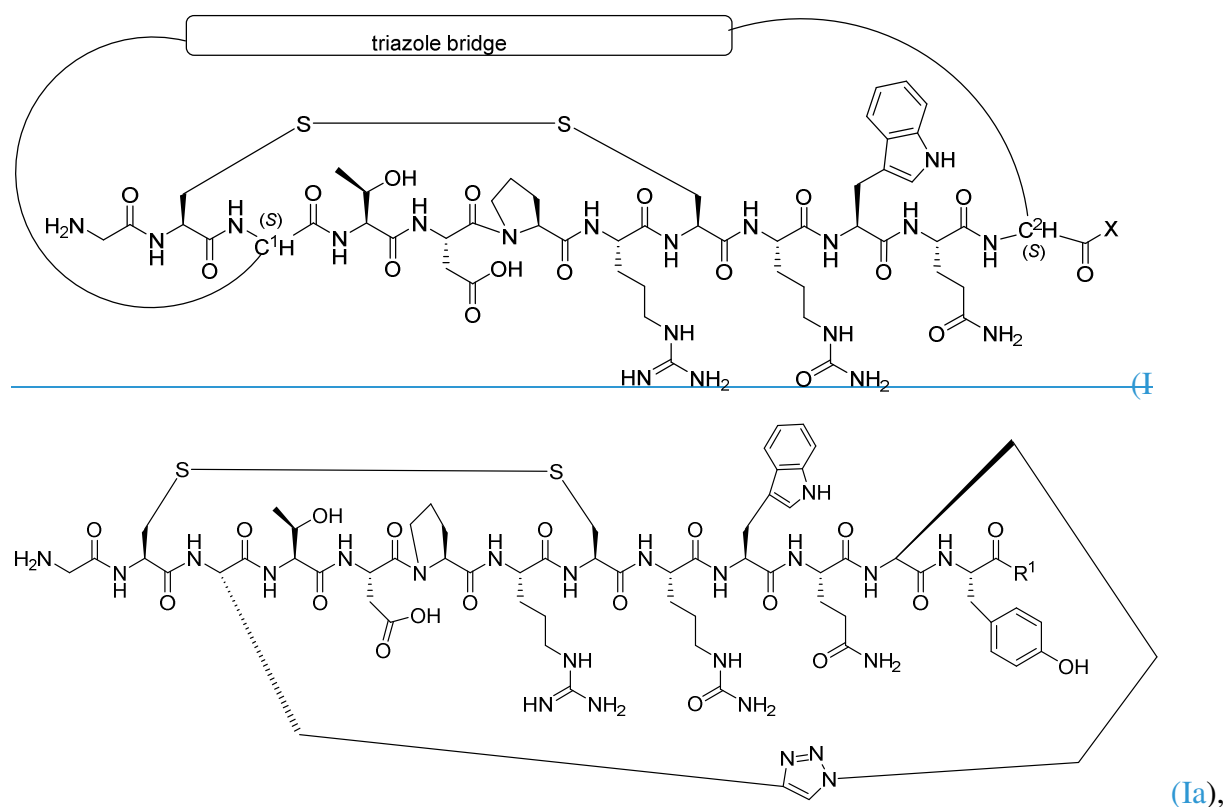


~~What is claimed is:~~

CLAIMS

1. 1. A PEGylated conotoxin peptide analog or pharmaceutically acceptable salt thereof, wherein the conotoxin peptide analog is of Formula (Ia) (SEQ ID NO:93):94)



wherein

XR^1 is X_{AA}^+ or $\text{X}_{\text{AA}}^+ \text{X}_{\text{AA}}^2$; wherein X_{AA}^+ is Tyr, Phe, Trp, or a D-isomer of Tyr, Phe, or Trp, and X_{AA}^2 is N-Me-Gly, D-Tyr, or N-Me-Tyr; OH,

wherein the C-terminus of the conotoxin peptide analog is a carboxylic acid or an amide group;

and

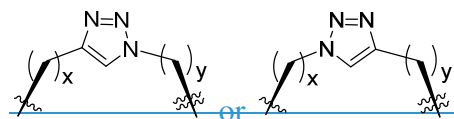
wherein the conotoxin peptide analog is covalently attached directly or via a linking group to one or more polyethylene glycol (PEG) polymers; polymer;

wherein the PEG polymer is covalently attached to the N-terminus of the conotoxin peptide analog; and

wherein the PEG polymer has a molecular weight in the range of 10 kDa to 40 kDa.

