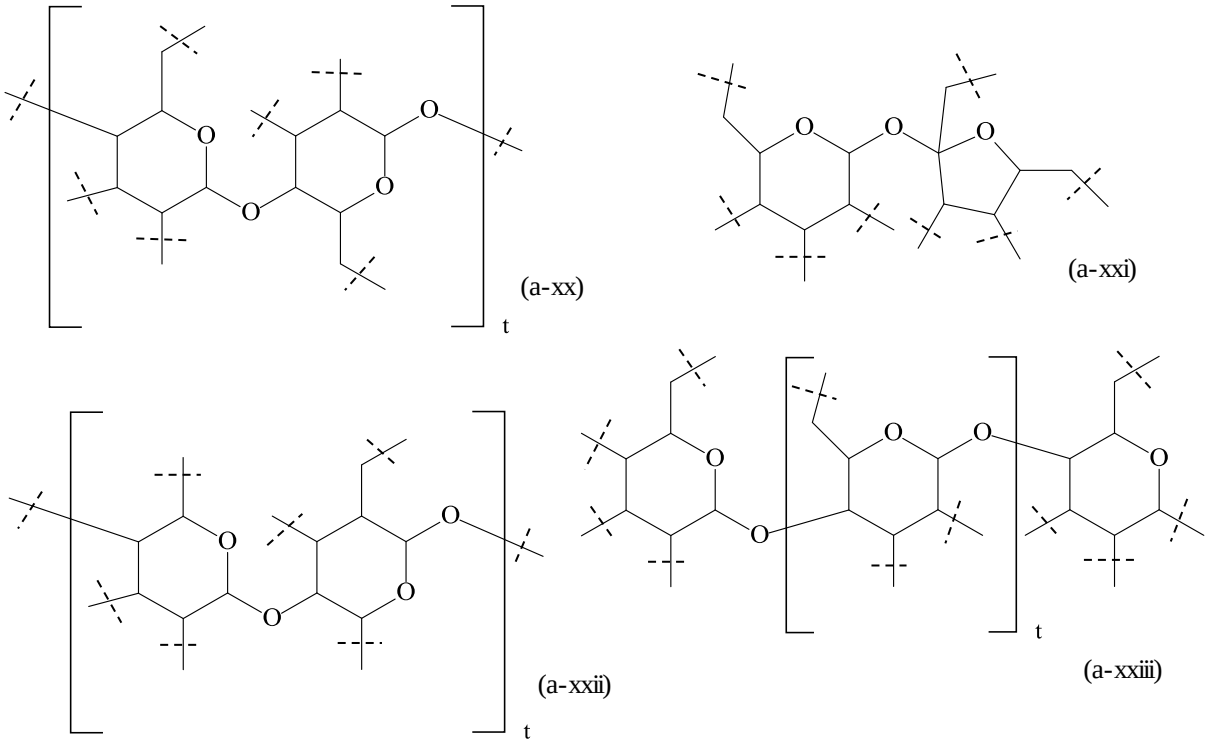


(a-xii)



(a-xiii)





wherein

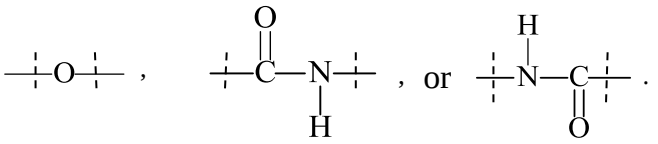
dashed lines indicate attachment to A^0 or, if x1 and x2 are both 0, to A^1,

t is 1 or 2; preferably t is 1,

v is 1, 2, 3, 4, 5, ,6 ,7 ,8 , 9, 10, 11, 12, 13 or 14; preferably, v is 2, 3, 4, 5, 6; more preferably, v is 2, 4 or 6; most preferably, v is 2.

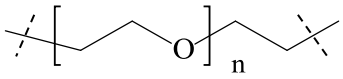
18. The use of any one of claims 14 to 17, wherein B is of formula (a-xiv).

19. The use of any one of claims 14 to 18, wherein A^0 is



20. The use of any one of claims 14 to 19, wherein x1 and x2 are 0.

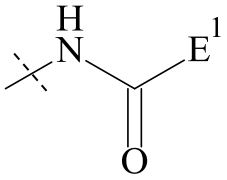
21. The use of any one of claims 14 to 20, wherein P has the structure of formula (c-i):



(c-i),

wherein n ranges from 6 to 900, more preferably n ranges from 20 to 700 and most preferably n ranges from 20 to 250.

22. The use of any one of claims 14 to 21, wherein the moiety $– A^2 – Hyp^1$ is a moiety of the formula



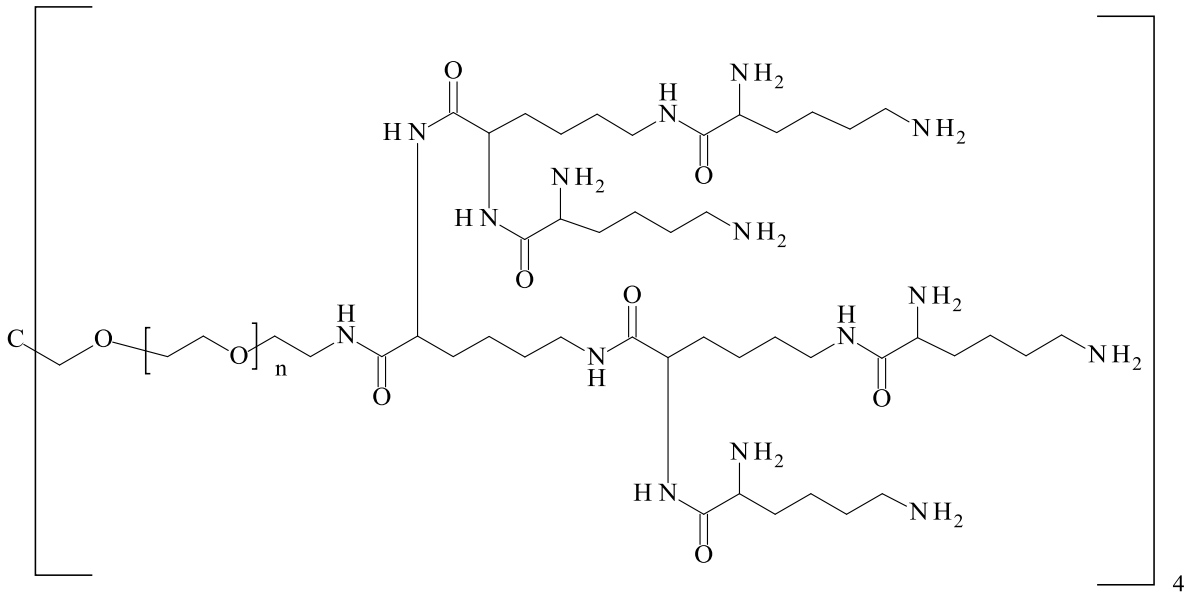
,

wherein

the dashed line indicates attachment to P; and

E^1 is selected from formulas (e-i) to (e-ix).

