unmarked dashed lines indicate attachment to a backbone moiety or to a spacer moiety -SP-;

$-R^{b1}$, $-R^{b1a}$, $-R^{b2}$, $-R^{b2a}$, $-R^{b3}$, $-R^{b3a}$, $-R^{a4}$, $-R^{a4a}$, $-R^{a5}$, $-R^{a5a}$, $-R^{a6}$ and $-R^{a6a}$ are independently selected from the group consisting of -H and C_{1-6} alkyl;

c1, c2, c3, c4, c5 and c6 are independently selected from the group consisting of 1, 2, 3, 4, 5 and 6;

d is an integer ranging from 2 to 250.

In certain embodiments d of formula (A-i) ranges from 3 to 200. In certain embodiments d of formula (A-i) ranges from 4 to 150. In certain embodiments d of formula (A-i) ranges from 5 to 100. In certain embodiments d of formula (A-i) ranges from 10 to 50. In certain embodiments d of formula (A-i) ranges from 15 to 30. In certain embodiments d of formula (A-i) is about 23.

In certain embodiments $-R^{b1}$ and $-R^{b1a}$ of formula (A-i) are -H. In certain embodiments $-R^{b2}$ and $-R^{b2a}$ of formula (A-i) are -H. In certain embodiments $-R^{b3}$ and-R^{b3a} of formula (A-i) are -H. In certain embodiments $-R^{b4}$ and $-R^{b4a}$ of formula (A-i) are -H. In certain embodiments $-R^{b5}$ and $-R^{b5a}$ of formula (A-i) are -H. In certain embodiments $-R^{b6}$ and $-R^{b6a}$ of formula (A-i) are -H.

In certain embodiments $-R^{b1}$, $-R^{b1a}$, $-R^{b2}$, $-R^{b2a}$, $-R^{b3}$, $-R^{b3a}$, $-R^{a4}$, $-R^{a4a}$, $-R^{a5}$, $-R^{a5a}$, $-R^{a6}$ and $-R^{a6a}$ of formula (A-i) are all -H.

In certain embodiments c1 of formula (A-i) is 1. In certain embodiments c1 of formula (A-i) is 2. In certain embodiments c1 of formula (A-i) is 3. In certain embodiments c1 of formula (A-i) is 4. In certain embodiments c1 of formula (A-i) is 5. In certain embodiments c1 of formula (A-i) is 6.

In certain embodiments c2 of formula (A-i) is 1. In certain embodiments c2 of formula (A-i) is 2. In certain embodiments c2 of formula (A-i) is 3. In certain embodiments c2 of formula (A-i) is 4. In certain embodiments c2 of formula (A-i) is 5. In certain embodiments c2 of formula (A-i) is 6.

Claims

1. A conjugate comprising a water-insoluble hydrogel Z, wherein said conjugate comprises a plurality of moieties -L^2-L^1-D covalently conjugated to Z,

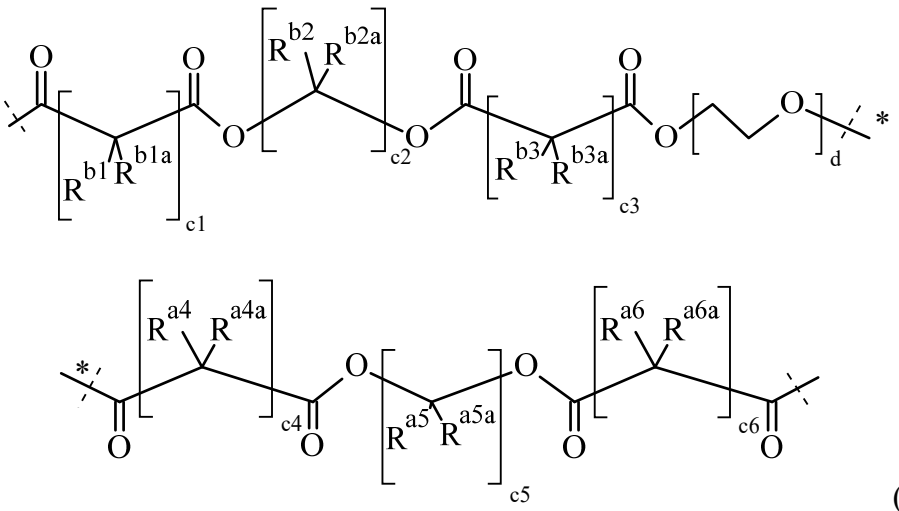
wherein

each -D is drug moiety;

each -L^1- is independently a linker moiety to which -D is covalently and reversibly conjugated;

each -L^2- is independently either a chemical bond or a spacer moiety;

Z is a PEG-based hydrogel comprising a plurality of backbone moieties that are crosslinked via crosslinker moieties -CL-, either directly or via a spacer moiety -SP- between a backbone moiety and -CL-, and wherein -CL- is of formula (A-i);



(A-i),

wherein

dashed lines marked with an asterisk indicate the connection point between the upper and the lower substructure,

unmarked dashed lines indicate attachment to a backbone moiety or to a spacer moiety -SP- ;

R^{b1}, R^{b1a}, R^{b2}, R^{b2a}, R^{b3}, R^{b3a}, R^{a4}, R^{a4a}, R^{a5}, R^{a5a}, R^{a6} and R^{a6a} are independently selected from the group consisting of -H and C_{1-6} alkyl;

c1, c2, c3, c4, c5 and c6 are independently selected from the group consisting of 1, 2, 3, 4, 5 and 6;

d is an integer ranging from 2 to 250.

