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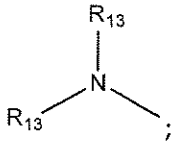
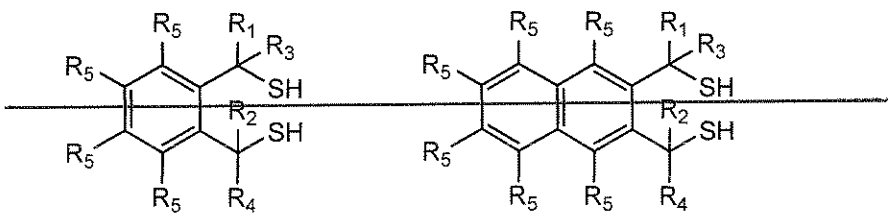
or  ;

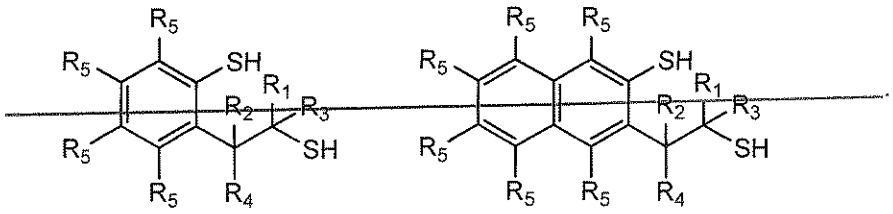
with the proviso that when any -CHOR^8- or –CH$_2$OR^8 groups are located 1,2- or 1,3- with respect to each other, the R^8 groups may, optionally, be taken together to form a cyclic mono- or di-substituted 1,3-dioxane or 1,3-dioxolane;

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

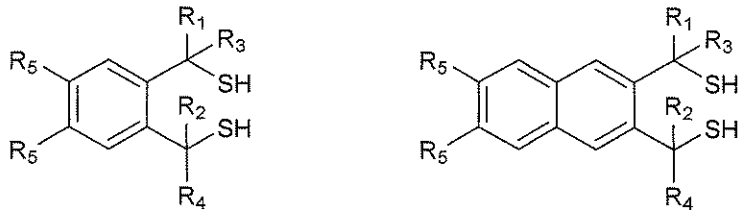
In one aspect, there is provided a compound represented by formula Ia~~,~~ or Ib~~, Ic or Id~~:



~~Ia~~ ~~Ib~~



~~Ic~~ ~~Id~~

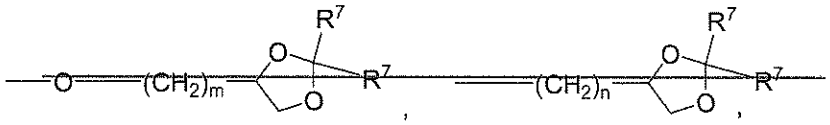


Ia Ib

wherein R^1, ~~and~~ R^2, R^3 and R^4 are each, independently, hydrogen, lower alkyl, halogen or triflouromethyl;

~~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;~~

each R^5 is, independently, hydrogen, halogen, trifluoromethyl, lower alkyl, ~~unsubstituted or substituted phenyl, lower alkyl thio, phenyl lower alkyl thio, lower alkyl sulfonyl, or phenyl lower alkyl sulfonyl, OH, $(CH_2)_m$-OR^8, -O-$(CH_2)_m$-OR^8,~~ -$(CH_2)_n$-NR^7R^{10}, ~~-$(CH_2)_n$-NR^7R^7, -O-$(CH_2)_m$-NR^7R^{10}, -O-$(CH_2)_m$-NR^7R^7, -$(CH_2)_n$($CHOR^8$)($CHOR^8$)$_n$-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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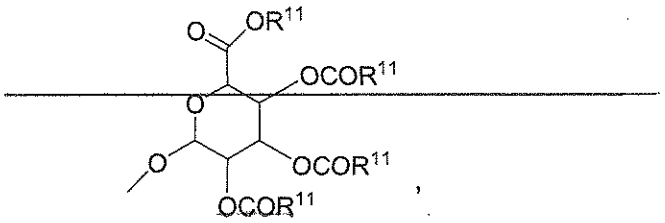

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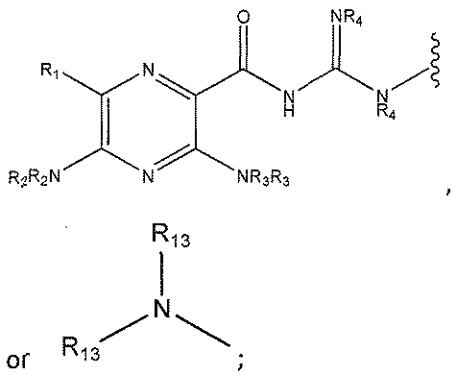
-Link-$(CH_2)_m$-CAP, -Link-$(CH_2)_n$($CHOR^8$)($CHOR^8$)$_n$-CAP, -Link-$(CH_2CH_2O)_m$-CH_2-CAP, -Link-$(CH_2CH_2O)_m$-CH_2CH_2-CAP, -Link-$(CH_2)_m$-$(Z)_g$-CAP, -Link-$(CH_2)_n(Z)_g$-$(CH_2)_m$-CAP, -Link-$(CH_2)_n$-NR^{13}-CH_2($CHOR^8$)($CHOR^8$)$_n$-CAP, -Link-$(CH_2)_n$-($CHOR^8$)$_m$$CH_2$-$NR^{13}$-$(Z)_g$-CAP, -Link-$(CH_2)_n$$NR^{13}$-$(CH_2)_m$($CHOR^8$)$_n$$CH_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 with the proviso that at least one R^5 group contains at least one basic nitrogen;

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

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

2-tetrahydropyranyl, or



with the proviso that when any -CHOR^8- or –CH_2OR^8 groups are located 1,2- or 1,3- with respect to each other, the R^8 groups may, optionally, be taken together to form a cyclic mono- or di-substituted 1,3-dioxane or 1,3-dioxolane;

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

The present disclosure also provides pharmaceutical compositions which comprise a compound as described herein.

In another aspect, there is provided a composition, comprising: (a) the compound described herein and (b) an osmotically active compound. In another aspect, there is provided a pharmaceutical composition, comprising the compound described herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided use of the compound described herein in the manufacture of a medicament for liquefying mucus from mucosal surfaces of a subject.

The present disclosure also provides a method of restoring mucosal defense, comprising: contacting mucus with an effective amount of compound described herein to a subject in need thereof.

The present disclosure also provides a method of decreasing mucus viscoelasticity, comprising: administering an effective amount of a compound described herein to a mucosal surface of a subject.

The present disclosure also provides a method of decreasing mucus viscoelasticity on a mucosal surface, comprising:

administering an effective amount of a compound described herein to a mucosal surface of a subject.

In another aspect, there is provided use of the compound described herein in the manufacture of a medicament for improving mucus penetration of therapeutic agents, wherein the medicament is to be administered with a second therapeutic agent.

In another aspect, there is provided use of the compound described herein in the manufacture of a medicament for decreasing mucosal oxygen free radicals.

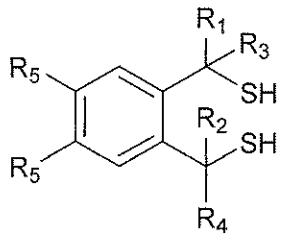
The present disclosure also provides a method of scavenging free radicals on a mucosal surface, comprising:

administering an effective amount of a compound described herein to a mucosal surface of a subject.