23. The use of any one of claims 1 to 22, wherein the backbone reagent has the following formula:

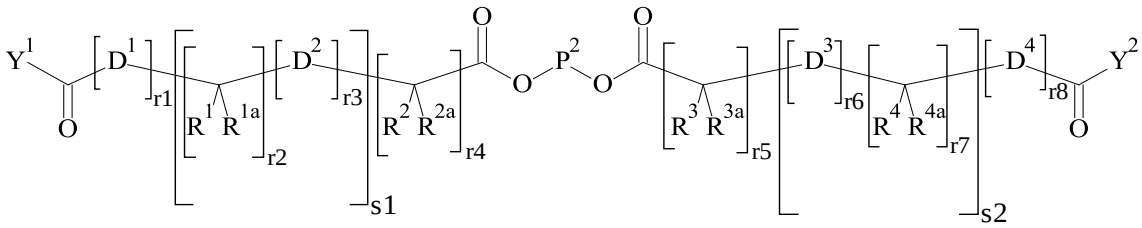


wherein

n ranges from 10 to 40, preferably from 10 to 30, more preferably from 10 to 20.

24. The use of any one of claims 1 to 23, wherein the backbone reagent is present in the form of its acidic salt.

25. The use of any one of claims 1 to 24, wherein the crosslinker reagent is a compound of formula (V):



(V),

wherein

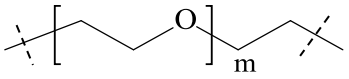
D^1, D^2, D^3 and D^4 are identical or different and each is independently of the others selected from the group comprising O, NR^5,S and CR^5R^{5a};

R^1, R^{1a}, R^2, R^2, R^3, R^{3a}, R^4, R^{4a}, R^5 and R^{5a} are identical or different and each is independently of the others selected from the group comprising H and $C_{1\text{-}6}$ alkyl; optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^3/R^{3a}, R^4/R^{4a}, R^1/R^2, R^3/R^4, R^{1a}/R^{2a}, and R^{3a}/R^{4a} form a chemical bond or are joined together with the atom to which they are attached to form a $C_{3\text{-}8}$ cycloalkyl or to form a ring A or are joined together

with the atom to which they are attached to form a 4- to 7-membered heterocyclyl or 8- to 11-membered heterobicyclyl or adamantyl;

A is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl and tetralinyl;

P^2 is



m ranges from 120 to 920, preferably from 120 to 460 and more preferably from 120 to 230;

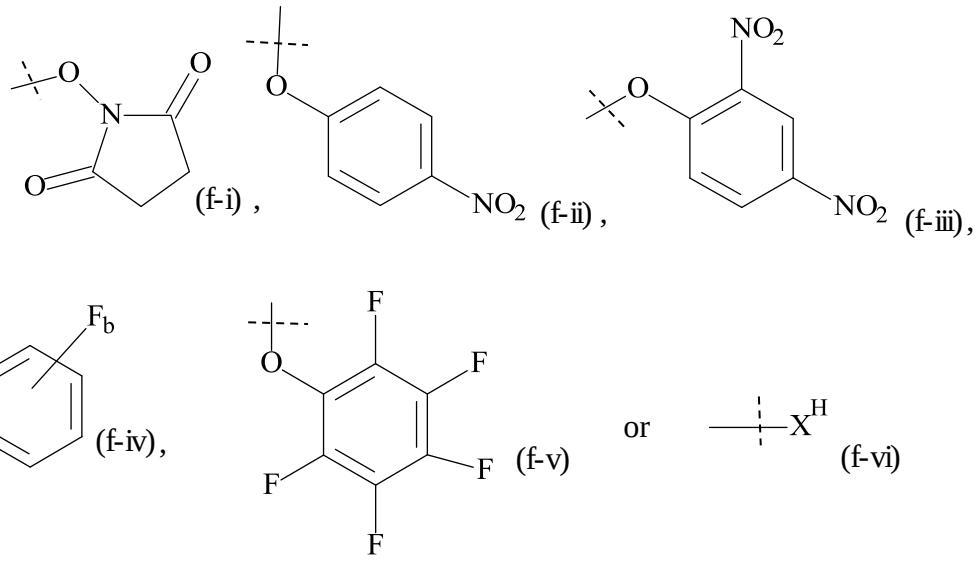
r1, r2, r7, r8 are independently 0 or 1;

r3, r6 are independently 0, 1, 2, 3, or 4;

r4, r5 are independently 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

s1, s2 are independently 1, 2, 3, 4, 5 or 6;

Y^1, Y^2 are identical or different and each is independently of the other selected from formulas (f-i) to (f-vi):



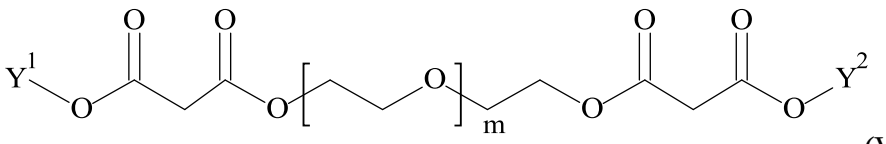
wherein

the dashed lines indicate attachment to the rest of the molecule,

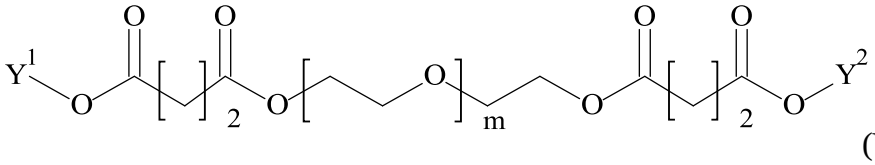
b is 1, 2, 3 or 4

X^H is Cl, Br, I, or F.