~~2. 2. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 1,~~

~~wherein the triazole bridge is~~



~~, wherein the single wavy line (~~~~~) indicates the point of attachment of the triazole bridge to the C¹ carbon of the conotoxin peptide analog, and the double wavy lines (~~~~~) indicate the point of attachment of the triazole bridge to the C² carbon of the conotoxin peptide analog; and wherein x is 1, 2, 3, or 4; and y is 2, 3 or 4.~~

~~3. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 2,~~



~~wherein the triazole bridge is~~

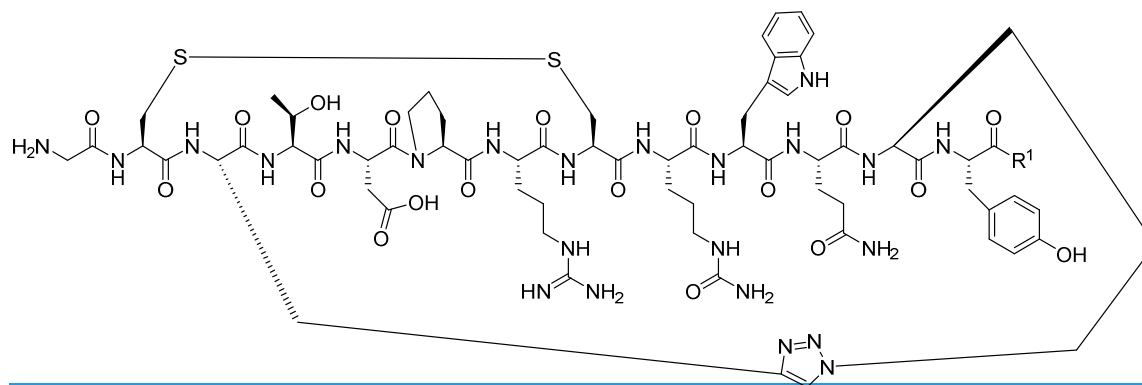
~~4. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 2,~~



~~wherein the triazole bridge is~~

~~5. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 1,~~

~~wherein the conotoxin peptide analog is of Formula (Ia) (SEQ ID NO:94)~~



~~(Ia),~~

~~wherein R¹ is OH or NH₂.~~

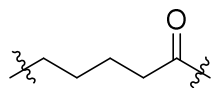
~~6. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 5, wherein R⁺ is OH.~~

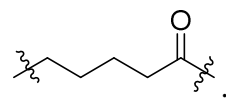
~~7. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 1-6, wherein the conotoxin peptide analog is covalently attached to one PEG polymer.~~

~~8. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 7, wherein the PEG polymer is covalently attached to the N-terminus of the conotoxin peptide analog.~~

~~9. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 7 or 8, wherein the PEG polymer is covalently attached to the conotoxin peptide analog via a linking group.~~

