T lymphocytes, where they mediate cell adhesion via binding to their respective primary ligands, vascular cell adhesion molecule (VCAM), and mucosal addressin cell adhesion molecule (MAdCAM), respectively. The proteins differ in binding specificity in that VCAM binds both α4β1 and to a lesser extent α4β7, while MAdCAM is highly specific for α4β7. In addition to pairing with the α4 subunit, the β7 subunit also forms a heterodimeric complex with αE subunit to form αEβ7, which is primarily expressed on intraepithelial lymphocytes (IEL) in the intestine, lung and genitourinary tract. αEβ7 is also expressed on dendritic cells in the gut. The αEβ7 heterodimer binds to E-cadherin on the epithelial cells. The IEL cells are thought to provide a mechanism for immune surveillance within the epithelial compartment. Therefore, blocking αEβ7 and α4β7 together may be a useful method for treating inflammatory conditions of the intestine.

[0006] Inhibitors of specific integrins-ligand interactions have been shown effective as anti-inflammatory agents for the treatment of various autoimmune diseases. For example, monoclonal antibodies displaying high binding affinity for α4β7 have displayed therapeutic benefits for gastrointestinal auto-inflammatory/autoimmune diseases, such as Crohn's disease, and ulcerative colitis (*Id*). However, these therapies interfered with α4β1 integrin-ligand interactions thereby resulting in dangerous side effects to the patient. Therapies utilizing small molecule antagonists have shown similar side effects in animal models, thereby preventing further development of these techniques.

[0007] Accordingly, there is a need in the art for integrin antagonist molecules having high affinity for the α4β7 integrin and high selectivity against the α4β1 integrin, as a therapy for various gastrointestinal autoimmune diseases.

[0008] Such integrin antagonist molecules are disclosed herein.

SUMMARY OF THE INVENTION

[0009] The present invention disclosure has been developed in response to the present state of the art, and in particular, in response to the problems and needs in the art that have not yet been fully solved by currently available integrin antagonists that are selective for α4β7. Thus, in certain examples, the present disclosure provides α4β7 antagonist thioether peptide monomers and dimers for use as anti-inflammatory and/or immunosuppressive agents. Further, the present disclosure provides α4β7 antagonist thioether peptides (e.g. monomers and dimers for use in treating a condition that is associated with a biological function of α4β7 or on cells or tissues expressing MAdCAM.

[0010] Aspects of the disclosure relate to a novel class of cyclized, thioether peptidic compounds exhibiting integrin antagonist activity, namely, exhibiting high specificity for α4β7 integrin. In certain examples, each peptide of the present disclosure comprises a downstream natural or unnatural amino acid and an upstream modified amino acid or aromatic group that are capable of bridging to form a cyclized structure through a thioether bond. Peptides of the present disclosure demonstrate increased stability when administered orally as a therapeutic agent. The peptides of the present disclosure further provide increased specificity and potency as compared to analogs that are cyclized through a bond other than a thioether bond, e.g., a disulfide bond.

[0011] In certain examples, cyclized, thioether peptidic compounds exhibiting integrin antagoinist activity are monomer peptides. In particular examples, the compounds of the present disclosure comprise dimerized peptides, each subunit of the dimer forming a cyclized structure through a thioether bond. The thioether cyclization feature provides the peptides of the present disclosure increased stability, specificity, and potency as compared to analogs that are cyclized through a bond other than a thioether bond, e.g., a disulfide bond. In some examples, dimerization of thioether peptide monomers further provides for increased specificity and potency as compared monomer anaologs.

[0011A] Disclosed is a peptide molecule comprising a structure of Formula (V): Xaa^1-Xaa^2-Xaa^3-Xaa^4-Xaa^5-Xaa^6-Xaa^7-Xaa^8-Xaa^9-Xaa^{10}-Xaa^{11}-Xaa^{12}-Xaa^{13}-Xaa^{14} (Formula (V)) or a pharmaceutically acceptable salt thereof, wherein the peptide comprises a thioether bond between Xaa^4 and Xaa^{10}, and wherein:

Xaa^1 is absent, or Xaa^1 is any amino acid; Xaa^2 is absent, or Xaa^2 is any amino acid; Xaa^3 is absent, or Xaa^3 is any amino acid; Xaa^4 is an amino acid, aliphatic acid, alicyclic acid, or modified 2-methyl aromatic acid having a side chain with one or two carbons, and capable of forming a thioether bond with Xaa^{10}; Xaa^5 is selected from the group consisting of N(alpha)-Me-Arg, Arg, HomoArg, Dap, Dab, Arg-Me-sym, Arg-Me-asym, 4-Guan, Cit,

