and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof,

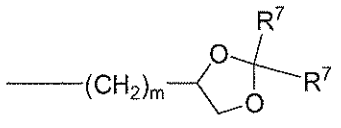
wherein:

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or $-N(R^2)_2$;

R^1 is hydrogen or lower alkyl;

each R^2 is, independently, $-R^7$, $-(CH_2)_m-OR^8$, $-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, or



;

R^3 and R^4 are each, independently, hydrogen, lower alkyl, hydroxyl-lower alkyl, phenyl, (phenyl)-lower alkyl, (halophenyl)-lower alkyl, ((lower-alkyl)phenyl)-lower-alkyl, ((lower-alkoxy)phenyl)-lower-alkyl, (naphthyl)-lower-alkyl, or (pyridyl)-lower-alkyl, or a group represented by formula A or formula B, with the proviso that at least one of R^3 and R^4 is a group represented by the formula A or formula B;

formula A: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^1$

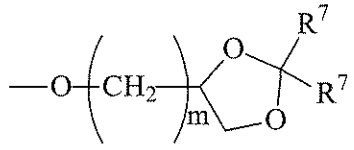
formula B: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^2$

A^1 is a C_6-C_{15}-membered aromatic carbocycle substituted with at least one R^5 and the remaining substituents are R^6;

A^2 is a six to fifteen-membered aromatic heterocycle substituted with at least one R^5 and the remaining substituents are R^6 wherein said aromatic heterocycle comprises 1-4 heteroatoms selected from the group consisting of O, N, and S;

each R^L is, independently, $-R^7$, $-(CH_2)_n-OR^8$, $-O-(CH_2)_m-OR^8$, $-(CH_2)_n-NR^7R^{10}$, $-O-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$,

$-O-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$,
$-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$,
$-O-(CH_2)_m-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-O-(CH_2)_m-(Z)_g-R^7$,
$-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$,
$-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$,
$-(CH_2)_n-CO_2R^7$, $-O-(CH_2)_m-CO_2R^7$, $-OSO_3H$, -O-glucuronide, -O-glucose,



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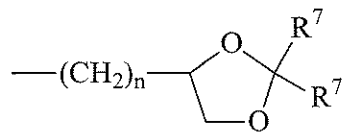


;

each o is, independently, an integer from 0 to 10;

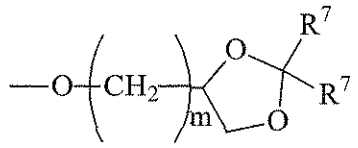
each p is, independently, an integer from 0 to 10;

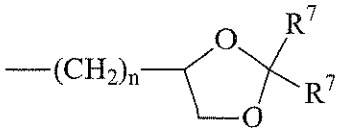
with the proviso that the sum of o and p in each contiguous chain is from 1 to 10;

each x is, independently, O, NR^{10}, C(=O), CHOH, $C(=N-R^{10})$, $CHNR^7R^{10}$, or a single bond;

each R^5 is, independently, $-Link-(CH_2)_m-CAP$, $-Link-(CH_2)_n(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2CH_2O)_m-CH_2-CAP$, $-Link-(CH_2CH_2O)_m-CH_2CH_2-CAP$, $-Link-(CH_2)_m-(Z)_g-CAP$, $-Link-(CH_2)_n(Z)_g-(CH_2)_m-CAP$, $-Link-(CH_2)_n-NR^{13}-CH_2(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2)_n-(CHOR^8)_mCH_2-NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_nNR^{13}-(CH_2)_m(CHOR^8)_nCH_2NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_m-(Z)_g-(CH_2)_m-CAP$, $-Link-NH-C(=O)-NH-(CH_2)_m-CAP$, $-Link-(CH_2)_m-C(=O)NR^{13}-(CH_2)_m-CAP$, $-Link-(CH_2)_n-(Z)_g-(CH_2)_m-(Z)_g-CAP$, or $-Link-Z_g-(CH_2)_m-Het-(CH_2)_m-CAP$;

each R^6 is, independently, R^5, $-R^7$, $-OR^{11}$, $-N(R^7)_2$, $-(CH_2)_m-OR^8$, $-O-(CH_2)_m-OR^8$, $-(CH_2)_n-NR^7R^{10}$, $-O-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-O-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-O-(CH_2)_m-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-O-(CH_2)_m-(Z)_g-R^7$, $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, $-O-(CH_2)_m-CO_2R^7$, $-OSO_3H$, -O-glucuronide, -O-glucose,

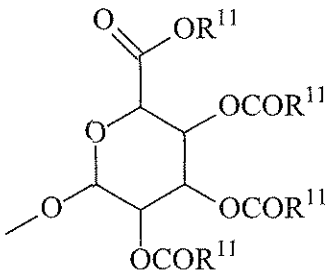


, or  ;

wherein when two R^6 are $-OR^{11}$ and are located adjacent to each other on the aromatic carbocycle or aromatic heterocycle, the two OR^{11} may form a methylenedioxy group;

each R^7 is, independently, hydrogen, lower alkyl, phenyl, substituted phenyl or $-CH_2(CHOR^8)_m-CH_2OR^8$;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or



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each R^9 is, independently, $-CO_2R^7$, $-CON(R^7)_2$, $-SO_2CH_3$, $-C(=O)R^7$, $-CO_2R^{13}$, $-CON(R^{13})_2$, $-SO_2CH_2R^{13}$, or $-C(=O)R^{13}$;

each R^{10} is, independently, -H, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, or $-CH_2-(CHOH)_n-CH_2OH$;

each Z is, independently, -(CHOH)-, -C(=O)-, $-(CHNR^7R^{10})-$, $-(C=NR^{10})-$, $-NR^{10}-$, $-(CH_2)_n-$, $-(CHNR^{13}R^{13})-$, $-(C=NR^{13})-$, or $-NR^{13}-$;

each R^{11} is, independently, hydrogen, lower alkyl, phenyl lower alkyl or substituted phenyl lower alkyl;

each R^{12} is, independently, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, $-CH_2(CHOH)_n-CH_2OH$, $-CO_2R^7$, $-C(=O)NR^7R^7$, or $-C(=O)R^7$;

each R^{13} is, independently, hydrogen, $-OR^7$, R^{10}, R^{11} or R^{12};

each g is, independently, an integer from 1 to 6;

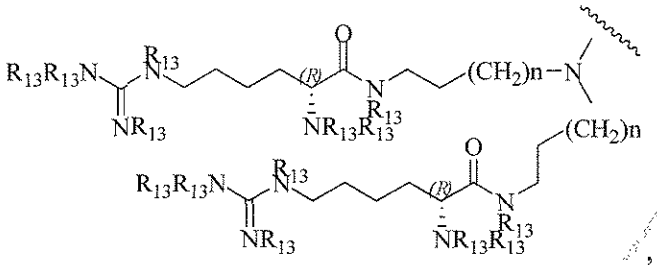
each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each –Het- is, independently, -N(R^7)-, -N(R^{10})-, -S-, -SO-, -SO_2-; -O-, -SO_2NH-, -NHSO_2-, -NR^7CO-, -CONR^7-, -N(R^{13})-, -SO_2NR^{13}-, -NR^{13}CO-, or -CONR^{13}-;

each Link is, independently, -O-, -$(CH_2)_n$-, -O$(CH_2)_m$-, -NR^{13}-C(=O)-NR^{13}-, -NR^{13}-C(=O)-$(CH_2)_m$-, -C(=O)NR^{13}-$(CH_2)_m$-, -$(CH_2)_n$-$(Z)_g$-$(CH_2)_n$-, -S-, -SO-, -SO_2-, -SO_2NR^7-, -SO_2NR^{10}-, or -Het-;

each CAP is



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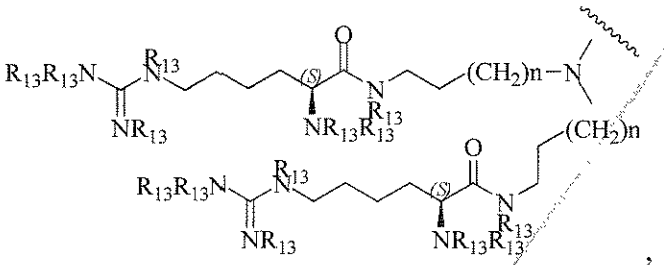

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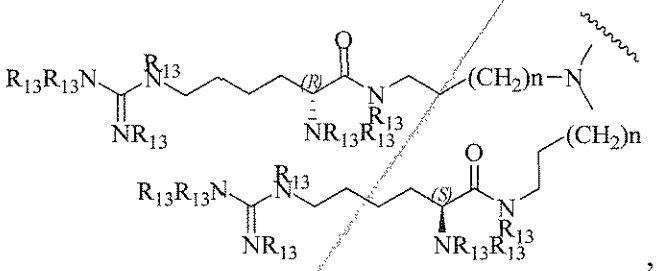

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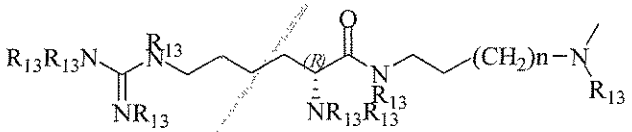

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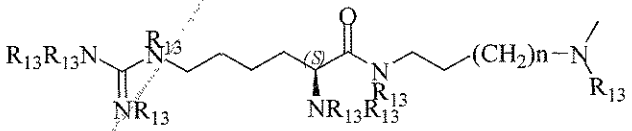

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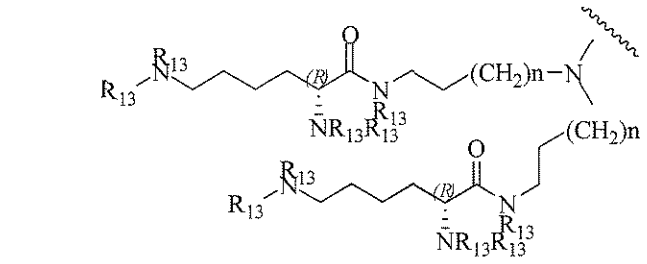

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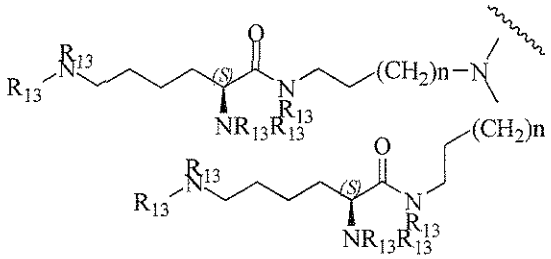

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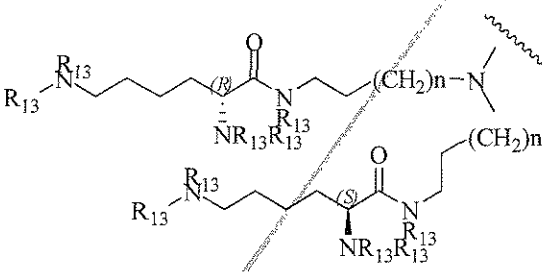

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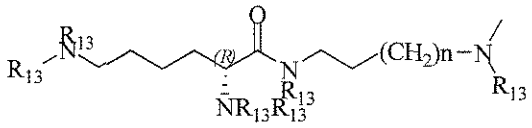

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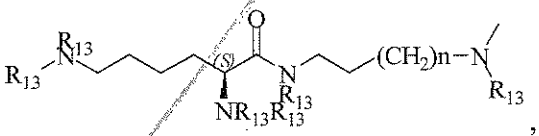

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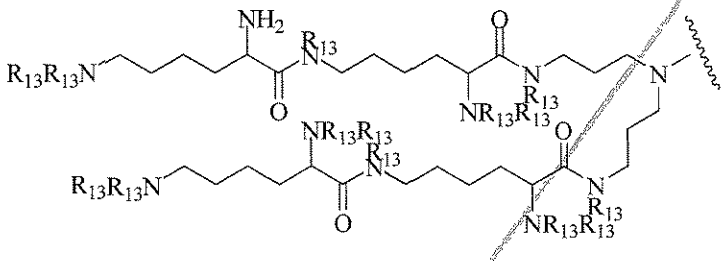

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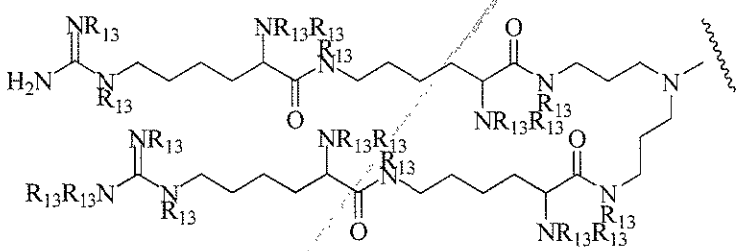

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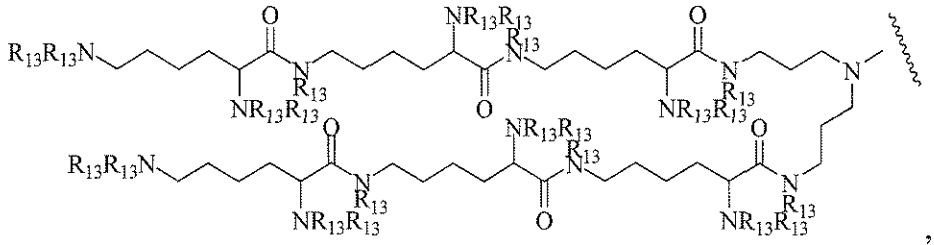

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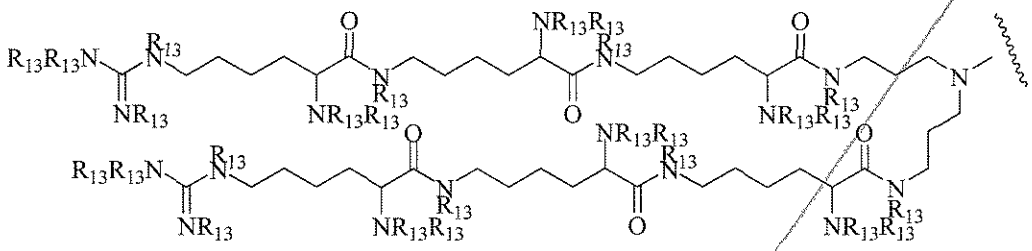

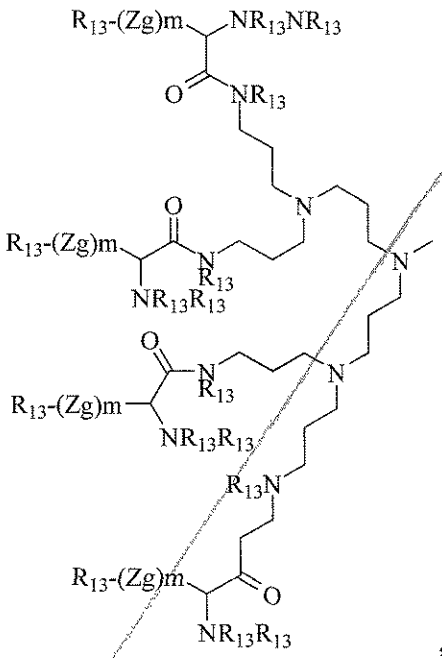

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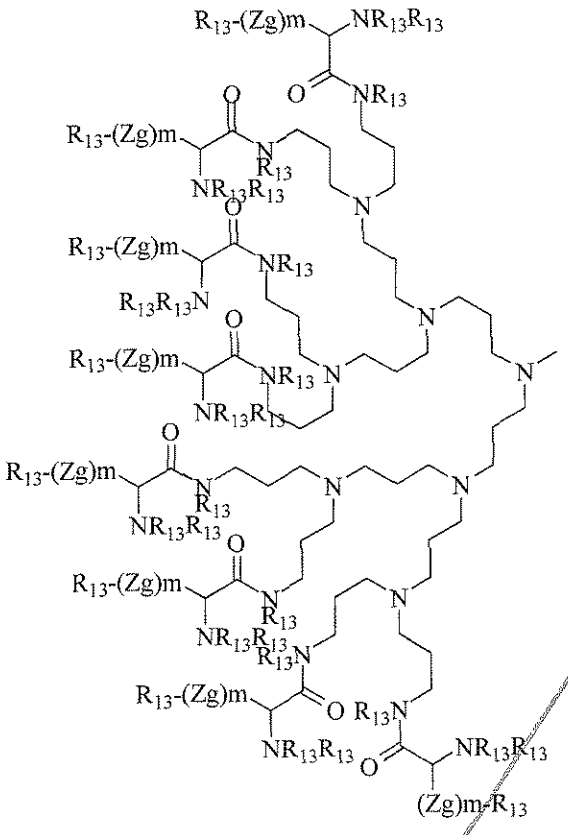

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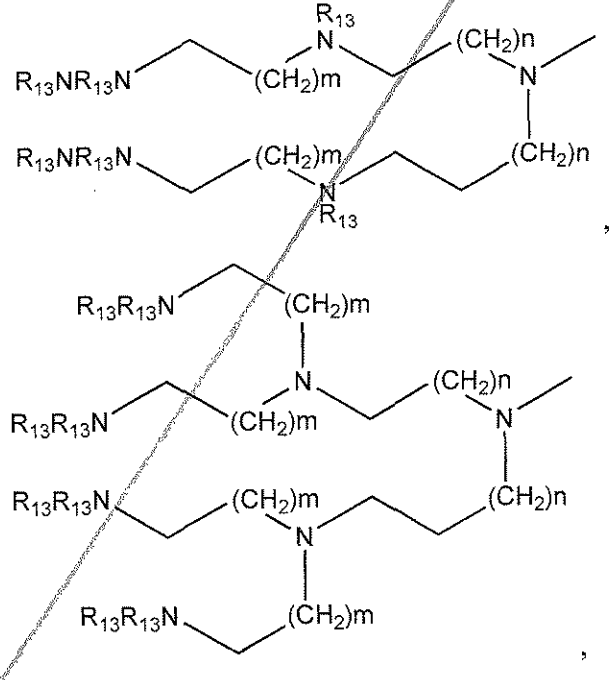


,

and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof,

wherein:

X is halogen, or trifluoromethyl;

Y is $-N(R^2)_2$;

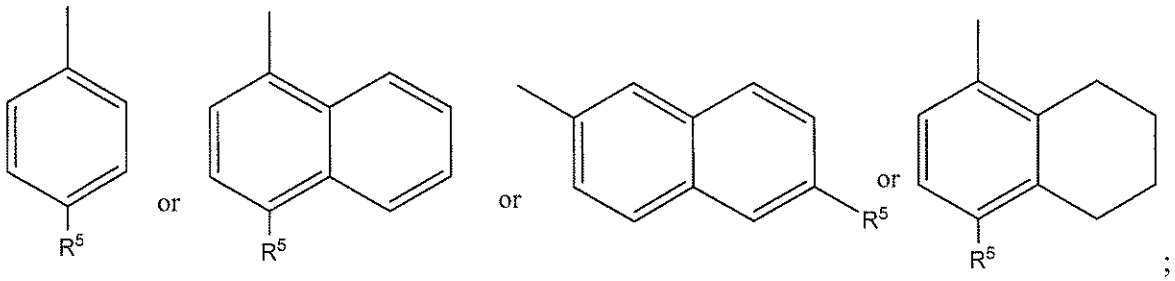
R^1 is hydrogen;

each R^2 is $-R^7$;

R^3 and R^4 are each, independently, hydrogen, or a group represented by formula A, with the proviso that at least one of R^3 and R^4 is a group represented by the formula A;

formula A: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^1$

A^1 is



;

each R^L is, independently, $-R^7$;

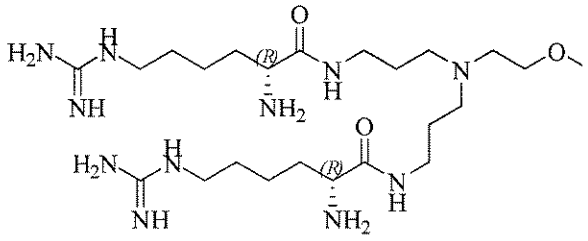
each o is, independently, an integer from 0 to 10;