~~10. 3. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of~~

~~claim 92, wherein the linking group is a valerate linker having a formula of~~ 



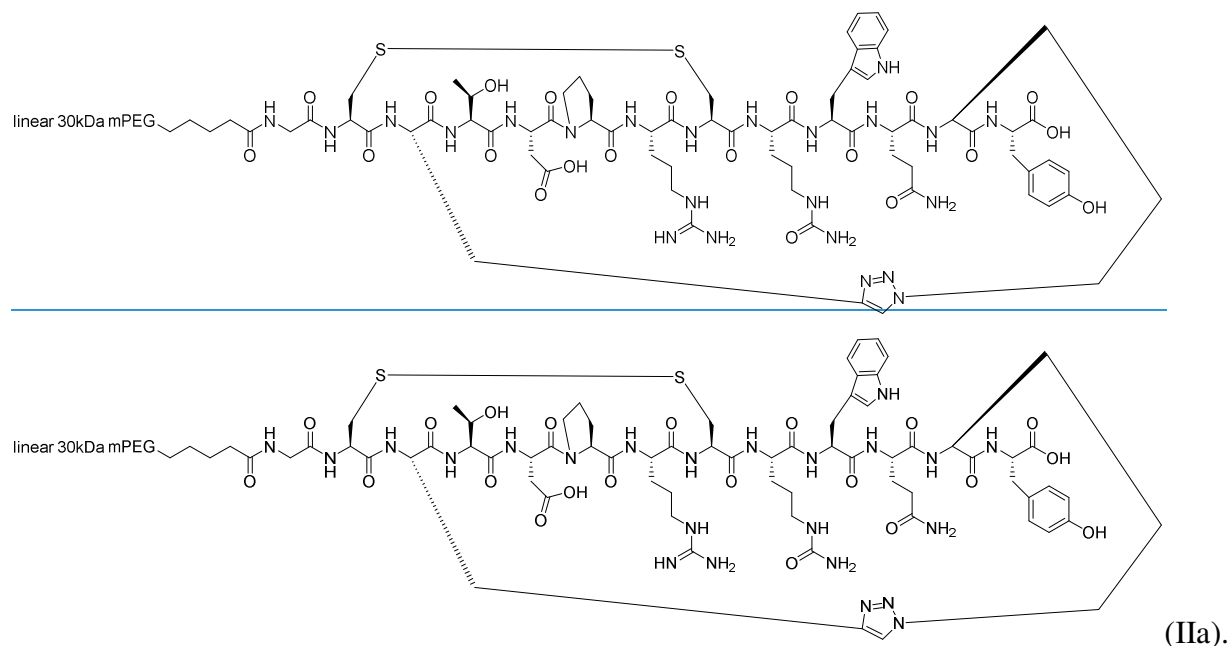
~~11. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 7-10, wherein the PEG polymer is a linear or branched PEG polymer.~~

~~12. 4. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 11, wherein the PEG polymer is a linear PEG polymer.~~

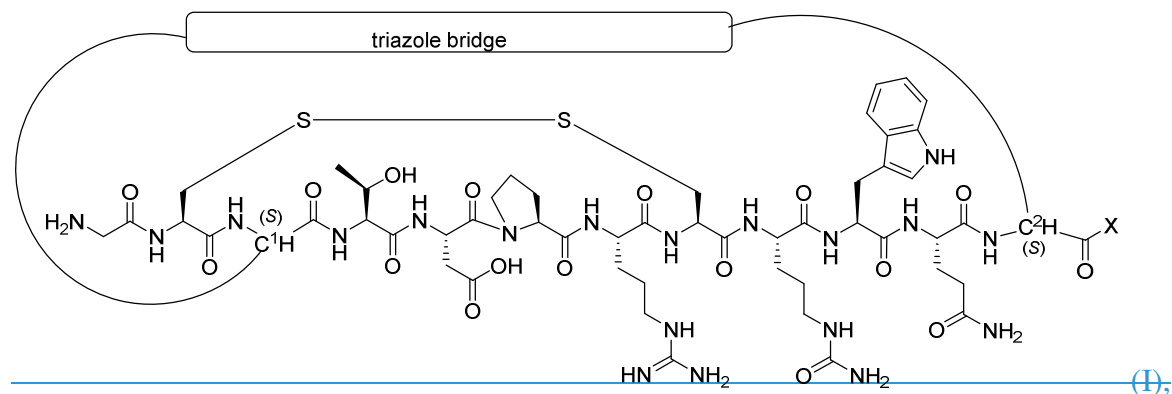
~~13. 5. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 12, wherein the PEG polymer has a molecular weight in the range of 10 kDa and 40 of 30 kDa.~~

~~14. 6. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 13, wherein the PEG polymer is a linear 30 kDa PEG polymer.~~

~~15.~~ 7. The PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 1, wherein the PEGylated conotoxin peptide analog is of Formula (IIa) (SEQ ID NO:83):



~~16-8.~~ A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of Formula (I) (SEQ ID NO:93):



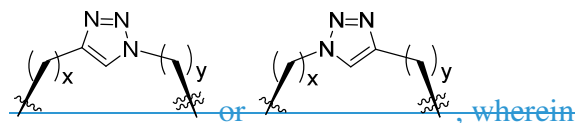
~~or~~ claim 7, and a pharmaceutically acceptable salt thereof, carrier,
wherein

X is X_{AA}^+ or X_{AA}^- ; wherein X_{AA}^+ is Tyr, Phe, Trp, or a D-isomer

9. Use of Tyr, Phe, or Trp, and X_{AA}^- is N Me Gly, D Tyr, or N Me Tyr;

wherein the C-terminus a therapeutically effective amount of the conotoxin peptide analog is a carboxylic acid or an amide group.