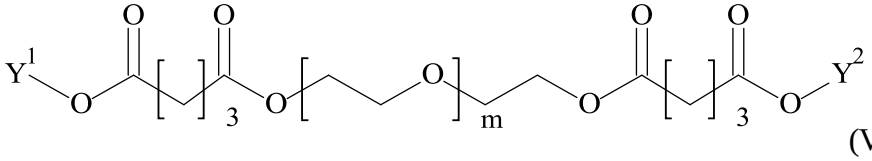
26. The use of any one of claims 1 to 25, wherein the crosslinker reagent is of formula (V-1) to (V-53):



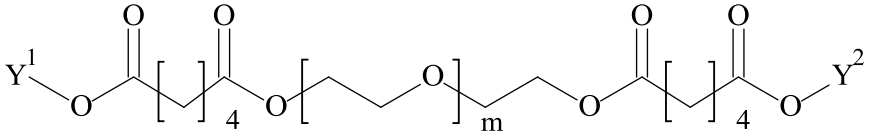
(V-1),



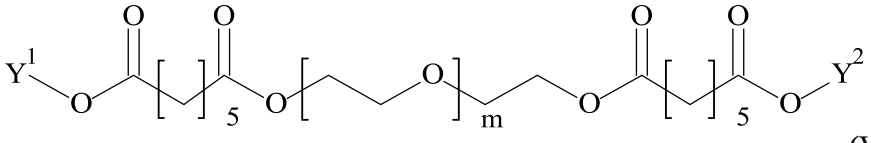
(V-2),



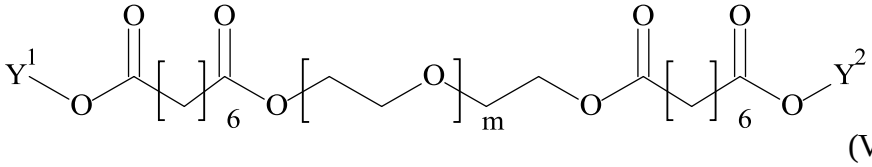
(V-3),



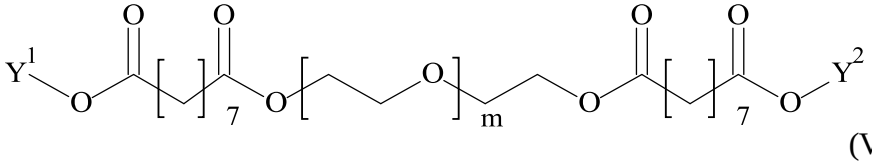
(V-4),



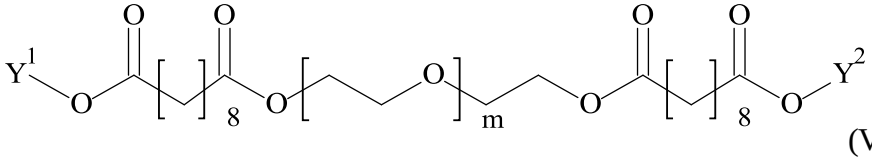
(V-5),



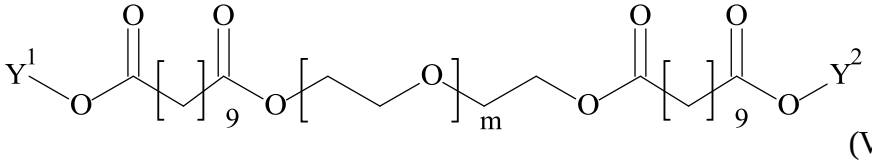
(V-6),



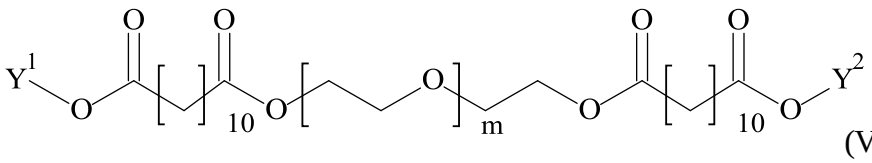
(V-7),



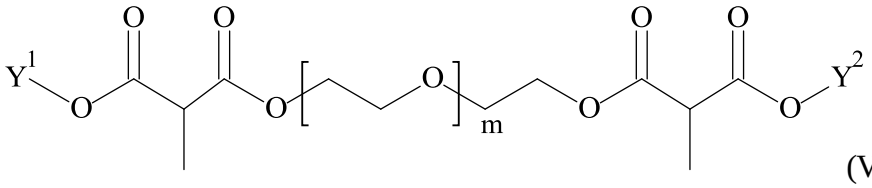
(V-8),



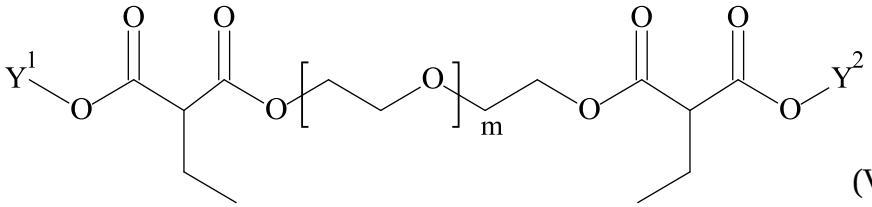
(V-9),



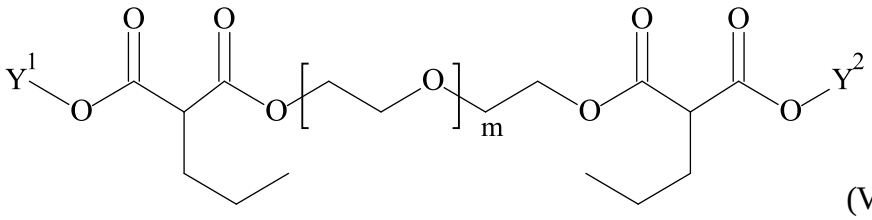
(V-10),



