Claims

1. A polyoxazoline (POZ) conjugate comprising a water-soluble POZ polymer and an agent linked to the water-soluble POZ polymer by a physiologically degradable linkage, or a pharmaceutically acceptable form thereof, wherein a release rate of the agent from the POZ conjugate is controlled by selecting a POZ polymer characteristic, an agent characteristic, a loading characteristic, or a combination of the foregoing.

2. The POZ conjugate of claim 1, wherein the agent is a phytocannabinoid, a dopamine agonist, an anticholinergic, a monamine oxidase-B inhibitor, a catechol-O-methyl transferase (COMT) inhibitor or an adenosine A_{2A} receptor antagonist, or a GABA-uptake inhibitor.

3. The POZ conjugate of claim 2, wherein the phytocannabinoid is selected from the group consisting of: cannabidiol, cannabigerol, cannabigerolic acid, cannabidiolic acid, cannabidiolmonomethylether, cannabidiol-C4, cannabidarinic acid, cannabidivarin, cannabidiol or cannabigerol propyl variant, cannabichromene, cannabichromenic acid, cannabichromevarinic acid, cannabichromevarin, cannabinol, cannabicyclol, tetrahydrocannabivarin, Δ^9-THC, ajulemic acid, and dexanabinol.

4. The POZ conjugate of claim 2, wherein the dopamine agonist is selected from the group consisting of: apomorphine, arbutamine, carbidopa, dobutamine, dopamine, entacapone, epinephrine, fenoldopam, isoetharine, isoproterenol, levopoda, levonordefrin, masaprocol, methyldopa, methyldopate, norepinephrine, protokylol, tolcapone, or (r)-(+)-fenoldopam, rotigotine, pramipexole, quinagolide, 5-OH-DPAT, ropinirole, pergolide, cabergoline, and bromocriptine.

5. The POZ conjugate of any one of claims 2 to 4 , wherein the release rate of the agent from the POZ conjugate is controlled by selecting the POZ polymer characteristic, wherein the POZ polymer characteristic is selecting a pendent moiety containing a hydrophilic or a hydrophobic portion, selecting a pendant group on the POZ polymer portion with a hydrophobic character, selecting a selected molecular weight for the POZ polymer portion, or a combination of the foregoing.

6. The POZ conjugate of any one of claims 2 to 4, wherein the release rate of the agent from the POZ conjugate is controlled by selecting the loading characteristic, wherein the loading characteristic is selecting a loading percentage of the agent.

7. The POZ conjugate of any one of claims 2 to 4, wherein the release rate of the agent from the POZ conjugate is controlled by selecting the agent characteristic, wherein the agent characteristic is selecting an agent with a selected solubility in water, selecting an agent with a selected molecular volume, selecting an agent with a selected total polar surface area, or a combination of the foregoing.

8. The POZ conjugate of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, having the structure

$$R\text{-}\{[N(CO\text{-}L_1\text{-}R_1)CH_2CH_2]_m\text{-}[N(COR_2\text{-}A)CH_2CH_2]o\text{-}[N(COX)CH_2CH_2]_n\}_a\text{-}T$$

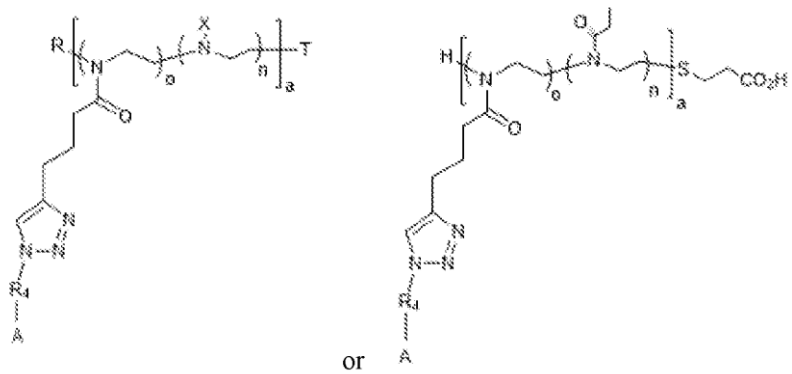
A is the agent;
R is hydrogen, unsubstituted alkyl or substituted alkyl;
R_1 is a pendent moiety containing a hydrophilic or a hydrophobic portion;
L_1 is a linking group linking R_1 to the POZ polymer or is absent;
R_2 is a pendent moiety comprising the physiologically degradable linkage linking the POZ polymer and A;
X is a pendant group;
T is a terminating group;
a is ran that indicates a random copolymer or block that indicates a block copolymer;
m is an integer from 0 to 100;
n is an integer from 0 to 1000, provided that if m is 0, the n is an integer from 1 to 1000; and
o is an integer from 1 to 50.