17. ~~The~~PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 16, ~~wherein the triazole bridge is 7 in the manufacture of a medicament for treating pain in a subject.~~



10. ~~A pharmaceutical composition comprising the single wavy line (~~~~~) indicates the point of attachment of the triazole bridge to the C¹ carbon of the conotoxin peptide analog, and the double wavy lines (~~~~~) indicate the point of attachment of the triazole bridge to the C² carbon of the conotoxin peptide analog; and wherein x is 1, 2, 3, or 4; and y is 2, 3 or 4.~~

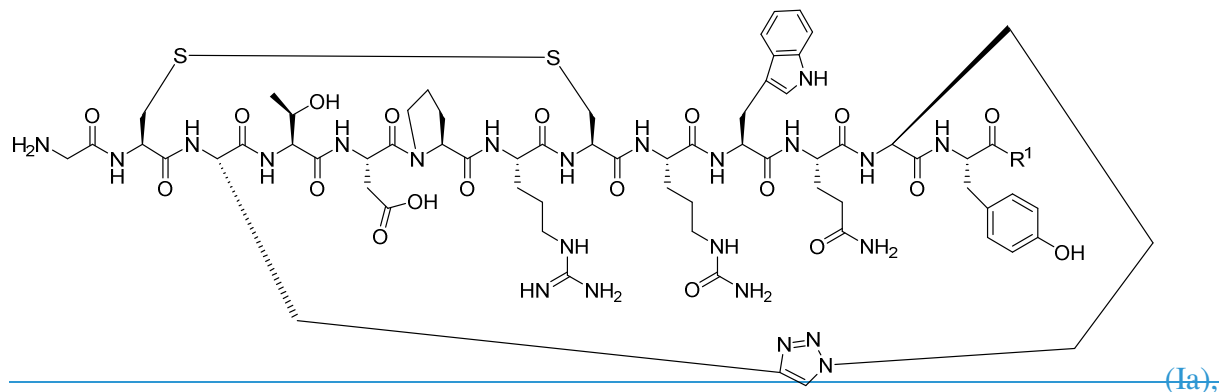
18. ~~The~~PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 17,

~~wherein the triazole bridge is~~ ~~1, and a pharmaceutically acceptable carrier.~~

19. ~~The conotoxin peptide analog or pharmaceutically acceptable salt of claim 17, wherein the~~



20. ~~The~~11. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 16, ~~wherein the conotoxin peptide analog is of Formula (Ia) (SEQ ID NO:94):~~ 1 in the manufacture of a medicament for treating pain in a subject.



~~wherein R¹ is OH or NH₂.~~

The

~~12.~~ 12. A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 2, and a pharmaceutically acceptable carrier.

~~21.~~ 13. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 20, wherein R⁺ is OH₂ in the manufacture of a medicament for treating pain in a subject.

~~14.~~ 14. A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 3, and a pharmaceutically acceptable carrier.

~~15.~~ 15. A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 4, and a pharmaceutically acceptable carrier.

~~22.~~ 16. A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 1-15, or the conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 16-21, claim 5, and a pharmaceutically acceptable carrier.

~~Use of 17.~~ 17. A pharmaceutical composition comprising the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 1-15, or the conotoxin peptide analog or claim 6, and a pharmaceutically acceptable salt of any one of claims 16-21, or the pharmaceutical composition of claim 22, carrier.

~~23.~~ 18. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 3 in the manufacture of a medicament for a method of treating or preventing pain or inflammation in a subject, the medicament is to be administered to thein a subject.