2. The conjugate of claim 1, wherein c1 is 3.

3. The conjugate of claim 1 or 2, wherein c2 is 2.

4. The conjugate of any one of claims 1 to 3, wherein c3 is 3.

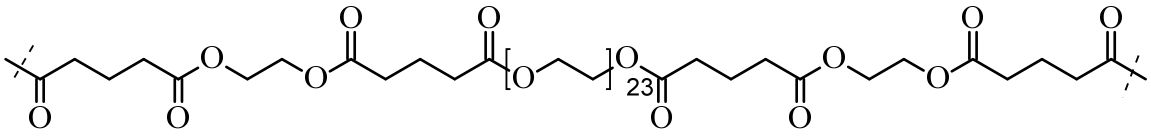
5. The conjugate of any one of claims 1 to 4, wherein c4 is 3.

6. The conjugate of any one of claims 1 to 5, wherein c5 is 2.

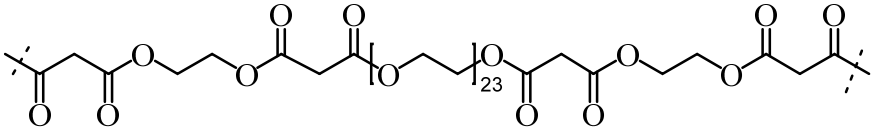
7. The conjugate of any one of claims 1 to 6, wherein c6 is 3.

8. The conjugate of any one of claims 1 to 7, wherein a moiety -CL- has a molecular weight ranging from 0.2 kDa to 25 kDa

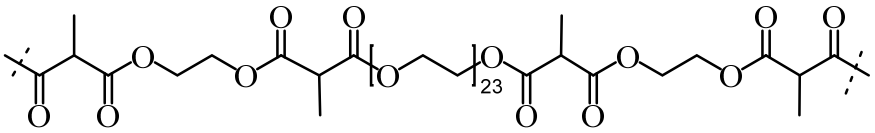
9. The conjugate of any one of claims 1 to 8, wherein a moiety -CL- is selected from the group consisting of