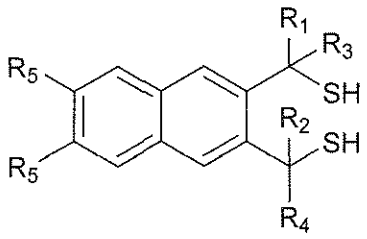
CLAIMS

That Which Is Claimed Is:

1. A compound represented by formula Ia or Ib:



Ia



Ib

wherein R^1, R^2, R^3 and R^4 are each, independently, hydrogen, lower alkyl, halogen or triflouromethyl;

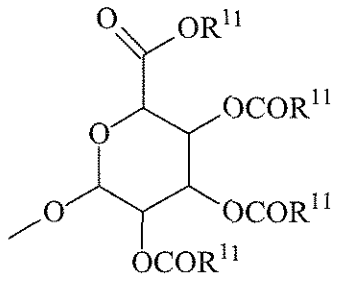
each R^5 is, independently, hydrogen, halogen, trifluoromethyl, lower alkyl, $-(CH_2)_n-NR^7R^{10}$,

$-Link–(CH_2)_m-CAP$, $-Link-(CH_2)_n(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2CH_2O)_m-CH_2-CAP$, $-Link-(CH_2CH_2O)_m-CH_2CH_2-CAP$, $-Link-(CH_2)_m-(Z)_g-CAP$, $-Link–(CH_2)_n(Z)_g-(CH_2)_m-CAP$, $-Link-(CH_2)_n-NR^{13}-CH_2(CHOR^8)(CHOR^8)_n-CAP$, $-Link-(CH_2)_n-(CHOR^8)_mCH_2-NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_nNR^{13}-(CH_2)_m(CHOR^8)_nCH_2NR^{13}-(Z)_g-CAP$, $-Link-(CH_2)_m-(Z)_g-(CH_2)_m-CAP$, -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 with the proviso that at least one R^5 group contains at least one basic nitrogen;

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

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

2-tetrahydropyranyl, or



;

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, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, $-CH_2(CHOH)_n-CH_2OH$, $-CO_2R^{13}$, $-C(=O)NR^{13}R^{13}$, or $-C(=O)R^{13}$;

each R^{13} is, independently, hydrogen, lower alkyl, phenyl, substituted phenyl or $-CH_2(CHOR^8)_m-CH_2OR^8$, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, $-CH_2-(CHOH)_n-CH_2OH$, $-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_m-NR^7R^7$, $-(CH_2)_m-NR^{11}R^{11}$, $-(CH_2)_m-(NR^{11}R^{11}R^{11})^+$, $-(CH_2)_m-(CHOR^8)_m-(CH_2)_mNR^{11}R^{11}$, $-(CH_2)_m-(CHOR^8)_m-(CH_2)_mNR^7R^{10}$, $-(CH_2)_m-NR^{10}R^{10}$, $-(CH_2)_m-(CHOR^8)_m-(CH_2)_m-(NR^{11}R^{11}R^{11})^+$, or $-(CH_2)_m-(CHOR^8)_m-(CH_2)_mNR^7R^7$;

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

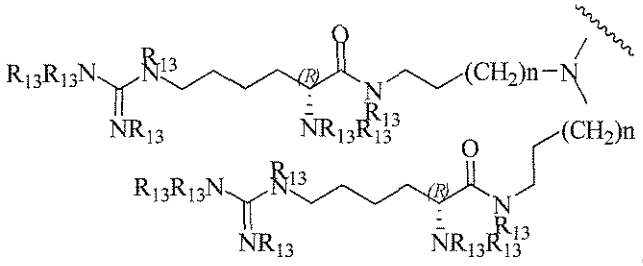
each m is, independently, an integer from 1 to 7;

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, independently



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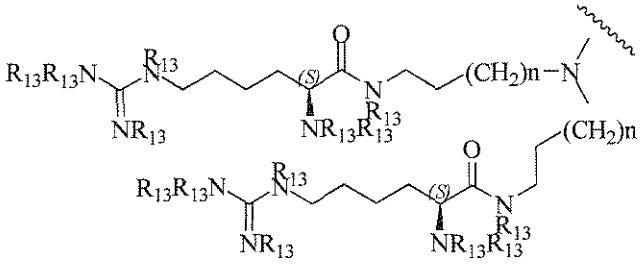

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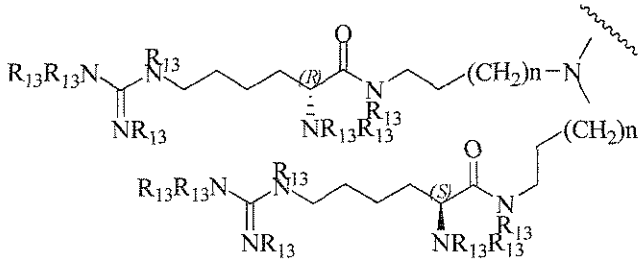

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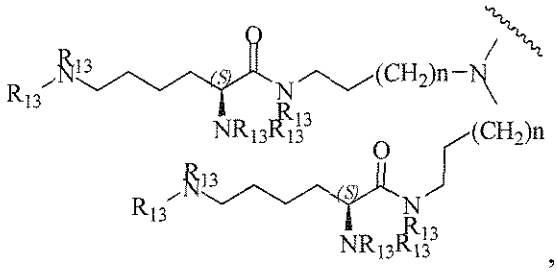

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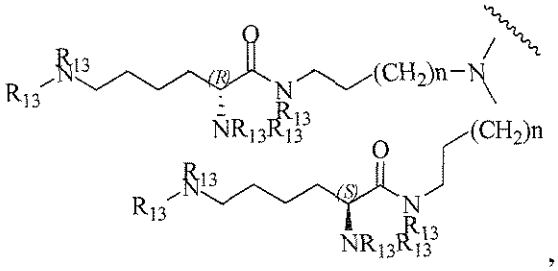

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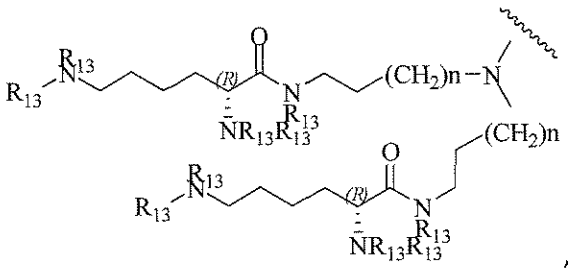
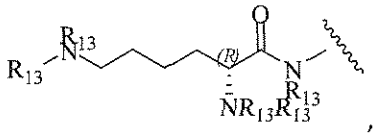
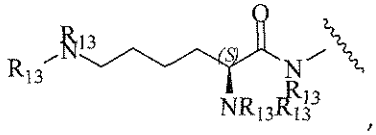
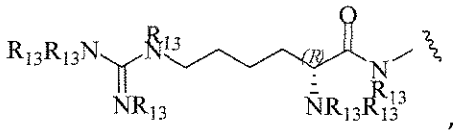
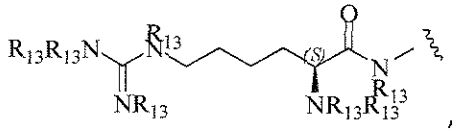
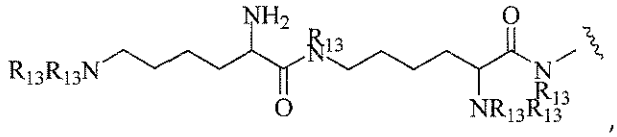