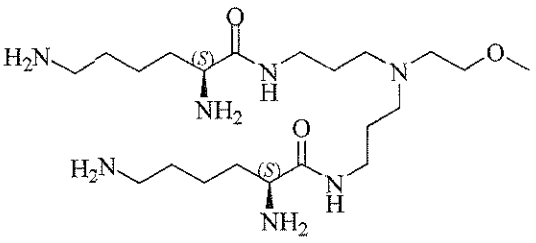
each p is, independently, an integer from 0 to 10;

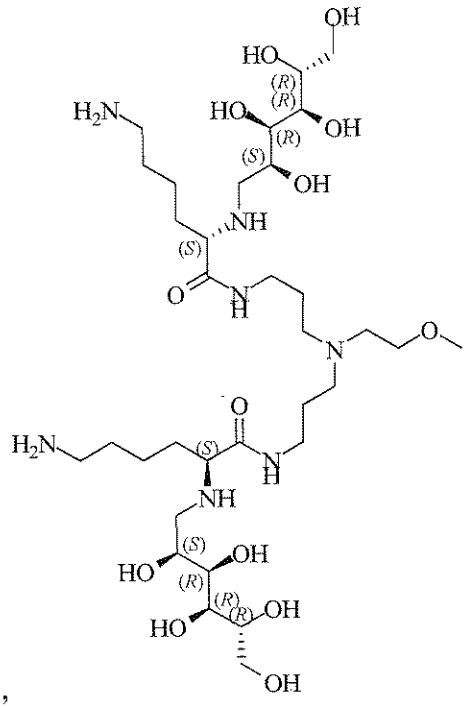
with the proviso that the sum of o and p in each contiguous chain is from 1 to 10;

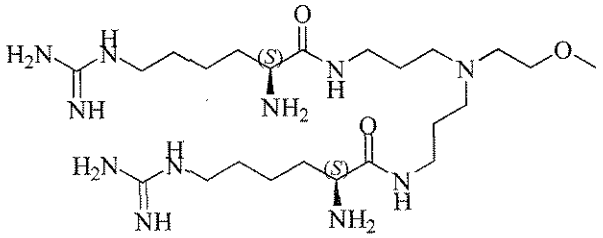
each x is, independently, a single bond;

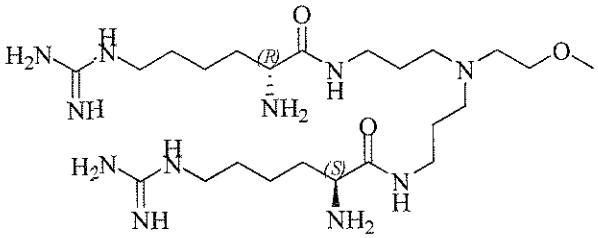
each R^5 is, independently, represented by one of the following formulas:

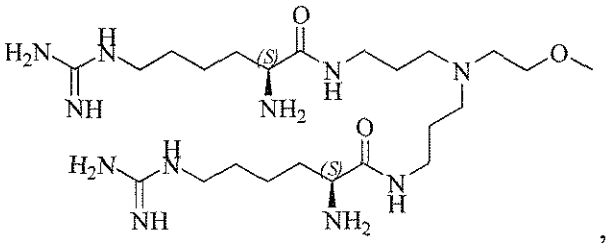












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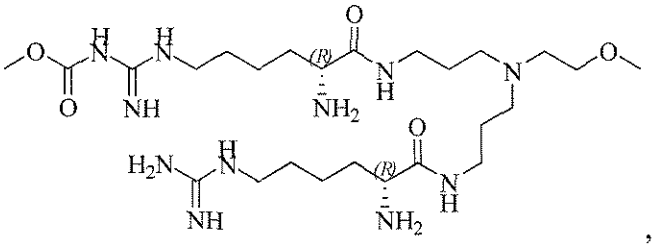

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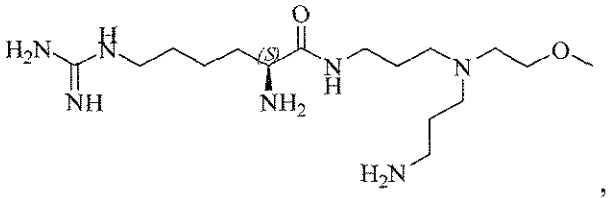

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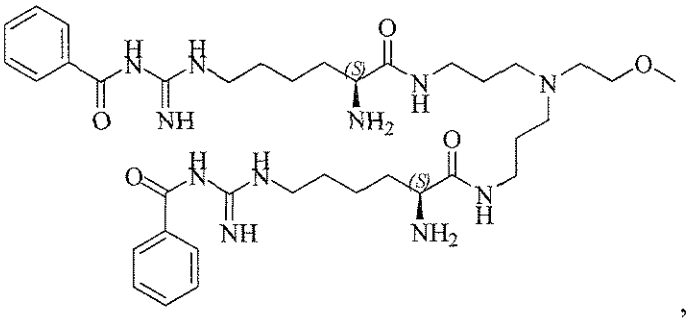

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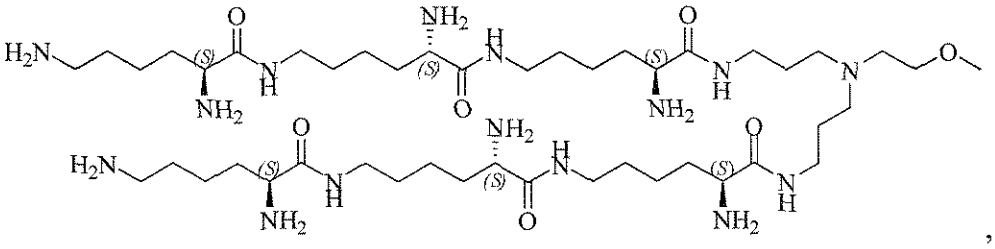

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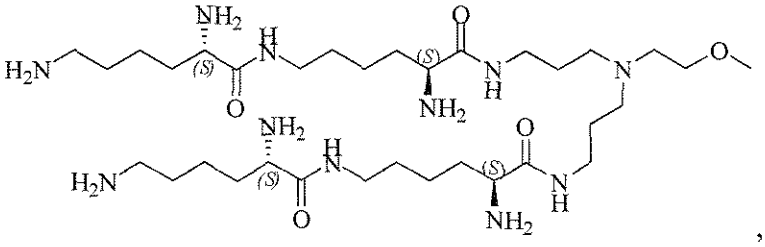

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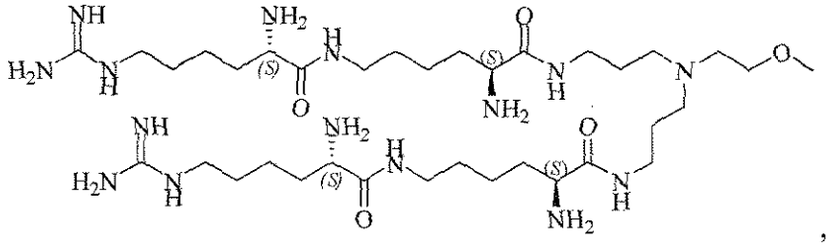

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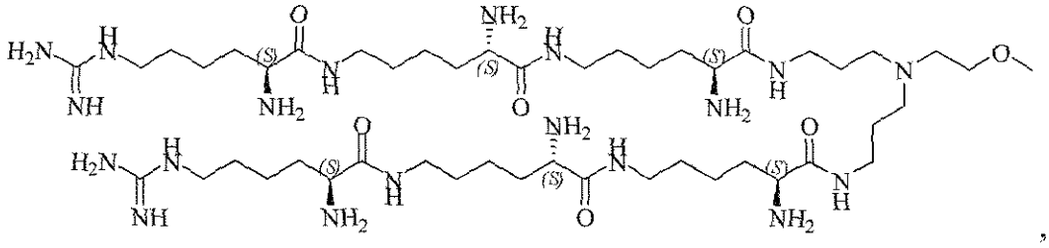

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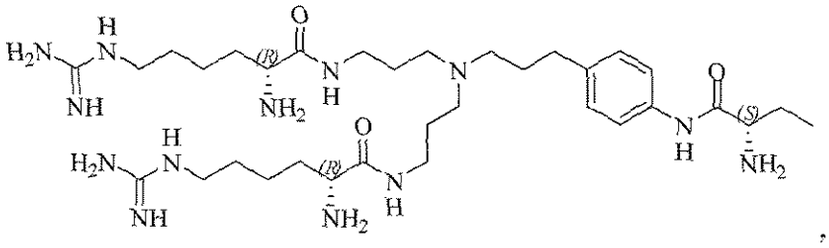

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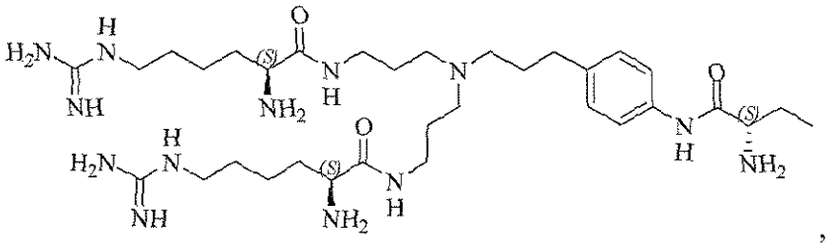

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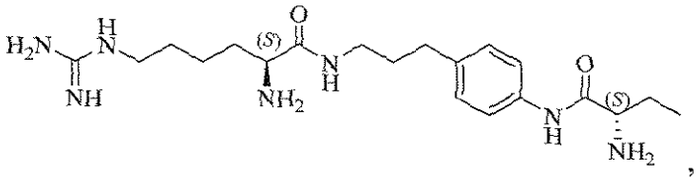

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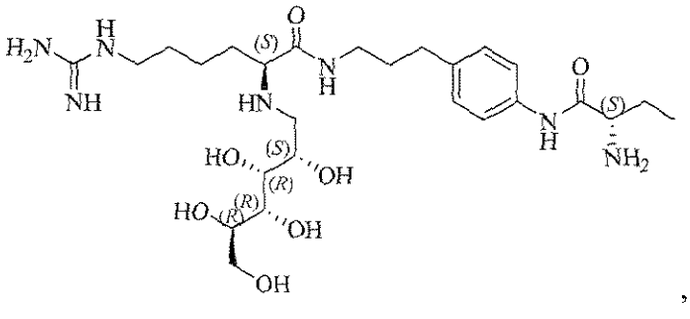

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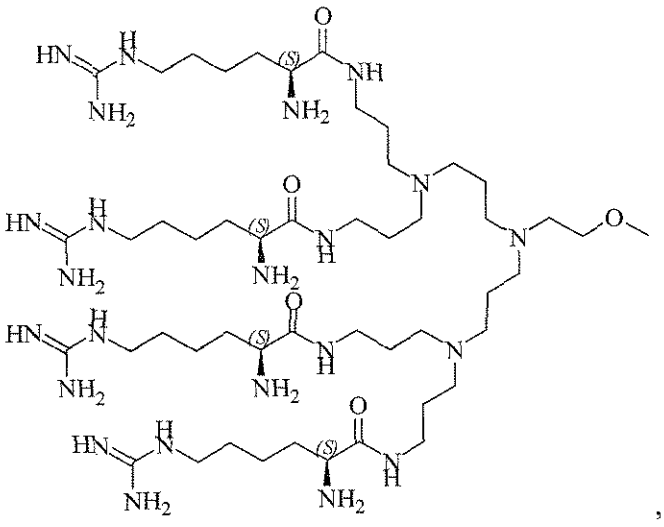

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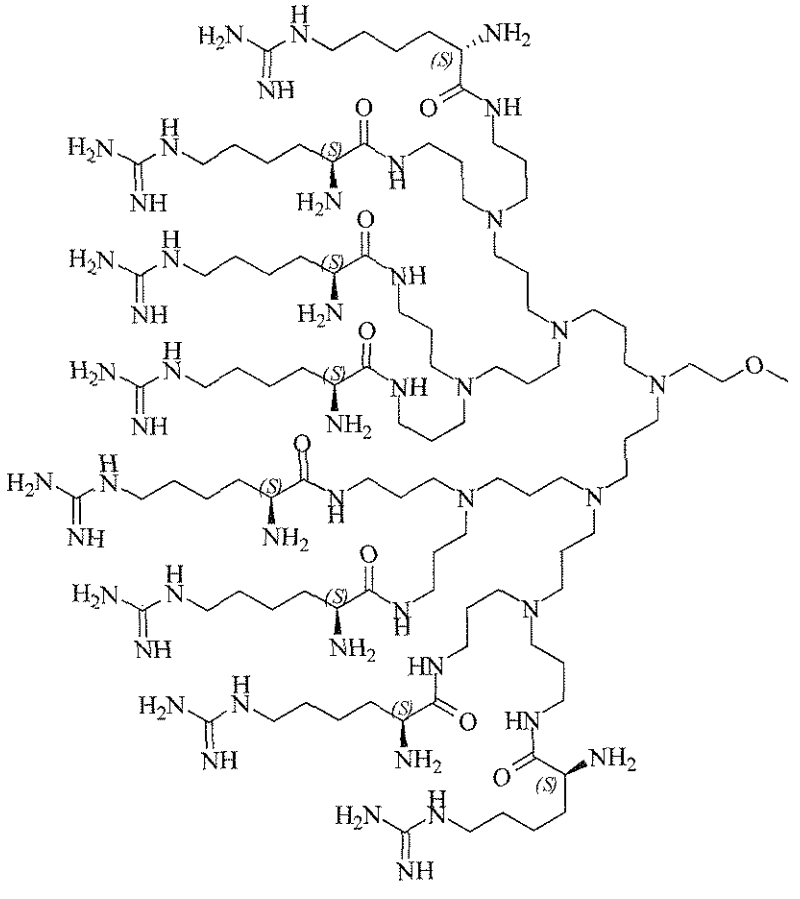

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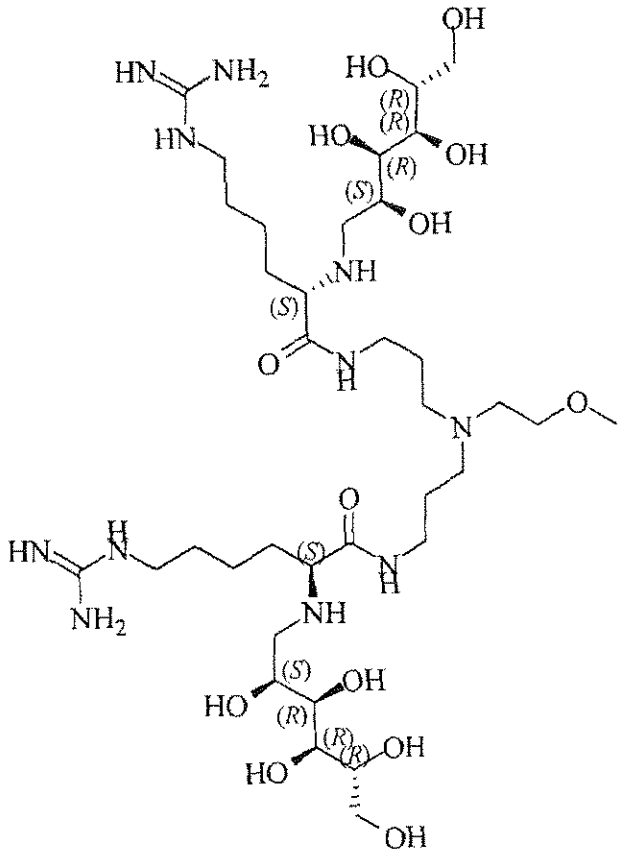
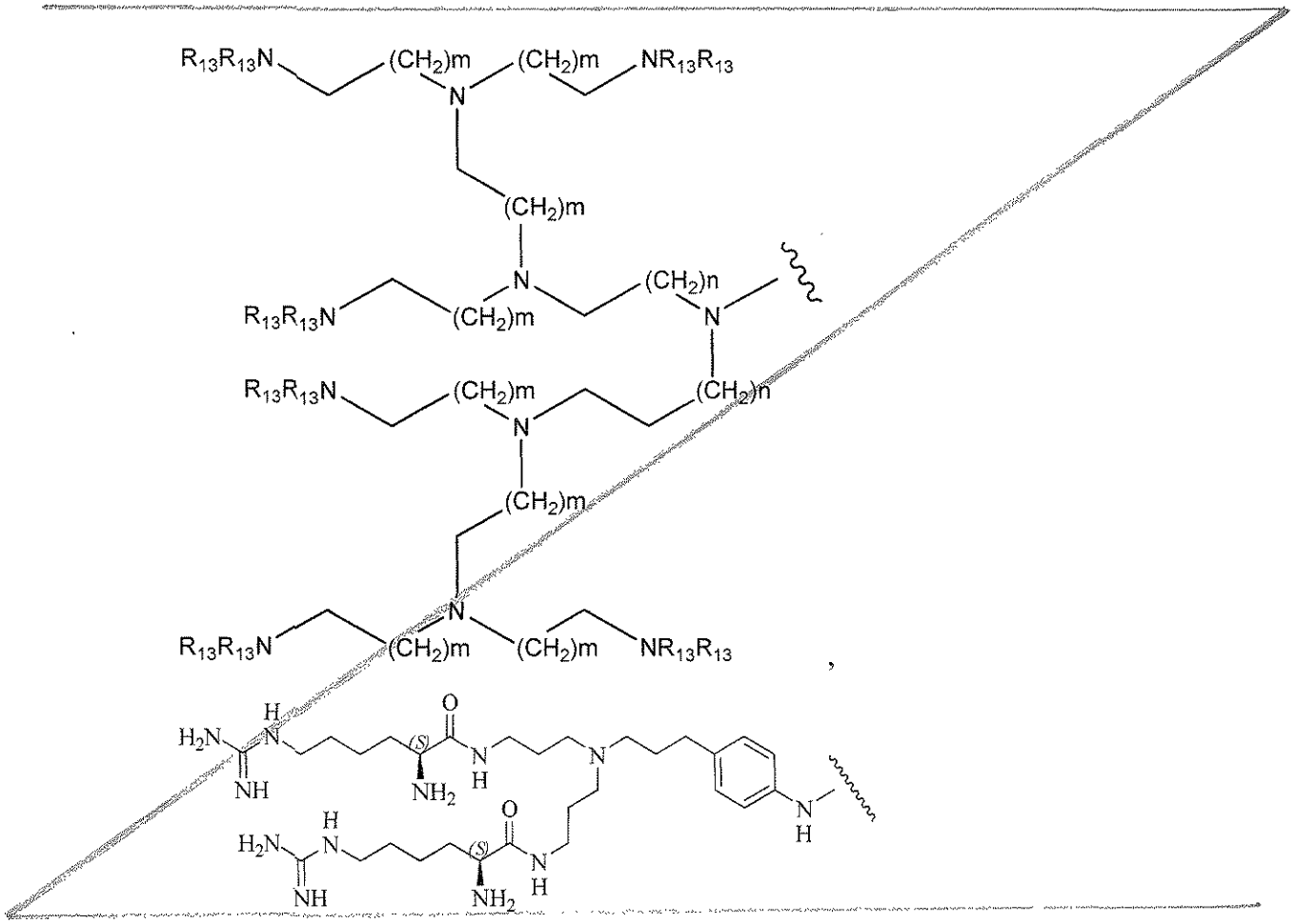
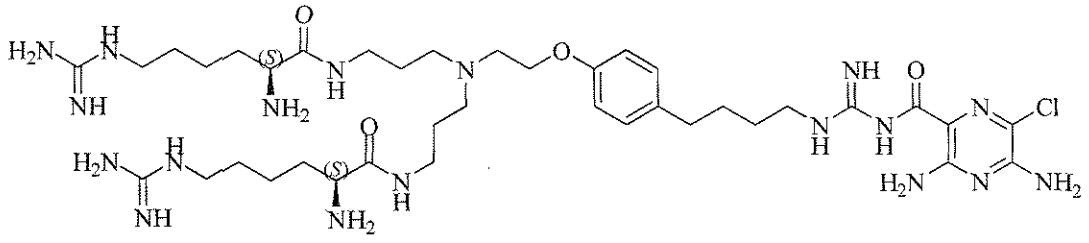


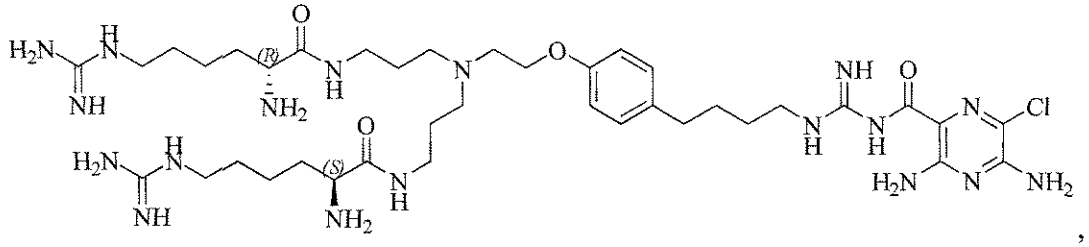
;

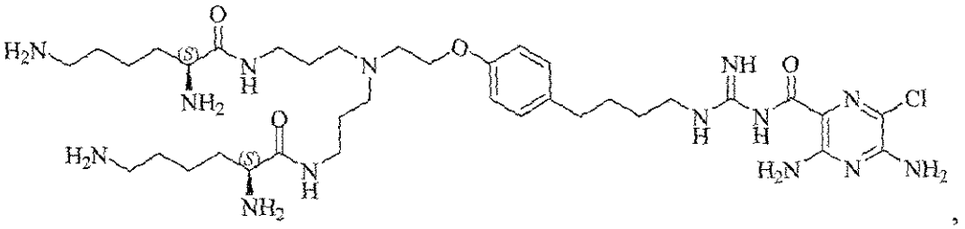
each R^7 is, independently, hydrogen.