Phe(4CF3), Bpa, Phe(3-Me), Phe(2-Me), Phe(2-CF3), □-Me-Phe, and corresponding D-amino acids and suitable isostere replacements;

Xaa^{12} is absent or selected from the group consisting of aromatic amino acids, substituted aromatic amino acids, Glu, D-Glu, HomoGlu, Beta-Homo-Glu, Asp, D-HomoGlu, Amide, Lys, COOH, $CONH_2$, Gln, Pro, Gly, His, Ala, Ile, Phe, Arg, Leu, Val, Tyr, Trp, Met, Gla, Ser, Asn, D-Glu, β-HGlu, 2-Nal, 1-Nal, D-Asp, Bip, β-HPhe, β-Glu, D-Tyr, D-Phe, D-Lys, Dap, Dab, Orn, D-Orn, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me Lys, D-Dap, D-Dab, D-His, F(4-COOH), Tic, D-Trp, D-Leu, D-Arg, D-Thr, N-Me-Glu, N-Me-Asp, alpha-H-Glu, isosteres, and corresponding D-amino acids;

Xaa^{13} is absent or any amino acid; and Xaa^{14} is absent or any amino acid;

wherein if the peptide molecule is a peptide dimer or subunit thereof, then Xaa^{14} is absent or selected from the group consisting of: any amino acid with an amine side chain, Lys, D-Lys, N-Me-Lys, D-N-Me-Lys, Orn, N-Me-Orn, Dab, N-Me-Dab, Dap, N-Me-Dap, Homo-Lys, D-Dap, D-Dab, D-Orn, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Cys, HomoCys, COOH, $CONH_2$, suitable isosteres, corresponding D-amino acids, and corresponding N-Methyl amino acids.

[0011A1] In one aspect, there is provided a peptide molecule comprising a structure of Formula (I-1):

$$Xaa^{1}\text{-}Xaa^{2}\text{-}Xaa^{3}\text{-}Xaa^{4}\text{-}Xaa^{5}\text{-}Xaa^{6}\text{-}Xaa^{7}\text{-}Xaa^{8}\text{-}Xaa^{9}\text{-}Xaa^{10}\text{-}Xaa^{11}\text{-}Xaa^{12}\text{-}Xaa^{13}\text{-}Xaa^{14}$$

(Formula (I-1))

or a pharmaceutically acceptable salt thereof, wherein the peptide comprises a thioether bond between Xaa^{4} and Xaa^{10}, and wherein:

Xaa^{1} is absent, or Xaa^{1} is any amino acid;

Xaa^{2} is absent, or Xaa^{2} is any amino acid;

Xaa^{3} is absent, or Xaa^{3} is any amino acid;

Xaa^{4} is 2-methylbenzoyl;

Xaa^5 is N-Me-Arg;

Xaa^6 is Ser;

Xaa^7 is Asp;

Xaa^8 is Thr;

Xaa^9 is Leu or Nle;

Xaa^{10} is Pen;

Xaa^{11} is absent or is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Phe (2-carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro-Trp, Ile, Leu, Ser, Arg, Thr, Sar, Ser, aromatic amino acids , substituted aromatic amino acids, Gly, Gln, Asn, Asp, Ala, Ile, Leu, Val, Met, Thr, Lys, Trp, Tyr, His, Glu, Ser, Arg, Pro, Phe, Sar, HPhe, D-Phe, D-Tyr, O-Me-Tyr, Dap, Dab, Dab(Ac), Orn, D-Orn, N-Me-Orn, N-Me-Dap, D-Dap, D-Dab, Bip, Ala(3,3diphenyl), Biphenyl-Ala, aromatic ring substituted Phe, aromatic ring substituted Trp, aromatic ring substituted His, hetero aromatic amino acids, N-Me-Lys, N-Me-Lys(Ac), 4-Me-Phe, Phe(4tBu), Phe(4-OMe), Phe(4-COOH), Phe(2-carbomyl), Phe(3-carbomyl), Phe(CF_3), Phe(2,4-diCl), Phe(3,4-diCl), Aic, N-Me-Tyr, N-Me-Phe, Tic, Phe(4-CF_3), and corresponding D-amino acids;