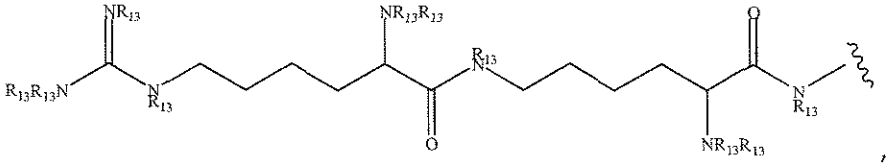


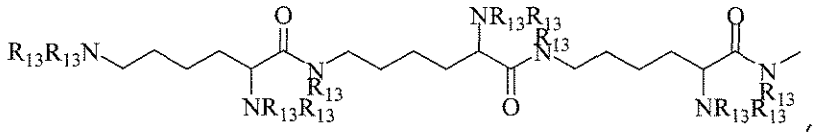


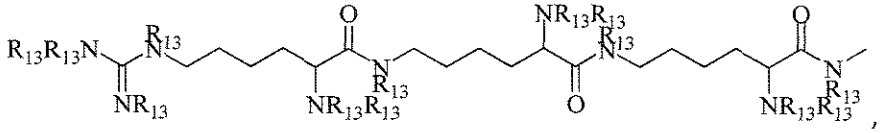


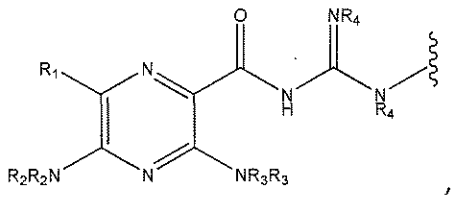


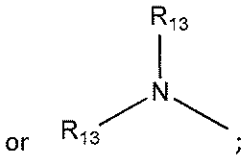












or ;

with the proviso that when any -CHOR^8- or –CH_2OR^8 groups are located 1,2- or 1,3- with respect to each other, the R^8 groups may, optionally, be taken together to form a cyclic mono- or di-substituted 1,3-dioxane or 1,3-dioxolane;

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

2. Use of the compound of Claim 1 in the manufacture of a medicament for liquefying mucus from mucosal surfaces of a subject.

3. Use of the compound of Claim 1 in the manufacture of a medicament for treating chronic bronchitis, treating bronchiectasis, treating cystic fibrosis, treating chronic obstructive pulmonary disease, treating asthma, treating sinusitis, treating vaginal dryness, treating dry eye, promoting ocular hydration, promoting corneal hydration, 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, treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating cystinosis, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, and/or treating rhinosinusitis in a subject.

4. Use of the compound of Claim 1 in the manufacture of a medicament for treating an eye disease characterized by the presence of ocular discharge in a subject.

5. The use of claim 4, wherein the eye disease is one or more conditions selected from the group consisting of blepharitis, allergies, conjunctivitis, corneal ulcer, trachoma, congenital herpes simplex, corneal abrasions, ectropion, eyelid disorders, gonococcal conjunctivitis, herpetic keratitis, ophthalmitis, Sjogren's Syndrome, or Stevens-Johnson Syndrome.

6. Use of the compound of 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 osmolyte.

7. The use of claim 6, wherein the disease is one or more conditions selected from the group consisting of chronic bronchitis, bronchiectasis, cystic fibrosis, asthma, sinusitis, vaginal dryness, dry eye, 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.

8. The use of claim 6, wherein the compound is to be administered preceding administration of the osmolyte.

9. The use of claim 6, wherein the compound is to be administered concurrent with administration of the osmolyte.

10. The use of claim 6, wherein the compound is to be administered following administration of the osmolyte.

11. The use of claim 6, wherein the osmolyte is hypertonic saline or mannitol.

12. The use of claim 6, wherein the osmolyte is sodium chloride which is delivered as a micronized particle of respirable size.

13. The use of claim 6, wherein the effective amount of an osmolyte and a compound of Formula (I) is to be administered by aerosolization using a device capable of delivering the formulation to the nasal passages or pulmonary airway wherein the aerosol is a respirable size.

14. A composition, comprising:
(a) the compound of Claim 1 and (b) an osmotically active compound.

15. Use of the compound of Claim 1 in the manufacture of a medicament for inducing sputum in a subject in need of increased mucociliary clearance and mucosal hydration, wherein the medicament is to be administered with an osmolyte.

16. Use of the compound of Claim 1 in the manufacture of a medicament for prophylactic, post-exposure prophylactic, preventive or therapeutic treatment against diseases or conditions caused by pathogens in a subject in need of increased mucociliary clearance and mucosal hydration.

17. The use of claim 16, wherein the pathogen is anthrax or plague.

18. Use of the compound of 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. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

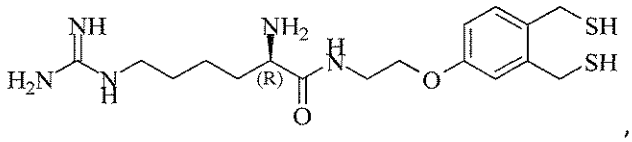
20. Use of the compound of Claim 1 in the manufacture of a medicament for improving mucus penetration of therapeutic agents, wherein the medicament is to be administered with a second therapeutic agent.

21. The use of claim 20, wherein the therapeutic agents is an osmolyte, a sodium channel blocker, a secretogogue, a bronchodilator, an anti-infective, an anti-inflammatory, or a gene carrier.

22. Use of the compound of Claim 1 in the manufacture of a medicament for decreasing mucosal inflammation.

23. Use of the compound of Claim 1 in the manufacture of a medicament for decreasing mucosal oxygen free radicals.

24. The compound of Claim 1, which is one of the following compounds:



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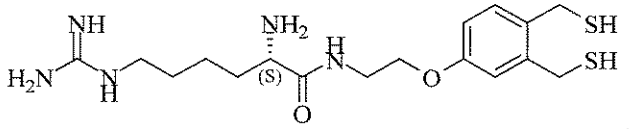

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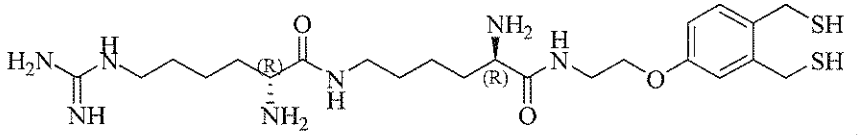

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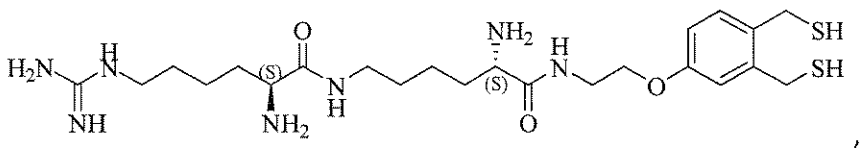

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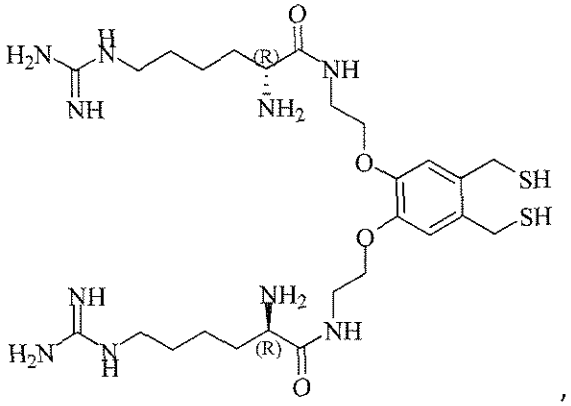