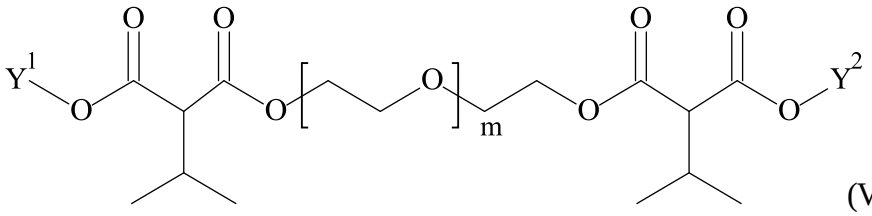
(V-11),



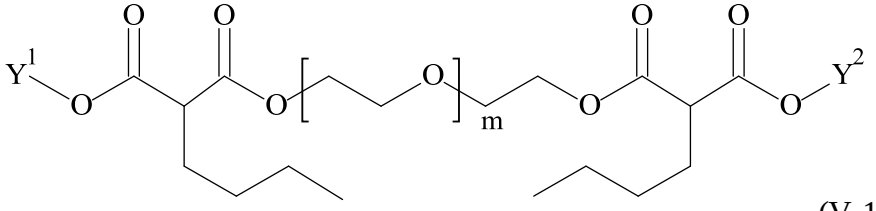
(V-12),



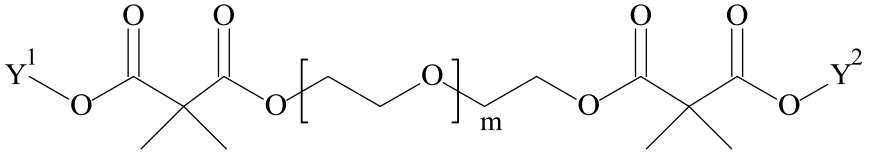
(V-13),



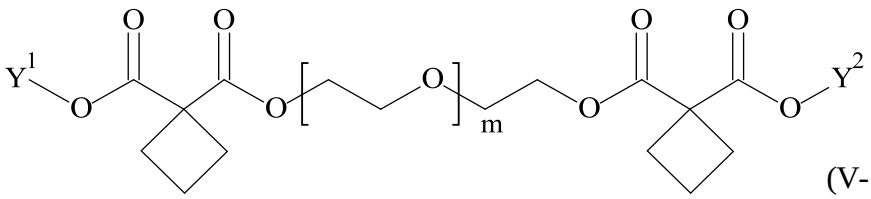
(V-14),



(V-15),

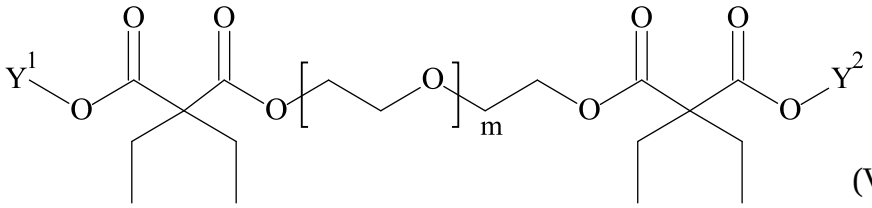


(V-16),



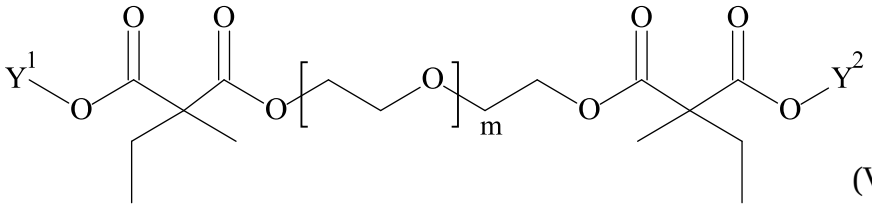
(V-17)

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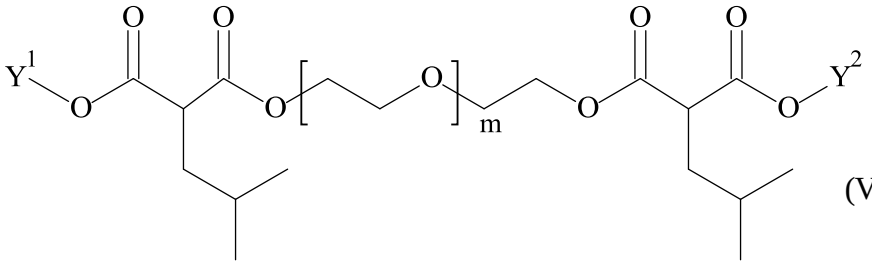


(V-18)

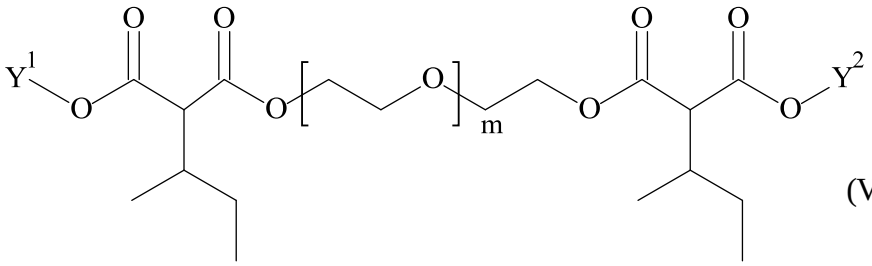
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(V-19)

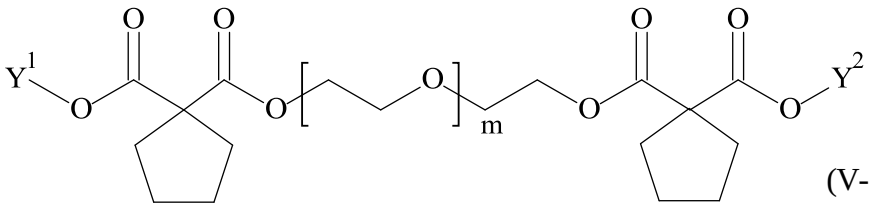


(V20)

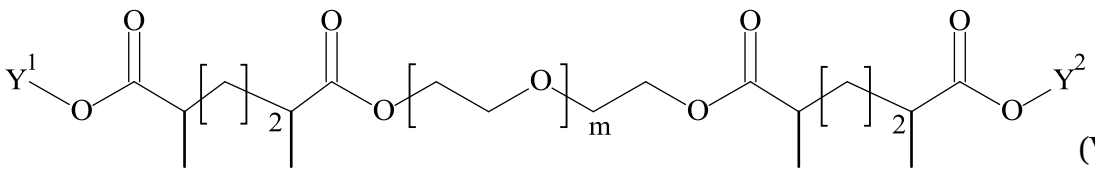


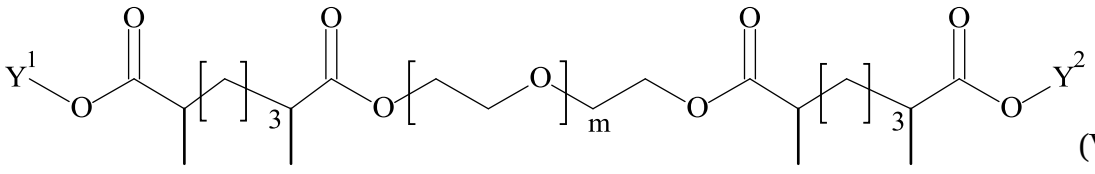
(V-21)