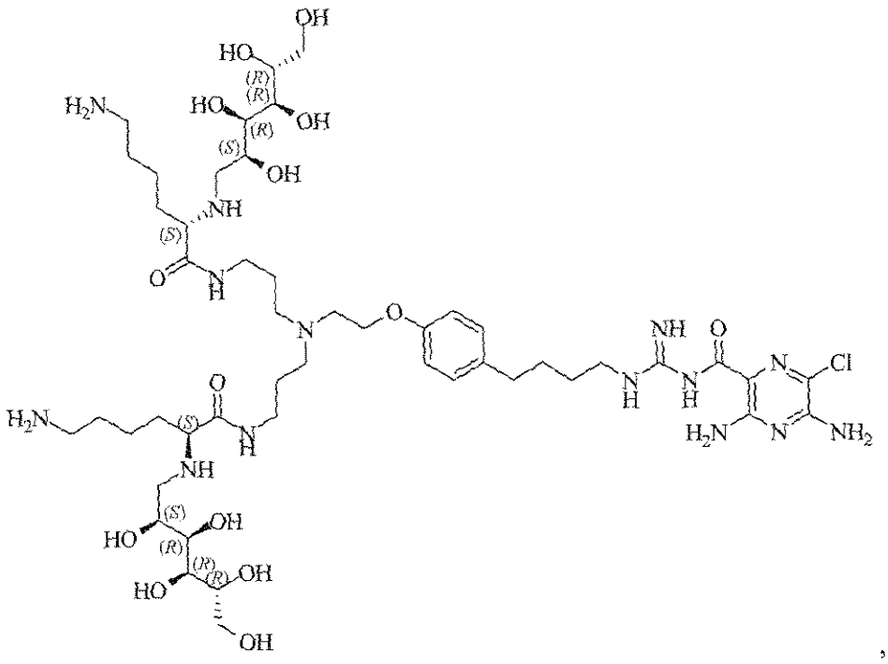


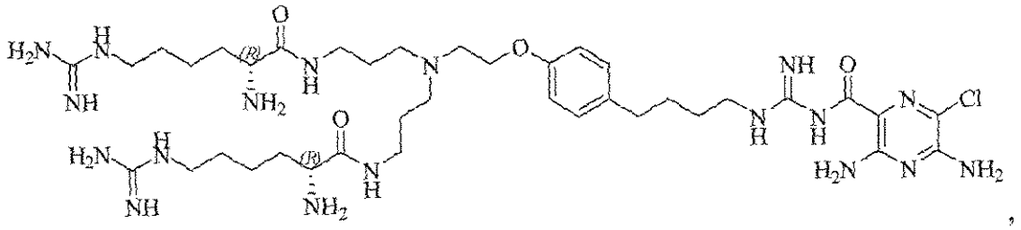
In one aspect, there is provided a compound represented by one of the following formulas:

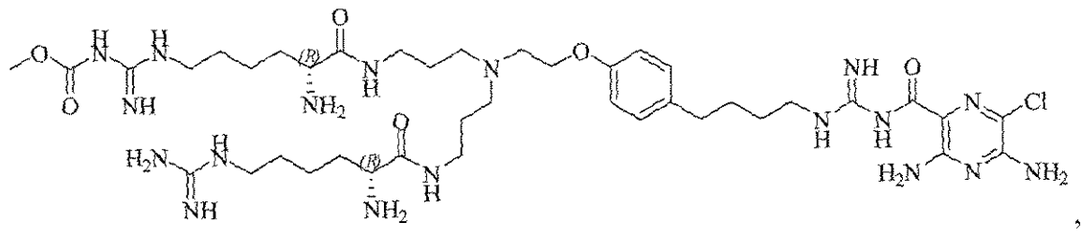


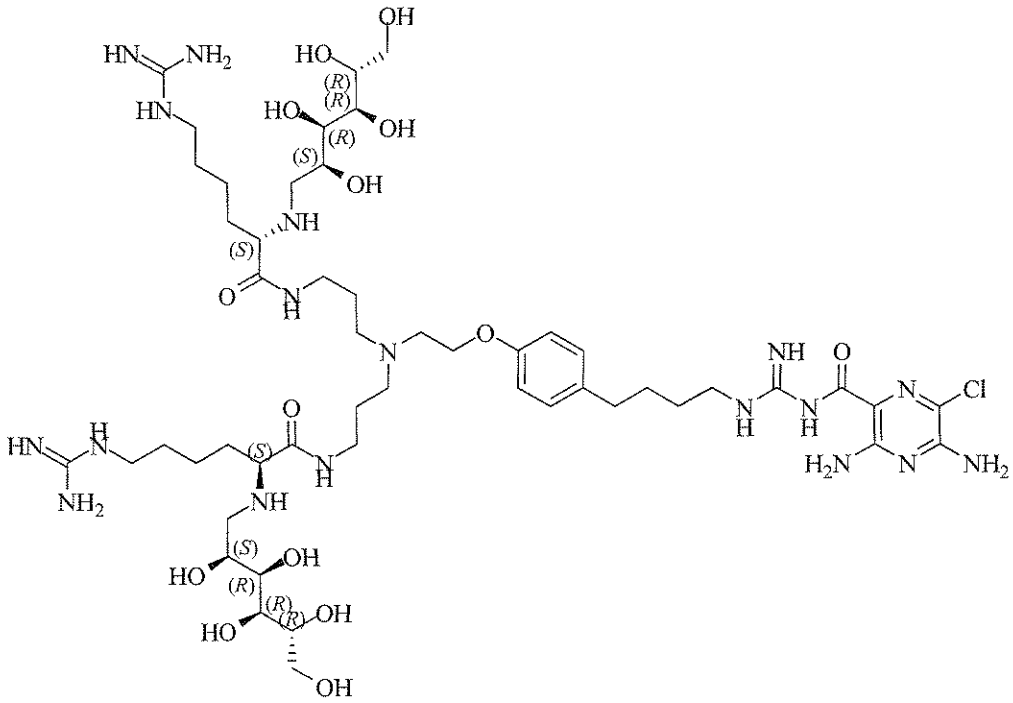


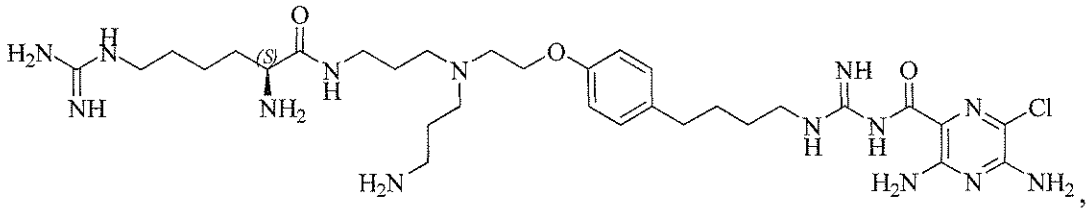












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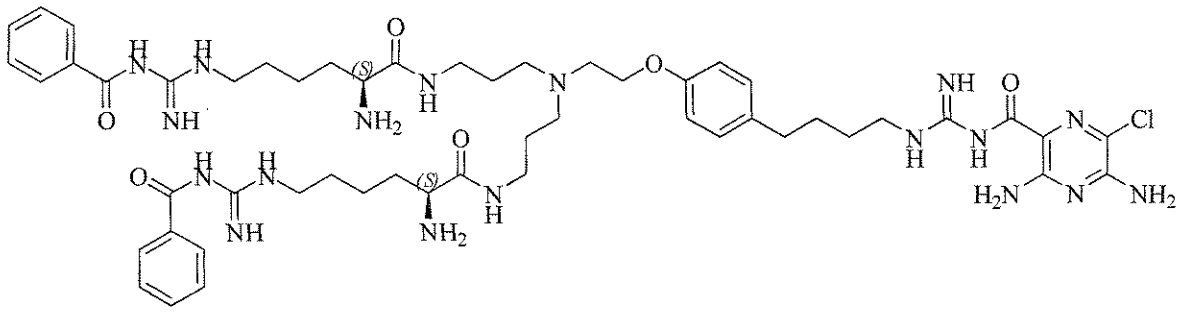

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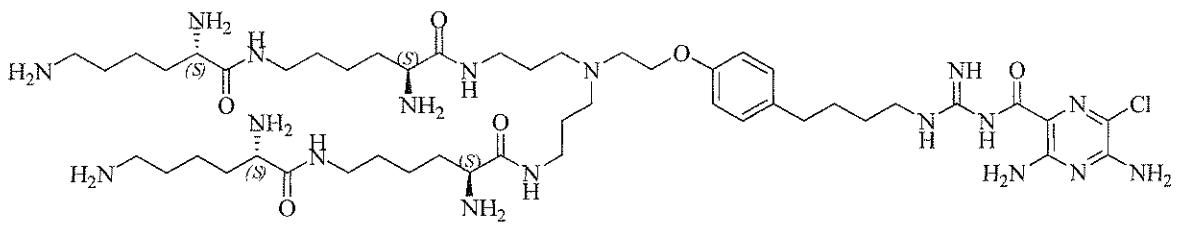

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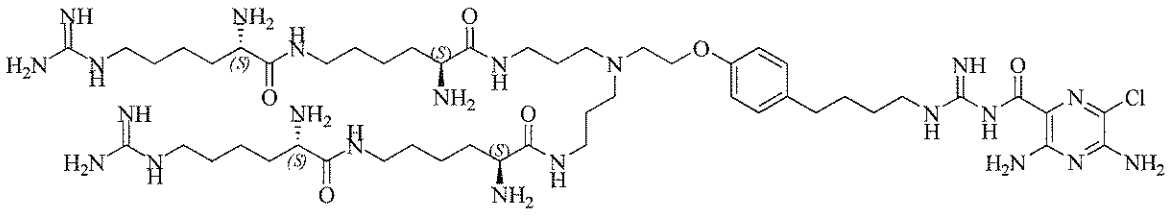

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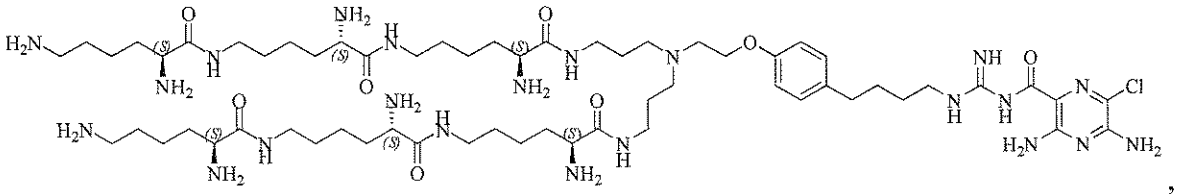

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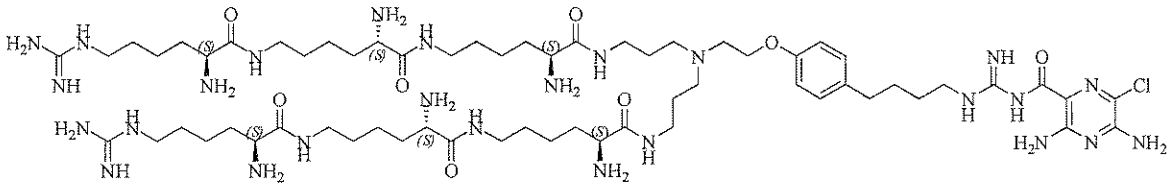

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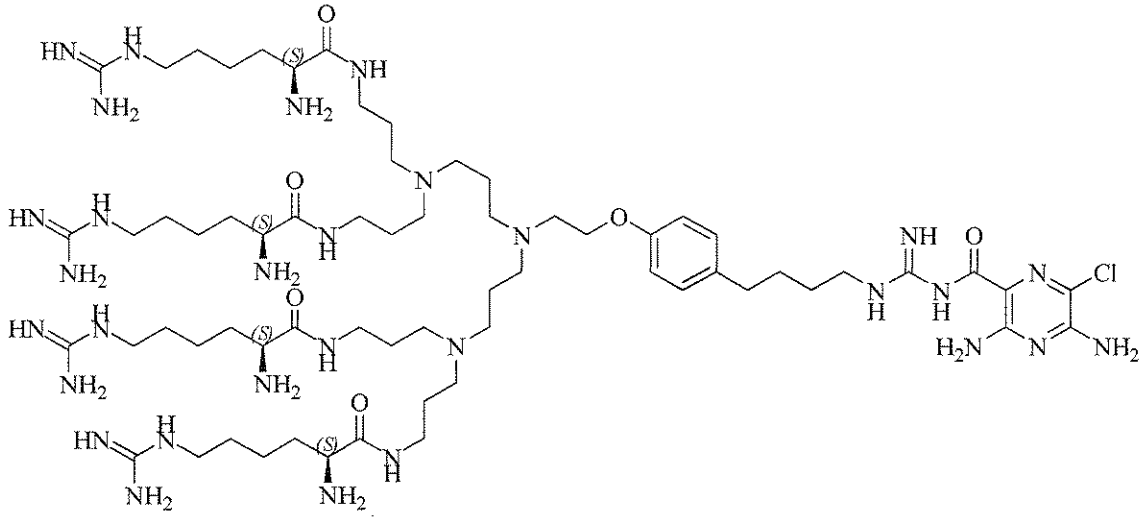

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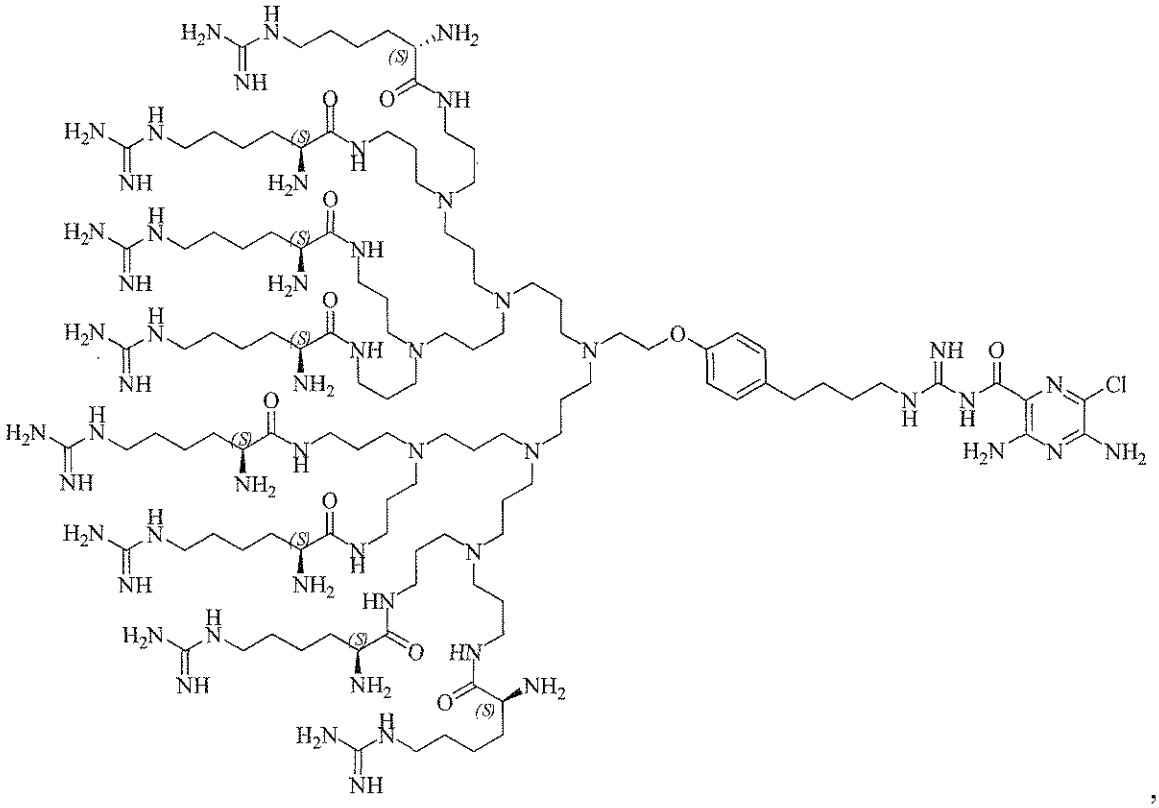
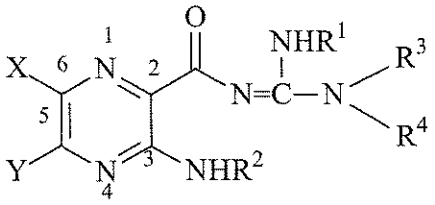


or a pharmaceutically active salt thereof.

The objects of the present disclosure may be accomplished with a class of pyrazinoylguanidine represented by a compound of formula (I):



(I)

and includes racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof, wherein:

caused by pathogens, particularly pathogens which may be used in bioterrorism, comprising administering an effective amount of a compound of formula (I) to a subject in need thereof.

In one aspect, there is provided a composition, comprising:

(a) a compound or a pharmaceutically acceptable salt thereof as described herein and

(b) an osmolotically active compound.

The objects of the disclosure may also be accomplished with a composition, comprising a compound of formula (I) as defined herein and an osmolyte as defined herein.

In one aspect, there is provided a composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and many of the advantages thereof may be readily obtained by reference to the information herein in conjunction with the following figures:

Figure 1: Tear volume assessments over 6 hours in ExLac rats with Amiloride. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 2: Tear volume assessments over 6 hours in ExLac rats with Compound **51**.

Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 3: Tear volume assessments over 6 hours in ExLac rats with Compound **75**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 4: Tear volume assessments over 6 hours in ExLac rats with Compound P-**59**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 5: Tear volume assessments over 6 hours in ExLac rats with Compound **46**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 6: Tear volume assessments over 6 hours in ExLac rats with Compound **45**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 7: Tear volume assessments over 6 hours in ExLac rats with Compound **145**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

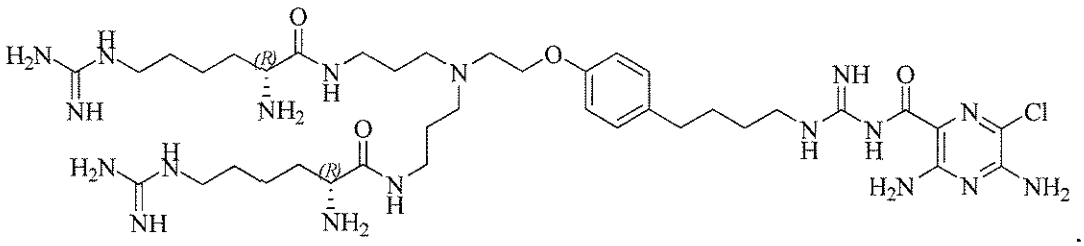
Figure 8: Tear volume assessments over 6 hours in ExLac rats with Compound **82**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

caused by pathogens, particularly pathogens which may be used in bioterrorism, comprising administering an effective amount of a compound of formula (I) to a subject in need thereof.
In one aspect, there is provided a composition, comprising:

(a) a compound or a pharmaceutically acceptable salt thereof as described herein and
(b) an osmolotically active compound.