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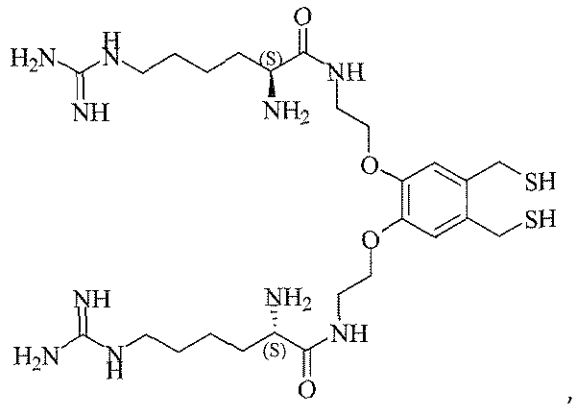

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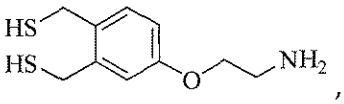

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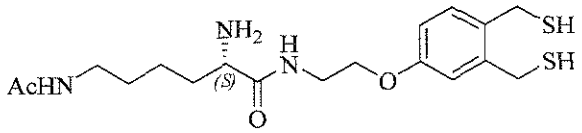

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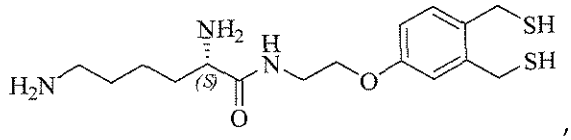

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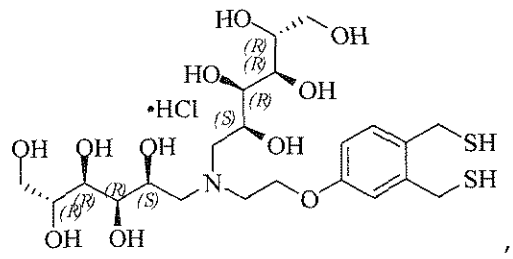

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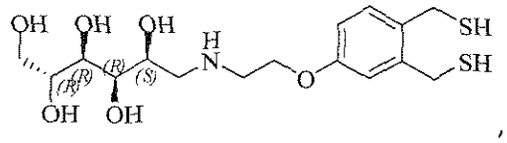
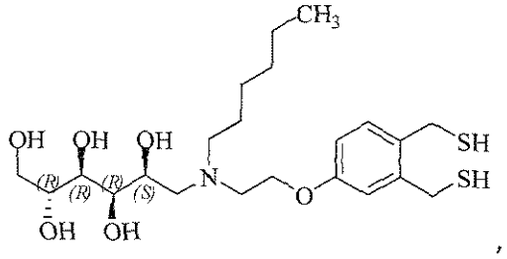
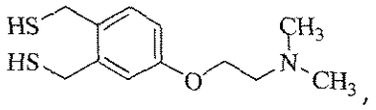
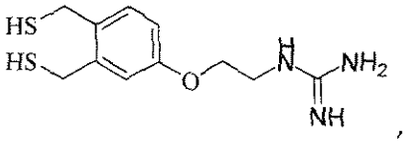
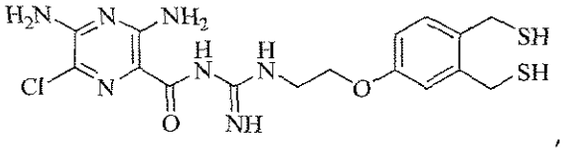
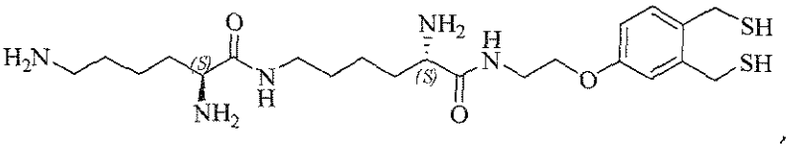