~~24. Use 19.~~ 19. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 1-15, or the conotoxin peptide analog or pharmaceutically acceptable salt of any one of claims 16-21, or the pharmaceutical composition of claim 22, 4 in the manufacture of a medicament for a method

~~of treating or preventing a condition conducive to treatment or prevention by inhibition of an $\alpha 9$ -containing nicotinic acetylcholine receptor (nAChR) in a subject, or a condition associated with activation of an $\alpha 9$ -containing nicotinic acetylcholine receptor (nAChR) in a subject, the medicament is to be administered to the subject.~~

~~25. The use of claim 24, wherein the condition conducive to treatment or prevention by inhibition of the $\alpha 9$ -containing nAChR is pain or inflammation in a subject.~~

~~26. The use of claim 25, wherein 20. Use of a therapeutically effective amount of the condition is pain.~~

~~27. The use of claim 26, wherein the pain is selected from the group consisting of general pain, chronic pain, neuropathic pain, nociceptive pain, inflammatory pain, visceral pain, somatic pain, pain induced by peripheral nerve damage, pain induced by an inflammatory disorder, pain induced by a metabolic disorder, pain induced by cancer, pain induced by chemotherapy, pain induced by a surgical procedure, and pain induced by a burn.~~

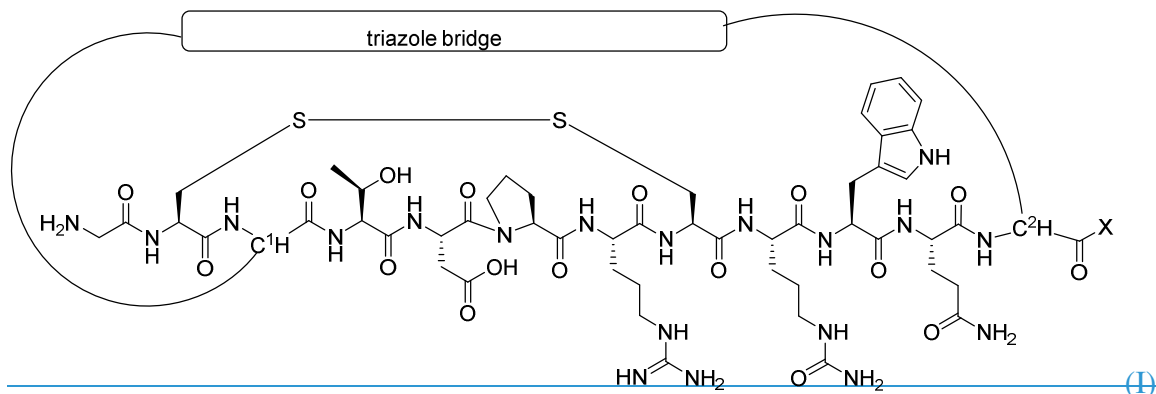
~~28. The use of claim 24, wherein the condition conducive to treatment or prevention by inhibition of the $\alpha 9$ -containing nAChR is an inflammatory condition.~~

~~29. The use of any one of claims 24-28, wherein the condition conducive to treatment or prevention by inhibition of an $\alpha 9$ -containing nicotinic acetylcholine receptor (nAChR) is a condition conducive to treatment or prevention by inhibition of the $\alpha 9\alpha 10$ -subtype of nAChR.~~

~~30. The use of any one of claims 23-29, wherein the subject is a human.~~

~~A method of making a PEGylated conotoxin peptide analog of Formula (I) (SEQ ID NO:93) or aor pharmaceutically acceptable salt of claim 5 in the manufacture of a medicament for treating pain in a subject.~~

34. 21. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt thereof, of claim 6 in the manufacture of a medicament for treating pain in a subject.



wherein

X is X_{AA}^1 or $X_{AA}^1X_{AA}^2$; wherein X_{AA}^1 is Tyr, Phe, Trp, or a D-isomer of Tyr, Phe, or Trp, and X_{AA}^2 is N-Me-Gly, D-Tyr, or N-Me-Tyr; and

wherein the C-terminus of the

22. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog of Formula (I) is a carboxylic acid or an amide group; comprising subjecting an intermediate conotoxin peptide analog or a pharmaceutically acceptable salt thereof to triazole formation conditions, wherein the amino acid sequence of the intermediate conotoxin peptide analog is Gly-Cys- X_{AA}^3 -Thr-Asp-Pro-Arg-Cys- X_{AA}^9 -Trp-Gln- X_{AA}^{12} -X (SEQ ID NO:106), of claim 1 in the manufacture of a medicament for treating inflammation in a subject.

wherein

X_{AA}^3 is selected from the group consisting

23. Use of (S)-propargyl-glycine, (S)-azidoalanine, (S)-homopropargyl-glycine, (S)-azidohomoalanine, (S)-azidonorvaline and (S)-bishomopropargyl-glycine;

