**Claims**:

1. A method of conjugating a water soluble polymer to an oxidized carbohydrate moiety of a blood coagulation protein comprising contacting the oxidized carbohydrate moiety with an activated water soluble polymer under conditions that allow conjugation;

said blood coagulation protein selected from the group consisting of Factor IX (FIX), Factor VIII (FVIII), Factor VIIa (FVIIa), Von Willebrand Factor (VWF), Factor FV (FV), Factor X (FX), Factor XI (FXI), Factor XII (FXII), thrombin (FII), protein C, protein S, tPA, PAI-1, tissue factor (TF) and ADAMTS 13 protease or a biologically active fragment, derivative or variant thereof;

said water soluble polymer containing an active aminooxy group and is selected from the group consisting of polyethylene glycol (PEG), branched PEG, polysialic acid (PSA), carbohydrate, polysaccharides, pullulane, chitosan, hyaluronic acid, chondroitin sulfate, dermatan sulfate, starch, dextran, carboxymethyl-dextran, polyalkylene oxide (PAO), polyalkylene glycol (PAG), polypropylene glycol (PPG), polyoxazoline, polyacryloylmorpholine, polyvinyl alcohol (PVA), polycarboxylate, polyvinylpyrrolidone, polyphosphazene, polyoxazoline, polyethylene-co-maleic acid anhydride, polystyrene-co-maleic acid anhydride, poly(1-hydroxymethylethylene hydroxymethylformal) (PHF), 2-methacryloyloxy-2'-ethyltrimethylammoniumphosphate (MPC); and

said carbohydrate moiety oxidized by incubation with a buffer comprising an oxidizing agent selected from the group consisting of sodium periodate ($NaIO_4$), lead tetraacetate ($Pb(OAc)_4$) and potassium perruthenate (KRuO4); wherein an oxime linkage is formed between the oxidized carbohydrate moiety and the active aminooxy group on the water soluble polymer.

2. The method according to claim 1 wherein the water soluble polymer is PSA.

3. The method according to claim 2 wherein the PSA is comprised of about 10 – 300 sialic acid units.

4. The method according to any one of claims 1-3 wherein the blood coagulation protein is FIX.

5. The method according to any one of claims 1-3 wherein the blood coagulation protein is FVIIa.

6. The method according to any one of claims 1-3 wherein the blood coagulation protein is FVIII.

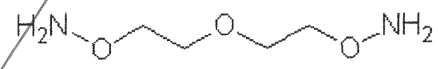
7. The method according to any one of claims 1-6 wherein the oxidizing agent is sodium periodate ($NaIO_4$).

8. The method according to any one of claims 4-7 wherein the oxidized carbohydrate moiety of the blood coagulation protein is located in the activation peptide of the blood coagulation protein.

9. The method according to claim 2 wherein the PSA is prepared by reacting an activated aminooxy linker with oxidized PSA;

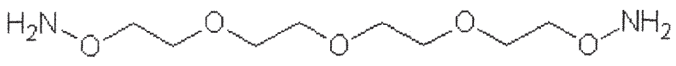
wherein the aminooxy linker is selected from the group consisting of:

a) a 3-oxa-pentane-1,5-dioxyamine linker of the formula:



and

b) a 3,6,9-trioxa-undecane-1,11-dioxyamine linker of the formula:



wherein the PSA is oxidized by incubation with a oxidizing agent to form a terminal aldehyde group at the non-reducing end of the PSA.

10. The method according to claim 7 wherein the aminooxy linker is 3-oxa-pentane-1,5-dioxyamine.

11. The method according to claim 7 wherein the oxidizing agent is $NaIO_4$.

12. The method according to any one of claims 1-9 wherein the contacting of the oxidized carbohydrate moiety with the activated water soluble polymer occurs in a buffer comprising a nucleophilic catalyst selected from the group consisting of aniline and aniline derivatives.

13. The method according to claim 2 further comprising the step of reducing an oxime linkage in the conjugated blood coagulation protein by incubating the conjugated blood coagulation protein in a buffer comprising a reducing compound selected from the group consisting of sodium cyanoborohydride ($NaCNBH_3$) and ascorbic acid (vitamin C).

14. The method according to claim 11 wherein the reducing compound is sodium cyanoborohydride ($NaCNBH_3$).

15. A modified blood coagulation protein produced by the method according to any one of claims 1-12.

16. A modified FIX comprising:

(a) a FIX molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PSA bound to the FIX molecule of (a), wherein said aminooxy PSA is attached to the FIX via one or more carbohydrate moieties.

17. A modified FVIIa comprising:

(a) a FVIIa molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PSA bound to the FVIIa molecule of (a), wherein said aminooxy PSA is attached to the FVIIa via one or more carbohydrate moieties.

18. A modified FVIII comprising:

(a) a FVIII molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PSA bound to the FVIII molecule of (a), wherein said aminooxy PSA is attached to the FVIII via one or more carbohydrate moieties.

19. A modified FIX comprising:

(a) a FIX molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PEG bound to the FIX molecule of (a), wherein said aminooxy PEG is attached to the FIX via one or more carbohydrate moieties.