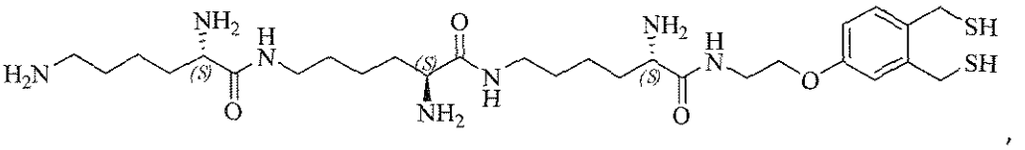


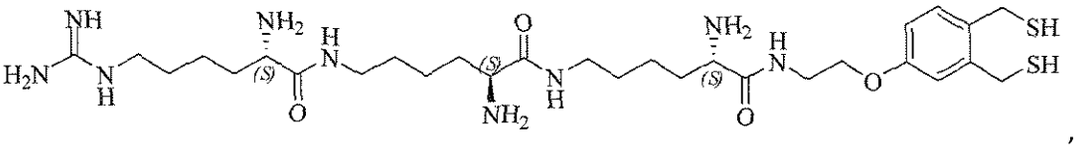


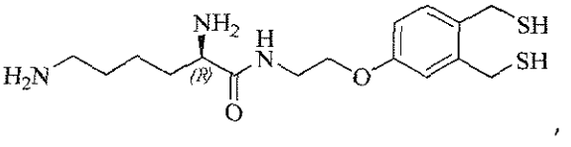


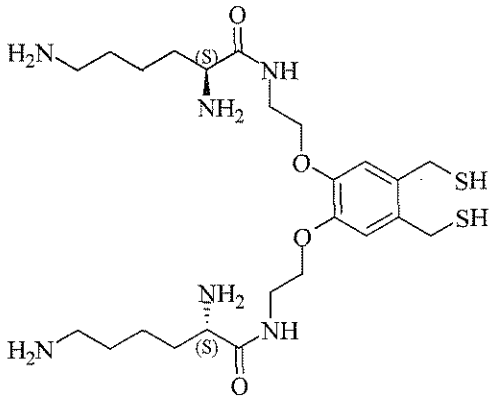


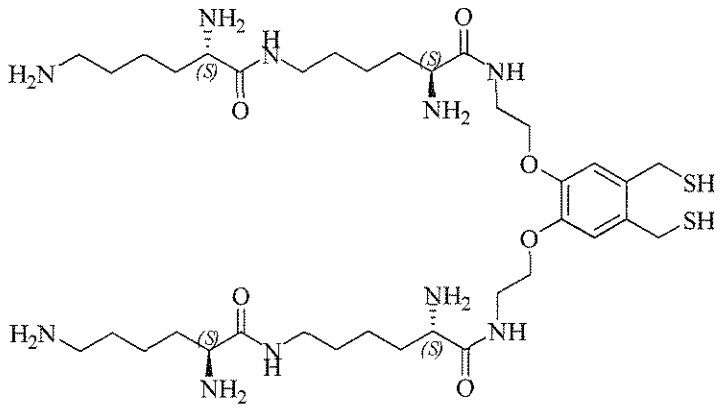


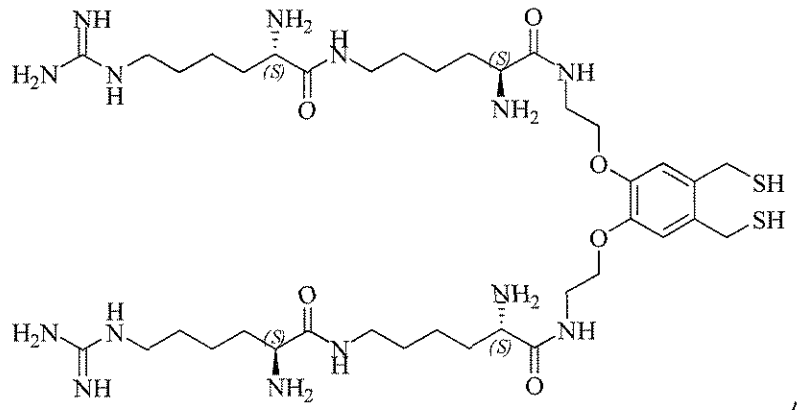


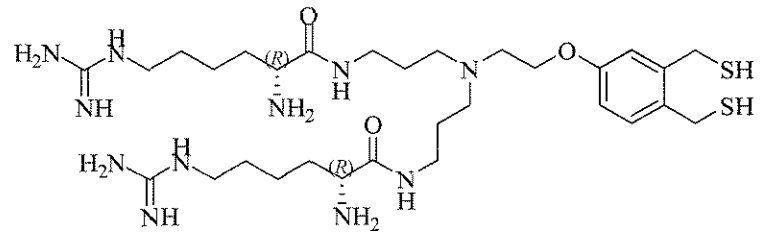










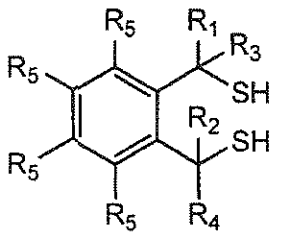


25. The compound of Claim 1, which is an acid addition salt of an inorganic acid or an organic acid selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, acetic acid, oxalic acid, tartaric acid, succinic acid, maleic acid, furmaric acid, gluconic acid, citric acid, malic acid, ascorbic acid, benzoic acid, tannic acid, palmitic acid, alginic acid, polyglutamic acid, naphthalensulfonic acid, methanesulfonic acid, p-toluenesulfonic acid, naphthalenedisulfonic acid, polygalacturonic acid, malonic acid, sulfosalicylic acid, glycolic acid, 2-hydroxy-3-naphthoate, pamoate, salicylic acid, stearic acid, phthalic acid, mandelic acid, and lactic acid.

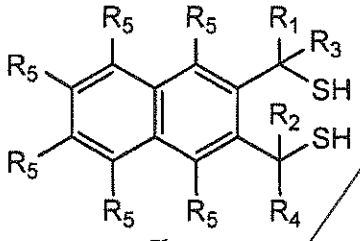
CLAIMS

That Which Is Claimed Is:

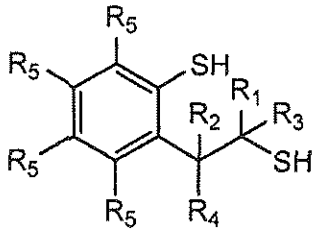
1. A compound represented by formula Ia, Ib, Ic or Id:



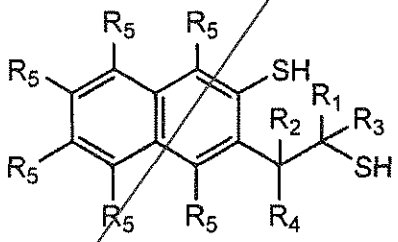
Ia



Ib



Ic

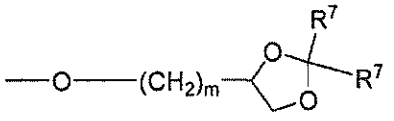


Id

wherein R^1 and R^2 are each, independently, hydrogen, lower alkyl, halogen or triflouromethyl;

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;

each R^5 is, independently, hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl, OH, $-(CH_2)_m-OR^8$, $-O-(CH_2)_m-OR^8$, $-(CH_2)_n-NR^7R^{10}$, $-(CH_2)_n-NR^7R^7$, $-O-(CH_2)_m-NR^7R^{10}$, $-O-(CH_2)_m-NR^7R^7$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-O-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-O-(CH_2)_m-C(=O)NR^7R^{10}$, $-(CH_2)_n-(Z)_g-R^7$, $-O-(CH_2)_m-(Z)_g-R^7$, $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, $-O-(CH_2)_m-CO_2R^7$, $-OSO_3H$, -O-glucuronide, -O-glucose,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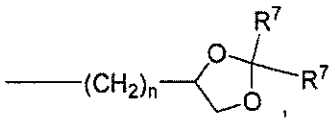
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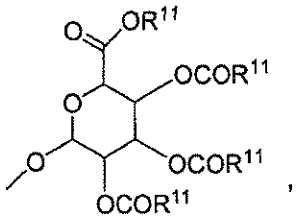
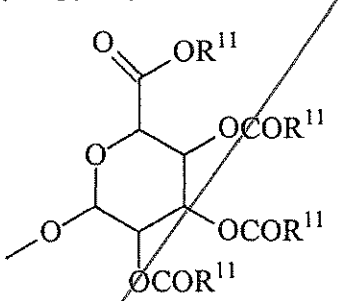

,

-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 with the proviso that at least one R^5 group contains at least one basic nitrogen;

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

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

2-tetrahydropyranyl, or


;

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^{7}R^{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$_2$CH$_3$, -CO$_2$R^{7}, -C(=O)NR^{7}R^{9}, -C(=O)R^{7}, -CH$_2$(CHOH)$_n$-CH$_2$OH, -CO$_2$R^{13}, -C(=O)NR^{13}R^{13}, or -C(=O)R^{13};

each R^{13} is, independently, hydrogen, lower alkyl, phenyl, substituted phenyl or -CH$_2$(CHOR^{8})$_m$-CH$_2$OR^{8}, -SO$_2$CH$_3$, -CO$_2$R^{7}, -C(=O)NR^{7}R^{9}, -C(=O)R^{7}, -CH$_2$-(CHOH)$_n$-CH$_2$OH, –(CH$_2$)$_m$-NR^{7}R^{10}, –(CH$_2$)$_m$- NR^{7}R^{7}, –(CH$_2$)$_m$-NR^{11}R^{11}, –(CH$_2$)$_m$-(NR^{11}R^{11}R^{11})$^{+}$, –(CH$_2$)$_m$-(CHOR^{8})$_m$-(CH$_2$)$_m$NR^{11}R^{11}, –(CH$_2$)$_m$-(CHOR^{8})$_m$-(CH$_2$)$_m$NR^{7}R^{10}, -(CH$_2$)$_m$-NR^{10}R^{10}, –(CH$_2$)$_m$-(CHOR^{8})$_m$-(CH$_2$)$_m$-(NR^{11}R^{11}R^{11})$^{+}$, or –(CH$_2$)$_m$-(CHOR^{8})$_m$-(CH$_2$)$_m$NR^{7}R^{7};

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

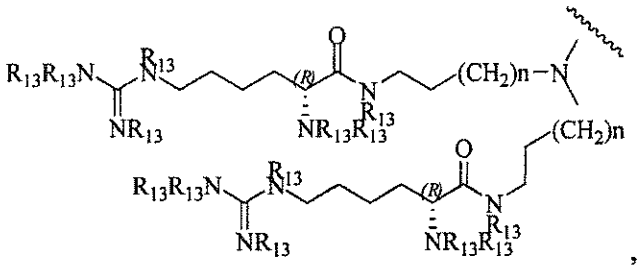
each m is, independently, an integer from 1 to 7;