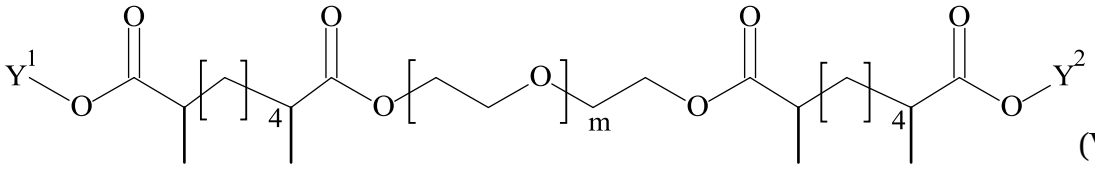
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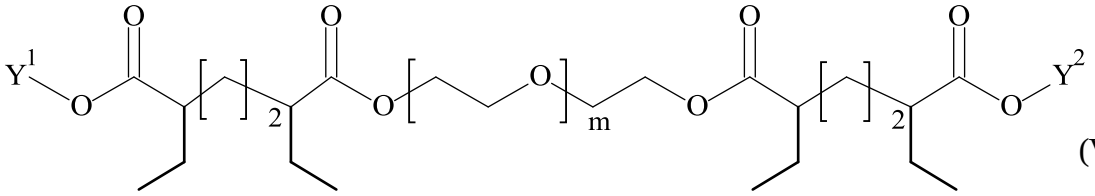


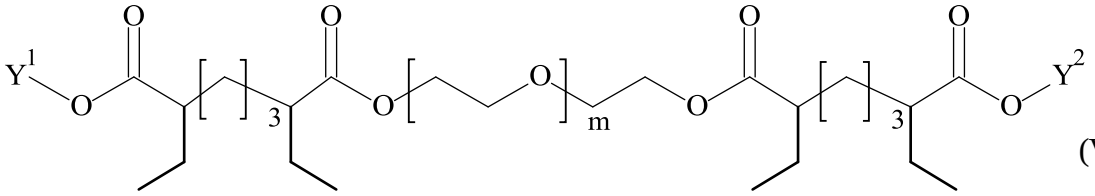
(V-22)

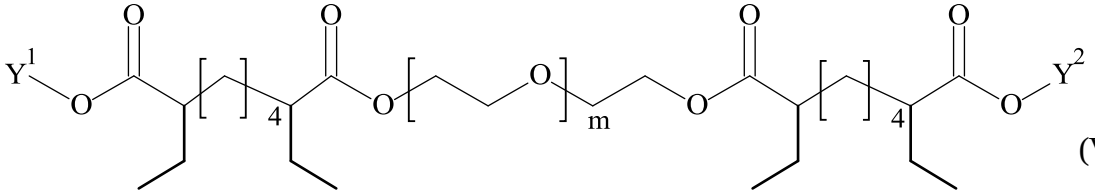

(V-23)

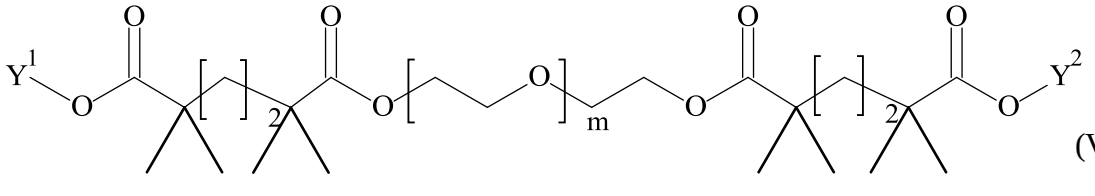

(V-24)

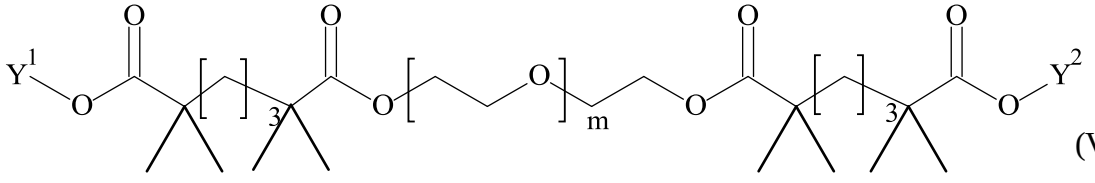

(V-25)

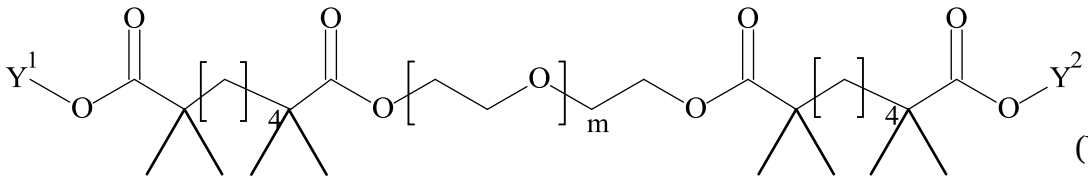

(V-26)


(V-27)

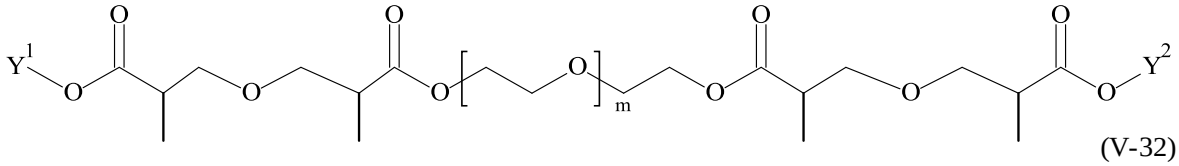

(V-28)


(V-29)

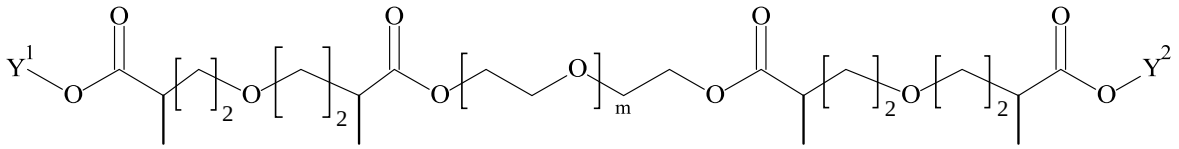

(V-30)



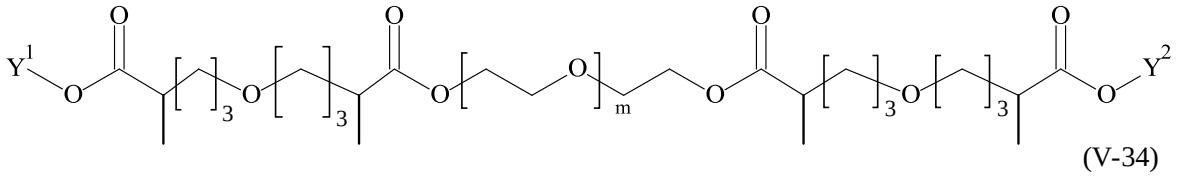
(V-31)