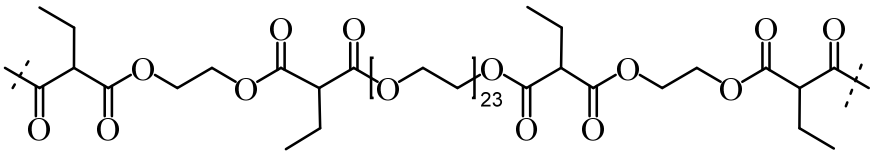
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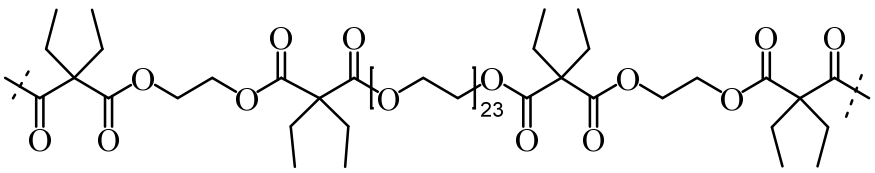
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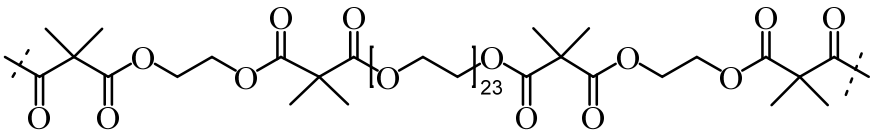
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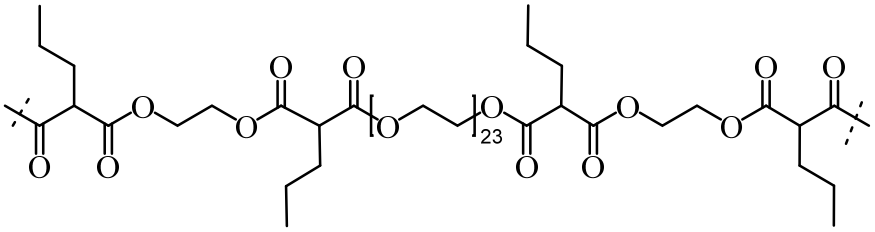
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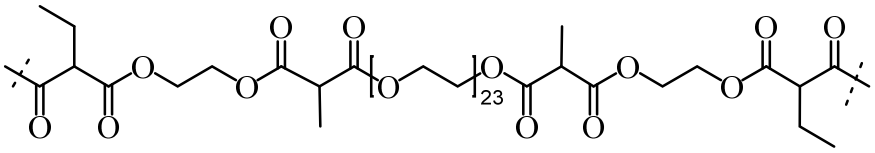
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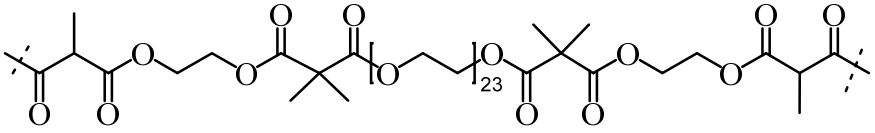
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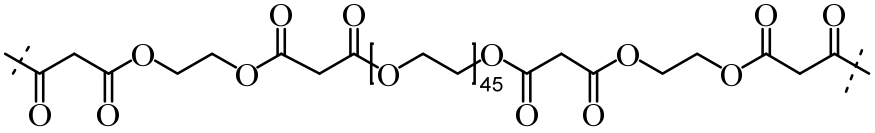
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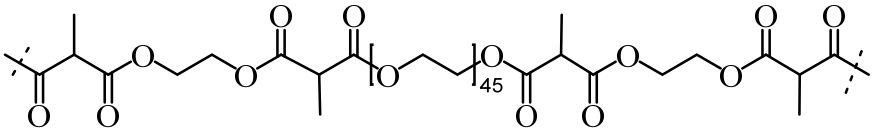
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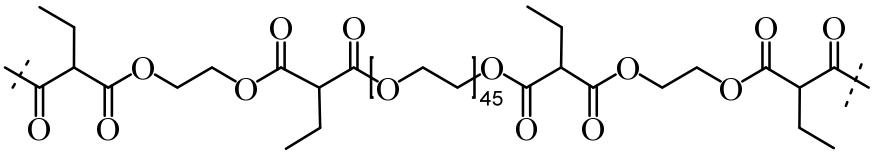
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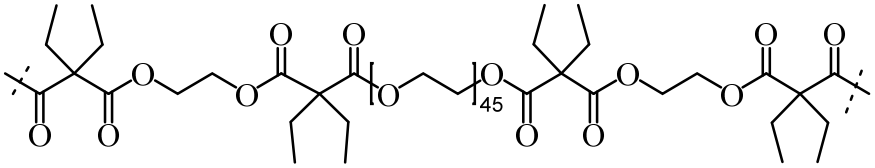
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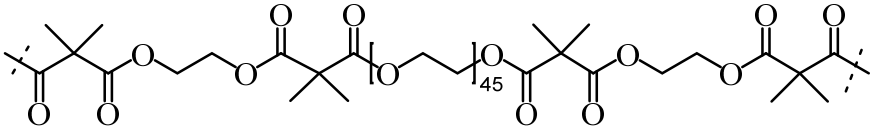
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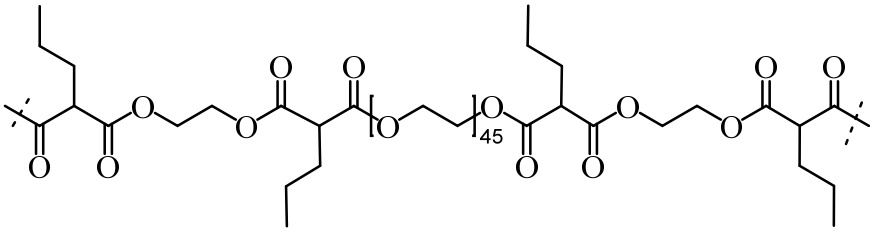
