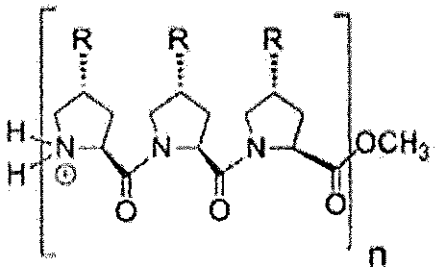
facilitate binding to their corresponding binding molecules.

There is a need to provide glycomimetics that overcome, or at least ameliorate, one or more of the disadvantages described above.

There is a need to provide glycomimetics that not only maintain key properties of natural polysaccharides, but also adopt a predictable, well-defined and stable conformation that enable binding or functional motifs to be more accurately and optimally positioned on its backbone and therefore, improved control of their multivalent interactions with binding molecules.

Summary

According to a first aspect, there is provided a glycopeptide, comprising a polyproline backbone and one or more carbohydrate molecules, wherein the polyproline backbone has the following general formula (I):



; wherein R is independently H or N_3; wherein at least one R is N_3; n is 1 or more; the one or more carbohydrate molecules is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a hyaluronan disaccharide, and a keratan sulfate disaccharide; and wherein the one or more carbohydrate molecules is alkyne-functionalized and attached to the polyproline backbone at R by forming a 1,2,3-triazole linkage when R is N_3.

Advantageously, the polyproline backbone provides conformational stability to the glycopeptide, and has 3-fold repeating units of the polyproline type II (PPII) helix that allows for the precise orientation of functional groups at desired sites along a rigid backbone.

The polyproline backbone may comprise (4R)-azidoproline (Azp). Advantageously, incorporation of Azp into polyproline stabilizes its PPII helix conformation via an azido gauche effect, and enables the polyproline to

the same face of the polyproline backbone. Advantageously, such pre-determined positioning of the carbohydrate molecules along the polyproline backbone improves the binding affinity of the glycopeptide to its target molecule(s).

According to a second aspect, there is provided a method of synthesizing a glycopeptide as defined above, comprising attaching one or more carbohydrate molecules to a polyproline backbone; wherein the one or more carbohydrate molecule is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a Hyaluronan disaccharide and a keratan sulfate disaccharide.

According to a third aspect, there is provided a glycopeptide as defined above for use in therapy.

According to a fourth aspect, there is provided the use of the glycopeptides as defined herein in the manufacture of a medicament for treating cancer or neurodegenerative disease in a patient in need of a target-specific therapy.

According to one embodiment, there is provided a method of treating a patient in need of a target-specific therapy, comprising the administration of a glycopeptide as defined above.

According to a fifth aspect, there is provided a target-specific therapeutic agent comprising a glycopeptide as defined above.

Disclosed is a glycopeptide as defined above for use as target-specific biopolymers.

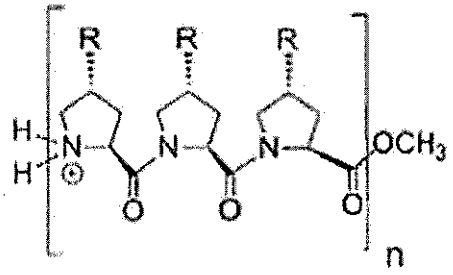
Disclosed is a glycopeptide as defined above for use in glycosaminoglycans (GAG)-based pharmaceutics.

Disclosed is a glycopeptide as defined above for use as diagnostic tools.

According to a sixth aspect, there is provided an *in vitro* method of controlling the binding affinity of a glycopeptide to one or more alkyne-functionalized binding molecules, comprising

attaching one or more carbohydrate molecules at pre-determined positions along an azido-functionalized polyproline backbone by forming a 1,2,3-triazole linkage; wherein the one or more carbohydrate molecules is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a hyaluronan disaccharide, and a keratan sulfate disaccharide.

Disclosed is a polyproline backbone having the



general formula (I), wherein R is independently H or N_3, and n is 1 or more, comprising (4R)-azidoproline (Azp).

Disclosed is a glycopeptide as defined herein, wherein the glycopeptide is capable of binding a cell adhesion molecule.

According to a seventh aspect, there is provided an *in vitro* method of inhibiting a cell adhesion molecule comprising contacting a glycopeptides as defined herein with the cell adhesion molecule.

According to an eighth aspect, there is provided the use of a glycopeptide as defined herein in the manufacture of a medicament for treating cancer.

