Claims

1. Use of an effective amount of a polyanion in the manufacture of a medicament for inhibiting the cytotoxic activity of extracellular histones in a subject, wherein the polyanion does not have substantial anticoagulant activity; and

wherein the polyanion is a polyanionic oligosaccharide having the general structure (I):

$A-(B)_n-D$ (I)

wherein A and B are each independently a cyclic monosaccharide or a cyclic deoxy monosaccharide;

D is a cyclic monosaccharide, a cyclic deoxy monosaccharide, a ring-opened monosaccharide, or a sugar alcohol;

n is an integer selected from 0, 1, 2, 3, 4, 5, 6, 7 and 8; and

wherein each of the cyclic monosaccharide, the cyclic deoxy monosaccharide, the ring-opened monosaccharide, or the sugar alcohol is independently optionally substituted with OSO_3^-, COO^-, OPO_3^-, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted aryl, or an optionally substituted aralkyl; and

wherein the polyanionic oligosaccharide includes at least two anionic substituents selected from the group consisting of OSO_3^-, COO^- and OPO_3^-.

2. Use of an effective amount of a polyanion for the manufacture of a medicament for inhibiting extracellular histone accumulation in a subject, wherein the polyanion does not have substantial anticoagulant activity; and

wherein the polyanion is a polyanionic oligosaccharide having the general structure (I):

$A-(B)_n-D$ (I)

wherein A and B are each independently a cyclic monosaccharide or a cyclic deoxy monosaccharide;

D is a cyclic monosaccharide, a cyclic deoxy monosaccharide, a ring-opened monosaccharide, or a sugar alcohol;

n is an integer selected from 0, 1, 2, 3, 4, 5, 6, 7 and 8; and

~~wherein each of the cyclic monosaccharide, the cyclic deoxy monosaccharide, the ring-opened monosaccharide, or the sugar alcohol is independently optionally substituted with OSO_3^-, COO^-, OPO_3^-, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted aryl, or an optionally substituted aralkyl; and~~

~~wherein the polyanionic oligosaccharide includes at least two anionic substituents selected from the group consisting of OSO_3^-, COO^- and OPO_3^-.~~

Claims

~~3~~1. Use of an effective amount of a polyanion for the manufacture of a medicament for the treatment of sepsis by inhibiting the cytotoxic activity of extracellular histones in a subject having sepsis, wherein the polyanion does not have substantial anticoagulant activity such that the polyanion increases prothrombin time (PT), partial thromboplastin time (PTT), activated partial thromboplastin time (APTT), thrombin clotting time (TCT), or activated clotting time (ACT) by 0 to 10% of the normal range; and

wherein the polyanion is a polyanionic oligosaccharide having the general structure (I):

$$A—(B)_n—D \qquad (I)$$

wherein A and B are each independently a cyclic monosaccharide or a cyclic deoxy monosaccharide;

D is a cyclic monosaccharide, a cyclic deoxy monosaccharide, a ring-opened monosaccharide, or a sugar alcohol;

n is an integer selected from 0, 1, ~~2, 3, 4, 5, 6, 7 and 8~~and 2; and

wherein each of the cyclic monosaccharide, the cyclic deoxy monosaccharide, the ring-opened monosaccharide, or the sugar alcohol is independently optionally substituted with OSO_3^-, COO^-, OPO_3^-, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted aryl, or an optionally substituted aralkyl; and

wherein the polyanionic oligosaccharide includes at least two anionic substituents selected from the group consisting of OSO_3^-, COO^- and OPO_3^-.

42. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the polyanion is substantially non-immunogenic.

53. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the cyclic monosaccharide is selected from the group consisting of glucose, galactose, fructose, ribose, arabinose, xylose, lyxose, allose, altrose, mannose, gulose, idose, talose, ribulose, xylulose, psicose, sorbose, tagatose and sedoheptulose.

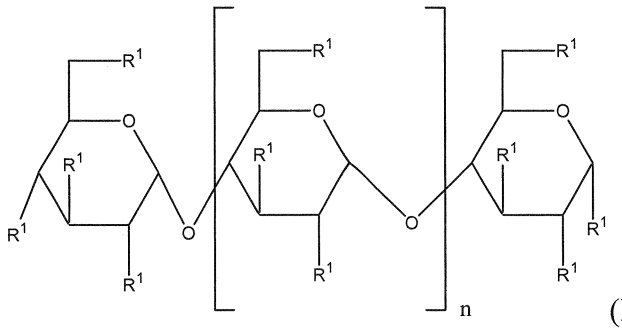
64. The use of ~~any one of~~ claim~~s~~ 1 ~~to 5~~ wherein the cyclic monosaccharide is selected from the group consisting of glucose, galactose and fructose.

75. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the cyclic deoxy monosaccharide is selected from the group consisting of fucose, deoxyribose and rhamnose.

~~86~~. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the sugar alcohol is selected from the group consisting of glycol, glycerol, erythritol, threitol, ribitol, arabitol, xylitol, sorbitol (glucitol), mannitol, dulcitol (galactitol), iditol and fucitol.

~~97~~. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the ring-opened monosaccharide is selected from the group consisting of glucose, galactose, fructose, erythrose, threose, erythrulose, ribose, arabinose, xylose, lyxose, allose, altrose, mannose, gulose, idose, talose, ribulose, xylulose, psicose, sorbose, tagatose and sedoheptulose.

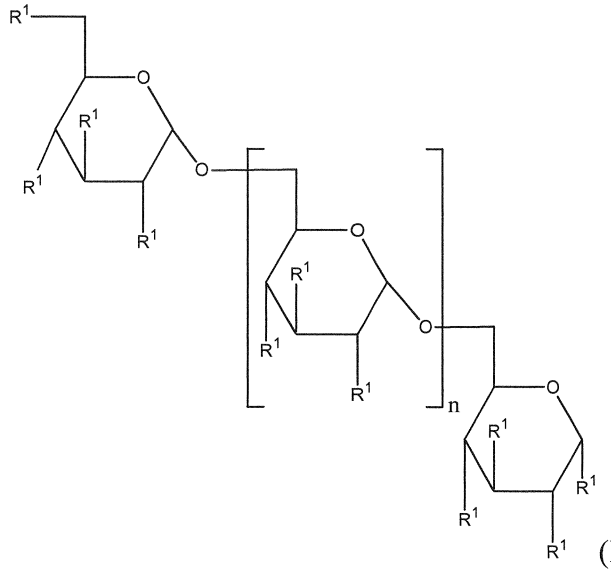
~~108~~. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the polyanionic oligosaccharide has the general structure (I-a):



(I-a)

wherein each R^1 is independently selected from OSO_3^-, COO^-, OPO_3^-, OH or H; and n is an integer between 0, 1, and 2~~, 3, 4, 5, 6, 7, and 8~~; and wherein at least two of R^1 are selected from the group consisting of OSO_3^-, COO^-, and OPO_3^-.

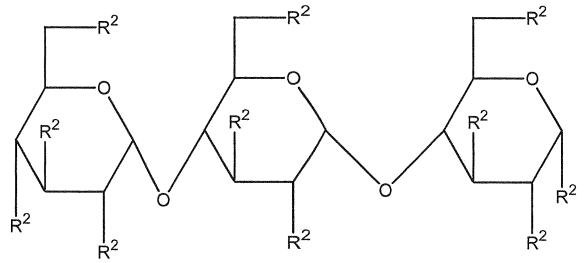
~~11~~9. The use of ~~any one of~~ claims 1 ~~to 3~~ wherein the polyanionic oligosaccharide has the general structure (I-b):

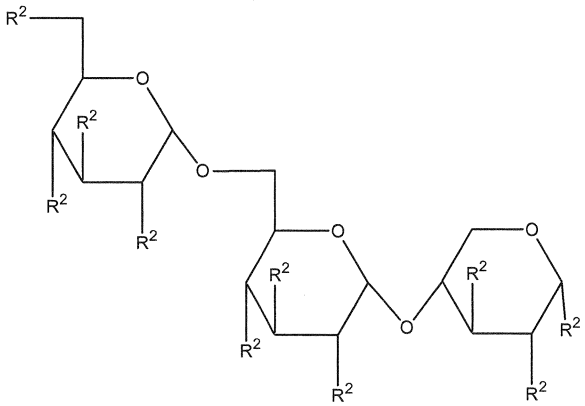


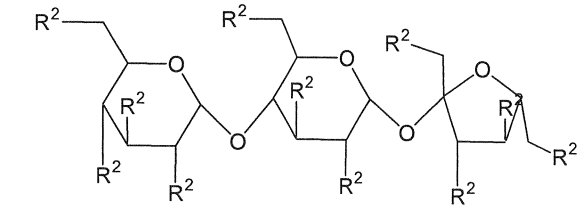
(I-b)