Xaa^{12} is absent or selected from the group consisting of aromatic amino acids, substituted aromatic amino acids, Glu, D-Glu, HomoGlu, Beta-Homo-Glu, Asp, D-HomoGlu, Amide, Lys, COOH, $CONH_2$, Gln, Pro, Gly, His, Ala, Ile, Phe, Arg, Leu, Val, Tyr, Trp, Met, Gla, Ser, Asn, D-Glu, β-HGlu, 2-Nal, 1-Nal, D-Asp, Bip, β-HPhe, β-Glu, D-Tyr, D-Phe, D-Lys, Dap, Dab, Orn, D-Orn, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me Lys, D-Dap, D-Dab, D-His, F(4-COOH), Tic, D-Trp, D-Leu, D-Arg, D-Thr, and corresponding D-amino acids;

Xaa^{13} is absent or any amino acid; and

Xaa^{14} is absent or any amino acid;

wherein if the peptide molecule is a peptide dimer or subunit thereof, then Xaa^{14} is absent or selected from the group consisting of: any amino acid with an amine side chain, Lys, D-Lys, N-Me-Lys, D-N-Me-Lys, Orn, N-Me-Orn, Dab, N-Me-Dab, Dap, N-Me-Dap, Homo-Lys, D-Dap, D-Dab, D-Orn, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Cys, HomoCys, COOH, $CONH_2$, corresponding D-amino acids, and corresponding N-Methyl amino acids.

[0011B] Also disclosed is a peptide molecule or pharmaceutically acceptable salt thereof comprising a structure of Formula (VI):

Xaa^1-Xaa^2-Xaa^3-Xaa^4-Xaa^5-Xaa^6-Xaa^7-Xaa^8-Xaa^9-Xaa^{10}-Xaa^{11}

(Formula VI)

or a pharmaceutically acceptable salt thereof, wherein

Xaa^1 is a 2-Me-benzoyl group capable of forming a thioether bond with Xaa^7;

Xaa^2 is selected from the group consisting of N(alpha)-Me-Arg, Arg, HArg, Dap, Dab, Arg-Me-sym, Arg-Me-asym, 4-Guan, Cit, Cav, and suitable isostere replacements;

Xaa^3 is selected from the group consisting of Ser, Gly, and suitable isostere replacements;

Xaa^{11} is selected from the group consisting of absent, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Dap, Dab, Orn, D-Orn, D-Lys, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me-Lys, D-Dap, D-Dab, COOH, $CONH_2$, suitable isosteres, and corresponding D-amino acids, wherein the peptide further comprises a thioether bond between Xaa^1 and Xaa^7, wherein the peptide further comprises a thioether bond between Xaa^1 and Xaa^7.

[0011B1] In another aspect, the present invention provides a peptide molecule or pharmaceutically acceptable salt thereof comprising a structure of Formula (VI):

$$Xaa^1\text{-}Xaa^2\text{-}Xaa^3\text{-}Xaa^4\text{-}Xaa^5\text{-}Xaa^6\text{-}Xaa^7\text{-}Xaa^8\text{-}Xaa^9\text{-}Xaa^{10}\text{-}Xaa^{11}$$

(Formula VI)

or a pharmaceutically acceptable salt thereof, wherein

Xaa^1 is 2-methyl benzoyl;

Xaa^2 is N-Me-Arg;

Xaa^3 is Ser;

Xaa^4 is Asp;

Xaa^5 is Thr;

Xaa^6 is Leu;

Xaa^7 is Pen;

Xaa^8 is selected from the group consisting of absent, Gly, Gln, Asn, Asp, Ala, Ile, Leu, Val, Met, Thr, Lys, Trp, Tyr, His, Glu, Ser, Arg, Pro, Phe, Sar, 1-Nal, 2-Nal, HPhe, Phe(4-F), O-Me-Tyr, dihydro-Trp, Dap, Dab, Dab(Ac), Orn, D-Orn, N-Me-Orn, N-Me-Dap, D-Dap, D-Dab, Bip, Ala(3,3diphenyl), Biphenyl-Ala, aromatic ring substituted Phe, aromatic ring substituted Trp, aromatic ring substituted His, hetero aromatic amino acids, N-Me-Lys, N-Me-Lys(Ac), and corresponding D-amino acids;