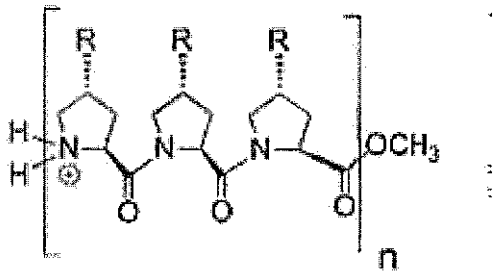
Disclosed is the use of a glycopeptide as defined herein in the manufacture of a medicament for inhibiting a cell adhesion molecule in a patient.

According to a ninth aspect, there is provided a glycopeptide, comprising a polyproline backbone and one or more carbohydrate molecules, wherein the one or more carbohydrate molecule is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a Hyaluronan disaccharide and a keratan sulfate disaccharide,

wherein the glycopeptide further comprises polyethylene glycol (PEG) at one end of the polyproline backbone, wherein the PEG is biotin-conjugated, wherein the glycopeptide has the following general formula (II):

Claims

1. A glycopeptide, comprising a polyproline backbone and one or more carbohydrate molecules, wherein the polyproline backbone has the following general formula (I):



(I)

; wherein R is independently H or N_3; wherein at least one R is N_3; n is 1 or more; the one or more carbohydrate molecules is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a hyaluronan disaccharide, and a keratan sulfate disaccharide; and wherein the one or more carbohydrate molecules is alkyne-functionalized and attached to the polyproline backbone at R by forming a 1,2,3-triazole linkage when R is N_3.

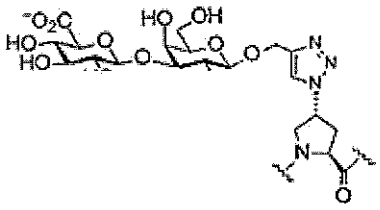
2. The glycopeptide according to claim 1, wherein n is 8 or more.

3. The glycopeptide according to any one of the preceding claims, wherein the carbohydrate molecules are attached at pre-determined positions along the polyproline backbone.

4. The glycopeptide according to claim 3, wherein the carbohydrate molecules are attached at equal distances from each other along the polyproline backbone.

5. The glycopeptide according to claim 3 or 4, wherein the carbohydrate molecules are attached along the same face of the polyproline backbone.

6. The glycopeptide according to any one of the preceding claims, wherein the polyproline backbone is rigid, or semi-flexible.



P_U is .

13. The glycopeptide according to any one of the preceding claims, further comprising a lipid.

14. A method of synthesising a glycopeptide according to any one of claims 1 to 13, comprising attaching one or more carbohydrate molecules to a polyproline backbone; wherein the one or more carbohydrate molecule is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a Hyaluronan disaccharide and a keratan sulfate disaccharide.

15. The method according to claim 14, wherein the one or more carbohydrate molecules are attached to the polyproline backbone via a click reaction.

16. The method according to claim 15, comprising conducting the click reaction in DMSO at ambient temperature for 7 days in the presence of copper(I) iodide, N,N-diisopropylethylamine (DIPEA) and tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (TBTA) under argon atmosphere.

17. The method according to claim 16, further comprising the steps of:

(i) precipitating the reaction mixture resulting from the click reaction from a THF/methanol mixture;

(ii) converting the reaction mixture into their sodium salt form; and

(iii) purifying the salt by size-exclusion chromatography.

20. The method according to any one of claims 14 to 19, comprising synthesising the polyproline backbone via solution-phase peptide synthesis.

21. The method according to claim 20, wherein the solution-phase peptide synthesis comprises the steps of:

(i) coupling the Bocprotected amino acid with amino acid methyl ester using O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate (TBTU) as the coupling reagent;

(ii) removing Boc and methyl ester protective groups of the resulting peptides prior to the next coupling reactions by treatment with a CF_3CO_2H/CH_2Cl_2 mixture and aquous NaOH, respectively;

(iii) repeating steps (i) and (ii) until the desired polyproline derivates are obtained; and

(iv) purifying the polyproline derivatives by flash column chromatography on silica or reverse phase HPLC.

22. The glycopeptide according any one of claims 1 to 13 for use in therapy.

23. Use of the glycopeptide according to any one of claims 1 to 13 in the manufacture of a medicament for treating cancer or neurodegenerative disease in a patient in need of a target-specific therapy.

24. The use of claim 23, wherein the glycopeptide binds to a target selected from the group consisting of E-selectin, L-selectin, P-selectin, nerve growth factor, and chemokine.