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$_2$NH-, -NHSO$_2$-, -NR^{7}CO-, -CONR^{7}-, -N(R^{13})-, -SO$_2$NR^{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$_2$NR^{7}-, -SO$_2$NR^{10}-, or -Het-;

each CAP is, independently



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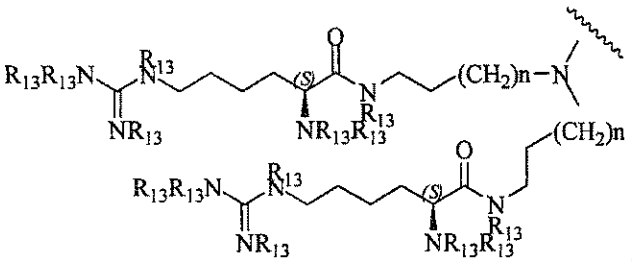

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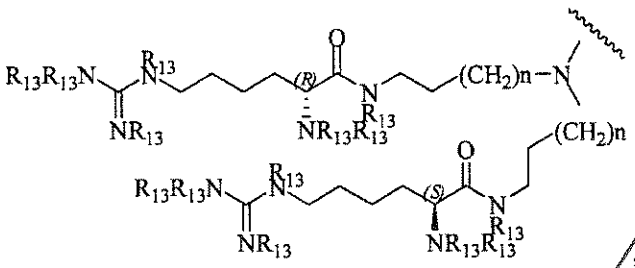

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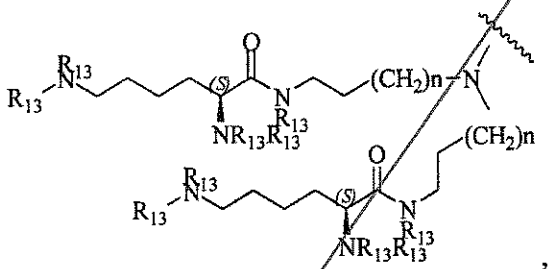

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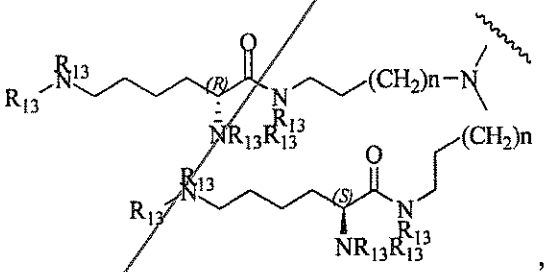

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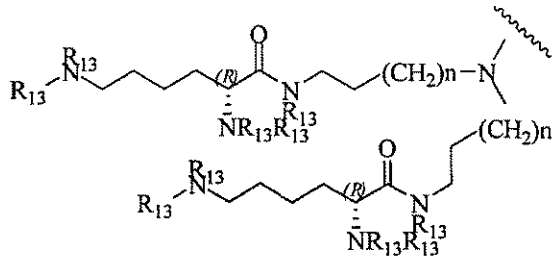
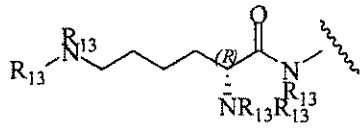
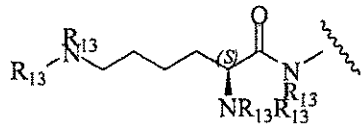
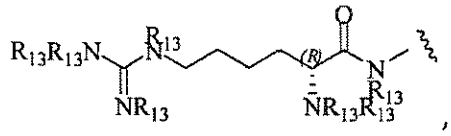
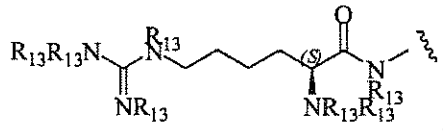
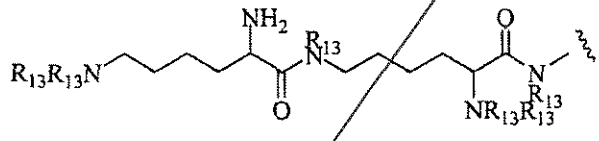


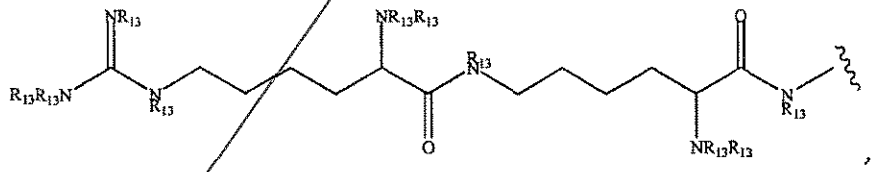


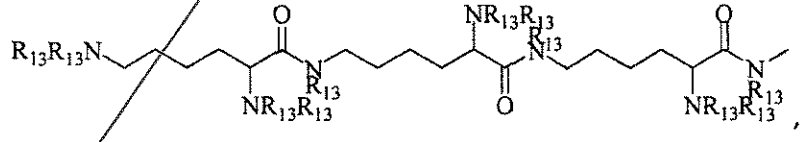


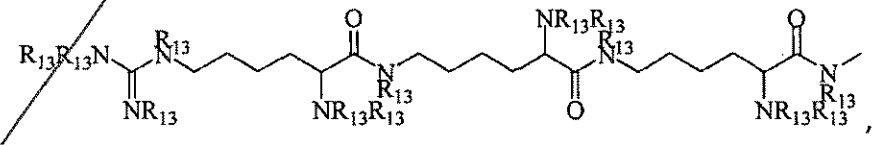


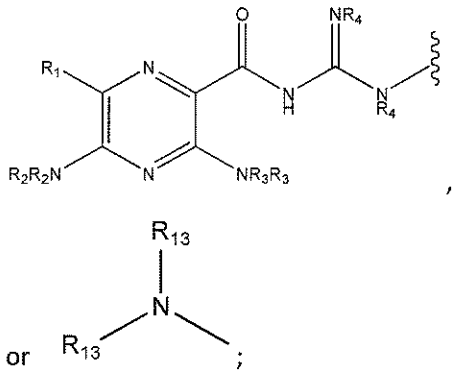












with the proviso that when any -CHOR^8- or –CH_2OR^8 groups are located 1,2- or 1,3- with respect to each other, the R^8 groups may, optionally, be taken together to form a cyclic mono- or di-substituted 1,3-dioxane or 1,3-dioxolane;

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

2. Use of the compound of Claim 1 in the manufacture of a medicament for liquefying mucus from mucosal surfaces of a subject.

3. Use of the compound of Claim 1 in the manufacture of a medicament for treating chronic bronchitis, treating bronchiectasis, treating cystic fibrosis, treating chronic obstructive pulmonary disease, treating asthma, treating sinusitis, treating vaginal dryness, treating dry eye, promoting ocular hydration, promoting corneal hydration, 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, treating ventilator-induced pneumonia, treating asthma, treating primary ciliary dyskinesia, treating otitis media, inducing sputum for diagnostic purposes, treating cystinosis, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, and/or treating rhinosinusitis in a subject.

4. Use of the compound of Claim 1 in the manufacture of a medicament for treating an eye disease characterized by the presence of ocular discharge in a subject.