X_{AA}^9 is Citrulline;

X_{AA}^{12} is selected from the group consisting a therapeutically effective amount of (S)-azidohomoalanine, (S)-homopropargyl-glycine, (S)-azidonorvaline, and (S)-bishomopropargyl-glycine;

wherein when X_{AA}^3 is selected from the group consisting of (S)-propargyl-glycine, (S)-homopropargyl-glycine, and (S)-bishomopropargyl-glycine, X_{AA}^{12} is (S)-azidohomoalanine or

~~(S)-azidonorvaline; when X_{AA}^3 is selected from the group consisting of (S)-azidoalanine, (S)-azidohomoalanine, and (S)-azidonorvaline, X_{AA}^{12} is (S)-homopropargyl-glycine or (S)-bishomopropargyl-glycine;~~

~~X is as defined above for the the PEGylated conotoxin peptide analog of Formula (I); and/or pharmaceutically acceptable salt of claim 7 in the manufacture of a medicament for treating inflammation in a subject.~~

~~wherein the C-terminus of the intermediate~~

24. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 2 in the manufacture of a medicament for treating inflammation in a subject.

25. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog or pharmaceutically acceptable salt of claim 3 in the manufacture of a medicament for treating inflammation in a subject.

26. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog is as defined above for the or pharmaceutically acceptable salt of claim 4 in the manufacture of a medicament for treating inflammation in a subject.

27. Use of a therapeutically effective amount of the PEGylated conotoxin peptide analog of Formula (I); and/or pharmaceutically acceptable salt of claim 5 in the manufacture of a medicament for treating inflammation in a subject.

~~wherein under said triazole formation conditions X_{AA}^3 reacts with X_{AA}^{12} to form the triazole bridge in the conotoxin peptide analog~~

28. Use of Formula (I).

32. A method a therapeutically effective amount of making at the PEGylated conotoxin peptide analog or a pharmaceutically acceptable salt thereof, comprising contacting under reaction conditions a conotoxin peptide analog or a salt thereof, with one or more reactive polyethylene glycol (PEG) polymers to form a PEGylated conotoxin peptide analog, wherein the reactive PEG polymers each comprise a reactive group covalently linked, optionally via a linking group, to a PEG polymer, and wherein each reactive group reacts under the reaction conditions to form a covalent bond with the conotoxin peptide analog whereby the conotoxin

peptide analog is covalently attached directly or via a linking group to the one or more PEG polymers;

wherein the amino acid sequence of the conotoxin peptide analog is Gly-Cys- X_{AA}^3 -Thr-Asp-Pro-Arg-Cys- X_{AA}^9 -Trp-Gln- X_{AA}^{12} -X (SEQ ID NO:106);

wherein

X_{AA}^3 is selected from the group consisting of (S)-propargyl-glycine, (S)-azidoalanine, (S)-homopropargyl-glycine, (S)-azidohomoalanine, (S)-azidonorvaline and (S)-bishomopropargyl-glycine;

X_{AA}^9 is Citrulline;

X_{AA}^{12} is selected from the group consisting of (S)-azidohomoalanine, (S)-homopropargyl-glycine, (S)-azidonorvaline, and (S)-bishomopropargyl-glycine;

wherein when X_{AA}^3 is selected from the group consisting of (S)-propargyl-glycine, (S)-homopropargyl-glycine, and (S)-bishomopropargyl-glycine, X_{AA}^{12} is (S)-azidohomoalanine or (S)-azidonorvaline; when X_{AA}^3 is selected from the group consisting of (S)-azidoalanine, (S)-azidohomoalanine, and (S)-azidonorvaline, X_{AA}^{12} is (S)-homopropargyl-glycine or (S)-bishomopropargyl-glycine;

X is X_{AA}^1 or $X_{AA}^1X_{AA}^2$; wherein X_{AA}^1 is Tyr, Phe, Trp, or a D-isomer of Tyr, Phe, or Trp, and X_{AA}^2 is N-Me-Gly, D-Tyr, or N-Me-Tyr; and

wherein the C-terminus of the conotoxin peptide analog is a carboxylic acid or an amide group.

a medicament for treating inflammation in a subject.