The objects of the disclosure may also be accomplished with a composition, comprising a compound of formula (I) as defined herein and an osmolyte as defined herein.
In one aspect, there is provided a composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis.

In one aspect, there is provided the hydrochloride salt of:



BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and many of the advantages thereof may be readily obtained by reference to the information herein in conjunction with the

following figures:

Figure 1: Tear volume assessments over 6 hours in ExLac rats with Amiloride. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

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Figure 3: Tear volume assessments over [21] s in ExLac rats with Compound **75**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 4: Tear volume assessments over 6 hours in ExLac rats with Compound P-**59**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

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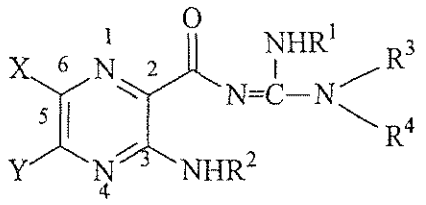
Figure 7: Tear volume assessments over 6 hours in ExLac rats with Compound **145**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

Figure 8: Tear volume assessments over 6 hours in ExLac rats with Compound **82**. Tear volume from ExLac and Normal rats treated with a vehicle are shown for comparison. Error bars are standard error.

What is claimed is:

1. A compound represented by formula (I):



(I)

and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof,

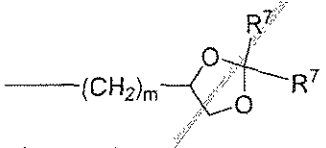
wherein:

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or $-N(R^2)_2$;

R^1 is hydrogen or lower alkyl;

each R^2 is, independently, $-R^7$, $-(CH_2)_m-OR^8$, $-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$,$-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, or



;

R^3 and R^4 are each, independently, hydrogen, lower alkyl, hydroxyl-lower alkyl, phenyl, (phenyl)-lower alkyl, (halophenyl)-lower alkyl, ((lower-alkyl)phenyl)-lower-alkyl, *((lower-alkoxy)phenyl)-lower-alkyl, (naphthyl)-lower-alkyl, or (pyridyl)-lower-alkyl, or* a group represented by formula A or formula B, with the proviso that at least one of R^3 and R^4 is a group represented by the formula A or formula B;

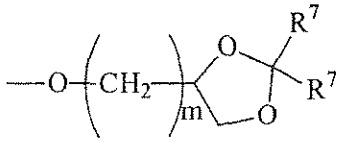
formula A: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^1$

formula B: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^2$

A^1 is a C_6-C_{15}-membered aromatic carbocycle substituted with at least one R^5 and the remaining substituents are R^6;

A^2 is a six to fifteen-membered aromatic heterocycle substituted with at least one R^5 and the remaining substituents are R^6 wherein said aromatic heterocycle comprises 1-4 heteroatoms selected from the group consisting of O, N, and S;

each R^L is, independently, $-R^7$, $-(CH_2)_n-OR^8$, $-O-(CH_2)_m-OR^8$, $-(CH_2)_n-NR^7R^{10}$, $-O-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-O-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-O-(CH_2)_m-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-O-(CH_2)_m-(Z)_g-R^7$, $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, $-O-(CH_2)_m-CO_2R^7$, $-OSO_3H$, -O-glucuronide, -O-glucose,



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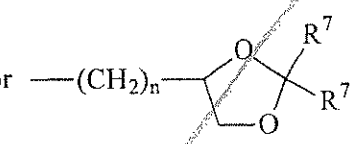


;

each o is, independently, an integer from 0 to 10;

each p is, independently, an integer from 0 to 10;

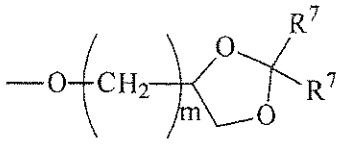
with the proviso that the sum of o and p in each contiguous chain is from 1 to 10;

each x is, independently, O, NR^{10}, C(=O), CHOH, $C(=N-R^{10})$, $CHNR^7R^{10}$, or a single bond;

each R^5 is, independently, $-Link-(CH_2)_m-CAP$, $-Link-(CH_2)_n(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2CH_2O)_m-CH_2-CAP$, $-Link-(CH_2CH_2O)_m-CH_2CH_2-CAP$, $-Link-(CH_2)_m-(Z)_g-CAP$, $-Link-(CH_2)_n(Z)_g-(CH_2)_m-CAP$, $-Link-(CH_2)_n-NR^{13}-CH_2(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2)_n-(CHOR^8)_mCH_2-NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_nNR^{13}-(CH_2)_m(CHOR^8)_nCH_2NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_m-(Z)_g-(CH_2)_m-CAP$, $-Link-NH-C(=O)-NH-(CH_2)_m-CAP$, $-Link-(CH_2)_m-C(=O)NR^{13}-(CH_2)_m-CAP$, $-Link-(CH_2)_n-(Z)_g-(CH_2)_m-(Z)_g-CAP$, or $-Link-Z_g-(CH_2)_m-Het-(CH_2)_m-CAP$;

each R^6 is, independently, R^5, $-R^7$, $-OR^{11}$, $-N(R^7)_2$, $-(CH_2)_m-OR^8$, $-O-(CH_2)_m-OR^8$, $-(CH_2)_n-NR^7R^{10}$, $-O-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-O-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-O-(CH_2)_m-$

$C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-O-(CH_2)_m-(Z)_g-R^7$, $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, $-O-(CH_2)_m-CO_2R^7$, $-OSO_3H$, -O-glucuronide, -O-glucose,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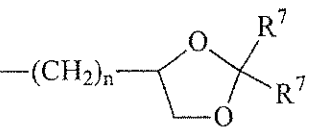
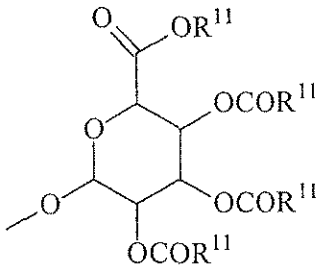

;

wherein when two R^6 are $-OR^{11}$ and are located adjacent to each other on the aromatic carbocycle or aromatic heterocycle, the two OR^{11} may form a methylenedioxy group;

each R^7 is, independently, hydrogen, lower alkyl, phenyl, substituted phenyl or $-CH_2(CHOR^8)_m-CH_2OR^8$;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or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each R^9 is, independently, $-CO_2R^7$, $-CON(R^7)_2$, $-SO_2CH_3$, $-C(=O)R^7$, $-CO_2R^{13}$, $-CON(R^{13})_2$, $-SO_2CH_2R^{13}$, or $-C(=O)R^{13}$;

each R^{10} is, independently, -H, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, or $-CH_2-(CHOH)_n-CH_2OH$;

each Z is, independently, -(CHOH)-, -C(=O)-, $-(CHNR^7R^{10})-$, $-(C=NR^{10})-$, $-NR^{10}-$, $-(CH_2)_n-$, $-(CHNR^{13}R^{13})-$, $-(C=NR^{13})-$, or $-NR^{13}-$;

each R^{11} is, independently, hydrogen, lower alkyl, phenyl lower alkyl or substituted phenyl lower alkyl;

each R^{12} is, independently, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, $-CH_2(CHOH)_n-CH_2OH$, $-CO_2R^7$, $-C(=O)NR^7R^7$, or $-C(=O)R^7$;

each R^{13} is, independently, hydrogen, $-OR^7$, R^{10}, R^{11} or R^{12};

each g is, independently, an integer from 1 to 6;

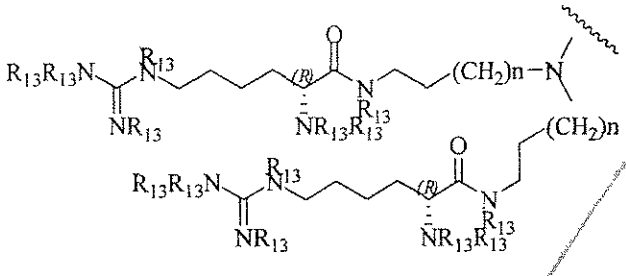
each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each –Het- is, independently, -N(R^7)-, -N(R^{10})-, -S-, -SO-, -SO_2-; -O-, -SO_2NH-, -$NHSO_2$-, -NR^7CO-, -$CONR^7$-, -N(R^{13})-, -SO_2NR^{13}-, -$NR^{13}CO$-, or -$CONR^{13}$-;

each Link is, independently, -O-, -$(CH_2)_n$-, -$O(CH_2)_m$-, -NR^{13}-C(=O)-NR^{13}-, -NR^{13}-C(=O)-$(CH_2)_m$-, -C(=O)NR^{13}-$(CH_2)_m$-, -$(CH_2)_n$-$(Z)_g$-$(CH_2)_n$-, -S-, -SO-, -SO_2-, -SO_2NR^7-, -SO_2NR^{10}-, or -Het-;

each CAP is



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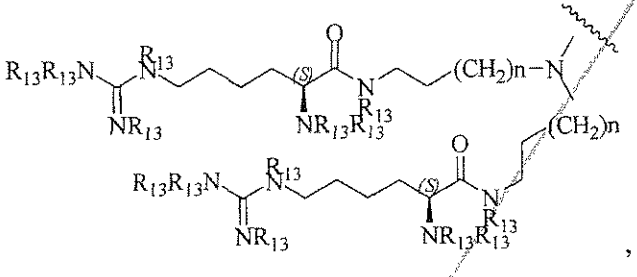

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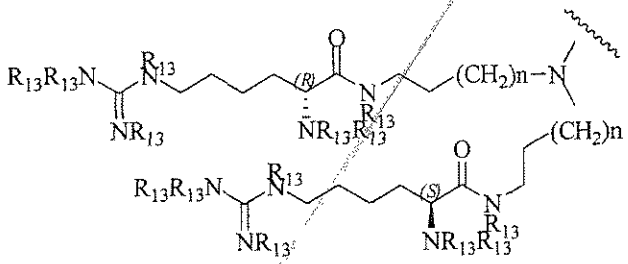

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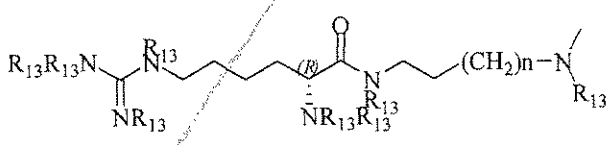

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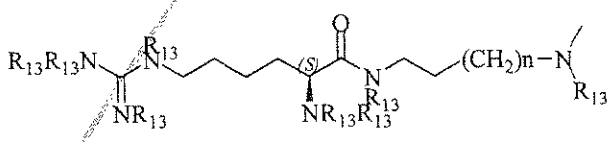

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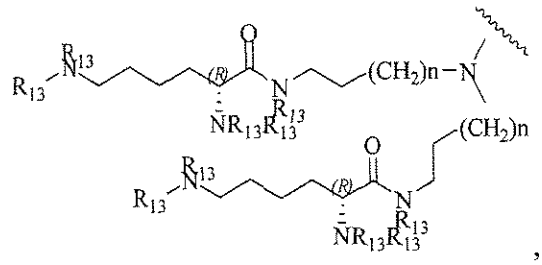

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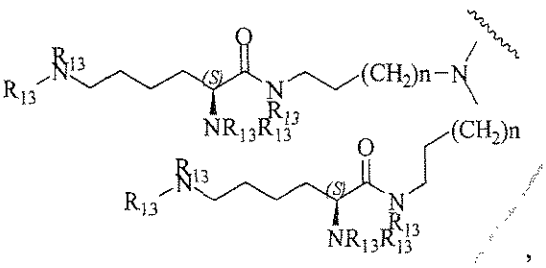

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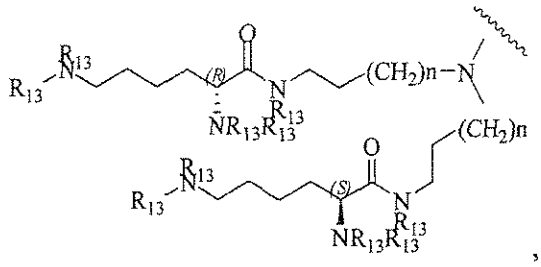

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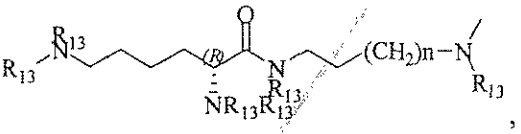

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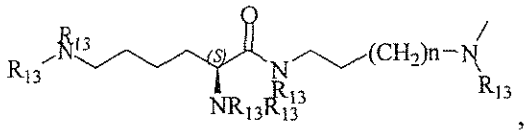

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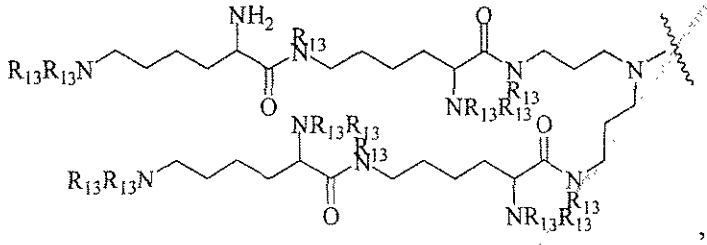

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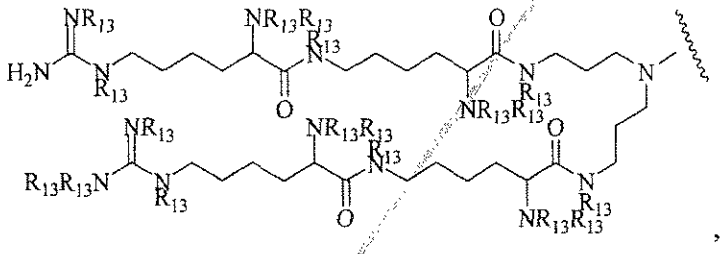

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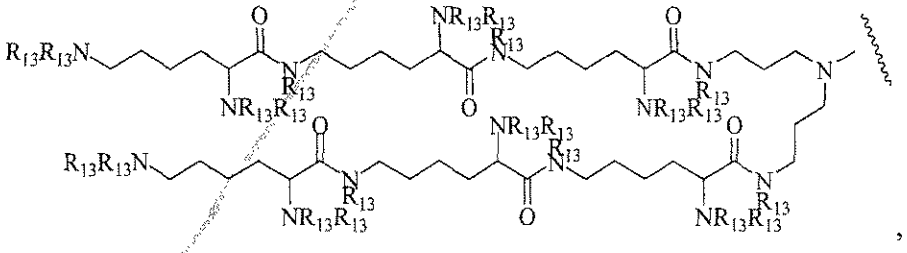

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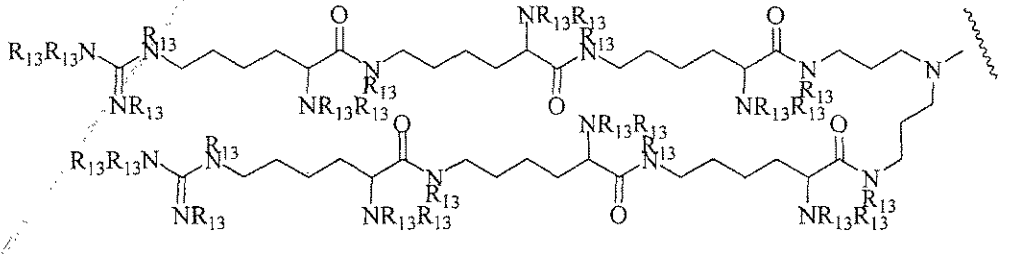

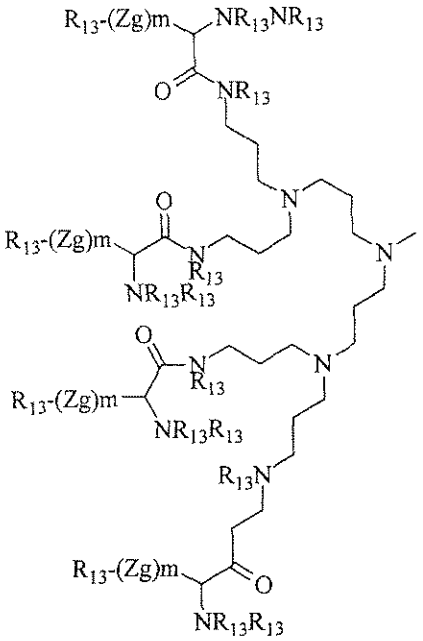

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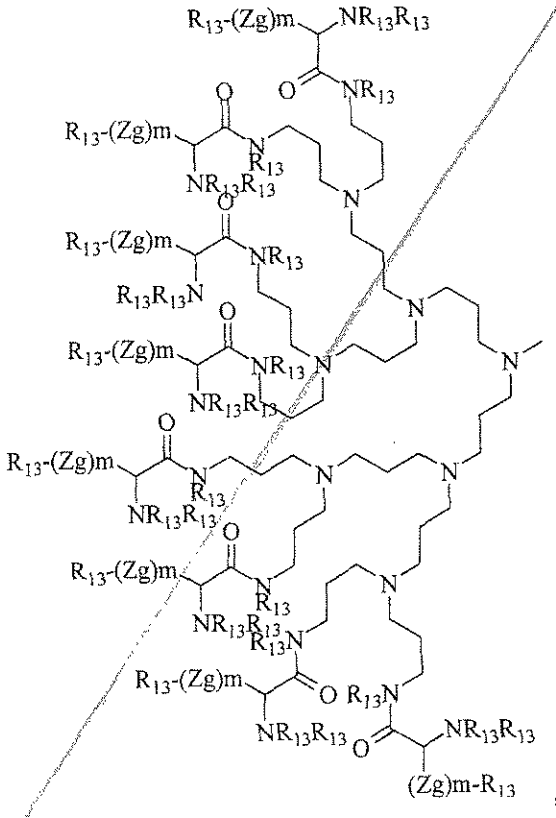

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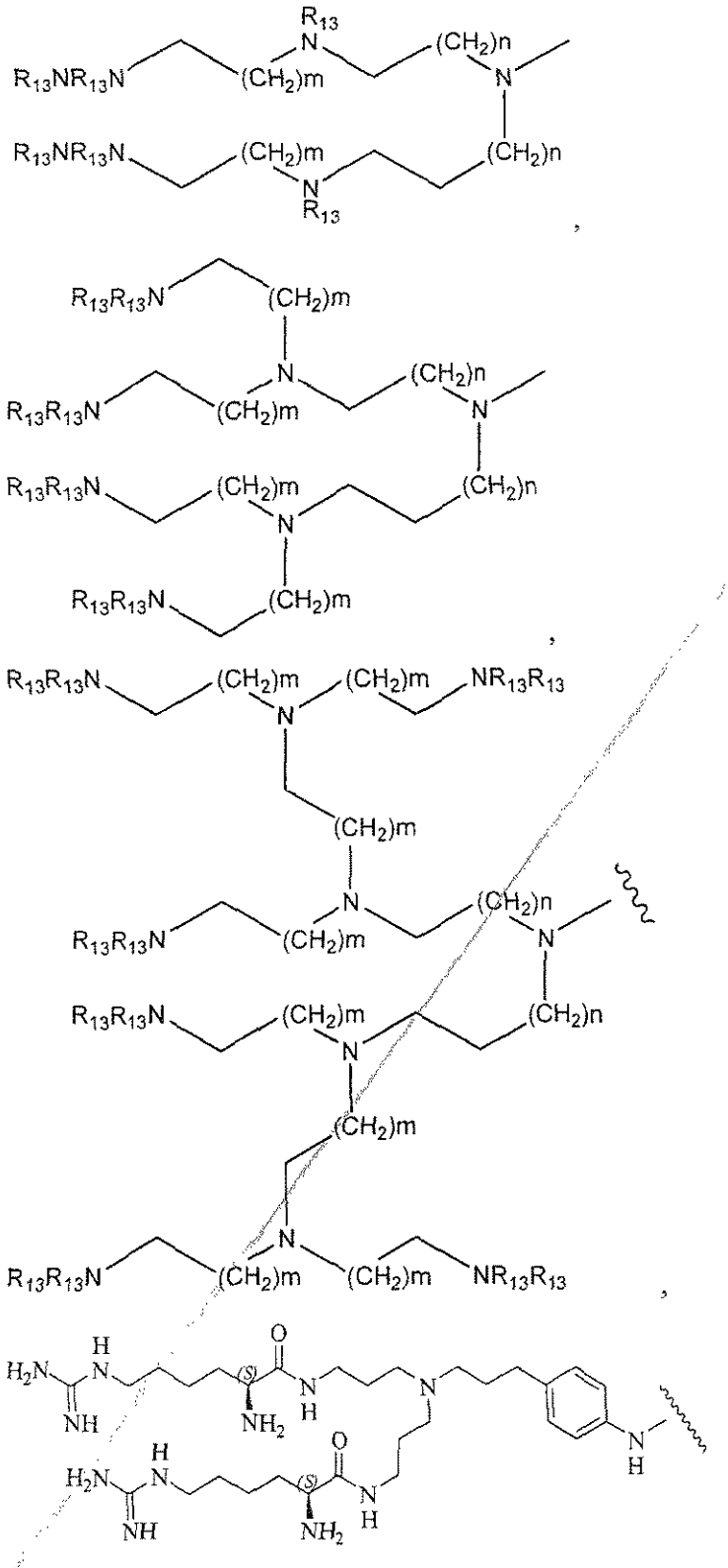
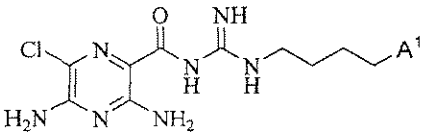
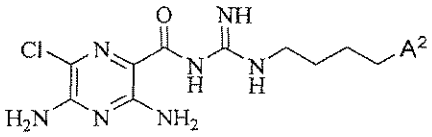