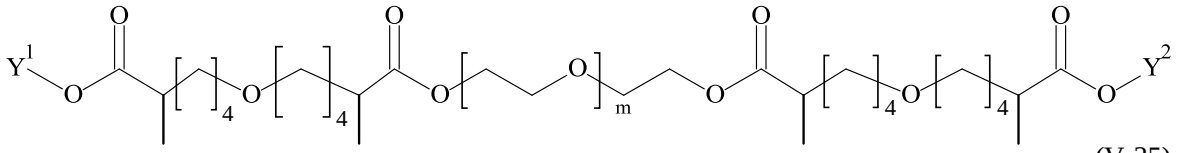
(V-32)



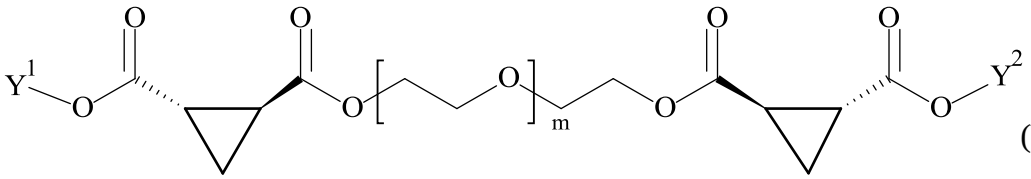
(V-33)



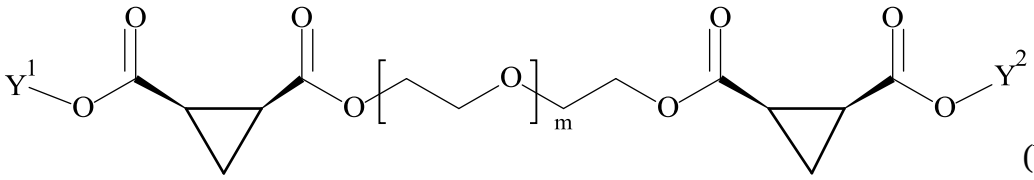
(V-34)



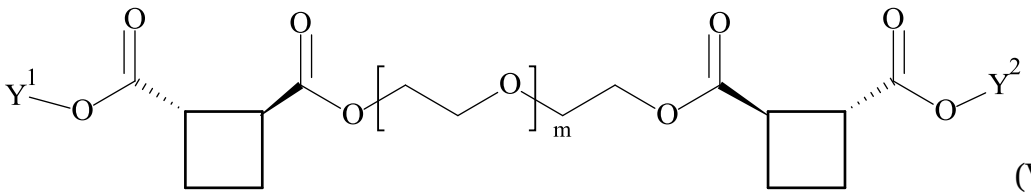
(V-35)



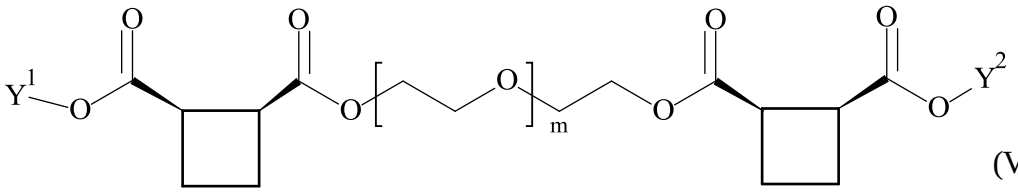
(V-36)



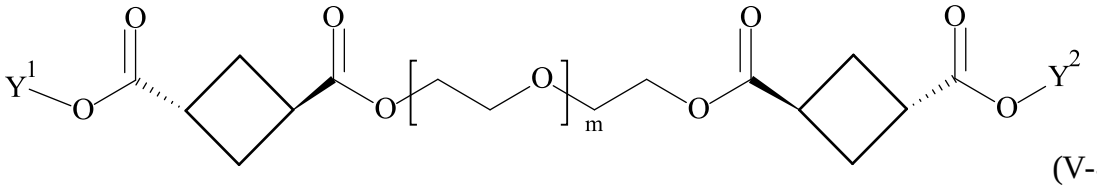
(V-37)



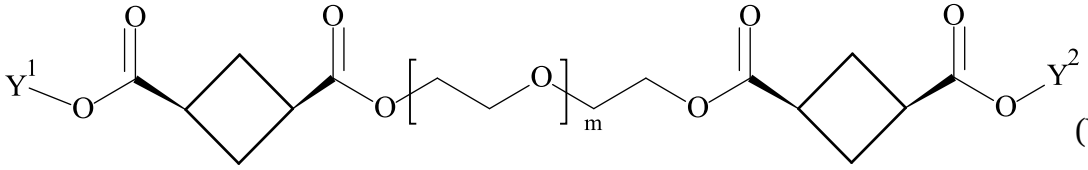
(V-38)



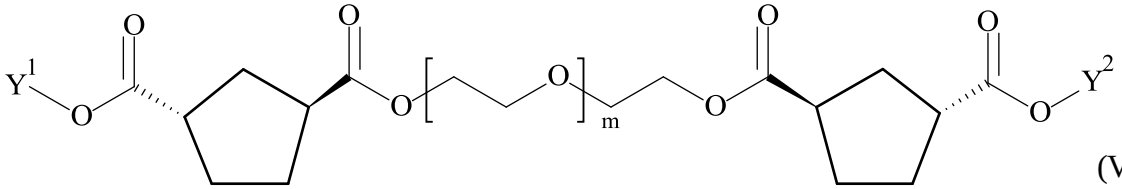
(V-39)



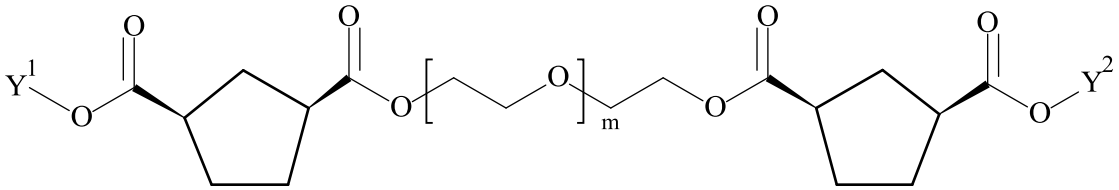
(V-40)