5. The use of claim 4, wherein the eye disease is one or more conditions selected from the group consisting of blepharitis, allergies, conjunctivitis, corneal ulcer, trachoma, congenital herpes simplex, corneal abrasions, ectropion, eyelid disorders, gonococcal conjunctivitis, herpetic keratitis, ophthalmitis, Sjogren's Syndrome, or Stevens-Johnson Syndrome

6. Use of the compound of 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 osmolyte.

7. The use of claim 6, wherein the disease is one or more conditions selected from the group consisting of chronic bronchitis, bronchiectasis, cystic fibrosis, asthma, sinusitis, vaginal dryness, dry eye, 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.

8. The use of claim 6, wherein the compound is to be administered preceding administration of the osmolyte.

9. The use of claim 6, wherein the compound is to be administered concurrent with administration of the osmolyte.

10. The use of claim 6, wherein the compound is to be administered following administration of the osmolyte.

11. The use of claim 6, wherein the osmolyte is hypertonic saline or mannitol.

12. The use of claim 6, wherein the osmolyte is sodium chloride which is delivered as a micronized particle of respirable size.

13. The use of claim 6, wherein the effective amount of an osmolyte and a compound of Formula (I) is to be administered by aerosolization using a device capable of delivering the formulation to the nasal passages or pulmonary airway wherein the aerosol is a respirable size.

14. A composition, comprising:

(a) the compound of Claim 1 and (b) an osmotically active compound.

15. Use of the compound of Claim 1 in the manufacture of a medicament for inducing sputum in a subject in need of increased mucociliary clearance and mucosal hydration, wherein the medicament is to be administered with an osmolyte.

16. Use of the compound of Claim 1 in the manufacture of a medicament for prophylactic, post-exposure prophylactic, preventive or therapeutic treatment against diseases or conditions caused by pathogens in a subject in need of increased mucociliary clearance and mucosal hydration.

17. The use of claim 16, wherein the pathogen is anthrax or plague.

18. Use of the compound of 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. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

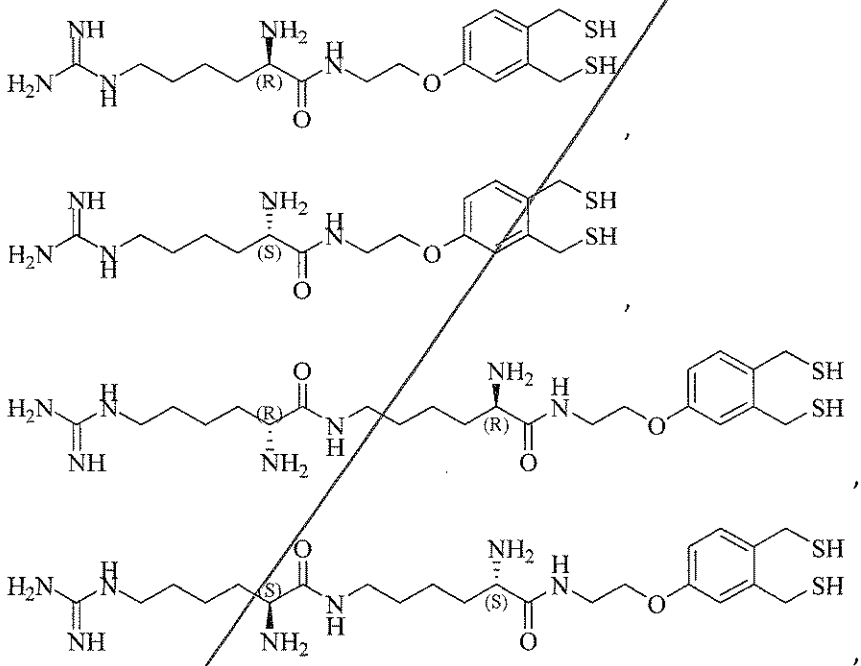
20. Use of the compound of Claim 1 in the manufacture of a medicament for improving mucus penetration of therapeutic agents, wherein the medicament is to be administered with a second therapeutic agent.

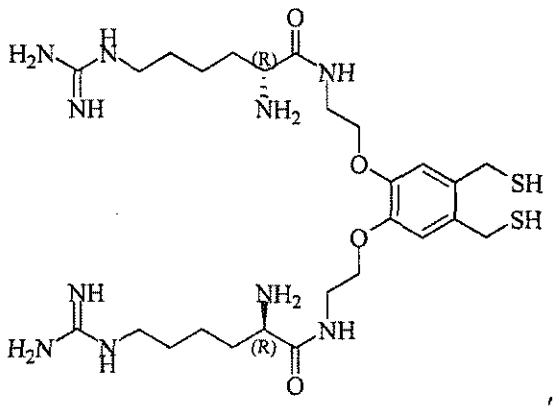
21. The use of claim 20, wherein the therapeutic agents is an osmolyte, a sodium channel blocker, a secretogogue, a bronchodilator, an anti-infective, an anti-inflammatory, or a gene carrier.

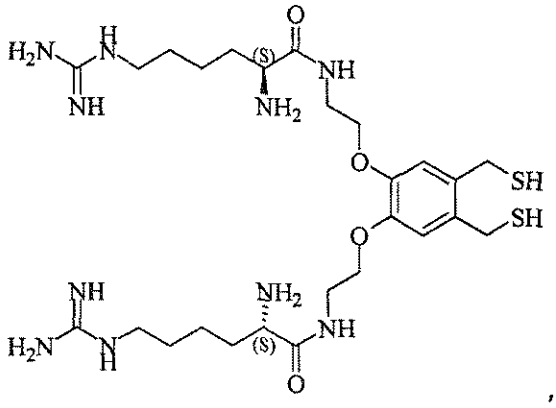
22. Use of the compound of Claim 1 in the manufacture of a medicament for decreasing mucosal inflammation.

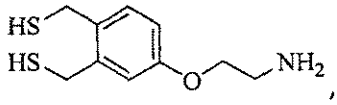
23. Use of the compound of Claim 1 in the manufacture of a medicament for decreasing mucosal oxygen free radicals.

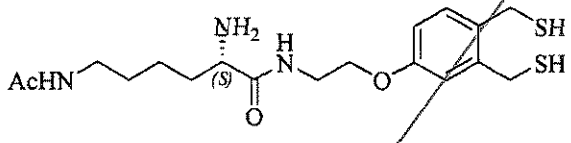
24. The compound of Claim 1, which is one of the following compounds:

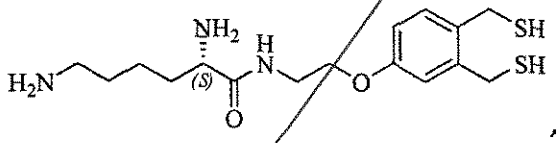


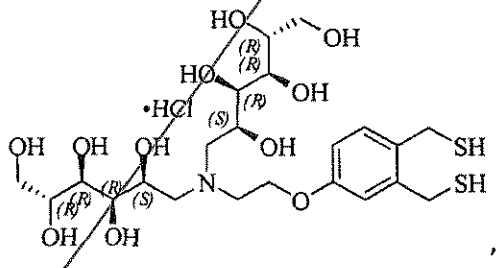


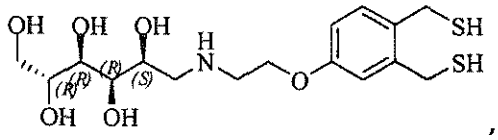


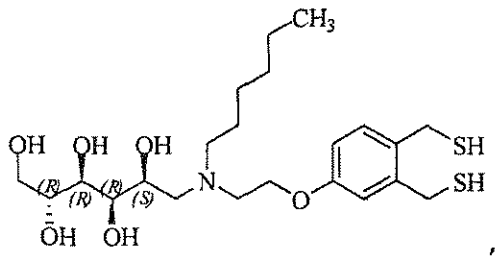


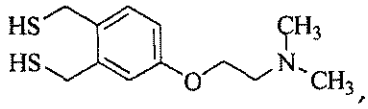


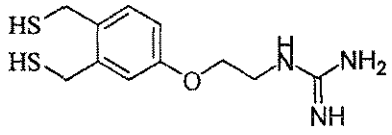


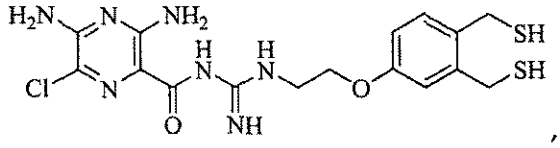


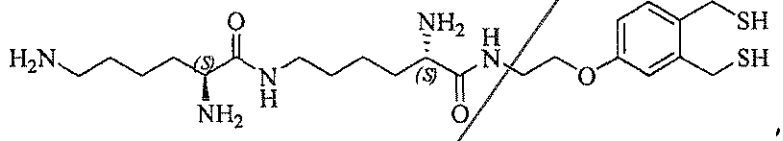


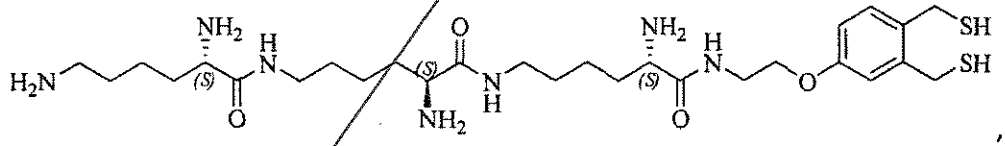


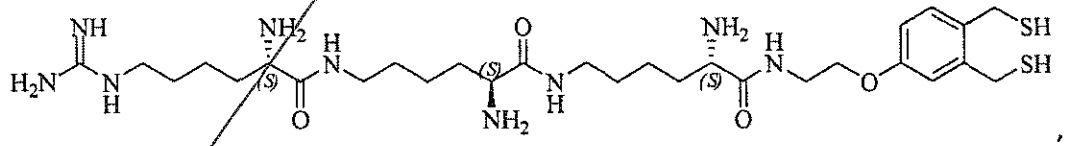


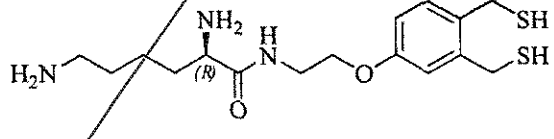


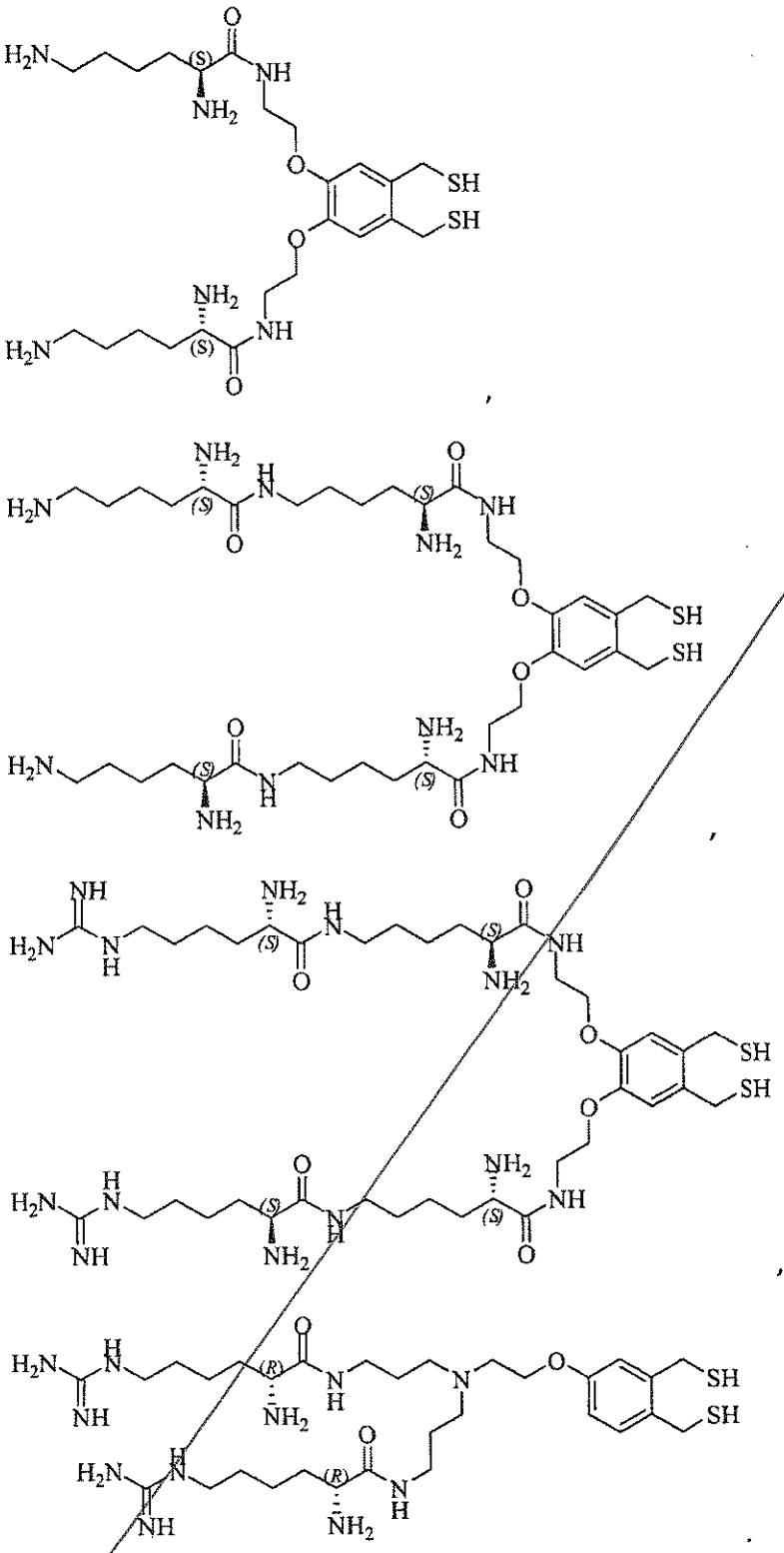












25. The compound of Claim 1, which is an acid addition salt of an inorganic acid or an organic acid selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, acetic acid, oxalic acid, tartaric acid, succinic acid, maleic acid, furmaric acid, gluconic acid, citric acid, malic acid, ascorbic acid, benzoic acid, tannic acid, palmitic acid, alginic acid, polyglutamic acid, naphthalensulfonic acid, methanesulfonic acid, p-toluenesulfonic acid, naphthalenedisulfonic acid, polygalacturonic acid, malonic acid, sulfosalicylic acid, glycolic acid, 2-hydroxy-3-naphthoate, pamoate, salicylic acid, stearic acid, phthalic acid, mandelic acid, and lactic acid.