20. A modified FVIIa comprising:

(a) a FVIIa molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PEG bound to the FVIIa molecule of (a), wherein said aminooxy PEG is attached to the FVIIa via one or more carbohydrate moieties.

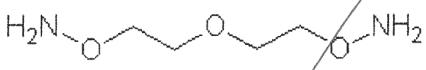
21. A modified FVIII comprising:

(a) a FVIII molecule or a biologically active fragment, derivative or variant thereof; and

(b) at least one aminooxy PEG bound to the FVIII molecule of (a), wherein said aminooxy PEG is attached to the FVIII via one or more carbohydrate moieties.

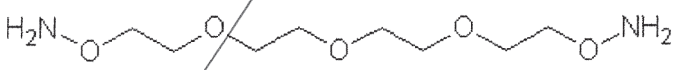
22. A water soluble polymer comprising an active aminooxy linker; said water soluble polymer selected from the group consisting of polyethylene glycol (PEG), branched PEG, polysialic acid (PSA), carbohydrate, polysaccharides, pullulane, chitosan, hyaluronic acid, chondroitin sulfate, dermatan sulfate, starch, dextran, carboxymethyl-dextran, polyalkylene oxide (PAO), polyalkylene glycol (PAG), polypropylene glycol (PPG), polyoxazoline, polyacryloylmorpholine, polyvinyl alcohol (PVA), polycarboxylate, polyvinylpyrrolidone, polyphosphazene, polyoxazoline, polyethylene-co-maleic acid anhydride, polystyrene-co-maleic acid anhydride, poly(1-hydroxymethylethylene hydroxymethylformal) (PHF), 2-methacryloyloxy-2'-ethyltrimethylammoniumphosphate (MPC), said active aminooxy linker is selected from the group consisting of:

a) a 3-oxa-pentane-1,5-dioxyamine linker of the formula:



and

b) a 3,6,9-trioxa-undecane-1,11-dioxyamine linker of the formula:



**Claims:**

1. A modified blood coagulation protein comprising:

(a) a blood coagulation protein selected from the group consisting of

(i) a blood coagulation protein with Factor IX (FIX) biological activity; and

(ii) a blood coagulation protein with Factor VIII (FVIII) biological activity; and

(b) at least one polysialic acid (PSA) containing an active aminooxy group bound to said blood coagulation protein of (a) at one or more oxidized carbohydrate moieties;

wherein said modified blood coagulation protein has an oxime linkage between said one or more oxidized carbohydrate moieties and the active aminooxy group on the PSA;

wherein said modified blood coagulation protein has a specific activity of at least 50% relative to an unmodified blood coagulation protein.

2. The modified blood coagulation protein of claim 1 wherein said blood coagulation protein is a blood coagulation protein with FIX biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 60% relative to an unmodified blood coagulation protein.

3. The modified blood coagulation protein of claim 1 wherein said blood coagulation protein is a blood coagulation protein with FVIII biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 70% relative to an unmodified blood coagulation protein.

4. A method of conjugating a polysialic acid (PSA) containing an active aminooxy group to an oxidized carbohydrate moiety of a blood coagulation protein, comprising contacting said oxidized carbohydrate moiety with at least one activated PSA under conditions that allow conjugation;

said blood coagulation protein selected from the group consisting of

(i) a blood coagulation protein with FIX biological activity; and

(ii) a blood coagulation protein with FVIII biological activity;

said carbohydrate moiety oxidized by incubation with a buffer comprising an oxidizing agent selected from the group consisting of sodium periodate ($NaIO_4$), lead tetraacetate ($Pb(OAc)_4$ ) and potassium perruthenate (KRuO4); wherein an oxime linkage is formed between the oxidized carbohydrate moiety and the active aminooxy group on the PSA;

said modified blood coagulation protein having a specific activity of at least 50% relative to an unmodified blood coagulation protein.

5. The method of claim 4 wherein said blood coagulation protein is a blood coagulation protein with FIX biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 60% relative to an unmodified blood coagulation protein.

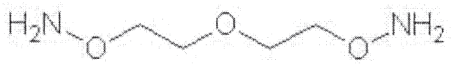
6. The method of claim 4 wherein said blood coagulation protein is a blood coagulation protein with FVIII biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 70% relative to an unmodified blood coagulation protein.

7. The method according claim 4 wherein the PSA is comprised of about 10 – 300 sialic acid units.

8. The method according to claim 4 wherein the PSA is prepared by reacting an activated aminooxy linker with oxidized PSA;

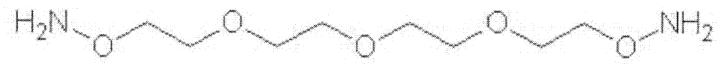
wherein the aminooxy linker is selected from the group consisting of:

(a) a 3-oxa-pentane-1,5-dioxyamine linker of the formula:



and

(b) a 3,6,9-trioxa-undecane-1,11-dioxyamine linker of the formula:



wherein the PSA is oxidized by incubation with a oxidizing agent to form a terminal aldehyde group at the non-reducing end of the PSA.

9. The method according to claim 8 wherein the aminooxy linker is 3-oxa-pentane-1,5-dioxyamine.