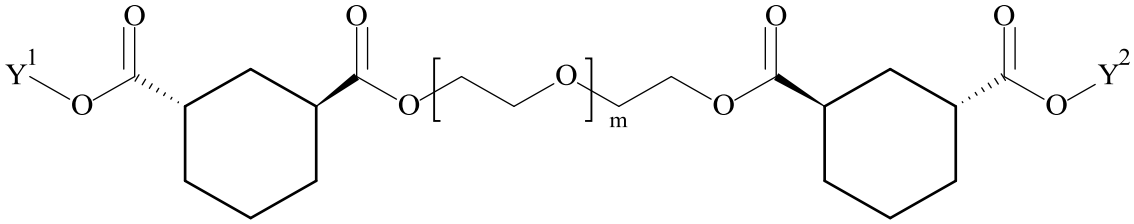
(V-41)



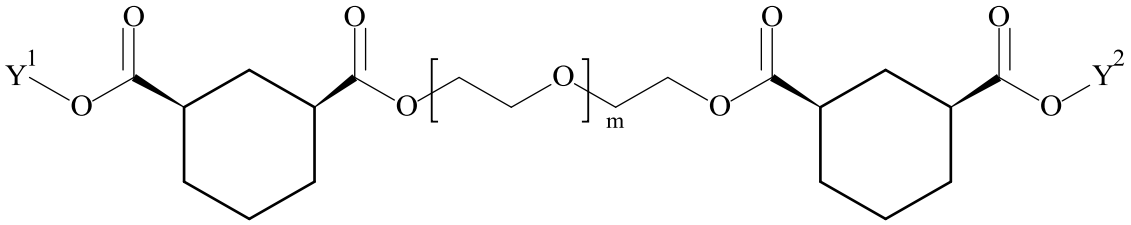
(V-42)



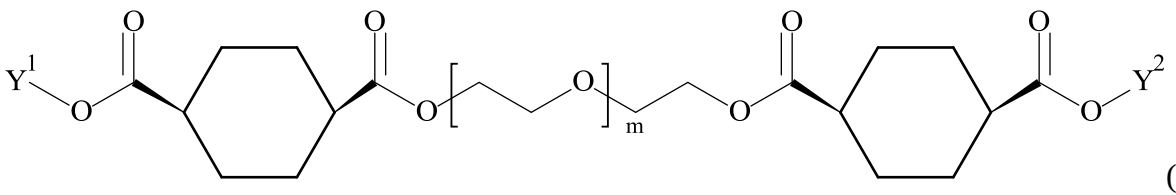
(V-43)



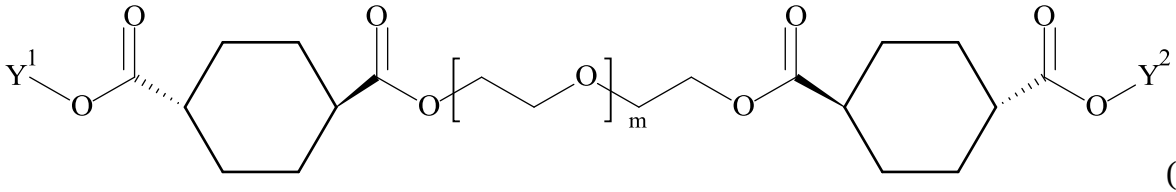
(V-43)



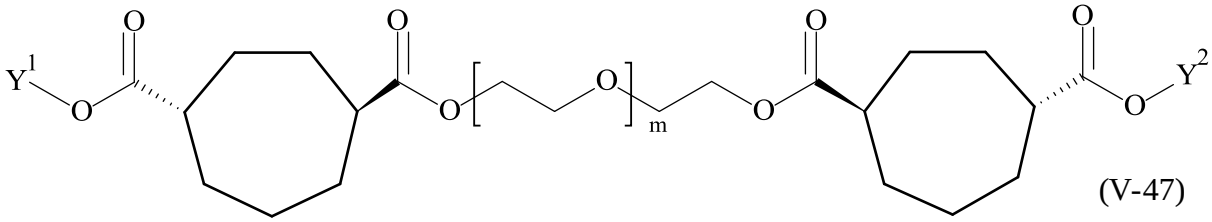
(V-44)



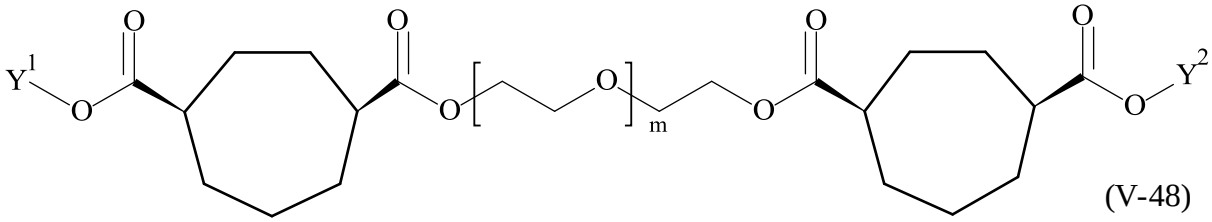
(V-45)



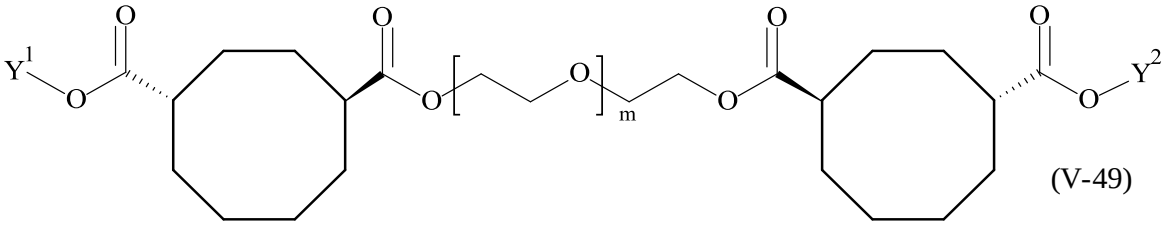
(V-46)



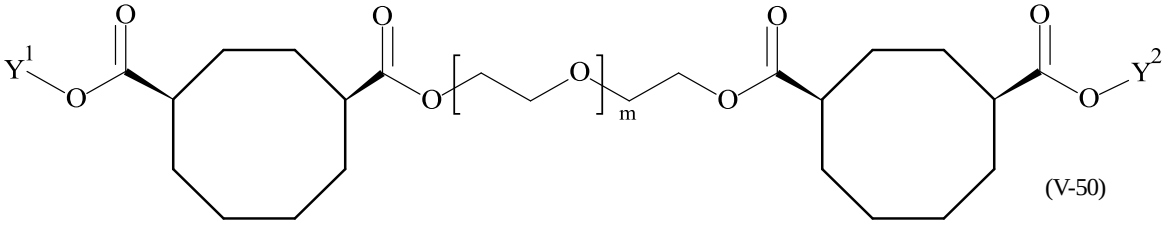
(V-47)