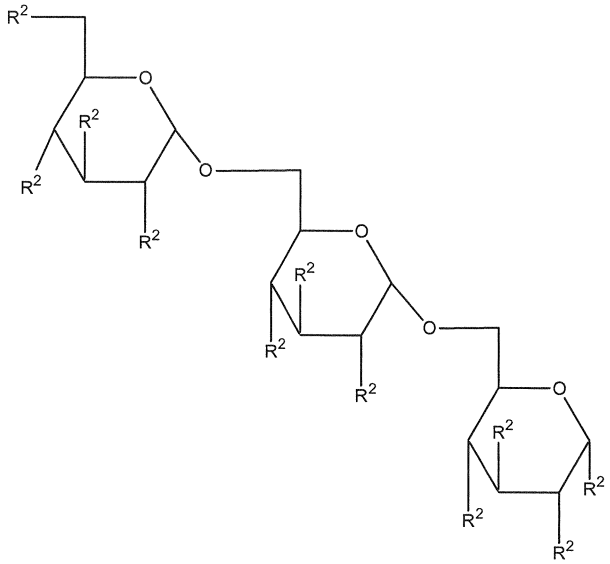
where each R^1 is independently selected from OSO_3^-, COO^-, OPO_3^-, OH or H; and n is an integer between 0, 1, and 2~~, 3, 4, 5, 6, 7, and 8~~; and wherein at least two of R^1 are selected from the group consisting of OSO_3^-, COO^-, and OPO_3^-.

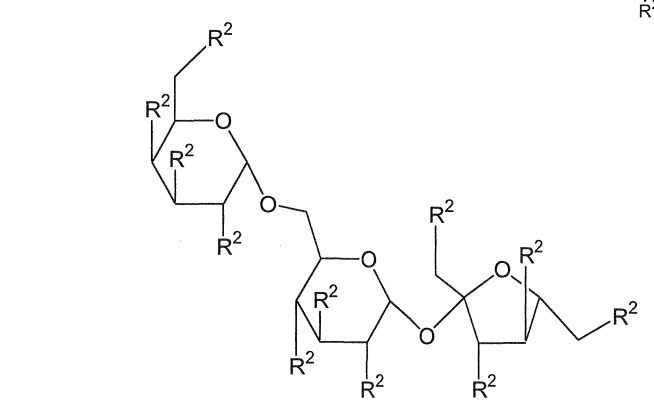
~~12~~10. The use of ~~any one of~~ claims ~~1~~ 1 ~~to 3~~ wherein the polyanionic oligosaccharide is selected from the group consisting of:

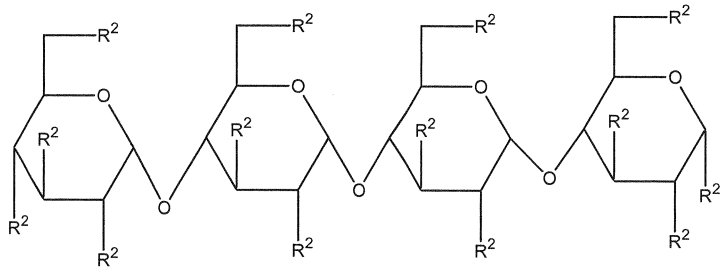




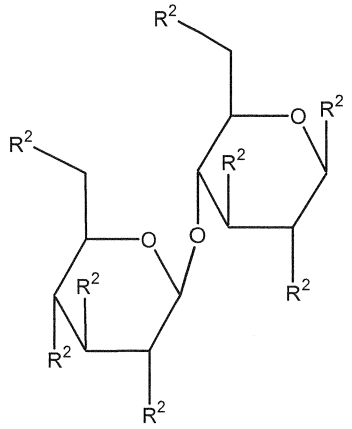








and



wherein each R^2 is independently selected from OSO_3^-, COO^-, OPO_3^-, OH or H; and wherein at least two of R^2 are selected from the group consisting of OSO_3^-, COO^-, and OPO_3^-.

~~13~~11. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the polyanionic oligosaccharide is selected from the group consisting of maltose sulfate, maltotriose sulfate, maltotetraose sulfate, ~~maltopentaose sulfate, maltohexaose sulfate, maltoheptaose sulfate, maltooctaose sulfate, maltononaose sulfate and maltodecaose sulfate,~~ panose sulfate, isomaltotriose sulfate, erlose sulfate, cellobiose sulfate and raffinose sulfate.

~~14~~12. The use of ~~any one of~~ claim~~s~~ 1 ~~to 3~~ wherein the polyanionic oligosaccharide is cellobiose sulfate.