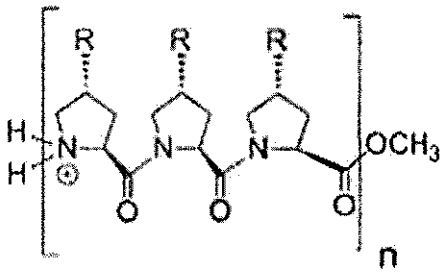
25. A target-specific therapeutic agent comprising a glycopeptide according to any one of claims 1 to 13.

26. The glycopeptide according to any one of claims 1 to 13 for use in glycosaminoglycans (GAG)-based pharmaceutics.

27. The glycopeptide according to any one of claims 1 to 13 for use as diagnostic tools.

28. An *in vitro* method of controlling the binding affinity of a glycopeptide to one or more binding molecules, comprising attaching one or more alkyne-functionalized carbohydrate molecules at pre-determined positions along an azido-functionalized polyproline backbone by forming a 1,2,3-triazole linkage; wherein the one or more carbohydrate molecules is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a hyaluronan disaccharide, and a keratan sulfate disaccharide.

29. The method according to claim 28, wherein the polyproline backbone is of the following general formula (I):



(I)

; wherein R is independently H or N_3; wherein at least one R is N_3, n is 1 or more; and wherein the one or more carbohydrate molecules are attached to the polyproline backbone at R by forming a 1,2,3-triazole linkage when R is N_3.

30. The method according to claim 29, wherein n is 8 or more.

31. The method according to any one of claims 28 to 30, comprising attaching the carbohydrate molecules at pre-determined positions along the polyproline backbone.

32. The method according to claim 31, comprising attaching the carbohydrate molecules at equal distances from each other along the polyproline backbone.

33. The method according to claim 31 or 32, wherein the carbohydrate molecules are attached along the same face of the polyproline backbone.

34. The method according to any one of claims 28 to 33, wherein the polyproline backbone is rigid, or semi-flexible.

35. An *in vitro* method of inhibiting a cell adhesion molecule comprising contacting a glycopeptide according to any one of claims 1-13 with the cell adhesion molecule.

36. The *in vitro* method of claim 35, wherein the cell adhesion molecule is selectin.

37. The *in vitro* method of claim 36, wherein the selectin is selected from the group consisting of E-selectin, L-selectin and P-selectin.

38. The *in vitro* method of claim 35, wherein the glycopeptide is selected from the group consisting of $(P_E)_{12}$, $(PP_EP_E)_6$, $(PP_E)_{12}$, $(PPP_E)_{12}$ and $(PPP_U)_{12}$.

39. Use of a glycopeptide according to any one of claims 1-13 in the manufacture of a medicament for treating cancer.

40. The use of claim 39, wherein the glycopeptide is one that binds to a selectin.

41. The use of claim 40, wherein the selectin is selected from the group consisting of E-selectin, L-selectin and P-selectin.

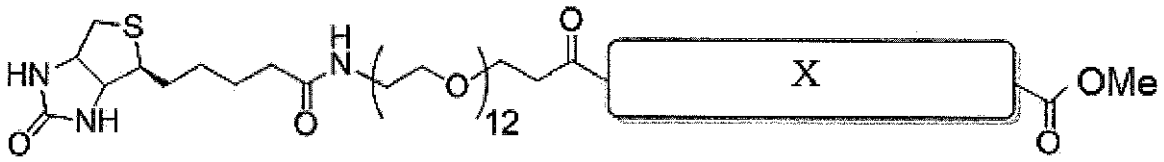
42. The use of claim 39, wherein the glycopeptide is selected from the group consisting of $(P_E)_{12}$, $(PP_EP_E)_6$, $(PP_E)_{12}$, $(PPP_E)_{12}$ and $(PPP_U)_{12}$.

43. A glycopeptide, comprising a polyproline backbone and one or more carbohydrate molecules, wherein the one or more carbohydrate molecule is selected from the group consisting of a chondroitin sulfate disaccharide, a heparin disaccharide, a heparan sulfate disaccharide, a dermatan sulfate disaccharide, a Hyaluronan disaccharide and a keratan sulfate disaccharide,

wherein the glycopeptide further comprises polyethylene glycol (PEG) at one end of the polyproline backbone,

wherein the PEG is biotin-conjugated,

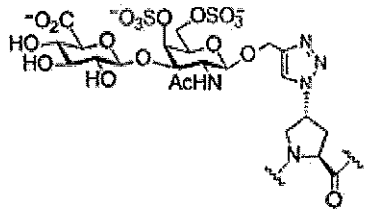
wherein the glycopeptide has the following general formula (II):



wherein X is $(P_E)_4G(P_E)_4G(P_E)_4$,

wherein P is proline;

G is glycine; and



P_E is .