2. The compound according to claim 1, which is represented by formula II or formula III:



formula II

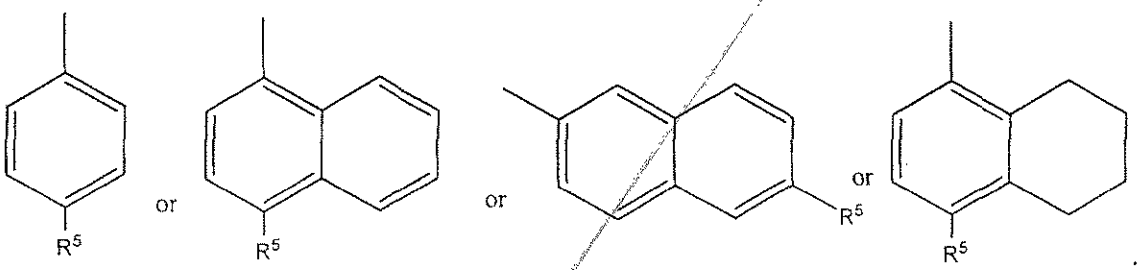


formula III

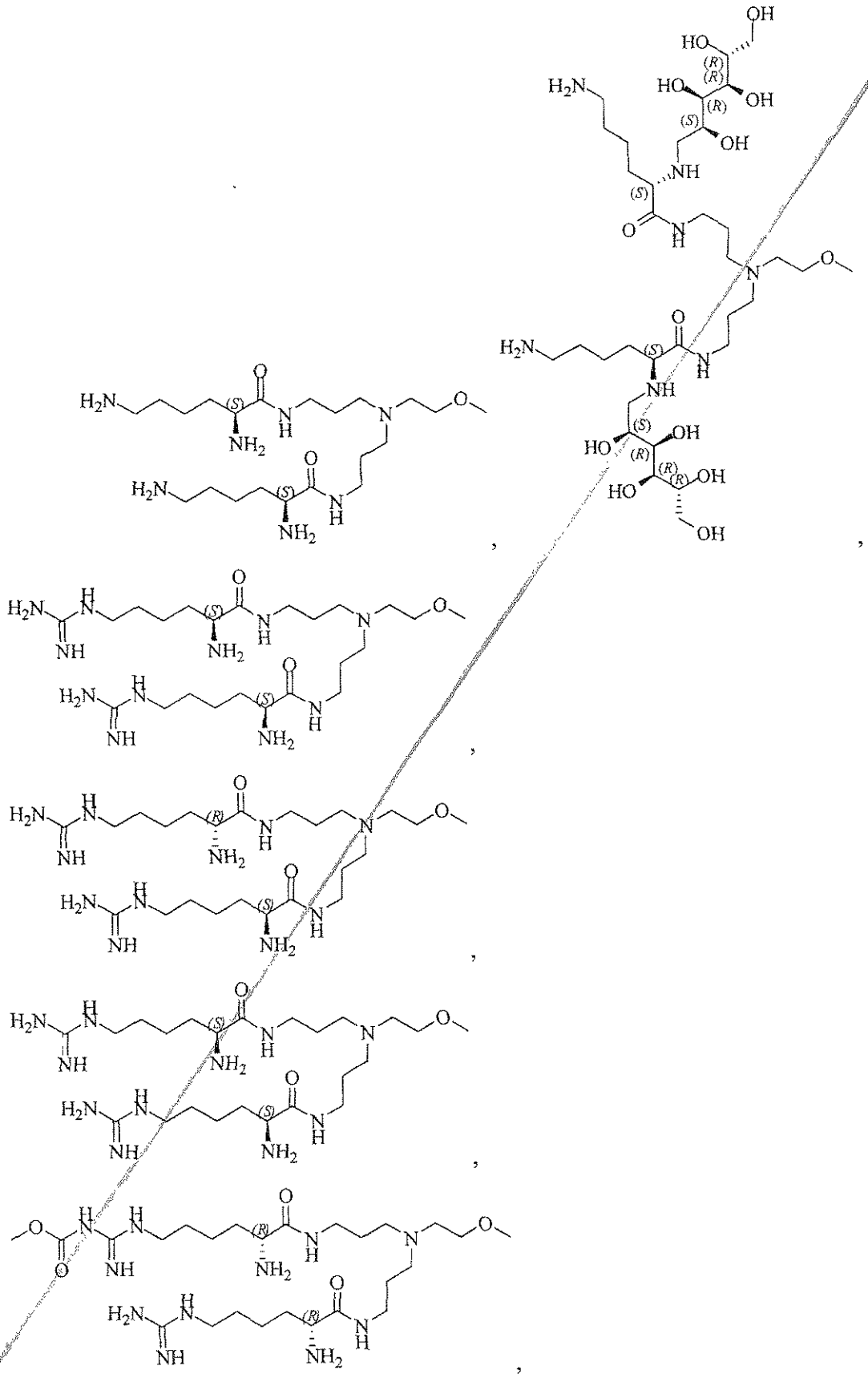
and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof.

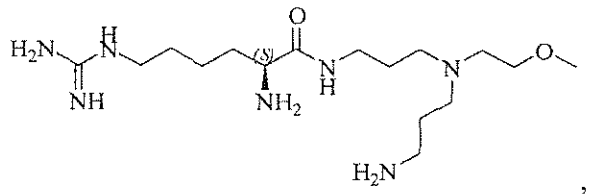
3. The compound according to claim 1, wherein the C_6-C_{15}-membered aromatic carbocycle of A^1 is selected from -phenyl, napthalenyl, 1,2-dihydronapthalenyl, and 1,2,3,4-tetrahydronapthalenyl.

4. The compound according to claim 1, wherein A^1 is



5. The compound according to claim 1, wherein R^5 is represented by one of the following formulas:





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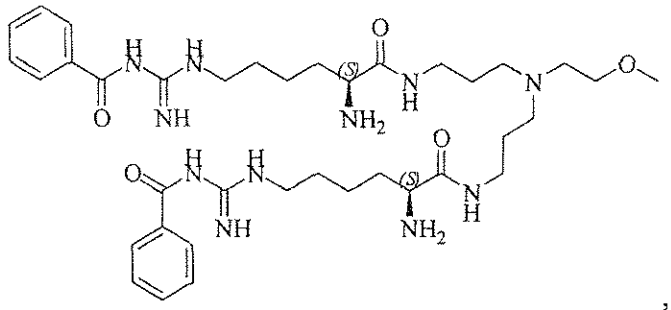

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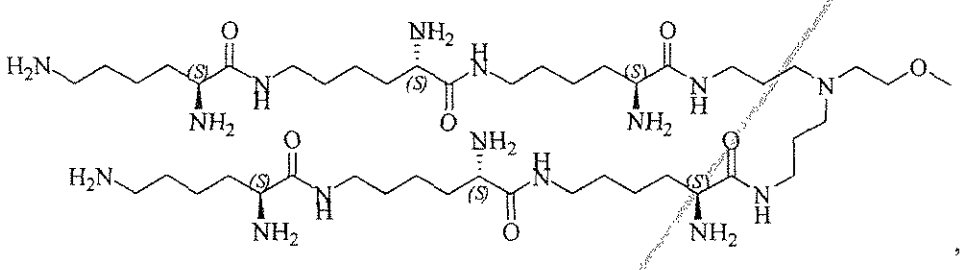

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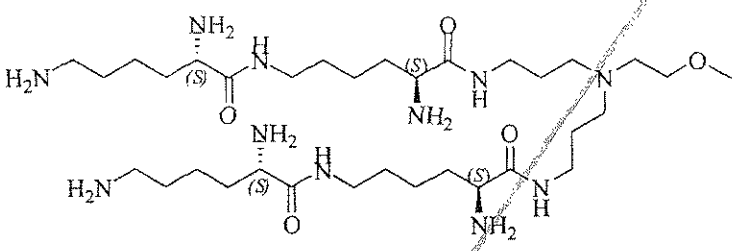

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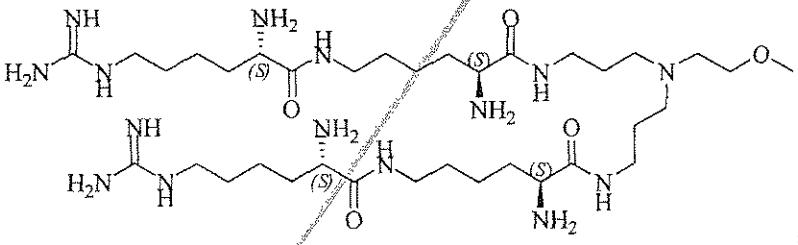

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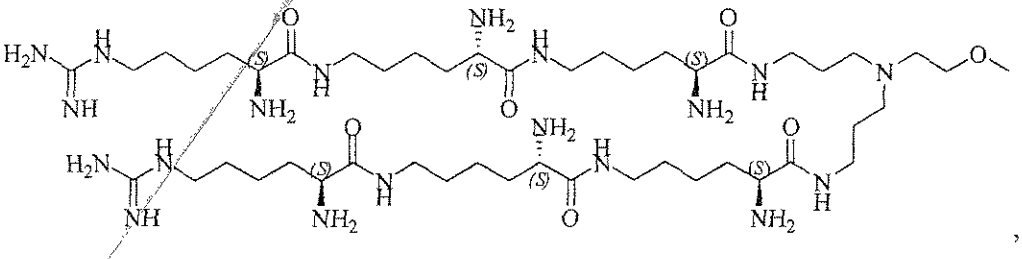

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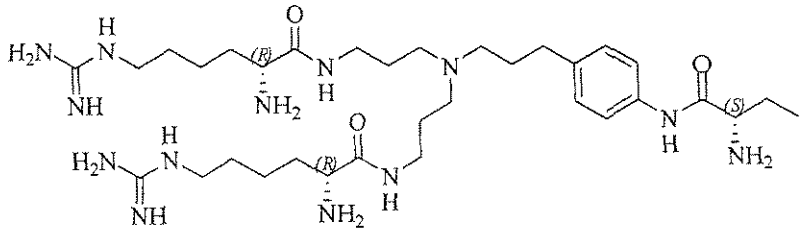

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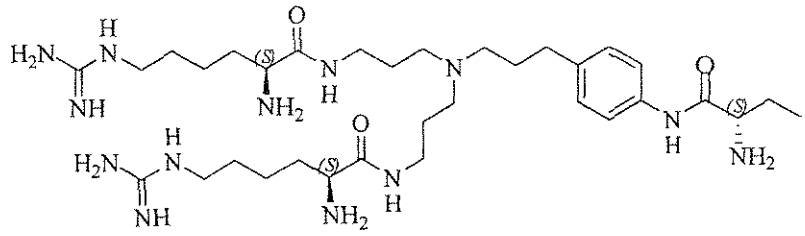

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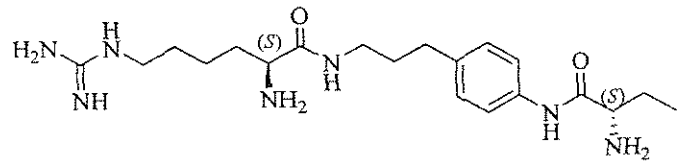

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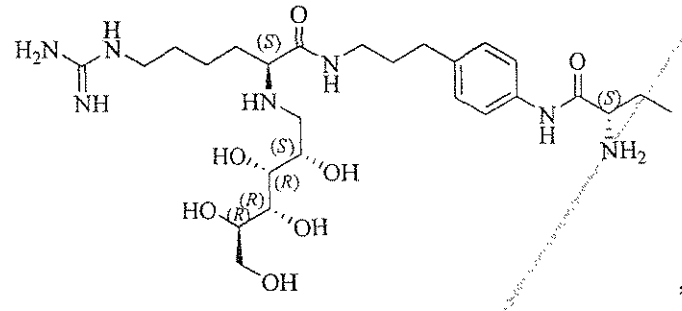

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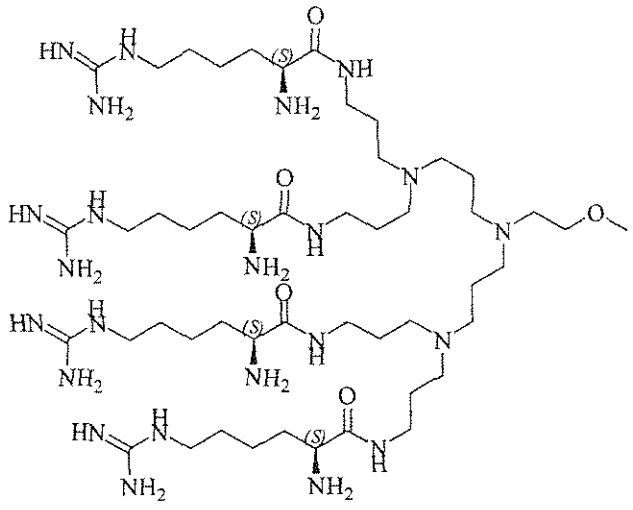

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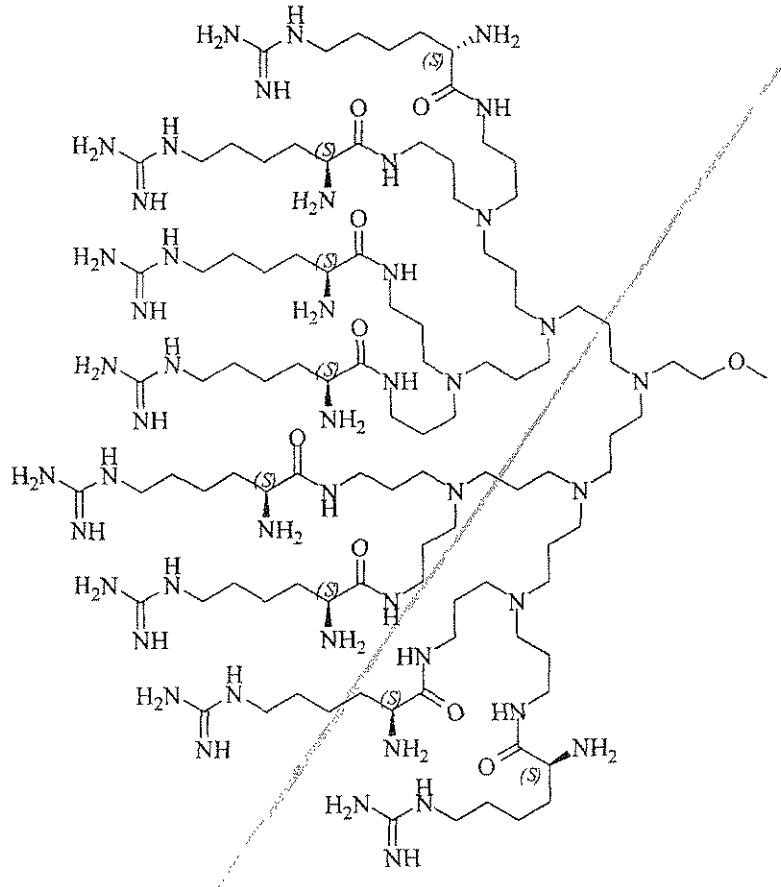
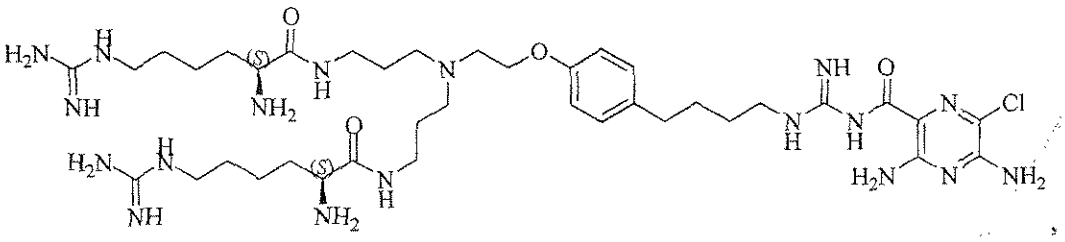
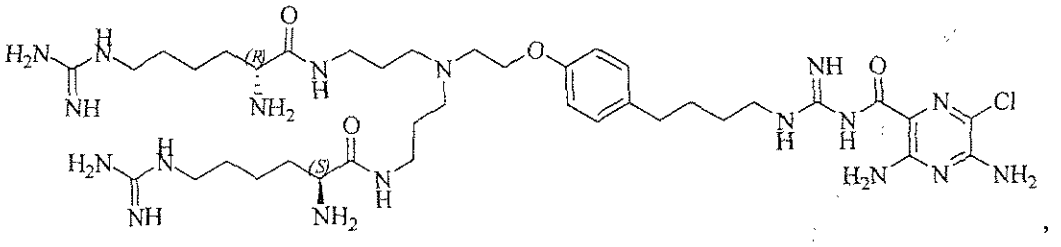
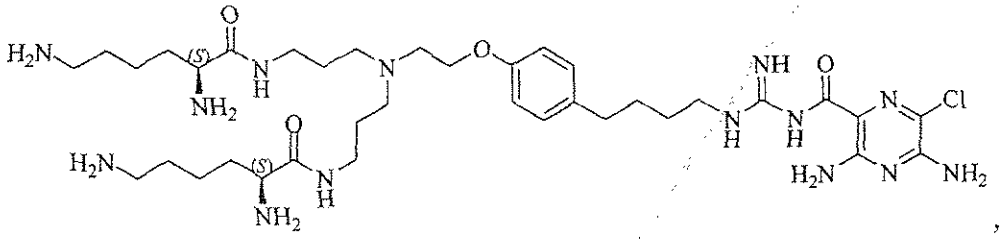
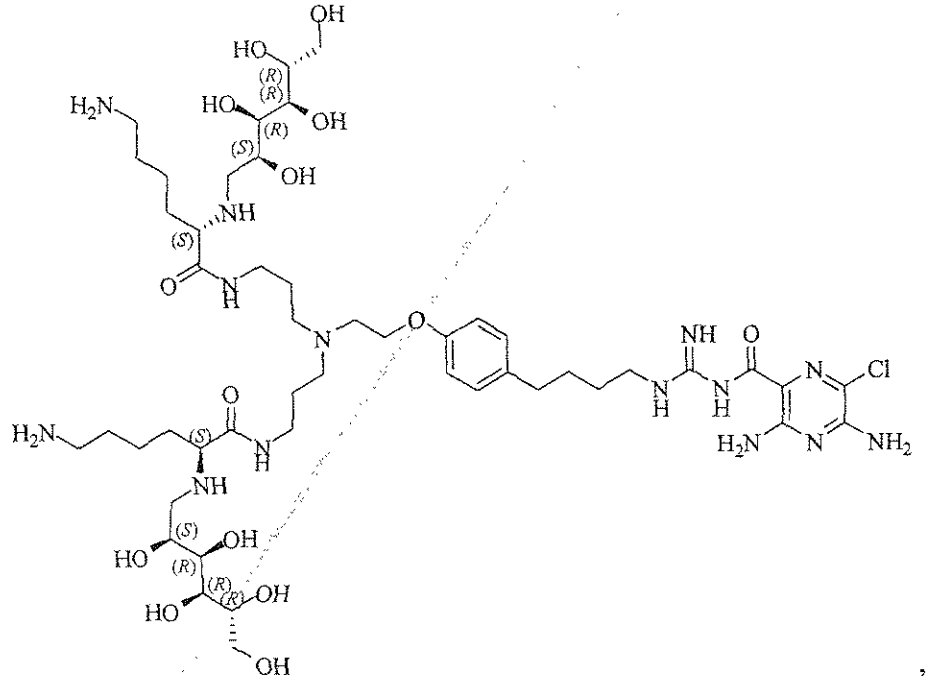