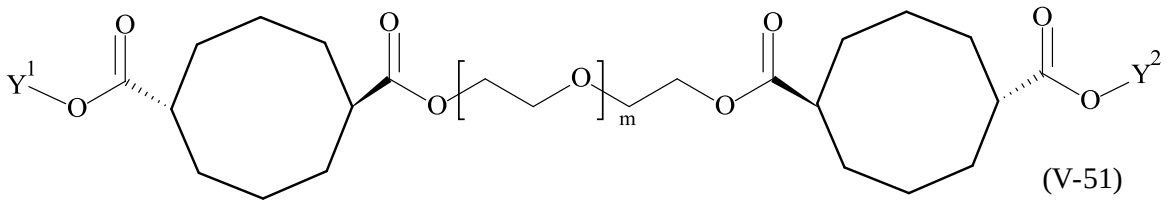
(V-48)



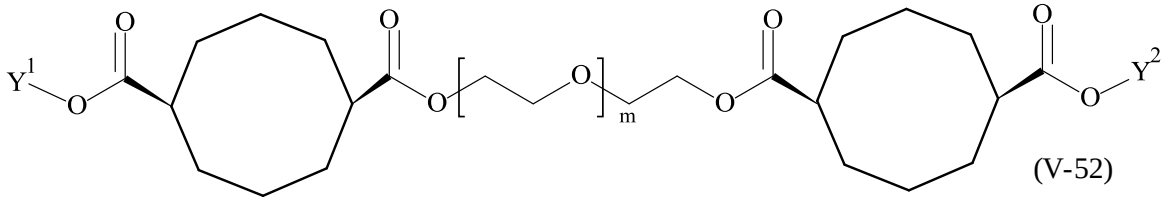
(V-49)



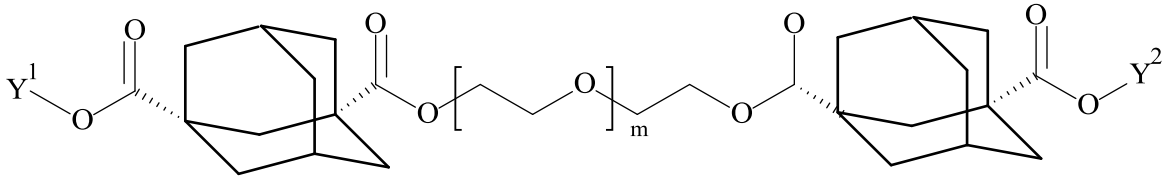
(V-50)



(V-51)



(V-52)



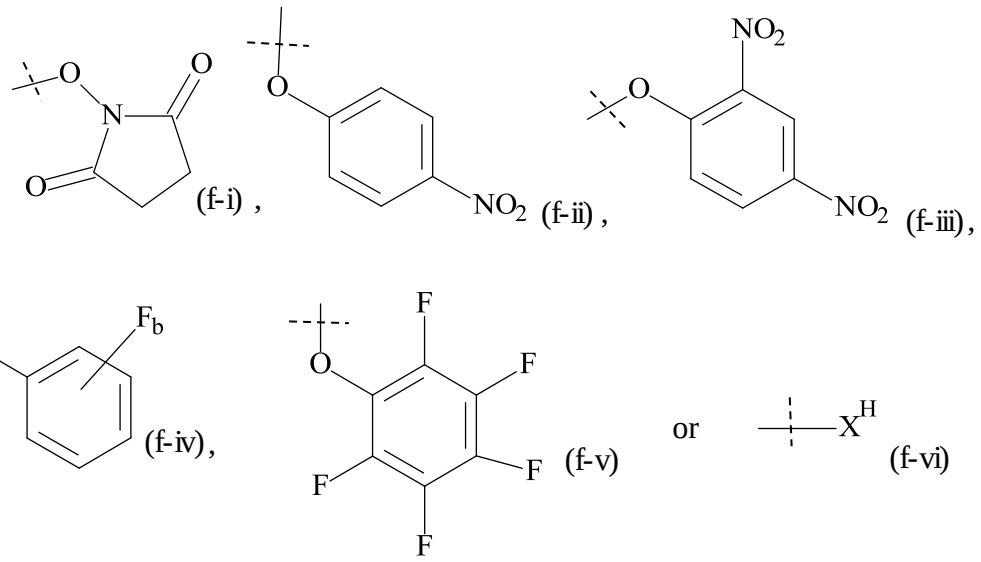
(V-53)

wherein

each crosslinker reagent may be in the form of its racemic mixture, where applicable; and

m ranges from 120 to 920, preferably from 120 to 460 and more preferably from 120 to 230*;*

Y^1, Y^2 are identical or different and each is independently of the other selected from formulas (f-i) to (f-vi):



(f-i) , (f-ii) , (f-iii), (f-iv), (f-v) or (f-vi)

wherein

the dashed lines indicate attachment to the rest of the molecule,

b is 1, 2, 3 or 4

X^H is Cl, Br, J, or F.

27. The use of any one of claims 1 to 26, wherein the hydrogel-linked prodrug comprises a biologically active moiety selected from the group consisting of anesthetics and analgesics, antiallergenics, antihistamines, anti-inflammatory agents, anti-cancer agents, antibiotics, antiinfectives, antibacterials, anti-fungal agents, anti-viral agents, cell transport/mobility impending agents, antiglaucoma drugs, antihypertensives, decongestants, immunological response modifiers, immunosuppresive agents, peptides and proteins, steroidal compounds (steroids), low solubility steroids, carbonic anhydrize inhibitors, diagnostic agents, antiapoptosis agents, gene therapy agents, sequestering agents, reductants, antipermeability agents, antisense compounds, antiproliferative agents, antibodies and antibody conjugates, bloodflow enhancers, antiparasitic agents, non-steroidal anti inflammatory agents, nutrients and vitamins, enzyme inhibitors, antioxidants, anticataract drugs, aldose reductase inhibitors, cytoprotectants, cytokines, cytokine inhibitors, and cytokine protectants, UV blockers, mast cell stabilizers, and anti neovascular agents such as antiangiogenic agents like matrix metalloprotease inhibitors and Vascular endothelial growth factor (VEGF) modulators, neuroprotectants, miotics and anti-cholinesterase, mydriatics, artificial tear/dry eye therapies, anti-TNFα, IL-1 receptor antagonists, protein kinase C-β inhibitors, somatostatin analogs and sympathomimetics.