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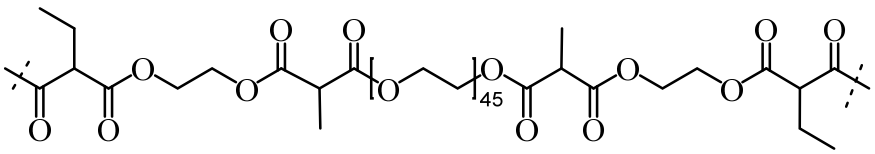
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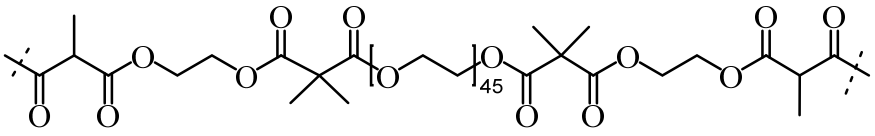
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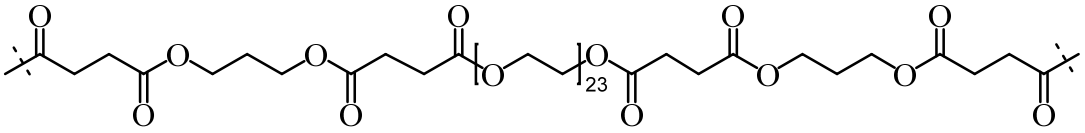
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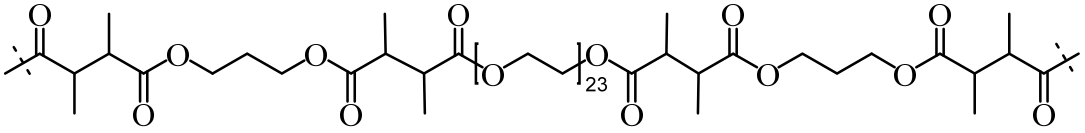
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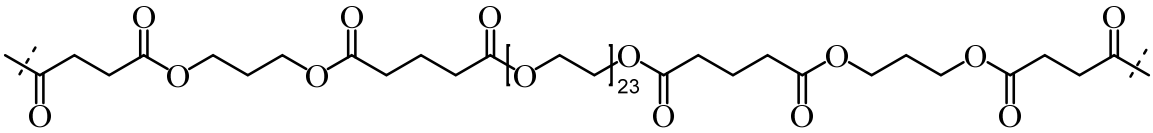
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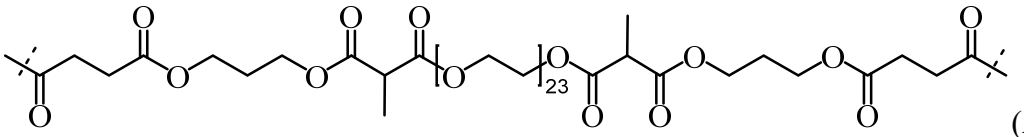
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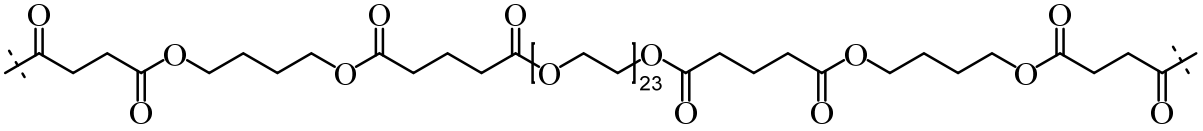
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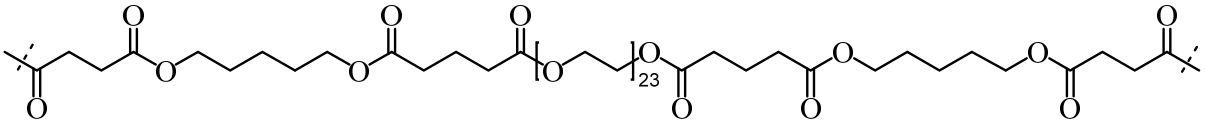
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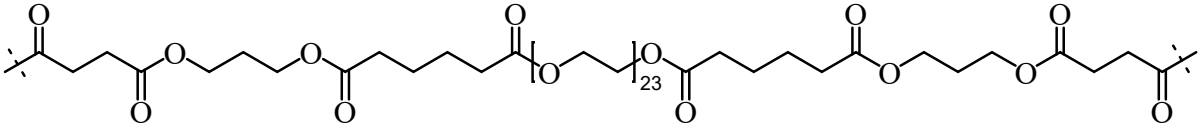
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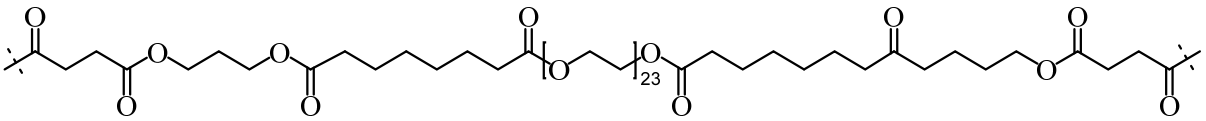
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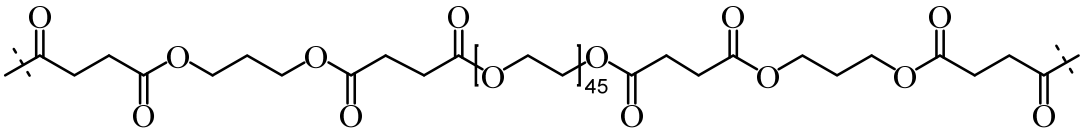
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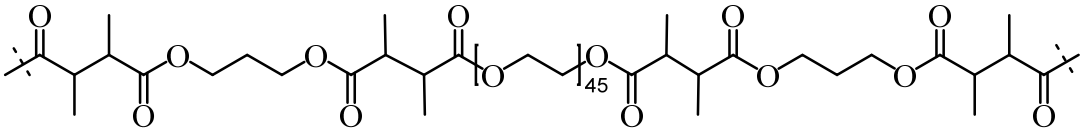