9. The POZ conjugate of claim 8, wherein m is from 1 to 100 and the release rate of the agent from the POZ conjugate is controlled by the loading percentage and R_1.

10. The POZ conjugate of claim 8, wherein the physiologically degradable linkage comprises a cleavable moiety selected from the group consisting of: esters, carboxylate esters, carbonate esters, carbamates, amides, disulfides, and peptides.

11. The POZ conjugate of any one of claims 8 or 10, wherein L_1 is non-degradable linkage, L_2 is a linking group containing the physiologically degradable linkage, wherein T is Z-B-Q, and wherein Z is S, B is -(CH2)y-, y is an integer from 1-3, and Q is -COOCH3, -COOH, or -NH2.

12. The POZ conjugate of claim 8 having the structure:



or

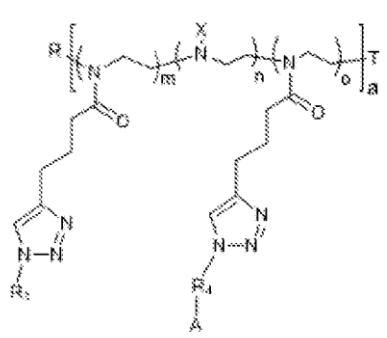
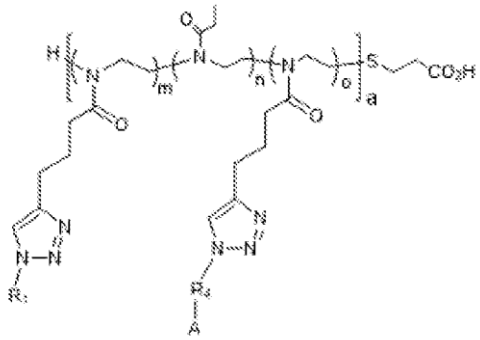
wherein

R_4 is independently selected for each repeating unit from $-(CH_2)_d-C(O)-$, $-CH_2-C(O)-$, $-CH_2-CH_2-C(O)-$, $-CH_2-CH_2-CH_2-C(O)-$, $-CH_2(CH_3)-C(O)-$, $-(CH_2)_d-C(O)-O-$, $-CH_2-C(O)-O-$, $-CH_2-CH_2-C(O)-O-$, $-CH_2-CH_2-CH_2-C(O)-O-$, or $-CH_2(CH_3)-C(O)-O-$;

d is an integer from 1 to 10; and

the release rate of the agent from the POZ conjugate is controlled by the loading percentage.

13. The POZ conjugate of claim 8 having the structure:

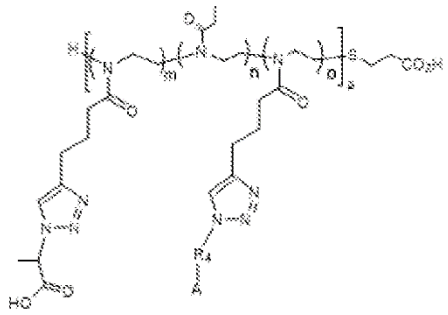
or

wherein:

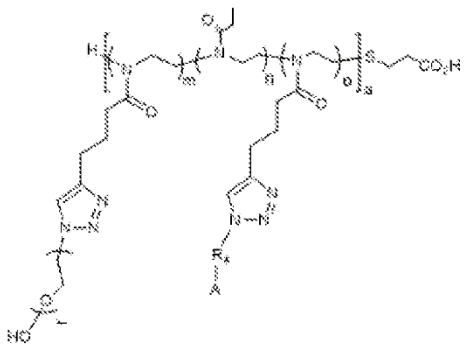
R_1 is independently selected for each repeating unit from a water soluble polymer, a substituted alkyl, a substituted alkenyl, a substituted alkynyl, a substituted aralkyl, or a substituted heterocyclylalkyl group;

R_4 is independently selected for each repeating unit from $-(CH_2)_d-C(O)-$, $-CH_2-C(O)-$, $-CH_2-CH_2-C(O)-$, $-CH_2-CH_2-CH_2-C(O)-$, $-CH_2(CH_3)-C(O)-$, $-(CH_2)_d-C(O)-O-$, $-CH_2-C(O)-O-$, $-CH_2-CH_2-C(O)-O-$, $-CH_2-CH_2-CH_2-C(O)-O-$, or $-CH_2(CH_3)-C(O)-O-$; d is an integer from 1 to 10; and the release rate of the agent from the POZ conjugate is controlled by the loading percentage and the R_1.

14. The POZ conjugate of claim 16 having the structure:



or



wherein:

f is an integer from 1-10;

R_4 is independently selected for each repeating unit from $-(CH_2)_d-C(O)-$, $-CH_2-C(O)-$, $-CH_2-CH_2-C(O)-$, $-CH_2-CH_2-CH_2-C(O)-$, $-CH_2(CH_3)-C(O)-$, $-(CH_2)_d-C(O)-O-$, $-CH_2-C(O)-O-$, $-CH_2-CH_2-C(O)-O-$, $-CH_2-CH_2-CH_2-C(O)-O-$, or $-CH_2(CH_3)-C(O)-O-$; d is an integer from 1 to 10; and the release rate of the agent from the POZ conjugate is controlled by the loading percentage and the hydrophilic portion.

15. A polyoxazoline (POZ) conjugate comprising a water-soluble POZ polymer and a phytocannabinoid linked to the water-soluble POZ polymer by a physiologically degradable linkage, or a pharmaceutically acceptable form thereof, wherein the POZ conjugate comprises a loading percentage of the phytocannabinoid from 1.6% ± 1% to 9.6% ± 1% (w/w phytocannabinoid to POZ polymer), and wherein a release rate of the phytocannabinoid from the POZ conjugate is controlled by the loading percentage.

16. The POZ conjugate of claim 15 further comprising a pendent moiety containing a hydrophilic or a hydrophobic portion linked to the POZ polymer and the release rate of the phytocannabinoid from the POZ conjugate is controlled by the loading percentage and the hydrophilic or the hydrophobic portion.

17. The POZ conjugate of claim 15, wherein the pendent moiety containing a hydrophilic or a hydrophobic portion is linked to the POZ polymer by a non-degradable linkage.

18. The POZ conjugate of claim 15, or a pharmaceutically acceptable salt thereof, having the structure

$$R-\{[N(CO-L_1-R_1)CH_2CH_2]_m-[N(COR_2-A)CH_2CH_2]o-[N(COX)CH_2CH_2]_n\}_a-T$$

A is the agent;

R is hydrogen, unsubstituted alkyl or substituted alkyl;

R_1 is a pendent moiety containing a hydrophilic or a hydrophobic portion;

L_1 is a linking group linking R_1 to the POZ polymer or is absent;

R_2 is a pendent moiety comprising the physiologically degradable linkage linking the POZ polymer and A;

X is a pendant group;

T is a terminating group;

a is ran that indicates a random copolymer or block that indicates a block copolymer;

m is an integer from 0 to 100;

n is an integer from 0 to 1000, provided that if m is 0, the n is an integer from 1 to 1000; and

o is an integer from 1 to 50.