Xaa^9 is selected from the group consisting of absent, Glu, Amide, Lys, COOH, $CONH_2$, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Gla, Ser, Asn, D-Glu, β-HGlu,

2-Nal, 1-Nal, D-Asp, Bip, β-HPhe, β-Glu, D-Tyr, D-Lys, Dap, Dab, Orn, D-Orn, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me Lys, D-Dap, D-Dab, and corresponding D-amino acids;

Xaa^{10} is selected from the group consisting of absent, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Dap, Dab, Orn, D-Orn, D-Lys, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me-Lys, D-Dap, D-Dab, COOH, $CONH_2$, and corresponding D-amino acids; and

Xaa^{11} is selected from the group consisting of absent, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Dap, Dab, Orn, D-Orn, D-Lys, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me-Lys, D-Dap, D-Dab, COOH, $CONH_2$, and corresponding D-amino acids, wherein the peptide further comprises a thioether bond between Xaa^1 and Xaa^7

[0011B2] In yet another aspect, the present invention provides a peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence shown in Table 4.

[0011B3] In yet another aspect, the present invention provides a peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence selected from the following:

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-(β-homoGlu)-(D-Lys) (SEQ ID NO: 61);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-(Phe-(4-COOH)-(β-homoGlu)-(D-Lys) (SEQ ID NO: 275);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-Lys) (SEQ ID NO: 62);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(D-Lys) (SEQ ID NO: 70);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(D-Lys) (SEQ ID NO: 282);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-Glu-(N-Me-Lys) (SEQ ID NO: 293);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys) (SEQ ID NO: 270);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 287);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 295);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 299);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-D-Lys) (SEQ ID NO: 62); or

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu) (SEQ ID NO: 134),

wherein the peptide molecule comprises a thioether bond between the 2-methylbenzoyl and the Pen.

[0011B4] In yet another aspect, the present invention provides a peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule is a dimer comprising a sequence or structure shown in Table 5.

[0011B5] In yet another aspect, the present invention provides a peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence or structure selected from the following:

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 151);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-(Phe-(4-COOH)-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 356);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 153);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 161);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 322);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-Glu-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 236);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 222);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys)-OH)$_2$ (SEQ ID NO: 223);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 366);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 338);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 325); or

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-D-Lys)-NH_2)$_2$ (SEQ ID NO: 152),

wherein the two peptide monomers are linked by DIG and comprise a thioether bond between the 2-methylbenzoyl and Pen.

[0011C] In yet another aspect, there is provided a pharmaceutical composition comprising a peptide molecule or pharmaceutically acceptable salt thereof as described herein and a pharmaceutically acceptable carrier, diluent or excipient.

[0011D] Also disclosed is use of an effective amount of the peptide molecule as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease or condition that is associated with a biological function of integrin α4β7.

[0011D1] In yet another aspect, the present invention provides use of an effective amount of the peptide molecule of any one of claims 1-18 or the pharmaceutical composition of any one of claims 19-21 in the manufacture of a medicament for treating or preventing a disease or condition selected from the group consisting of Inflammatory Bowel Disease (IBD), adult IBD, pediatric IBD, adolescent IBD, ulcerative colitis, Crohn's disease, Celiac disease (*nontropical Sprue)*, enteropathy associated with seronegative arthropathies, microscopic colitis, collagenous colitis, eosinophilic gastroenteritis, radiotherapy, chemotherapy, pouchitis resulting after proctocolectomy and ileoanal anastomosis, gastrointestinal cancer, pancreatitis, insulin-dependent diabetes mellitus, mastitis, cholecystitis, cholangitis, pericholangitis, chronic bronchitis, chronic sinusitis, asthma, primary sclerosing cholangitis, human immunodeficiency virus (HIV) infection in the GI tract, eosinophilic asthma, eosinophilic esophagitis, gastritis, colitis, microscopic colitis and graft versus host disease (GVDH).