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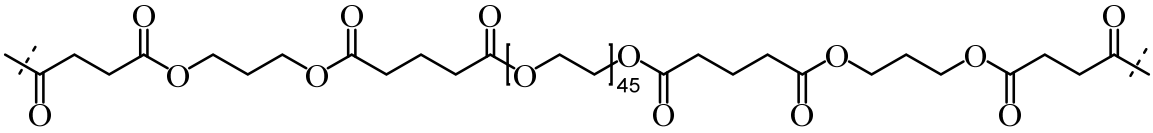
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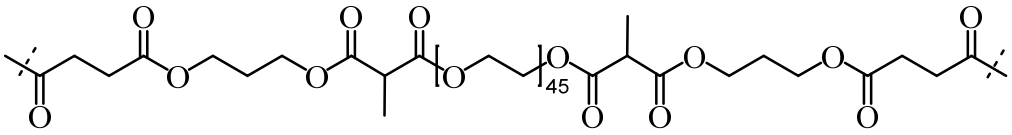
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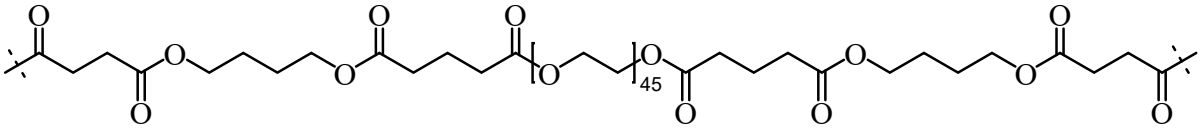
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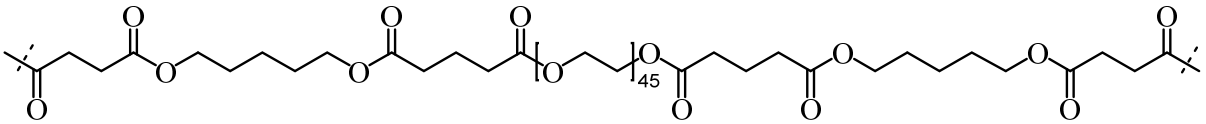
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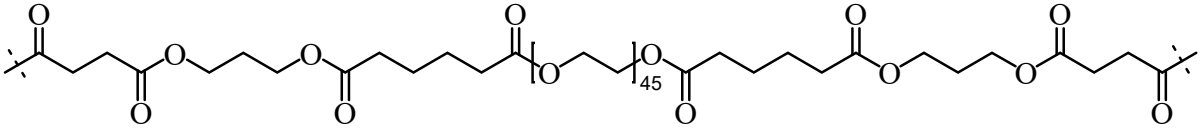
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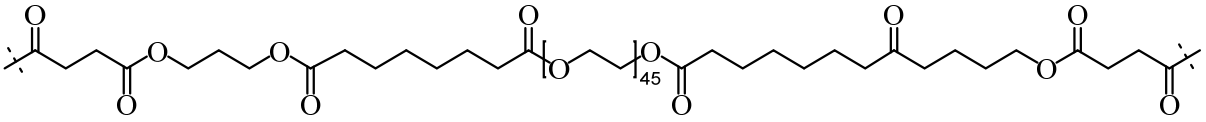
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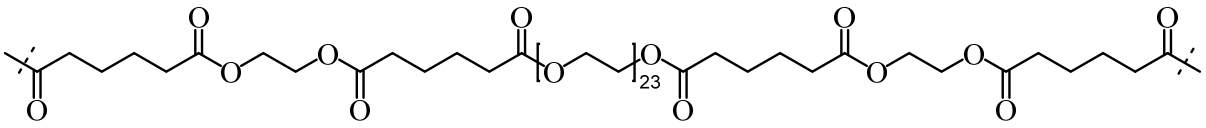
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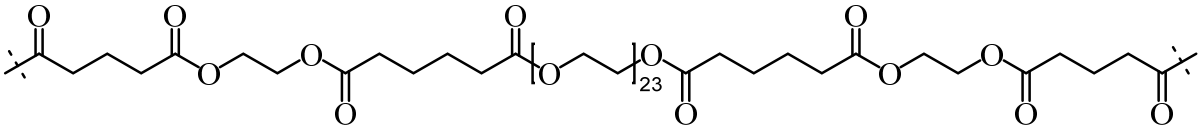
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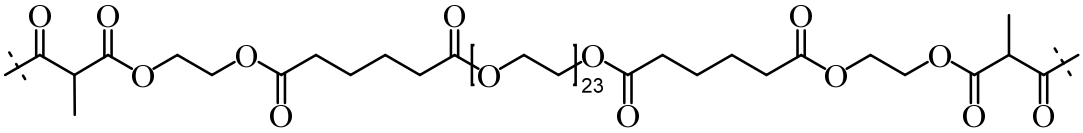
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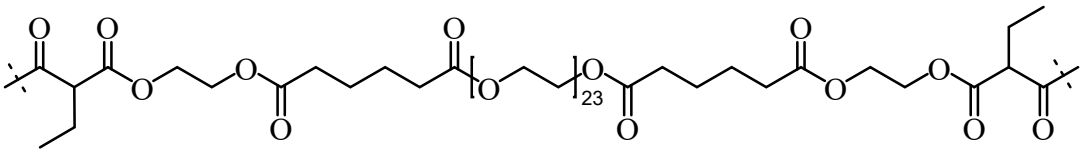
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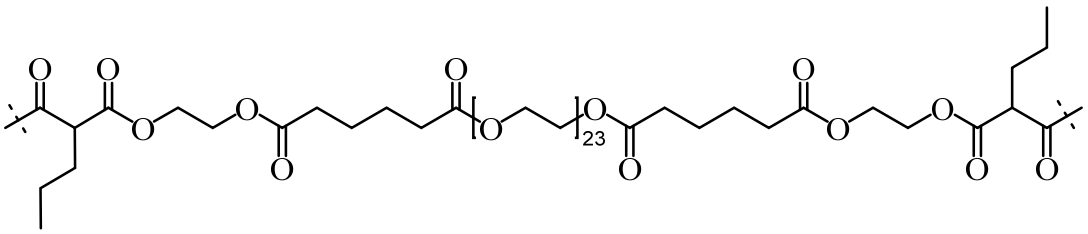
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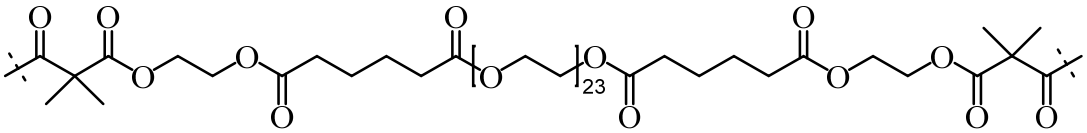
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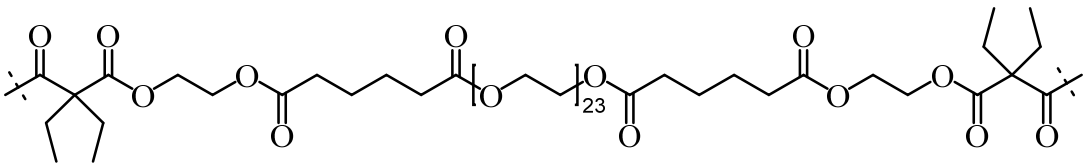
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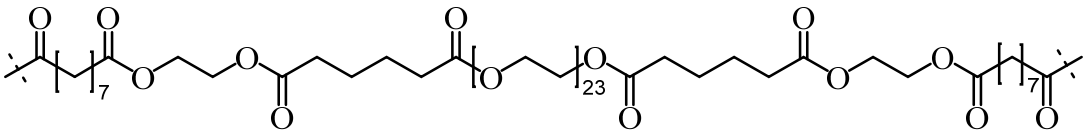
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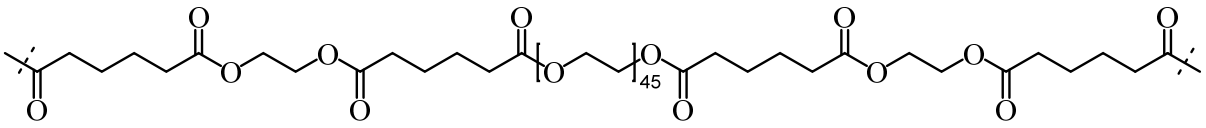
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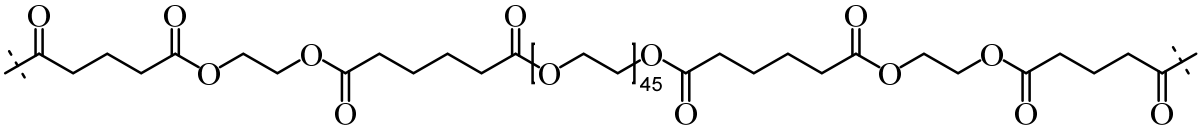
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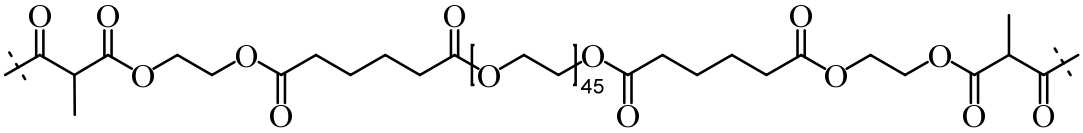
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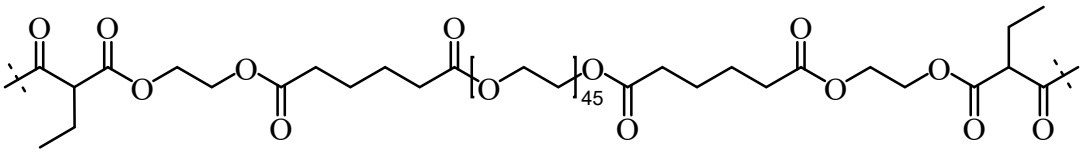
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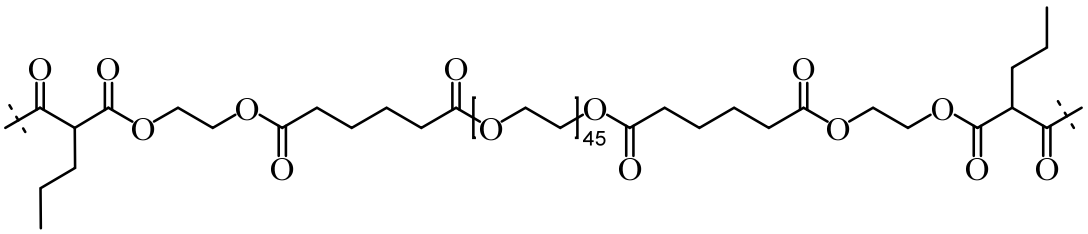
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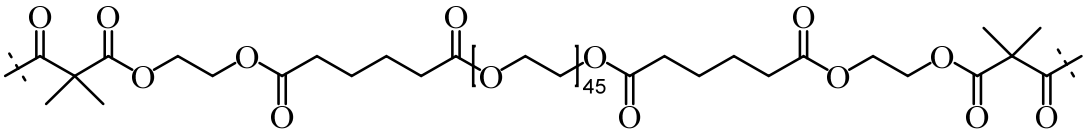
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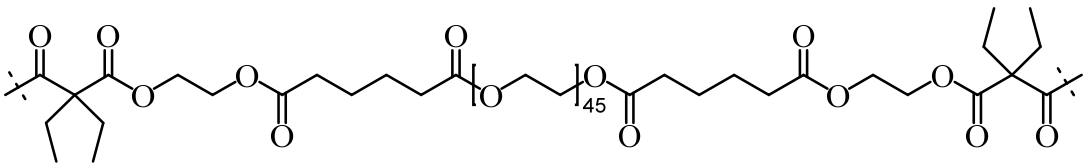
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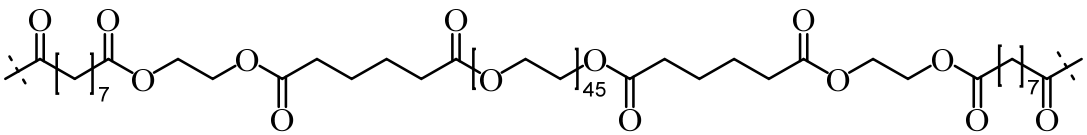
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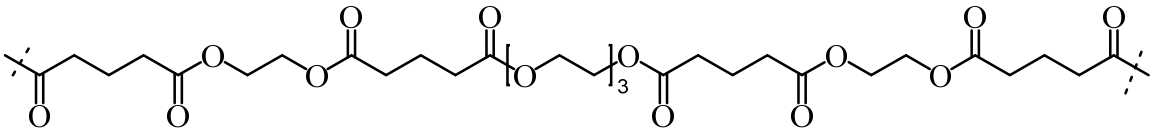
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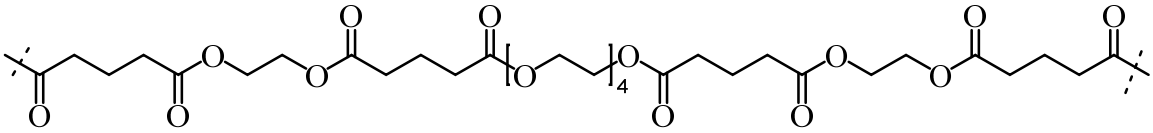
(A-i48),



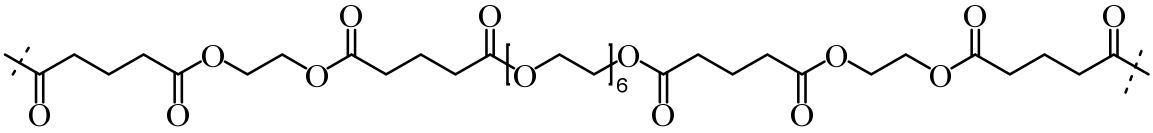
(A-i49),



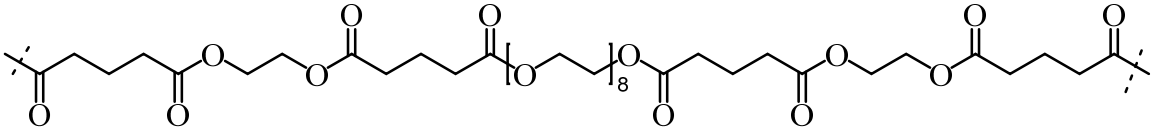
(A-i50),



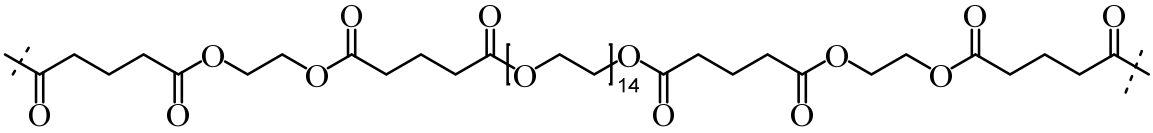
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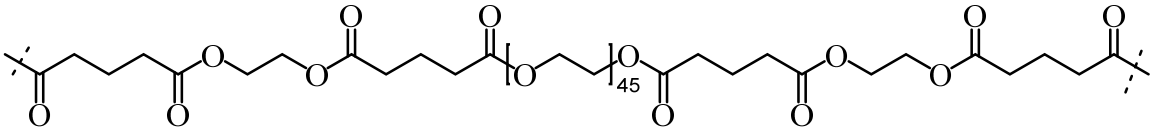
(A-i52),



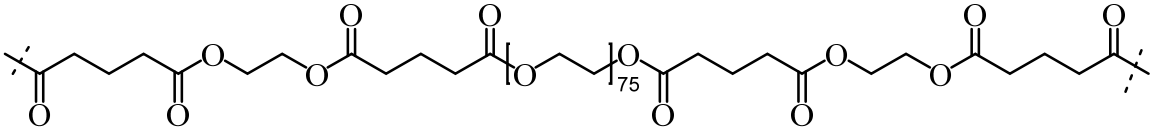
(A-i53),



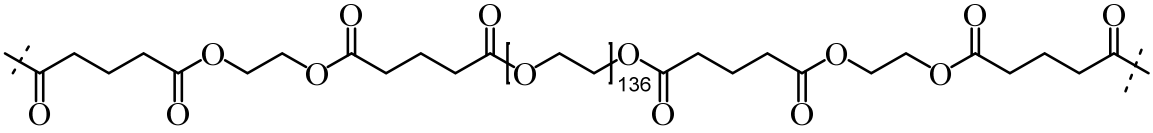
(A-i54),



(A-i55),



(A-i56),



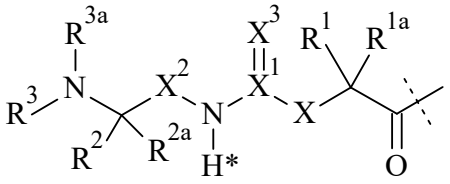
(A-i57),

wherein

dashed lines indicate attachment to a backbone moiety or to a spacer moiety -SP-.

10. The conjugate of any one of claims 1 to 9, wherein a backbone moiety has a molecular weight ranging from 1 kDa to 20 kDa.

11. The conjugate of any one of claims 1 to 10, wherein -L^1- is of formula (I):



,

wherein the dashed line indicates the attachment to a nitrogen, hydroxyl or thiol of -D;

-X- is selected from the group consisting of -C(R^4R^{4a})-, -N(R^4)-, -O-, -C(R^4R^{4a})-C(R^5R^{5a})-, -C(R^5R^{5a})-C(R^4R^{4a})-, -C(R^4R^{4a})-N(R^6)-, -N(R^6)-C(R^4R^{4a})-, -C(R^4R^{4a})-O-, -O-C(R^4R^{4a})-, and -C(R^7R^{7a})-,

X^1 is selected from the group consisting of C and S(O);

-X^2- is selected from the group consisting of -C(R^8R^{8a})- and -C(R^8R^{8a})-C(R^9R^{9a})-;

=X^3 is selected from the group consisting of =O, =S, and =N-CN;

-R^1, -R^{1a}, -R^2, -R^{2a}, -R^4, -R^{4a}, -R^5, -R^{5a}, -R^6, -R^8, -R^{8a}, -R^9 and -R^{9a} are independently selected from the group consisting of -H and C_{1-6} alkyl;

-R^3 and -R^{3a} are independently selected from the group consisting of -H and C_{1-6} alkyl, provided that in case one of -R^3 and -R^{3a} or both are other than -H they are connected to N to which they are attached through an sp^3-hybridized carbon atom;

-R^7 is selected from the group consisting of -N($R^{10}R^{10a}$) and -NR^{10}-(C=O)-R^{11};

-R^{7a}, -R^{10}, -R^{10a} and -R^{11} are independently selected from the group consisting of -H and C_{1-6} alkyl;

alternatively, one or more of the pairs -R^{1a}/-R^{4a}, -R^{1a}/-R^{5a}, -R^{1a}/-R^{7a}, -R^{4a}/-R^{5a} and -R^{8a}/-R^{9a} form a chemical bond;

alternatively, one or more of the pairs -R^1/-R^{1a}, -R^2/-R^{2a}, -R^4/-R^{4a}, -R^5/-R^{5a}, -R^8/-R^{8a} and -R^9/-R^{9a} are joined together with the atom to which they are attached to form a C_{3-10} cycloalkyl or 3- to 10-membered heterocyclyl;

alternatively, one or more of the pairs -R^1/-R^4, -R^1/-R^5, -R^1/-R^6, -R^1/-R^{7a}, -R^4/-R^5, -R^4/-R^6, -R^8/-R^9 and -R^2/-R^3 are joined together with the atoms to which they are attached to form a ring A;

alternatively, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 3- to 10-membered heterocycle;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 3- to 10-membered heterocyclyl; and 8- to 11-membered heterobicyclyl; and

wherein $-L^1-$ is substituted with $-L^2-$ and wherein $-L^1-$ is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (II) is not replaced by $-L^2-$ or a substituent.

12. The conjugate of any one of claims 1 to 11, wherein $-L^2-$ is a spacer moiety.

13. The conjugate of any one of claims 1 to 12, wherein -D is released in its free form from $-L^1-$.

14. The conjugate of any one of claims 1 to 13, wherein -D is selected from the group consisting of peptides, proteins, oligonucleotides and small molecule drug moieties.

15. The conjugate of any one of claims 1 to 14, wherein -D is an antibiotic moiety.

16. The conjugate of any one of claims 1 to 15, wherein -D is selected from the group consisting of aminoglycosides, tetracycline antibiotics, amphenicols, pleuromutilins, macrolid antibiotics, lincosamides, steroid antibiotics, antifolate antibiotics, sulfonamides, topoisomerase inhibitors, quinolones, fluoroquinolones, nitroimidazole antibiotics, nitrofuran antibiotics, rifamycins, glycopeptides, penicillins, cephalosporins, monobactams, beta-lactamase inhibitors, polymyxin antibiotics, lipopeptide antibiotics, oxazolidinon, antimicrobial peptides, antimicrobial proteins, porphyrins, azole antifungals, polyenes, antiprotozoal drugs, fosfomycin**,** cycloserine, and bacitracin.

17. The conjugate of any one of claims 1 to 16, wherein -D is daptomycin.

18. A pharmaceutical composition comprising the conjugate of any one of claims 1 to 17 and at least one excipient.

19. The conjugate of any one of claims 1 to 17 or the pharmaceutical composition of claim 18 for use as a medicament.

20. The conjugate of any one of claims 1 to 17 or the pharmaceutical composition of claim 18 for the manufacture of an antibiotic.

21. Use of the conjugate of any one of claims 1 to 17, or the pharmaceutical composition of claim 18, in the manufacture of a medicament for the prevention or treatment of a joint infection.