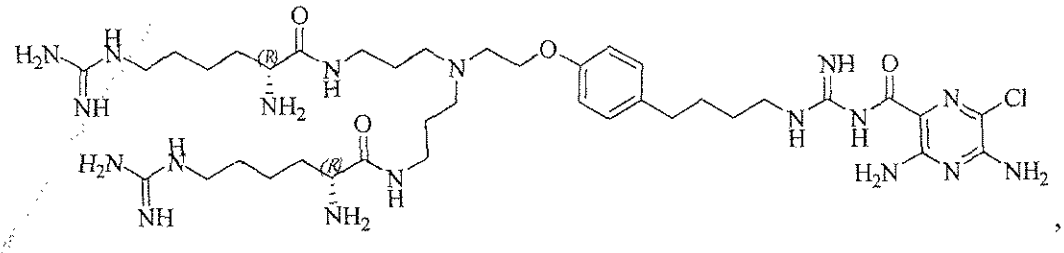
6. A compound represented by one of the following formulas:

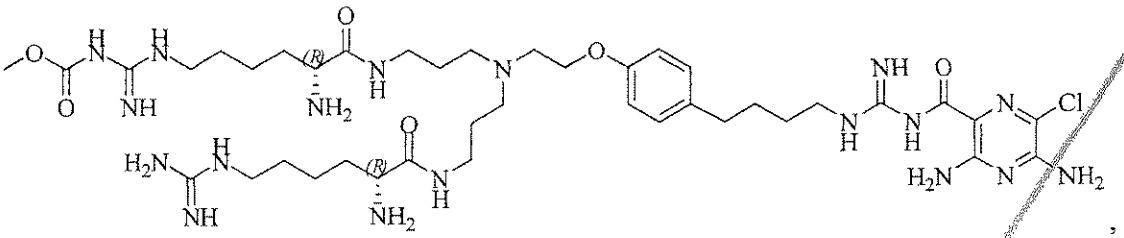












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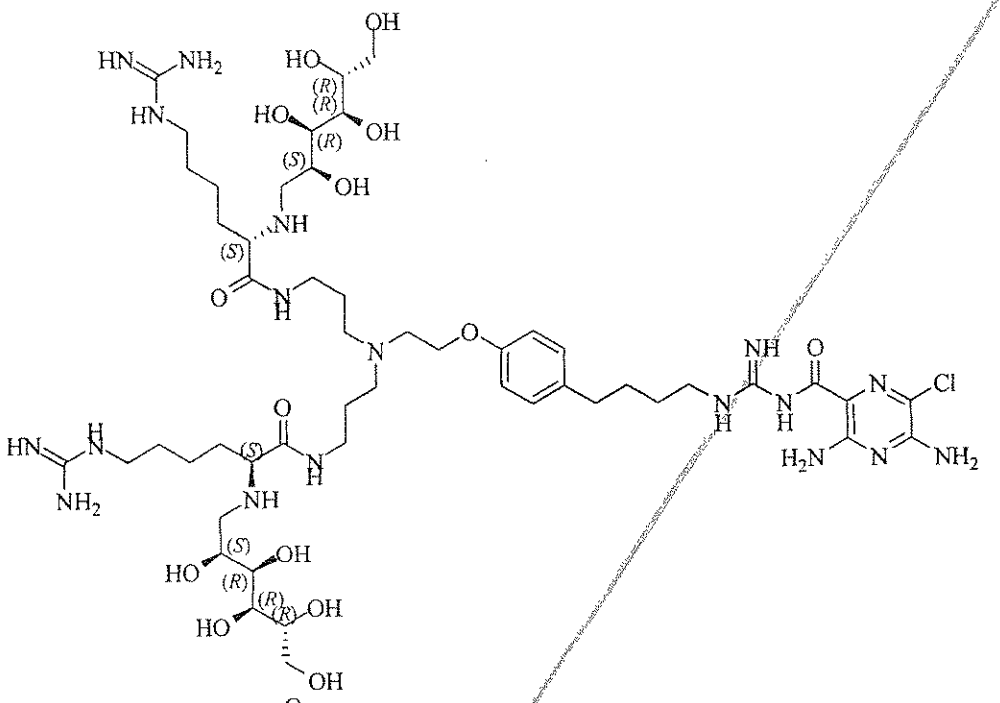

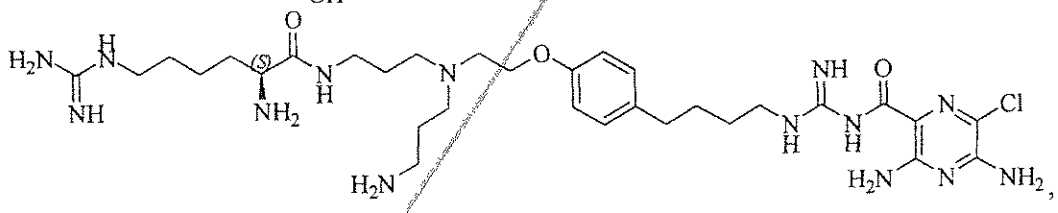

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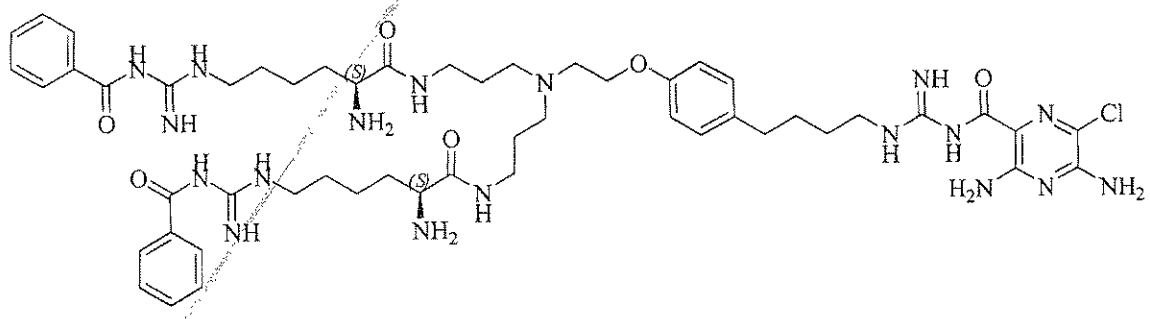

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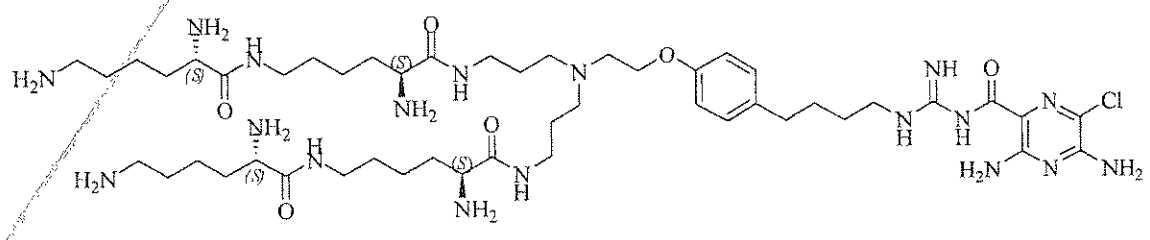

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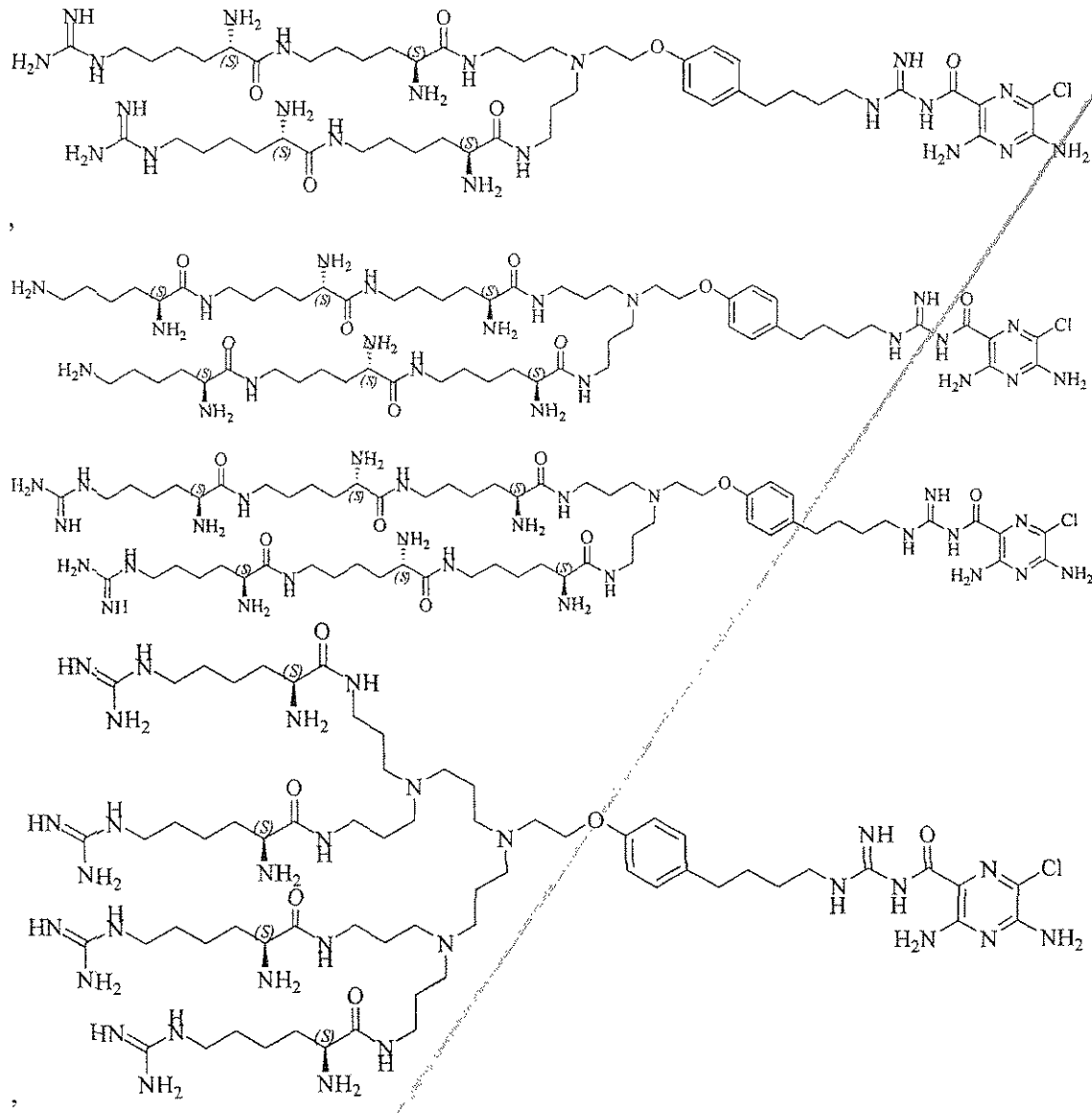
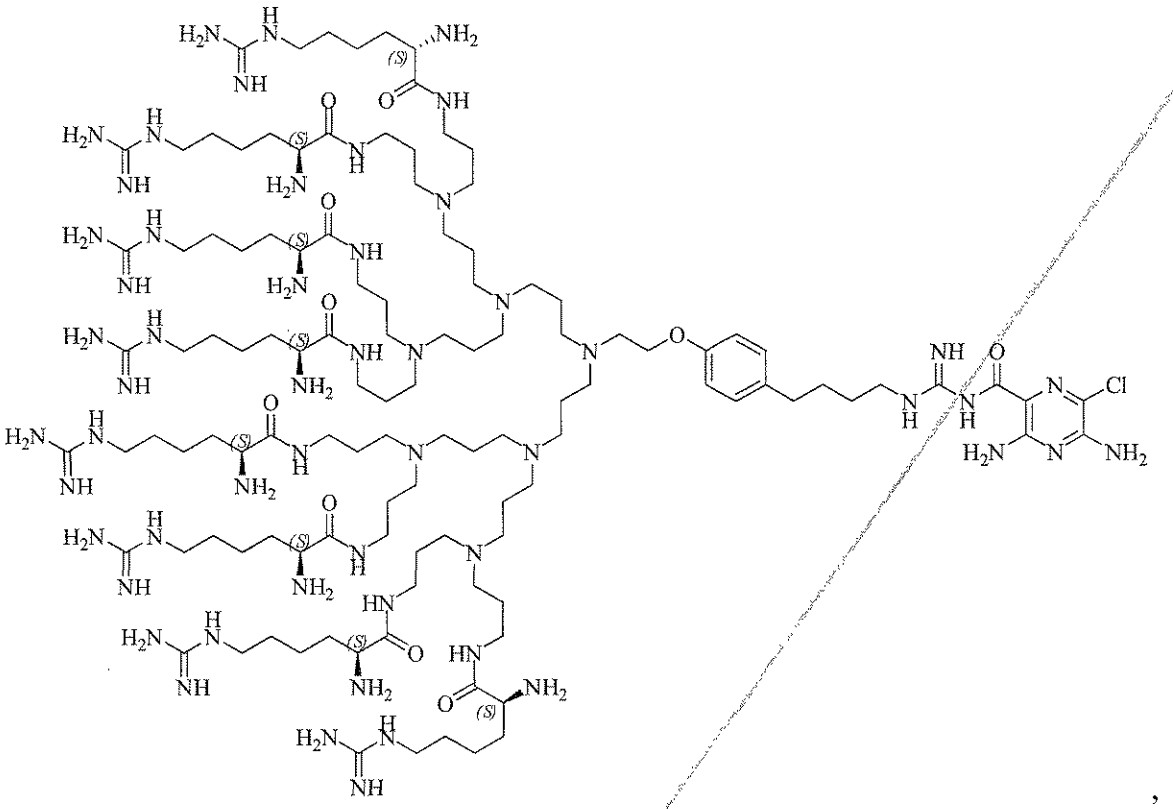




or a pharmaceutically active salt thereof.

7. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

8. The pharmaceutical composition according to claim 7, wherein the compound is (2R, 2'R)-N,N'-(3,3'-(2-(4-(4-(3-(3,5-diamino-6-chloropyrazine-2-carbonyl)guanidino)butyl)phenoxy)ethylazanediyl)bis(propane-3,1-diyl))bis(2-amino-6-guanidinohexanamide), or a pharmaceutically acceptable salt thereof.

9. The composition according to claim 7, wherein said composition is a solution for administration by eye drops.

10. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for blocking sodium channels in a human.

11. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for promoting hydration of mucosal surfaces or restoring mucosal defense in a human.

12. Use of an effective amount of the compound according to claim 1 in the manufacture of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis in a subject in need thereof.

13. Use of an effective amount of the compound according to claim 1 in the manufacture of a medicament for treating a disease ameliorated by increased mucociliary clearance and mucosal hydration in a subject in need of increased mucociliary clearance and mucosal hydration, wherein the medicament is to be administered with an effective amount of an osmolyte .

14. The use according to claim 12, wherein the disease is one or more conditions selected from the group consisting of dry eye, chronic bronchitis, bronchiectasis, cystic fibrosis, sinusitis, vaginal dryness, Sjogren's disease, distal intestinal obstruction syndrome, dry skin, esophagitis, dry mouth (xerostomia), nasal dehydration, asthma, primary ciliary dyskinesia, otitis media, chronic obstructive pulmonary disease, emphysema, pneumonia, diverticulitis, rhinosinusitis, and airborne infections.

15. A composition, comprising:

(a) a compound or a pharmaceutically acceptable salt thereof according to claim 1 and (b) an osmolotically active compound.

16. The composition according to claim 7, further comprising a pharmaceutically effective amount of a therapeutically active agent selected from anti-inflammatory agents, anticholinergic agents, β-agonists, P2Y2 receptor agonists, peroxisome proliferator-activated receptor agonists, kinase inhibitors, antiinfective agents and antihistamines.

17. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament.

18. A compound according to claim 1, or a pharmaceutically acceptable salt thereof for use as a medicament.

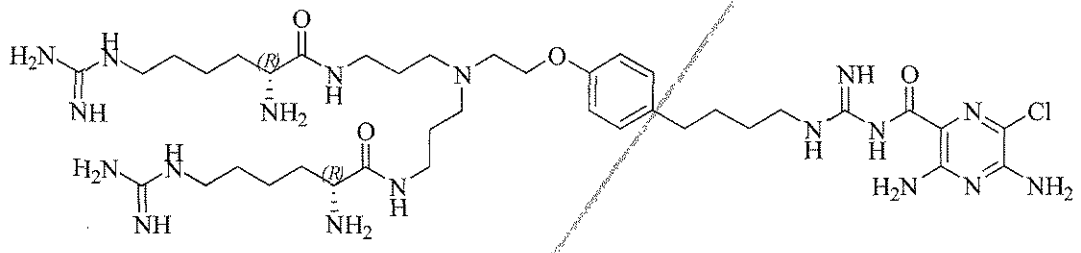
19. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis in a human in need thereof.

20. A composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in

mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis.

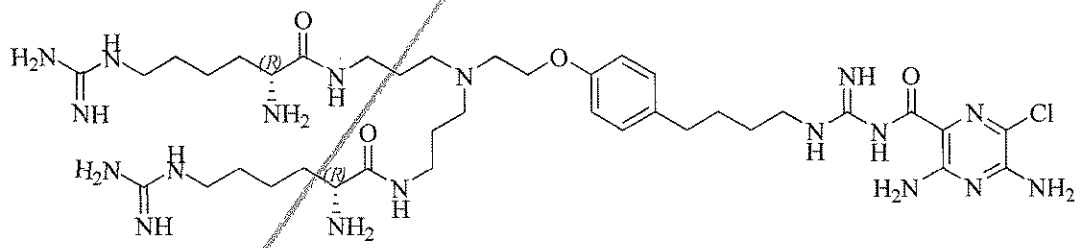
21. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for preventing, mitigating, and/or treating deterministic health effects to the respiratory tract and/or other bodily organs caused by respirable aerosols containing radionuclides in a human in need thereof.

22. The method according to claim 10, wherein the compound is:



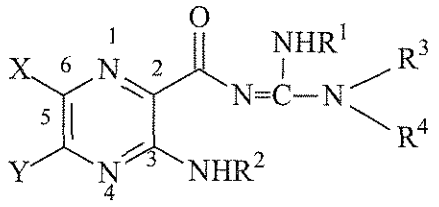
or a pharmaceutically acceptable salt thereof.