[0012] In one example, the disclosure provides a peptide molecule comprising a structure of Formula (V):

Xaa^{1}-Xaa^{2}-Xaa^{3}-Xaa^{4}-Xaa^{5}-Xaa^{6}-Xaa^{7}-Xaa^{8}-Xaa^{9}-Xaa^{10}-Xaa^{11}-Xaa^{12}-Xaa^{13}-Xaa^{14}

(Formula (V) (SEQ ID NO: 49)

[0013] or a pharmaceutically acceptable salt thereof, wherein the peptide comprises a thioether bond between Xaa^{4} and Xaa^{10}, and wherein:

[0014] Xaa^{1} is absent, or Xaa^{1} is any amino acid;

[0015] Xaa^{2} is absent, or Xaa^{2} is any amino acid;

[0016] Xaa^{3} is absent, or Xaa^{3} is any amino acid;

[0017] Xaa^4 is an amino acid, aliphatic acid, alicyclic acid, or modified 2-methyl aromatic acid having a side chain with one or two carbons, and capable of forming a thioether bond with Xaa^{10};

[0018] Xaa^5 is selected from the group consisting of N(alpha)-Me-Arg, Arg, HomoArg, Dap, Dab, Arg-Me-sym, Arg-Me-asym, 4-Guan, Cit, Cav, N-Me-Lys, Phe(4-quanidino), Phe(4-carbamoyl amino), Phe(4-NH_2), N-Me-HomoArg, Tyr, His, and suitable isostere replacements;

CLAIMS

1. A peptide molecule comprising a structure of Formula (I-1):

Xaa^1-Xaa^2-Xaa^3-Xaa^4-Xaa^5-Xaa^6-Xaa^7-Xaa^8-Xaa^9-Xaa^{10}-Xaa^{11}-Xaa^{12}-Xaa^{13}-Xaa^{14}

(Formula (I-1))

or a pharmaceutically acceptable salt thereof, wherein the peptide comprises a thioether bond between Xaa^4 and Xaa^{10}, and wherein:

Xaa^1 is absent, or Xaa^1 is any amino acid;

Xaa^2 is absent, or Xaa^2 is any amino acid;

Xaa^3 is absent, or Xaa^3 is any amino acid;

Xaa^4 is 2-methylbenzoyl;

Xaa^5 is N-Me-Arg;

Xaa^6 is Ser;

Xaa^7 is Asp;

Xaa^8 is Thr;

Xaa^9 is Leu or Nle;

Xaa^{10} is Pen;

Xaa^{11} is absent or is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Phe (2-carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro-Trp, Ile, Leu, Ser, Arg, Thr, Sar, Ser, aromatic amino acids , substituted aromatic amino acids, Gly, Gln, Asn, Asp, Ala, Ile, Leu, Val, Met, Thr, Lys, Trp, Tyr, His, Glu, Ser, Arg, Pro, Phe, Sar, HPhe, D-Phe, D-Tyr, O-Me-Tyr, Dap, Dab, Dab(Ac), Orn, D-Orn, N-Me-Orn, N-Me-Dap, D-Dap, D-Dab, Bip, Ala(3,3diphenyl), Biphenyl-Ala, aromatic ring substituted Phe, aromatic ring substituted Trp, aromatic ring substituted His, hetero aromatic amino acids, N-Me-Lys, N-Me-Lys(Ac), 4-Me-Phe, Phe(4tBu), Phe(4-OMe), Phe(4-COOH), Phe(2-carbomyl), Phe(3-carbomyl), Phe(CF_3), Phe(2,4-diCl), Phe(3,4-diCl), Aic, N-Me-Tyr, N-Me-Phe, Tic, Phe(4-CF_3), and corresponding D-amino acids;

Xaa^{12} is absent or selected from the group consisting of aromatic amino acids, substituted aromatic amino acids, Glu, D-Glu, HomoGlu, Beta-Homo-Glu, Asp, D-HomoGlu, Amide, Lys,

COOH, $CONH_2$, Gln, Pro, Gly, His, Ala, Ile, Phe, Arg, Leu, Val, Tyr, Trp, Met, Gla, Ser, Asn, D-Glu, β-HGlu, 2-Nal, 1-Nal, D-Asp, Bip, β-HPhe, β-Glu, D-Tyr, D-Phe, D-Lys, Dap, Dab, Orn, D-Orn, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me Lys, D-Dap, D-Dab, D-His, F(4-COOH), Tic, D-Trp, D-Leu, D-Arg, D-Thr, and corresponding D-amino acids;

Xaa^{13} is absent or any amino acid; and

Xaa^{14} is absent or any amino acid;

wherein if the peptide molecule is a peptide dimer or subunit thereof, then Xaa^{14} is absent or selected from the group consisting of: any amino acid with an amine side chain, Lys, D-Lys, N-Me-Lys, D-N-Me-Lys, Orn, N-Me-Orn, Dab, N-Me-Dab, Dap, N-Me-Dap, Homo-Lys, D-Dap, D-Dab, D-Orn, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Cys, HomoCys, COOH, $CONH_2$, corresponding D-amino acids, and corresponding N-Methyl amino acids.

2. The peptide molecule or pharmaceutically acceptable salt thereof of claim 1, wherein(a) Xaa^{11} is absent or selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Phe (2-carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro Trp, Ile, Leu, Arg, and Thr;

Xaa^{12} is absent or selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, homoGlu, Asp, D-Asp, D-homoGlu, D-Asp, Gla, beta-homo-Glu, and corresponding D-amino acids; and

Xaa^{14} is any amino acid;

(b) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro Trp, Ile, Leu, Ser, Arg, Thr, Sar, any substituted aromatic amino acid, and corresponding D-amino acids;

Xaa^{12} is selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, homoGlu, Asp, D-Asp, D-homoGlu, Gla, beta-homo-Glu, and corresponding D-amino acids;

Xaa^{13} is absent; and

Xaa^{14} is any amino acid;

(c) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Sar, Dihydro Trp, Ile, Leu, Ser, Arg, Thr, and Sar;

Xaa^{12} is selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, homoGlu, Asp, D-Asp, D-homoGlu, Gla, beta-homo-Glu, and corresponding D-amino acids; and

Xaa^{14} is any amino acid;

(d) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro Trp, Ile, Leu, Ser, Arg, Thr, and Sar;

Xaa^{12} is absent or selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, homoGlu, Asp, D-Asp, D-homoGlu, Gla, beta-homo-Glu, and corresponding D-amino acids;

Xaa^{13} is absent; and

Xaa^{14} is any amino acid;

(e) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro Trp, Ile, Leu, Ser, Arg, Thr, and Sar;

Xaa^{12} is absent or selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, and beta-homo-Glu;

Xaa^{13} is absent; and,

Xaa^{14} is any amino acid;

(f) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3), Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), HomoPhe, N-Me-Phe, N-Me-Tyr, Ser, Sar, Dihydro Trp, Ile, Leu, Ser, Arg, Thr, and Sar;

Xaa^{12} is selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, beta-homo-Glu, and corresponding D-amino acid;

Xaa^{13} is absent; and

Xaa^{14} is any amino acid; or

(g) Xaa^{11} is selected from the group consisting of: Trp, Phe, 2-Nal, 1-Nal, Tyr, His, Phe(4-F), Phe(4-CF_3), Phe (4-CH_3). Phe (4-tBu), Bip, Phe(4-COOH), Gly, 3,3-DiPhenylGly, 3,3 diPhenyl Ala, Tic, b-homo-Trp, D-1-Nal, D-2-Nal, Phe(2,4-diCl), Phe(3,4-diCl), Phe(4-carbomyl), Phe(3-Carbomyl), Tyr(Me), and HomoPhe;

Xaa^{12} is selected from the group consisting of: any aromatic amino acid, Glu, D-Glu, and beta-homo-Glu;

Xaa^{13} is absent; and

Xaa^{14} is any amino acid.

3. The peptide molecule or pharmaceutically acceptable salt thereof of claim 1 or 2, wherein Xaa^{1}, Xaa^{2} and Xaa^{3} are absent.

4. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein Xaa^{14} is selected from the group consisting of: Lys, D-Lys, N-Me-Lys, D-N-Me-Lys, Orn, Dab, Dap, Homo-Lys, D-Dap, D-Dab, Cys, HomoCys, Pen, or D-Orn, optionally Xaa^{14} is selected from the group consisting of: D-Lys, N-Me-Lys, and D-N-Me-Lys.

5. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-4, comprising N(alpha)methylation of at least one position selected from the group consisting of Xaa^{3}, Xaa^{5}, Xaa^{7}-Xaa^{9}, and Xaa^{11}-Xaa^{13}.

6. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-5, comprising acylation for at least one position selected from the group consisting of Xaa^1-Xaa^3 and Xaa^{11}-Xaa^{14}.

7. A peptide molecule or pharmaceutically acceptable salt thereof comprising a structure of Formula (VI):

$$Xaa^1\text{-}Xaa^2\text{-}Xaa^3\text{-}Xaa^4\text{-}Xaa^5\text{-}Xaa^6\text{-}Xaa^7\text{-}Xaa^8\text{-}Xaa^9\text{-}Xaa^{10}\text{-}Xaa^{11}$$

(Formula VI)

or a pharmaceutically acceptable salt thereof, wherein

Xaa^1 is 2-methyl benzoyl;

Xaa^2 is N-Me-Arg;

Xaa^3 is Ser;

Xaa^4 is Asp;

Xaa^5 is Thr;

Xaa^6 is Leu;

Xaa^7 is Pen;

Xaa^8 is selected from the group consisting of absent, Gly, Gln, Asn, Asp, Ala, Ile, Leu, Val, Met, Thr, Lys, Trp, Tyr, His, Glu, Ser, Arg, Pro, Phe, Sar, 1-Nal, 2-Nal, HPhe, Phe(4-F), O-Me-Tyr, dihydro-Trp, Dap, Dab, Dab(Ac), Orn, D-Orn, N-Me-Orn, N-Me-Dap, D-Dap, D-Dab, Bip, Ala(3,3diphenyl), Biphenyl-Ala, aromatic ring substituted Phe, aromatic ring substituted Trp, aromatic ring substituted His, hetero aromatic amino acids, N-Me-Lys, N-Me-Lys(Ac), and corresponding D-amino acids;

Xaa^9 is selected from the group consisting of absent, Glu, Amide, Lys, COOH, $CONH_2$, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Gla, Ser, Asn, D-Glu, β-HGlu, 2-Nal, 1-Nal, D-Asp, Bip, β-HPhe, β-Glu, D-Tyr, D-Lys, Dap, Dab, Orn, D-Orn, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me Lys, D-Dap, D-Dab, and corresponding D-amino acids;

Xaa^{10} is selected from the group consisting of absent, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Dap, Dab, Orn, D-Orn, D-Lys, N-Me-Orn, N-Me-

Dap, N-Me-Dab, N-Me-Lys, D-Dap, D-Dab, COOH, $CONH_2$, and corresponding D-amino acids; and

Xaa^{11} is selected from the group consisting of absent, Gln, Pro, Gly, His, Ala, Ile, Phe, Lys, Arg, Leu, Val, Tyr, Trp, Met, Glu, Ser, Asn, Gla, Dap, Dab, Orn, D-Orn, D-Lys, N-Me-Orn, N-Me-Dap, N-Me-Dab, N-Me-Lys, D-Dap, D-Dab, COOH, $CONH_2$, and corresponding D-amino acids, wherein the peptide further comprises a thioether bond between Xaa^1 and Xaa^7.

8. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-7, further comprising a terminal modifying group selected from the group consisting of DIG, PEG4, PEG13, PEG25, PEG1K, PEG2K, PEG4K, PEG5K, Polyethylene glycol having molecular weight from 400Da to 40,000Da, IDA, Ac-IDA, ADA, Glutaric acid, Isophthalic acid, 1,3-phenylenediacetic acid, 1,4-phenylenediacetic acid, 1,2-phenylenediacetic acid, AADA, suitable aliphatic acids, suitable aromatic acids, and heteroaromatic acids.

9. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-8, wherein the C-terminus of the peptide molecule further comprises a modifying group.

10. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-9, wherein the peptide molecule is a monomer.

11. The peptide molecule or pharmaceutically acceptable salt thereof of any one of claims 1-9, wherein the peptide molecule is a dimer, optionally comprising two peptide molecules dimerized by a linker, optionally wherein the linker is selected from the group consisting of: DIG, PEG4, PEG4-biotin, PEG13, PEG25, PEG1K, PEG2K, PEG3.4K, PEG4K, PEG5K, IDA, ADA, Boc-IDA, Glutaric acid, Isophthalic acid, 1,3-phenylenediacetic acid, 1,4-phenylenediacetic acid, 1,2-phenylenediacetic acid, Triazine, Boc-Triazine, IDA-biotin, PEG4-Biotin, AADA, suitable aliphatics, aromatics, heteroaromatics, and polyethylene glycol based linkers having a molecular weight from approximately 400Da to approximately 40,000Da.

12. The peptide molecule or pharmaceutically acceptable salt thereof of claim 11, wherein the two peptide molecules are dimerized via their C-termini.

13. A peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence shown in Table 4.

14. A peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence selected from the following:

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-(β-homoGlu)-(D-Lys) (SEQ ID NO: 61);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-(Phe-(4-COOH)-(β-homoGlu)-(D-Lys) (SEQ ID NO: 275);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-Lys) (SEQ ID NO: 62);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(D-Lys) (SEQ ID NO: 70);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(D-Lys) (SEQ ID NO: 282);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-Glu-(N-Me-Lys) (SEQ ID NO: 293);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys) (SEQ ID NO: 270);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 287);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 295);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(N-Me-Lys) (SEQ ID NO: 299);

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-D-Lys) (SEQ ID NO: 62); or

(2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu) (SEQ ID NO: 134),

wherein the peptide molecule comprises a thioether bond between the 2-methylbenzoyl and the Pen.

15. The peptide molecule or pharmaceutically acceptable salt thereof of any of claims 1-14, wherein the peptide molecule or the two peptide monomers of the dimer comprise C-terminal NH_2 or OH groups.

16. A peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule is a dimer comprising a sequence or structure shown in Table 5.

17. A peptide molecule or pharmaceutically acceptable salt thereof, wherein the peptide molecule comprises a sequence or structure selected from the following:

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 151);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-(Phe-(4-COOH)-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 356);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 153);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 161);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 322);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-Glu-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 236);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys)-NH_2)$_2$ (SEQ ID NO: 222);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(D-Lys)-OH)$_2$ (SEQ ID NO: 223);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Phe(4-tBu)-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 366);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-2-Nal-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 338);

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-1-Nal-(β-homoGlu)-(N-Me-Lys)-NH_2)$_2$ (SEQ ID NO: 325); or

((2-methylbenzoyl)-(N-Me-Arg)-Ser-Asp-Thr-Leu-Pen-Trp-Glu-(N-Me-D-Lys)-NH_2)$_2$ (SEQ ID NO: 152),

wherein the two peptide monomers are linked by DIG and comprise a thioether bond between the 2-methylbenzoyl and Pen.

18. The peptide molecule or pharmaceutically acceptable salt thereof of any of claims 1-17, wherein the peptide dimer or the two peptide monomers of the dimer comprise a thioether bond between the 2-methyl group of the 2-methylbenzoyl and Xaa^7.

19. A pharmaceutical composition comprising a peptide molecule or pharmaceutically acceptable salt thereof of any one of claims1-18 and a pharmaceutically acceptable carrier, diluent or excipient.

20. The pharmaceutical composition of claim 19, wherein the pharmaceutical composition is formulated for oral delivery.

21. The pharmaceutical composition of claim 19 or claim 20, further comprising an enteric coating, optionally wherein the enteric coating releases the pharmaceutical composition within a subject's lower gastrointestinal system.

22. Use of an effective amount of the peptide molecule of any one of claims 1-18 or the pharmaceutical composition of any one of claims 19-21 in the manufacture of a medicament for

treating or preventing a disease or condition selected from the group consisting of Inflammatory Bowel Disease (IBD), adult IBD, pediatric IBD, adolescent IBD, ulcerative colitis, Crohn's disease, Celiac disease (*nontropical Sprue)*, enteropathy associated with seronegative arthropathies, microscopic colitis, collagenous colitis, eosinophilic gastroenteritis, radiotherapy, chemotherapy, pouchitis resulting after proctocolectomy and ileoanal anastomosis, gastrointestinal cancer, pancreatitis, insulin-dependent diabetes mellitus, mastitis, cholecystitis, cholangitis, pericholangitis, chronic bronchitis, chronic sinusitis, asthma, primary sclerosing cholangitis, human immunodeficiency virus (HIV) infection in the GI tract, eosinophilic asthma, eosinophilic esophagitis, gastritis, colitis, microscopic colitis and graft versus host disease (GVDH).

23. The use of claim 22, wherein the disease or condition is an inflammatory bowel disease.

24. The use of claim 23, wherein the inflammatory bowel disease is (a) ulcerative colitis or (b) Crohn's disease.

25. The use of claim 22, wherein the disease or condition is eosinophilic esophagitis.

26. The use of any one of claims 22-25, wherein the peptide molecule or pharmaceutically acceptable salt thereof inhibits binding of $\alpha 4\beta 7$ to MAdCAM.

27. The use of any one of claims 22-26, wherein the peptide molecule or pharmaceutically acceptable salt thereof or the pharmaceutical composition is to be administered orally, parenterally, or topically.