23. The hydrochloride salt of:



What is claimed is:

1. A compound represented by formula (I):



(I)

and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof,

wherein:

X is halogen, or trifluoromethyl;

Y is $-N(R^2)_2$;

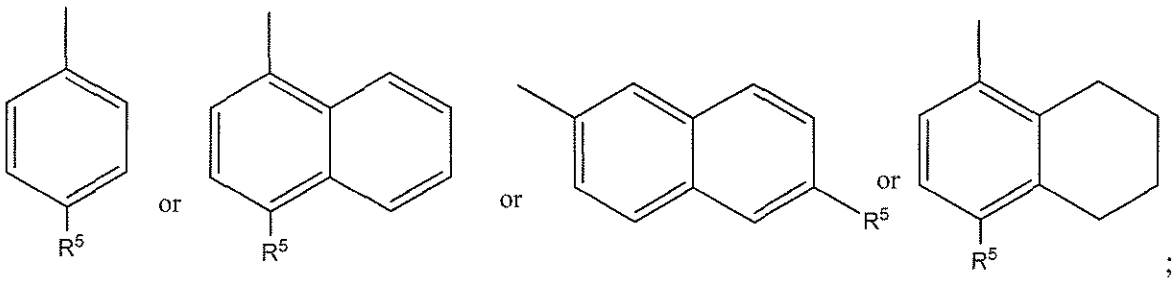
R^1 is hydrogen;

each R^2 is $-R^7$;

R^3 and R^4 are each, independently, hydrogen, or a group represented by formula A, with the proviso that at least one of R^3 and R^4 is a group represented by the formula A;

formula A: $-(C(R^L)_2)_o-x-(C(R^L)_2)_pA^1$

A^1 is



;

each R^L is, independently, $-R^7$;

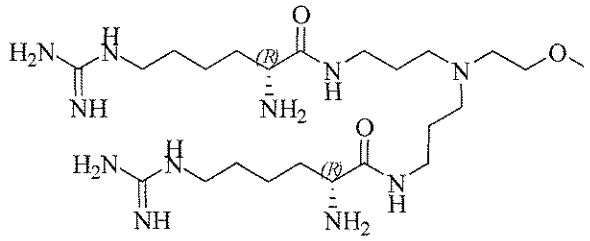
each o is, independently, an integer from 0 to 10;

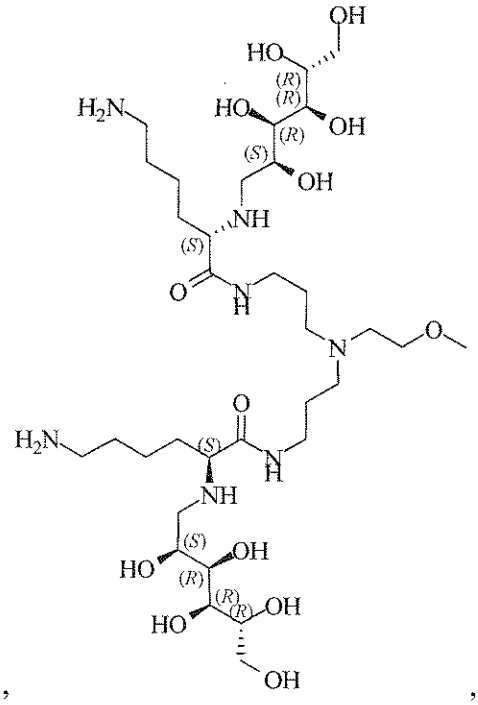
each p is, independently, an integer from 0 to 10;

with the proviso that the sum of o and p in each contiguous chain is from 1 to 10;

each x is, independently, a single bond;

each R^5 is, independently, represented by one of the following formulas:





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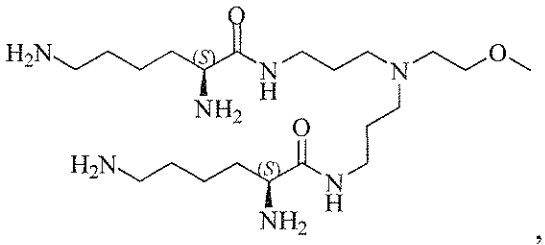

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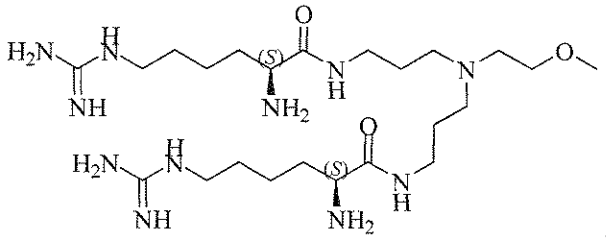

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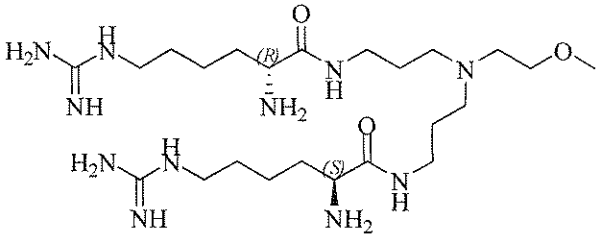

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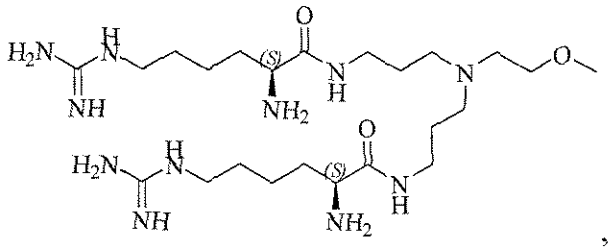

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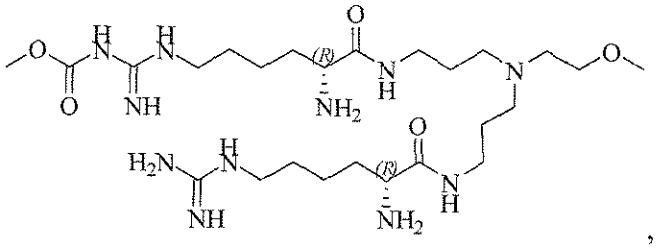

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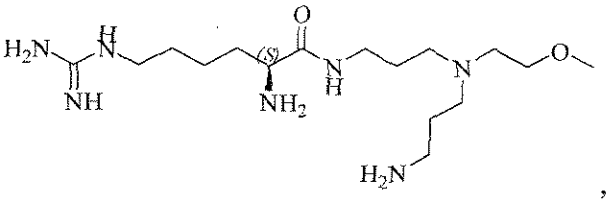

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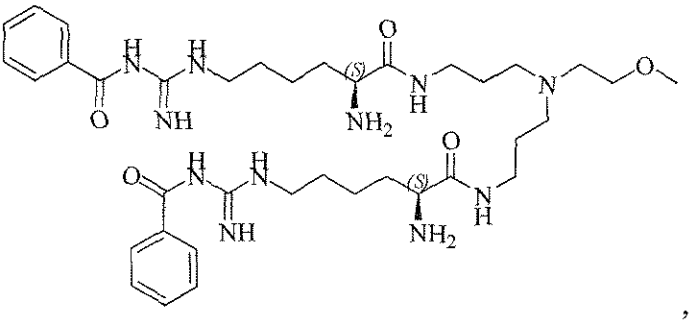

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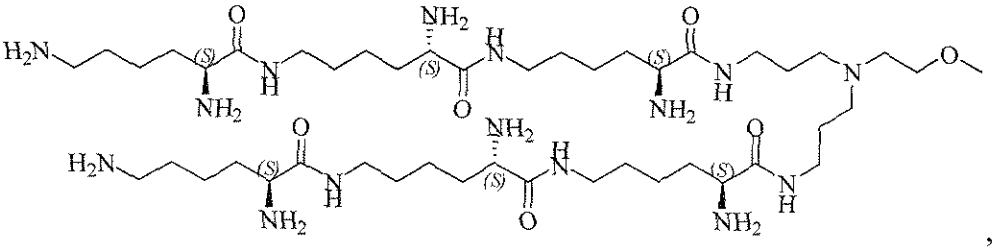

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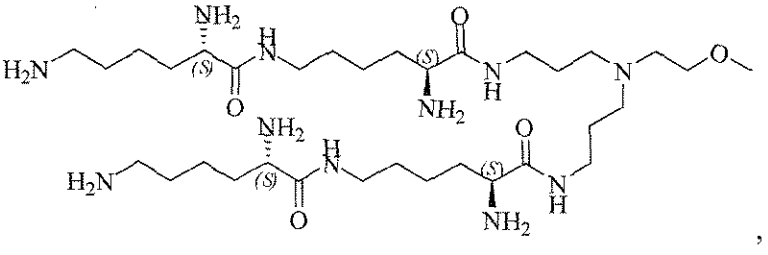

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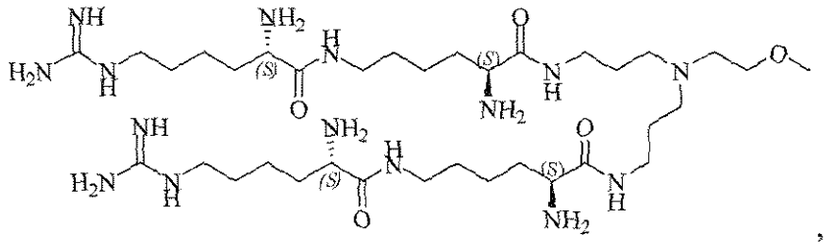

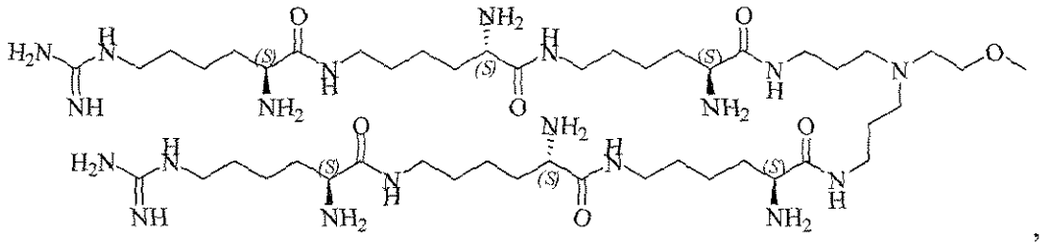

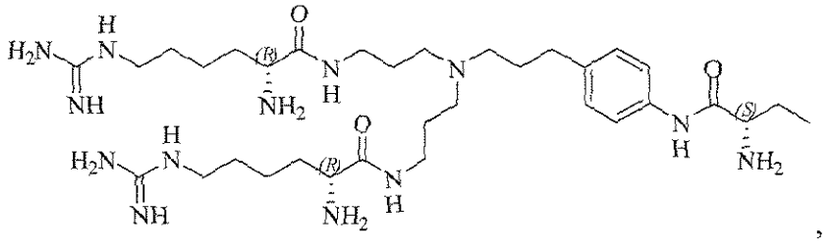

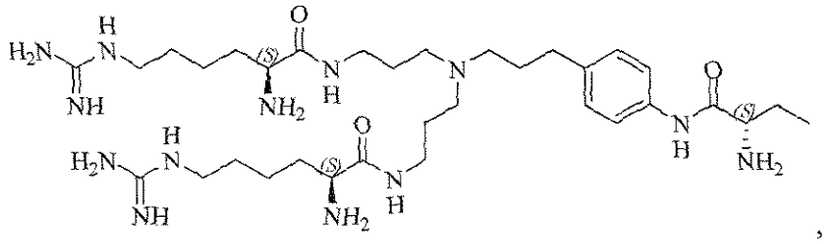

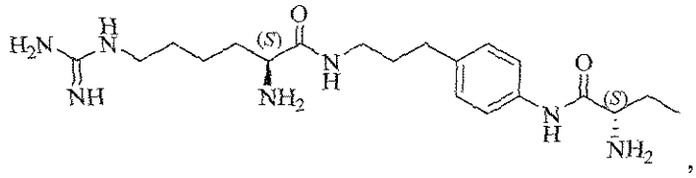

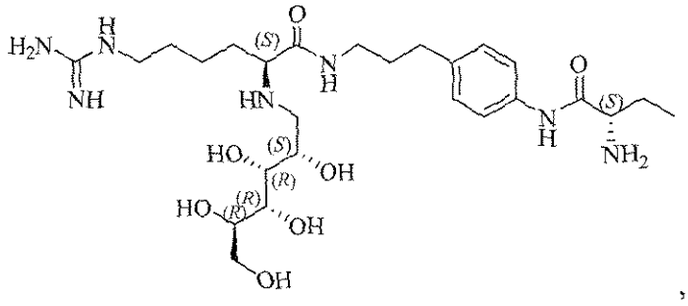

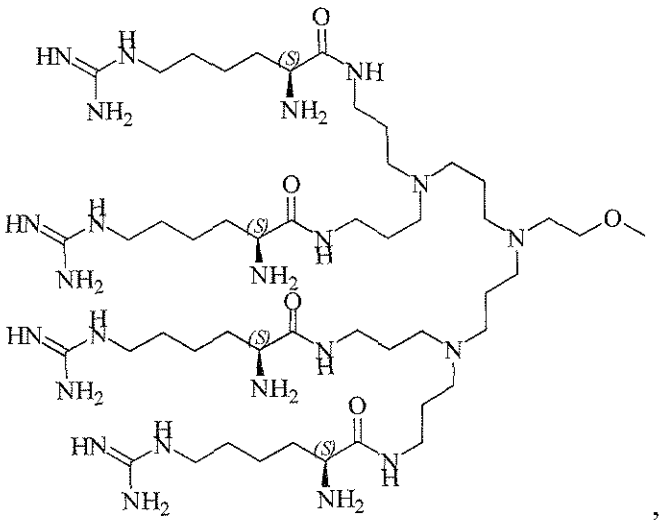

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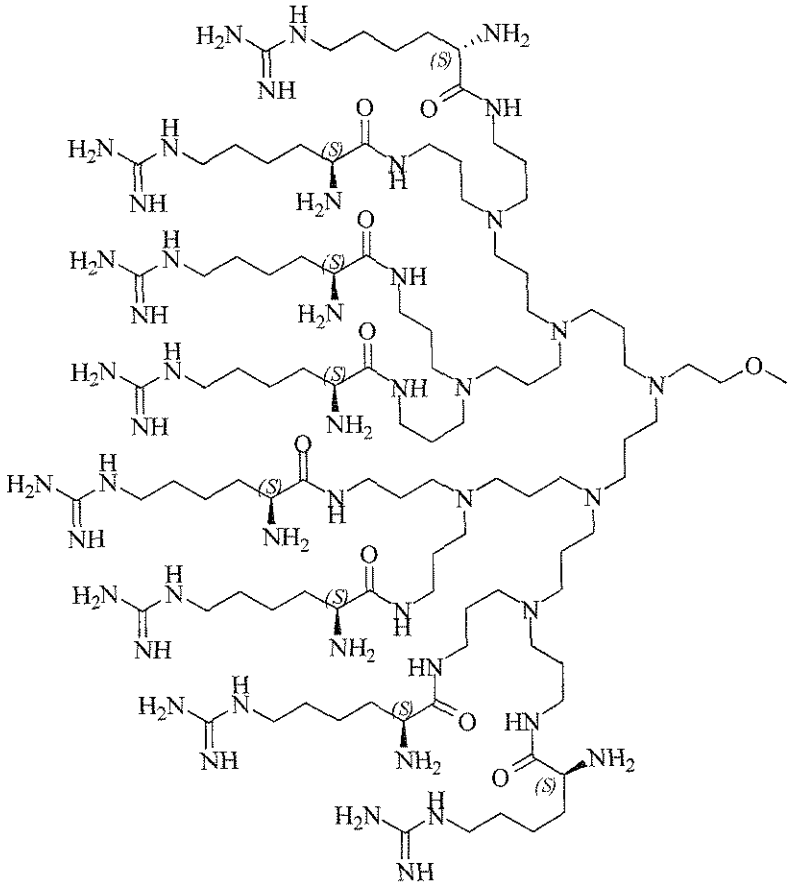

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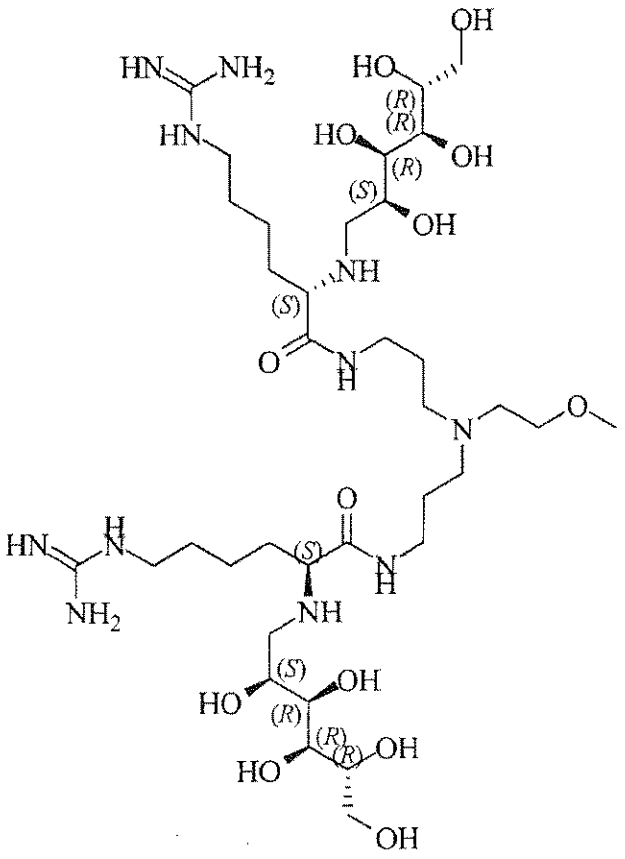
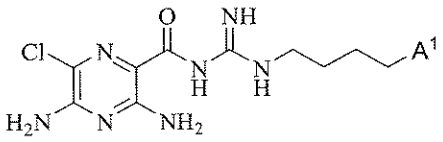


;

each R^7 is, independently, hydrogen.

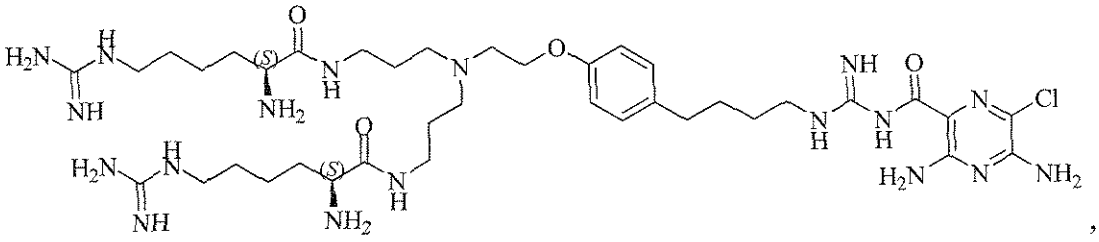
2. The compound according to claim 1, which is represented by formula II:



formula II

and racemates, enantiomers, diastereomers, tautomers, polymorphs, pseudopolymorphs and pharmaceutically acceptable salts, thereof.

3. A compound represented by one of the following formulas:



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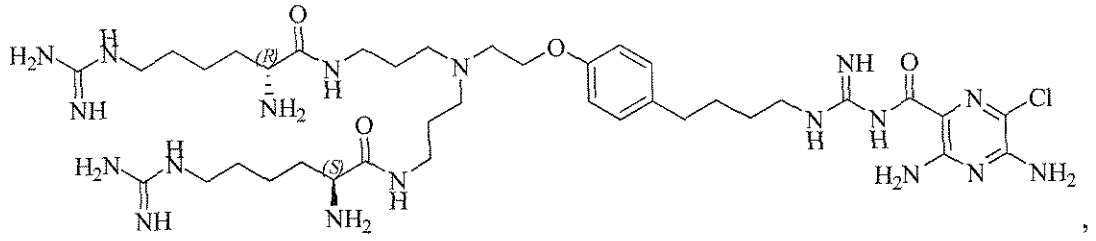

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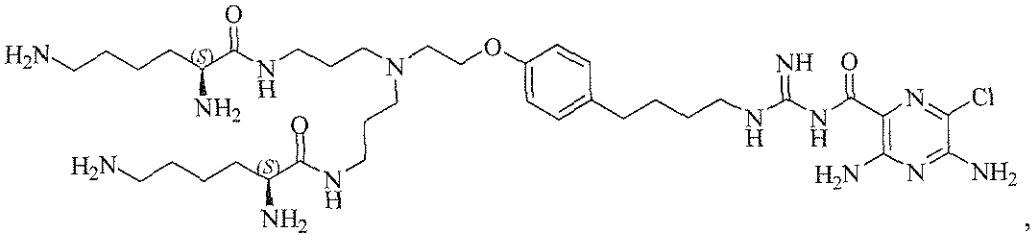

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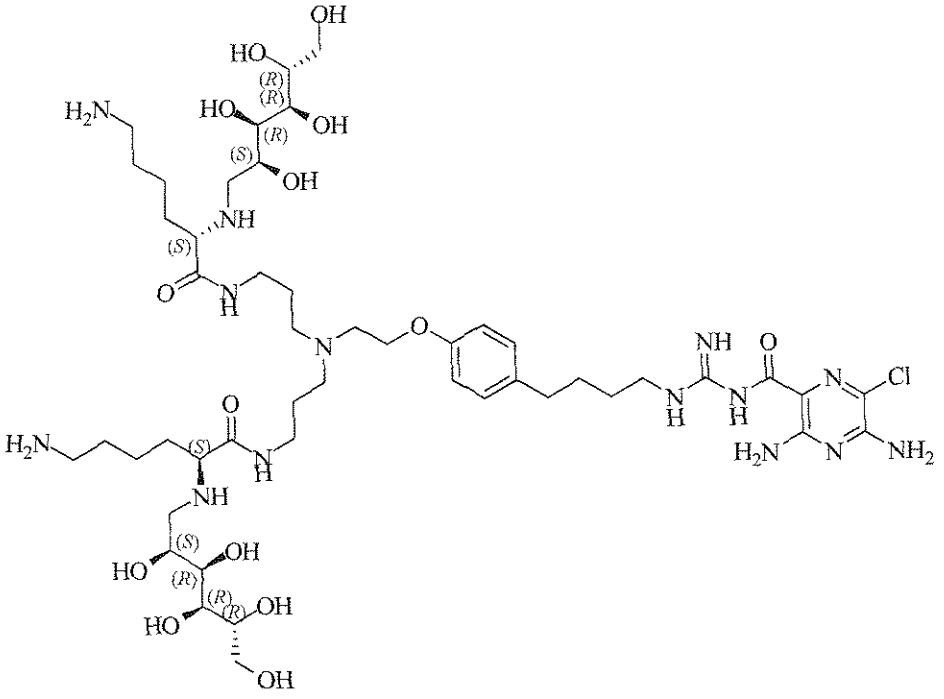

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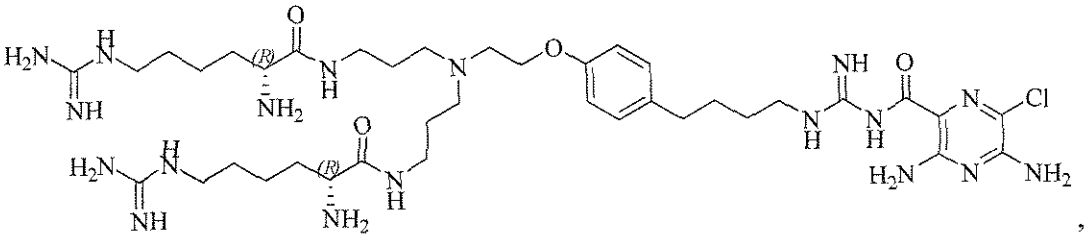

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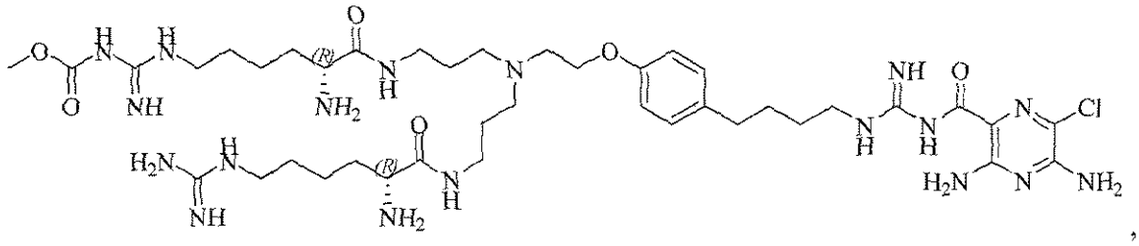

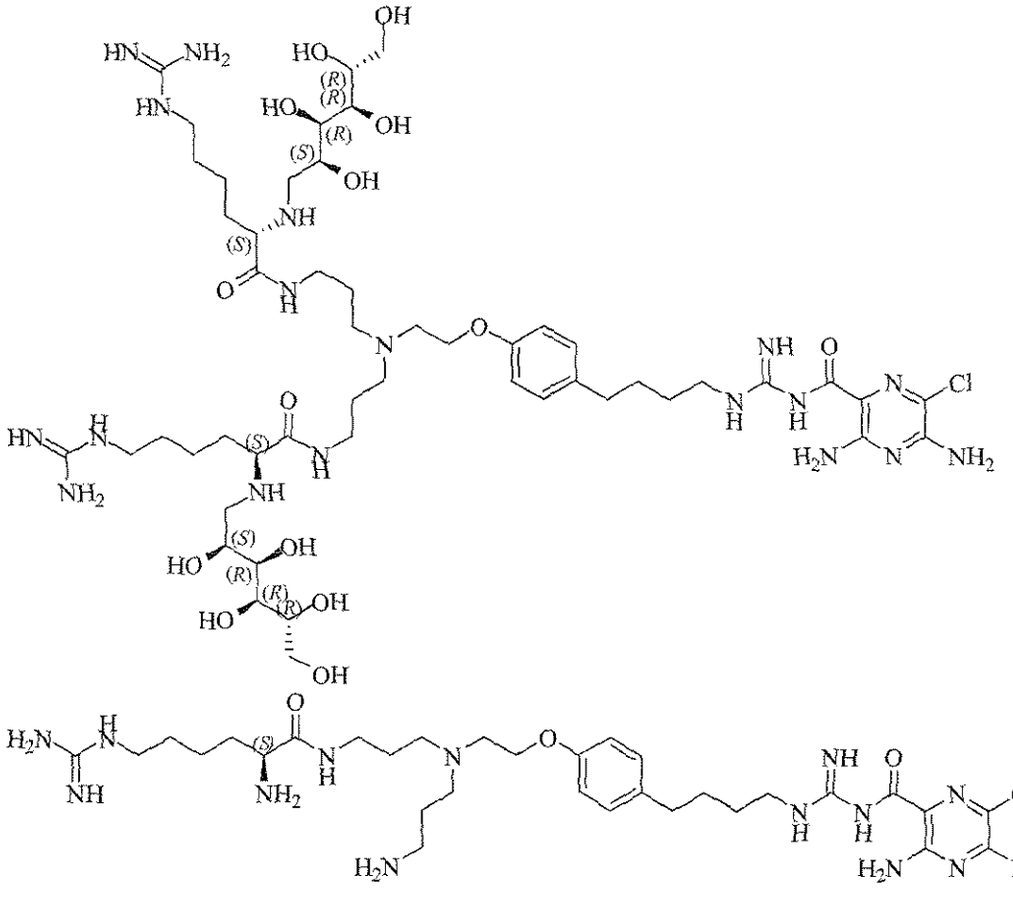

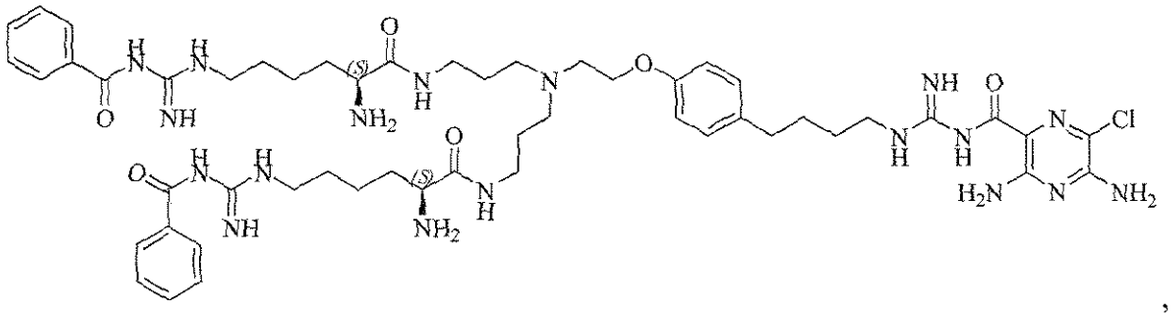

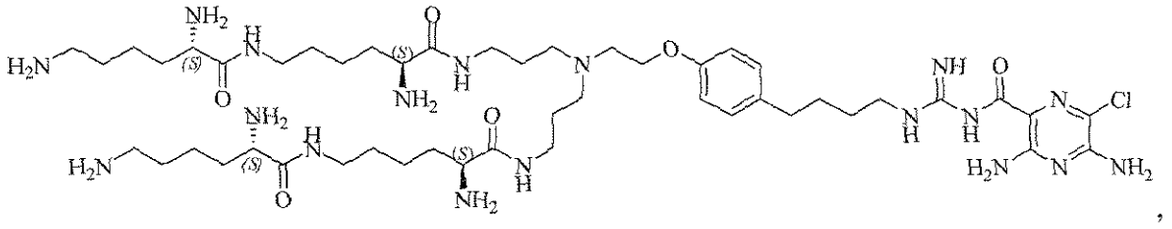

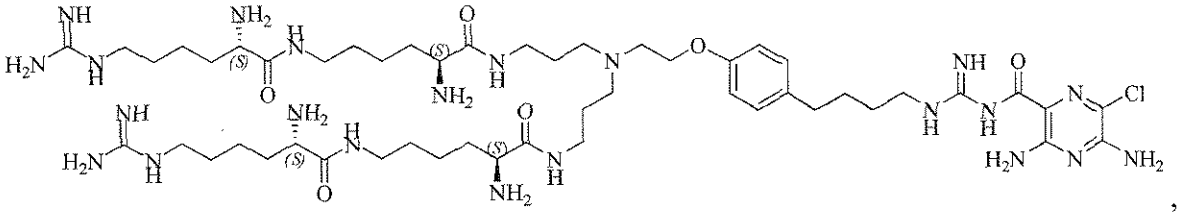

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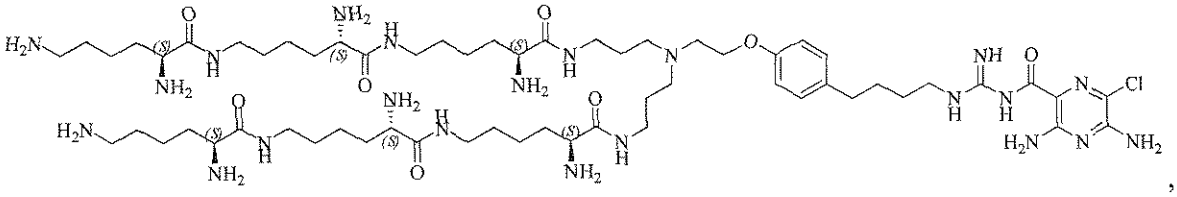

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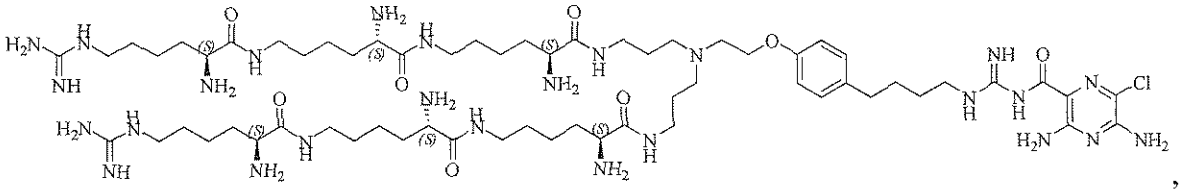

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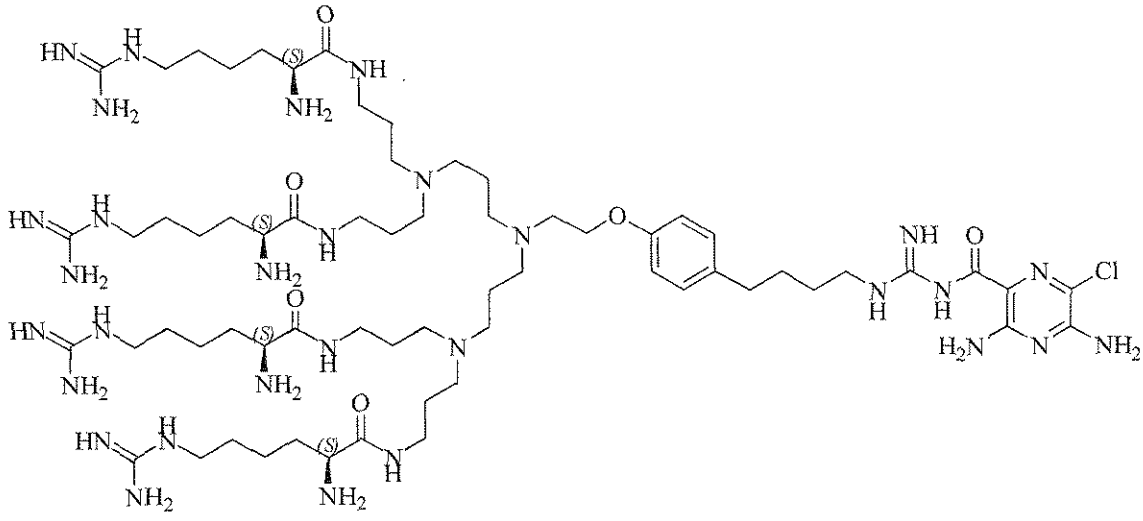
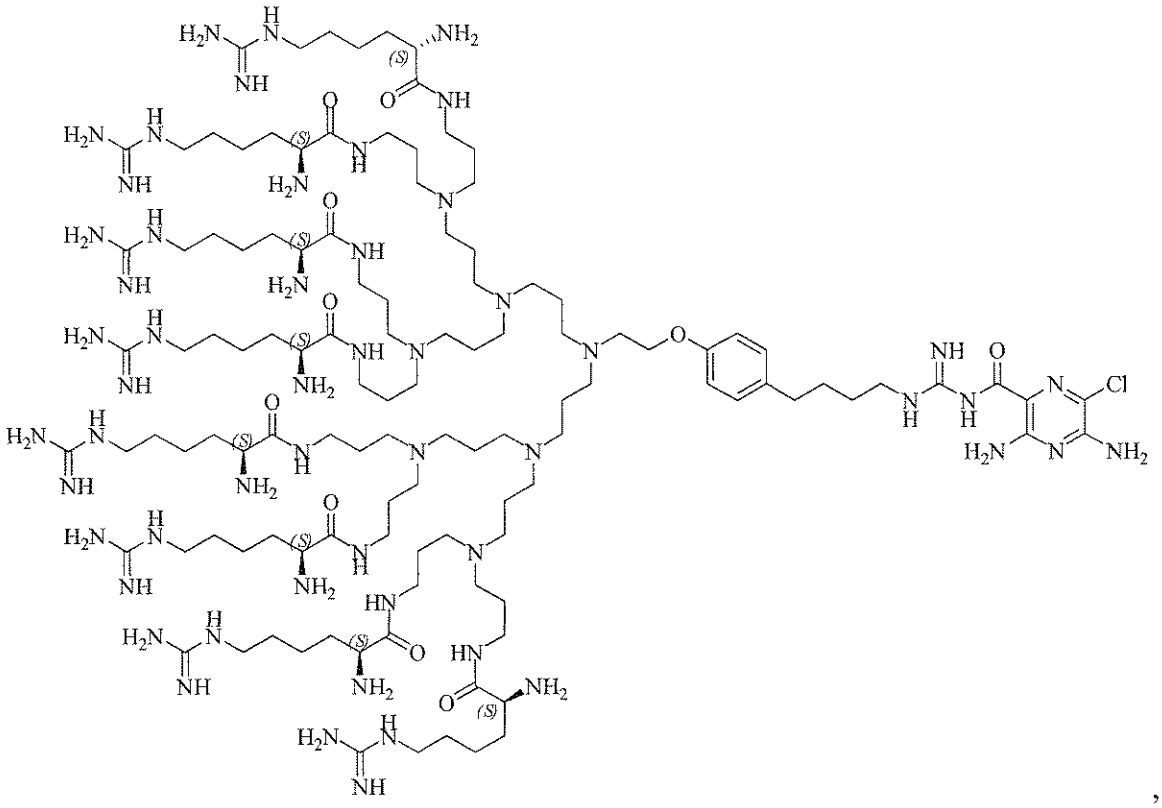




or a pharmaceutically active salt thereof.

4. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

5. The pharmaceutical composition according to claim 4, wherein the compound is (2R, 2'R)-N,N'-(3,3'-(2-(4-(4-(3-(3,5-diamino-6-chloropyrazine-2-carbonyl)guanidino)butyl)phenoxy)ethylazanediyl)bis(propane-3,1-diyl))bis(2-amino-6-guanidinohexanamide), or a pharmaceutically acceptable salt thereof.

6. The composition according to claim 4, wherein said composition is a solution for administration by eye drops.

7. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for blocking sodium channels in a human.

8. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for promoting hydration of mucosal surfaces or restoring mucosal defense in a human.

9. Use of an effective amount of the compound according to claim 1 in the manufacture of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis in a subject in need thereof.

10. Use of an effective amount of the compound according to claim 1 in the manufacture of a medicament for treating a disease ameliorated by increased mucociliary clearance and mucosal hydration in a subject in need of increased mucociliary clearance and mucosal hydration, wherein the medicament is to be administered with an effective amount of an osmolyte .

11. The use according to claim 9, wherein the disease is one or more conditions selected from the group consisting of dry eye, chronic bronchitis, bronchiectasis, cystic fibrosis, sinusitis, vaginal dryness, Sjogren's disease, distal intestinal obstruction syndrome, dry skin, esophagitis, dry mouth (xerostomia), nasal dehydration, asthma, primary ciliary dyskinesia, otitis media, chronic obstructive pulmonary disease, emphysema, pneumonia, diverticulitis, rhinosinusitis, and airborne infections.

12. A composition, comprising:

(a) a compound or a pharmaceutically acceptable salt thereof according to claim 1 and

(b) an osmolotically active compound.

13. The composition according to claim 4, further comprising a pharmaceutically effective amount of a therapeutically active agent selected from anti-inflammatory agents, anticholinergic agents, β-agonists, P2Y2 receptor agonists, peroxisome proliferator-activated receptor agonists, kinase inhibitors, antiinfective agents and antihistamines.

14. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament.

15. A compound according to claim 1, or a pharmaceutically acceptable salt thereof for use as a medicament.

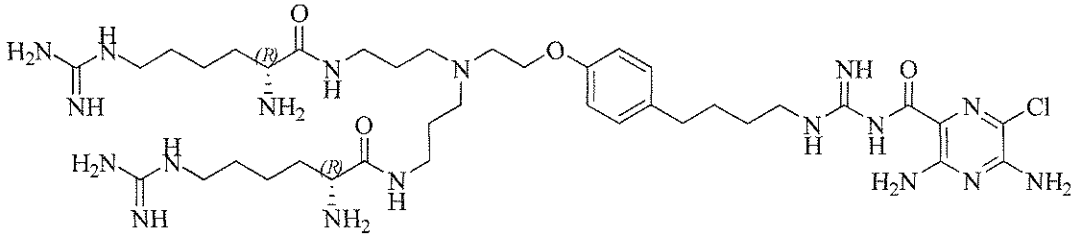
16. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis in a human in need thereof.

17. A composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for treating dry eye, treating Sjogren's disease-associated dry eye, treating eye inflammation caused by dry eye , promoting ocular hydration, promoting corneal hydration, treating chronic bronchitis, treating bronchiectasis (including bronchiectasis due to conditions other than cystic fibrosis), treating cystic fibrosis, treating sinusitis, treating vaginal dryness, promoting mucus clearance in

mucosal surfaces, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth, treating nasal dehydration (including nasal dehydration brought on by administering dry oxygen to the subject), treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, or treating rhinosinusitis.

18. Use of an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for preventing, mitigating, and/or treating deterministic health effects to the respiratory tract and/or other bodily organs caused by respirable aerosols containing radionuclides in a human in need thereof.

19. The use according to claim 7, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

20. The hydrochloride salt of:

