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(54) Titre : DERIVES CYCLOPEPTIDIQUES
(54) Title: CYCLOPEPTIDE DERIVATIVES

(57) **Abrégé/Abstract:**

The invention relates to compounds of the formula (I) $R^1-Q^1-X-Q^2-R^2$, in which: Q^1 , Q^2 , each independent of one another, are missing or are $-NH-(CH_2)_n-CO-$; R^1 , R^2 , each independent of one another, are missing or are cyclo-(Arg-Gly-Asp-Z), wherein Z is missing in the side chain of Q^1 or Q^2 or if Q^1 and/or Q^2 are missing, is bound to X, at least one of the groups R^1 or R^2 always having to be included; X is $-CO-R^{18}-CO-$, and if R^1-Q^1- or R^2-Q^2- are missing is R^{10} , R^{13} , R^{16} , Het-CO or a fluorescent pigment residue linked through a $-CONH-$, $-COO-$, $-NH-C(=S)-NH-$, $-NH-C(=O)-NH-$, $-SO_2NH-$ or $-NHCO-$ bond; and Z, R^{10} , R^{13} , R^{16} , R^{18} , Het and n have the meanings given in claim 1. The invention also relates to the salts of said compounds. Said compounds and their salts can be used as integrin inhibitors, in particular for the prevention and treatment of circulatory diseases, thrombosis, heart infarct, coronary heart diseases, arteriosclerosis, angiogenic diseases and in tumour therapy.

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(54) Title: CYCLOPEPTIDE DERIVATIVES (54) Bezeichnung: CYCLOPEPTIDDERIVATE				
(57) Abstract The invention relates to compounds of the formula (I) $R^1-Q^1-X-Q^2-R^2$, in which: Q^1, Q^2, each independent of one another, are missing or are $-NH-(CH_2)_n-CO-$; R^1, R^2, each independent of one another, are missing or are cyclo-(Arg-Gly-Asp-Z), wherein Z is missing in the side chain of Q^1 or Q^2 or if Q^1 and/or Q^2 are missing, is bound to X, at least one of the groups R^1 or R^2 always having to be included; X is $-CO-R^{18}-CO-$, and if R^1-Q^1- or R^2-Q^2- are missing is R^{10}, R^{13}, R^{16}, Het-CO or a fluorescent pigment residue linked through a $-CONH-$, $-COO-$, $-NH-C(=S)-NH-$, $-NH-C(=O)-NH-$, $-SO_2NH-$ or $-NHCO-$ bond; and Z, $R^{10}, R^{13}, R^{16}, R^{18}$, Het and n have the meanings given in claim 1. The invention also relates to the salts of said compounds. Said compounds and their salts can be used as integrin inhibitors, in particular for the prevention and treatment of circulatory diseases, thrombosis, heart infarct, coronary heart diseases, arteriosclerosis, angiogenic diseases and in tumour therapy.				
(57) Zusammenfassung Verbindungen der Formel (I) $R^1-Q^1-X-Q^2-R^2$ worin Q^1, Q^2 jeweils unabhängig voneinander fehlt oder $-NH-(CH_2)_n-CO-$, R^1, R^2 jeweils unabhängig voneinander fehlt oder cyclo-(Arg-Gly-Asp-Z), wobei Z in der Seitenkette an Q^1 oder Q^2 oder, falls Q^1 und/oder Q^2 fehlt, an X gebunden ist, und wobei mindestens einer der Reste R^1 oder R^2 immer enthalten sein muß, X $-CO-R^{18}-CO-$, und falls R^1-Q^1- oder R^2-Q^2- fehlen R^{10}, R^{13}, R^{16}, Het-CO oder einen über eine $-CONH-$, $-COO-$, $-NH-C(=S)-NH-$, $-NH-C(=O)-NH-$, $-SO_2NH-$ oder $-NHCO-$ Bindung verknüpften fluoreszierenden Farbstoffrest, bedeutet, und Z, $R^{10}, R^{13}, R^{16}, R^{18}$, Het und n die in Anspruch 1 angegebenen Bedeutungen besitzen, sowie deren Salze, können als Integrin-Inhibitoren insbesondere zur Prophylaxe und Behandlung von Erkrankungen des Kreislaufs, bei Thrombose, Herzinfarkt, koronaren Herzerkrankungen, Arteriosklerose, angiogenen Erkrankungen und in der Tumorthherapie verwendet werden.				

**FILE, ~~PIN IN THIS AMENDED~~
~~TEXT~~ TRANSLATION**

Cyclopeptide derivatives

The invention relates to compounds of the formula I



5

in which

Q^1, Q^2 are, in each case independently of each other, either absent or $-NH-(CH_2)_n-CO-$,

10

R^1, R^2 are, in each case independently of each other, either absent or cyclo-(Arg-Gly-Asp-Z), where Z is bonded in the side chain to Q^1 or Q^2 or, if Q^1 and/or Q^2 is/are absent, to X, and

15

where at least one of the radicals R^1 or R^2 must always be present,

20

X is $-CO-R^{18}-CO-$, and if R^1-Q^1- or R^2-Q^2- is absent, R^{10}, R^{13}, R^{16} , Het-CO or a fluorescent dye residue which is linked by way of a $-CONH-$, $-COO-$, $-NH-C(=S)-NH-$, $-NH-C(O)-NH-$, $-SO_2NH-$ or $-NHCO-$ bond,

25

Z

is, in each case independently of each other, an amino acid residue or a di-, tri- or tetrapeptide residue, where the amino acids are selected, independently of each other, from a group consisting of Ala, Asn, Asp, Arg, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, Val or M,

30

35

where the said amino acids can also be derivatized and the amino acid residues are linked to each other, in peptide manner, by way of the α -amino and α -carboxyl groups, and

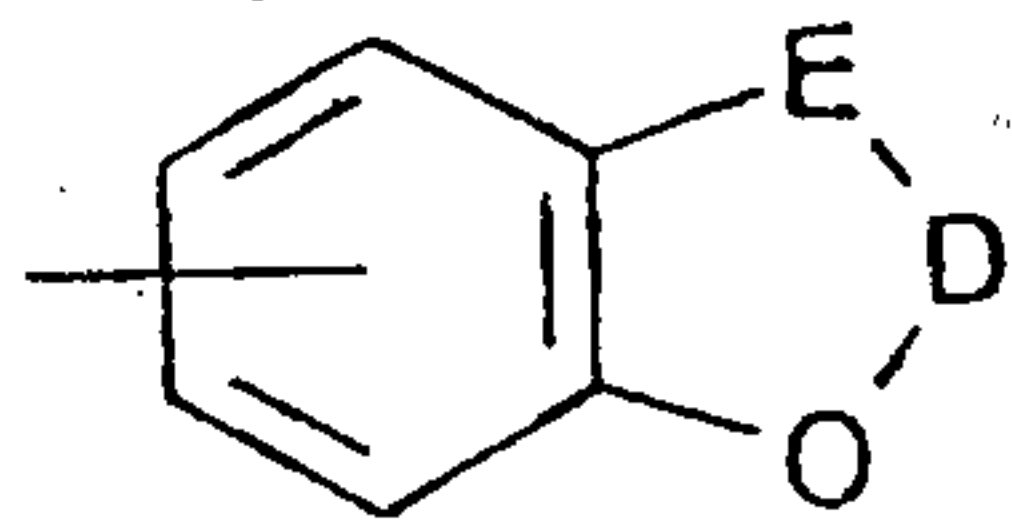
where M is always present,

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- M is $\text{NH}(\text{R}^8) - \text{CH}(\text{R}^3) - \text{COOH}$,
- R^3 is $-\text{R}^5 - \text{R}^4$, $-\text{R}^6 - \text{R}^4$ or $-\text{R}^7 - \text{R}^4$,
- 5 R^4 is OH, NH_2 , SH or COOH,
- R^5 is alkylene having 1-6 carbon atoms,
- R^6 is alkylenephenylene having 7-14 carbon atoms,
- 10 R^7 is alkylenephenylalkylene having 8-15 carbon atoms,
- R^8 is H, A or alkylphenyl having 7-12 carbon atoms,
- 15 A is alkyl having 1-6 carbon atoms,
- R^{10} is alkanoyl having 1-18 carbon atoms which is unsubstituted or substituted once by COOH, COOA, SR^{11} or $\text{NR}^{12}\text{R}^{12'}$,
- 20 R^{11} is H or trityl, pyridyl-2-thio or alkylthio having 1-6 carbon atoms,
- 25 R^{12} , $\text{R}^{12'}$ are, in each case independently of each other, H, alkyl having 1-8 carbon atoms or an amino-protecting group,
- 30 R^{13} is aroyl having 7-11 carbon atoms which is unsubstituted or substituted once or twice by alkyl having 1-6 carbon atoms, alkoxy having 1-4 carbon atoms, alkanoyl having 1-8 carbon atoms, Hal, SR^{14} or $\text{NR}^{15}\text{R}^{15'}$,
- 35 R^{14} is H or A,
- R^{15} , $\text{R}^{15'}$ are, in each case independently of each other, H or A,

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R^{16} is aralkanoyl having 7-19 carbon atoms which is unsubstituted or substituted once, twice or three times in the aryl moiety by Hal, alkoxy having 1-6 carbon atoms or OH and in which the aryl moiety can also be a



group,

E is CH_2 or O,

D is carbonyl or $[C(R^{17}R^{17'})]_m$,

R^{17} , $R^{17'}$ are, in each case independently of each other, H or A,

R^{18} is absent, or

is R^{19} , R^{20} , $R^{19}-R^{20}-R^{19}$, or phenylene which is unsubstituted or substituted once or twice by R^5 , where the chain length of R^5 is in each case independent of each other,

R^{19} is alkylene having 1-8 carbon atoms, where 1 or 2 methylene groups can be replaced by S, $-CH=CH-$ or $-C\equiv C-$,

R^{20} is cycloalkylene having 3-7 carbon atoms,

Hal is F, Cl, Br or I,

Het is a mononuclear or binuclear saturated, unsaturated or aromatic heterocycle having from 1 to 4 N, O and/or S atoms, bonded via N or C, which can be unsubstituted or substituted once, twice or three times by Hal, A, R^3 , $NR^{15}R^{15'}$, CN, NO_2 and/or carbonyl oxygen,

n is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10,

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and

m is 1 or 2,

5 where, provided that the residues are residues of optically active amino acids and amino acid derivatives, both the D and the L forms are included, and the salts thereof.

Similar compounds of cyclic peptides are
10 disclosed in DE 43 10 643.

The invention was based on discovering novel compounds possessing valuable properties, in particular those compounds which can be used for preparing pharmaceuticals.

15 It was found that the compounds of the formula I, and their salts, possess very valuable pharmacological properties while being well tolerated. In particular, they act as integrin inhibitors, in which connection they particularly inhibit the
20 interactions of the α_v -, β_3 - or β_5 -integrin receptors with ligands, such as the binding of fibrinogen to the β_3 -integrin receptor. The compounds exhibit particular activity in the case of the $\alpha_v\beta_3$, $\alpha_v\beta_5$ and $\alpha_{IIb}\beta_3$ integrins and also the $\alpha_v\beta_1$, $\alpha_v\beta_6$ and $\alpha_v\beta_8$ integrins.
25 This effect can be demonstrated, for example, using the method described by J.W. Smith et al. in J. Biol. Chem. 265, 12267-12271 (1990).

PC Brooks, R.A. Clark and D.A. Cheresh have reported, in Science 264, 569-71 (1994), that the development of
30 angiogenesis depends on the interaction between vascular integrins and extracellular matrix proteins.

The possibility of using a cyclic peptide to inhibit this interaction, and thereby initiate apoptosis (programmed cell death) of angiogenic
35 vascular cells, has been described by P.C. Brooks, A.M. Montgomery, M. Rosenfeld, R.A. Reisfeld, T.-Hu, G. Klier and D.A. Cheresh in Cell 72, 1157-64 (1994).

Compounds of the formula I, which block the interaction of integrin receptors and ligands, such as

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that of fibrinogen to the fibrinogen receptor (Glycoprotein IIb/IIIa), prevent, as GPIIb/IIIa antagonists, the spread of tumour cells as a result of metastasis. This is substantiated by the following observations:

The compounds are able to inhibit the binding of metalloproteinases to integrines and therefore avoid that the cells can use the enzymatic activity of the proteinases. This is for example described by the inhibition of the binding from matrix metalloproteinase-2 (MMP-2) to the vitronection receptor $\alpha_v\beta_3$ by a cyclic RGD peptide in Cell 85, 683-693 (1996) by P.C. Brooks et al..

The spread of tumour cells from a local tumour into the vascular system takes place by the formation of microaggregates (microthrombi) as a result of the interaction of the tumour cells with blood platelets. The tumour cells are shielded as a result of the protection afforded by the microaggregate and are not recognized by the cells of the immune system. The microaggregates can settle on vessel walls, thereby facilitating further penetration of tumour cells into the tissue. Since the formation of the microthrombi is mediated by the binding of fibrinogen to the fibrinogen receptors on activated blood platelets, the GPIIa/IIIb antagonists can be regarded as effective inhibitors of metastasis.

The compounds of the formula I may be employed as pharmaceutical active compounds in human and veterinary medicine, in particular for the prophylaxis and/or therapy of thrombosis, myocardial infarct, arteriosclerosis, inflammations, stroke, angina pectoris, tumour diseases, osteolytic diseases such as osteoporosis, pathologically angiogenic diseases such as inflammations, ophthalmological diseases, diabetic retinopathy, macular degeneration, myopia, ocular histoplasmosis, rheumatic arthritis, osteoarthritis,

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rubeotic glaucoma, ulcerative colitis, Crohn's disease, atherosclerosis, psoriasis, restenosis following angioplasty, viral infection, bacterial infection, fungal infection, in acute liver failure and for
5 supporting the healing processes in wound healing.

The compounds of the formula I may be employed as substances having an antimicrobial effect in operations in which biomaterials, implants, catheters or heart pacemakers are used. In this context, they
10 have an antiseptic effect. The efficacy of the antimicrobial activity can be demonstrated using the method described by P. Valentin-Weigund et al., in Infection and Immunity, 2851-2855 (1988).

The amino acid residue abbreviations which are
15 cited in the above text and in that which follows represent the residues of the following amino acids:

	Abu	4-Aminobutyric acid
	Aha	6-Aminohexanoic acid, 6-aminocaproic acid
20	Ala	Alanine
	Asn	Asparagine
	Asp	Aspartic acid
	Arg	Arginine
	Cys	Cysteine
25	Dab	2,4-Diaminobutyric acid
	Dap	2,3-Diaminopropionic acid
	Gln	Glutamine
	Glp	Pyroglutamic acid
	Glu	Glutamic acid
30	Gly	Glycine
	His	Histidine
	homo-Phe	homo-Phenylalanine
	Ile	Isoleucine
	Leu	Leucine
35	Lys	Lysine
	Met	Methionine
	Nle	Norleucine
	Orn	Ornithine
	Phe	Phenylalanine

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	Phg	Phenylglycine
	4-Hal-Phe	4-Halo-phenylalanine
	Pro	Proline
	Ser	Serine
5	Thr	Threonine
	Trp	Tryptophan
	Tyr	Tyrosine
	Val	Valine.

10 In addition, the abbreviations below have the following meanings:

	Ac	Acetyl
	BOC	tert-Butoxycarbonyl
15	CBZ or Z	Benzyloxycarbonyl
	DCCI	Dicyclohexylcarbodiimide
	DMF	Dimethylformamide
	EDCI	N-Ethyl-N,N'-(dimethylaminopropyl) carbodiimide
20	Et	Ethyl
	FCA	Fluoresceincarboxylic acid
	FITC	Fluorescein isothiocyanate
	Fmoc	9-Fluorenylmethoxycarbonyl
	FTH	Fluorescein thiourea
25	HOBt	1-Hydroxybenzotriazole
	Me	Methyl
	MBHA	4-Methylbenzhydramine
	Mtr	4-Methoxy-2,3,6-trimethylphenylsulphonyl
	HONSu	N-Hydroxysuccinimide
30	OBu	tert-Butyl ester
	Oct	Octanoyl
	OMe	Methyl ester
	OEt	Ethyl ester
	POA	Phenoxyacetyl
35	Sal	Salicyloyl
	TFA	Trifluoroacetic acid
	Trt	Trityl (triphenylmethyl).

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Provided that the abovementioned amino acids are able to appear in several enantiomeric forms, all these forms, and also their mixtures (for example the DL forms) are included both above and below, for example as an integral part of the compounds of the formula I. In addition, the amino acids can, for example as an integral part of compounds of the formula I, be provided with appropriate protecting groups which are known per se.

The compounds according to the invention also include so-called prodrug derivatives, that is compounds of the formula I which are modified with, for example, alkyl or acyl groups, sugars or oligopeptides, and which are rapidly cleaved in the organism to give the effective compounds according to the invention. This also includes biodegradable polymer derivatives of the compounds according to the invention, as described, for example, in Int. J. Pharm. 115, 61-67 (1995).

The invention furthermore relates to a process for preparing compounds of the formula I according to the invention, and their salts, characterized in that

(a) a compound of the formula II

$$\text{H-Q}^1\text{-R}^1 \qquad \text{II}$$

in which

Q^1 and R^1 have the meaning given above, is reacted, in an acylation reaction,

with a compound of the formula III

$$\text{X-L} \qquad \text{III}$$

in which

X has the meaning given above, and

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L is Cl, Br, I or a free or reactive functionally modified OH group,

or

5

b) in that a compound of the formula IV



10 in which

Q^2 and R^2 have the meaning given above, is reacted, in an acylation reaction, with a compound of the formula V



in which

R^1 , Q^1 , X and L have the given meaning,

20

or

c) in that a compound of the formula II



in which

Q^1 and R^1 have the meaning given above,

30

is reacted, in an addition reaction, with a compound of the formula VI



in which

X has the meaning given above, and

U is $-\text{N}=\text{C}=\text{O}$, $-\text{N}=\text{C}=\text{S}$ or maleimidyl,

- 10 -

or

d) in that they are liberated from one of their
 5 functional derivatives by treatment with a solvolysing
 or hydrogenolysing agent,

and/or in that a basic or acidic compound of the
 formula I is converted into one of its salts by
 10 treatment with an acid or base.

In the above text, and in that which follows,
 the radicals Q^1 , Q^2 , R^1 , R^2 , X and L have the meanings
 given in the formulae I, II and III provided another
 alternative is not expressly indicated.

15 In the above formulae, alkyl is preferably
 methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-
 butyl or tert-butyl, and, in addition, also pentyl, 1-,
 2- or 3-methylbutyl, 1,1-, 1,2- or 2,2-dimethylpropyl,
 1-ethylpropyl, hexyl, 1-, 2-, 3- or 4-methylpentyl,
 20 1,1-, 1,2-, 1,3-, 2,2-, 2,3- or 3,3-dimethylbutyl,
 1- or 2-ethylbutyl, 1-ethyl-1-methylpropyl, 1-ethyl-2-
 methylpropyl, or 1,1,2- or 1,2,2-trimethylpropyl.

Alkylene is preferably methylene, ethylene,
 propylene, butylene, pentylene or hexylene.
 25 Alkylenephenyl is preferably benzyl or phenethyl.
 Alkylenephenylalkylene is preferably 4-methylenebenzyl
 or 4-ethylenebenzyl.

Q^1 and Q^2 are preferably, in each case
 independently of each other, 6-aminohexanoic acid
 30 (6-aminocaproic acid) or are absent, where, preferably,
 for example Q^1 is 6-aminohexanoic acid and Q^2 is absent.

M is preferably Dap, Ser, Cys, Asp, D-Asp, Dab,
 homoserine, homocysteine, Glu, D-Glu, Thr, Orn, Lys,
 D-Lys, 4-aminomethyl-Phe or 4-aminomethyl-D-Phe.

35 The amino acids and amino acid residues which
 are mentioned for Z in the meanings can also be
 derivatized, with the N-methyl, N-ethyl, N-propyl,
 N-benzyl or C_α -methyl derivatives being preferred.
 Preference is also given to derivatives of Asp and Glu,

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in particular the methyl, ethyl, propyl, butyl, tert-butyl, neopentyl or benzyl esters of the side-chain carboxyl groups, and also to derivatives of Arg, which can be substituted on the $-NH-C(=NH)-NH_2$ group by an
 5 acetyl, benzoyl, methoxycarbonyl or ethoxycarbonyl radical.

Z is preferably M, with preference also being given to D-Phe-M, D-Trp-M, D-Tyr-M, D-Phe-Lys, D-Phe-D-Lys, D-Trp-Lys, D-Trp-D-Lys, D-Tyr-Lys, D-Tyr-D-Lys,
 10 D-Phe-Orn, D-Phe-Dab, D-Phe-Dap, D-Phe-D-Orn, D-Phe-D-Dab, D-Phe-D-Dap, D-Phe-4-aminomethyl-Phe, D-Phe-4-aminomethyl-D-Phe, D-Trp-4-aminomethyl-Phe, D-Trp-4-aminomethyl-D-Phe, D-Tyr-4-aminomethyl-Phe, D-Tyr-4-aminomethyl-D-Phe, D-Phe-Asp, D-Phe-D-Asp, D-Trp-Asp,
 15 D-Trp-D-Asp, D-Tyr-Asp, D-Tyr-D-Asp, D-Phe-Cys, D-Phe-D-Cys, D-Trp-Cys, D-Trp-D-Cys, D-Tyr-Cys, D-Tyr-D-Cys, Phe-D-Lys, Trp-D-Lys, Tyr-D-Lys, Phe-Orn, Phe-Dab, Phe-Dap, Trp-Orn, Trp-Dab, Trp-Dap, Tyr-Orn, Tyr-Dab, Tyr-Dap, Phe-4-aminomethyl-D-Phe, Trp-4-aminomethyl-D-Phe,
 20 Tyr-4-aminomethyl-D-Phe, Phe-D-Asp, Trp-D-Asp, Tyr-D-Asp, Phe-D-Cys, Trp-D-Cys, Tyr-D-Cys, D-Phe-Lys-Gly, D-Phe-M-Gly, D-Trp-Lys-Gly, D-Trp-M-Gly, D-Tyr-Lys-Gly, D-Tyr-M-Gly, D-Phe-Val-Lys, D-Phe-Gly-Lys, D-Phe-Ala-Lys, D-Phe-Ile-Lys, D-Phe-Leu-Lys, D-Trp-Val-Lys,
 25 D-Trp-Gly-Lys, D-Trp-Ala-Lys, D-Trp-Ile-Lys, D-Trp-Leu-Lys, D-Tyr-Val-Lys, D-Tyr-Gly-Lys, D-Tyr-Ala-Lys, D-Tyr-Ile-Lys, D-Tyr-Leu-Lys, and also M-Pro-Ala-Ser-Ser.

The radical $-R^6-R^4$ is preferably 2-, 3- or 4-hydroxybenzyl, 2-, 3- or 4-aminobenzyl, 2-, 3- or 4-mercaptobenzyl, 2-, 3- or 4-carboxybenzyl, and also, preferably, 2-, 3- or 4-hydroxyphenethyl, 2-, 3- or 4-aminophenethyl, 2-, 3- or 4-mercaptophenethyl or 2-, 3- or 4-carboxyphenethyl.

35 Alkanoyl is preferably formyl, acetyl, propionyl, butyryl, pentanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl or octadecanoyl.

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Aroyl is preferably benzoyl or naphthoyl.

R^{13} is unsubstituted, preferably - as indicated
 - monosubstituted benzoyl, with individual preference
 being given to benzoyl, o-, m- or p-methylbenzoyl, o-,
 5 m- or p-ethylbenzoyl, o-, m- or p-propylbenzoyl, o-, m-
 or p-isopropylbenzoyl, o-, m- or p-tert-butylbenzoyl,
 o-, m- or p-aminobenzoyl, o-, m- or p-(N-methylamino)-
 benzoyl, o-, m- or p-methoxybenzoyl, o-, m- or p-
 ethoxybenzoyl, o-, m- or p-(N,N-dimethylamino)-benzoyl,
 10 o-, m- or p-(N-ethylamino)-benzoyl, o-, m- or p-(N,N-
 diethylamino)-benzoyl, o-, m- or p-fluorobenzoyl, o-,
 m- or p-bromobenzoyl, o-, m- or p-chlorobenzoyl, o-, m-
 or p-formylbenzoyl, o-, m- or p-acetylbenzoyl, o-, m-
 or p-propionylbenzoyl, o-, m- or p-butyrylbenzoyl, o-,
 15 m- or p-pentanoylbenzoyl, o-, m- or p-methylthiobenz-
 oyl, with preference also being given to 2,3-, 2,4-,
 2,5-, 2,6-, 3,4- or 3,5-difluorobenzoyl, 2,3-, 2,4-,
 2,5-, 2,6-, 3,4- or 3,5-dichlorobenzoyl, 2,3-, 2,4-,
 2,5-, 2,6-, 3,4- or 3,5-dibromobenzoyl, 2-chloro-3-
 20 methyl-, 2-chloro-4-methyl-, 2-chloro-5-methyl-,
 2-chloro-6-methyl-, 2-methyl-3-chloro-, 2-methyl-4-
 chloro-, 2-methyl-5-chloro-, 2-methyl-6-chloro-,
 3-chloro-4-methyl-, 3-chloro-5-methyl- or 3-methyl-4-
 chlorobenzoyl, 2-bromo-3-methyl-, 2-bromo-4-methyl-,
 25 2-bromo-5-methyl-, 2-bromo-6-methyl-, 2-methyl-3-bromo-
 , 2-methyl-4-bromo-, 2-methyl-5-bromo-, 2-methyl-6-
 bromo-, 3-bromo-4-methyl-, 3-bromo-5-methyl- or 3-
 methyl-4-bromobenzoyl, or 2,5- or 3,4-dimethoxybenzoyl.

R^{16} is unsubstituted, preferably - as indicated
 30 - monosubstituted phenylacetyl, with individual
 preference being given to phenylacetyl, o-, m- or p-
 methoxyphenylacetyl, o-, m- or p-hydroxyphenylacetyl,
 o-, m- or p-ethoxyphenylacetyl, o-, m- or p-fluoro-
 phenylacetyl, o-, m- or p-bromophenylacetyl, o-, m- or
 35 p-chlorophenylacetyl, with preference also being given
 to 3-phenylpropionyl, 4-phenylbutyryl, 5-phenylpentan-
 oyl, 6-phenylhexanoyl, 7-phenylheptanoyl, 8-phenyl-
 octanoyl, 9-phenylnonanoyl, 10-phenyldecanoyl, 11-
 phenylundecanoyl, 12-phenyldodecanoyl or 13-phenyl-

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tridecanoyl, and, in addition, 2,3-methylene-dioxyphenyl, 3,4-methylenedioxyphenyl, 2,3-dihydro-benzofuranyl or 2,3-dihydro-2-oxobenzofuranyl.

Cycloalkylene is preferably cyclopropylene, 1,2- or 1,3-cyclobutylene, 1,2- or 1,3-cyclopentylene, 1,2-, 1,3- or 1,4-cyclohexylene and, in addition, 1,2-, 1,3- or 1,4-cycloheptylene.

D is preferably CH₂, with carbonyl also being preferred.

Het is preferably 2- or 3-furyl, 2- or 3-thienyl, 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, and preferably also 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -3- or 5-yl, 1- or 5- tetrazolyl, 1,2,3-oxadiazol-4- or 5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 2-, 3-, 4-, 5- or 6-2H-thiopyranyl, 2-, 3- or 4-4-H-thiopyranyl, 3- or 4-pyridazinyl, pyrazinyl, 2-, 3-, 4-, 5-, 6- or 7-benzofuryl, 2-, 3-, 4-, 5-, 6- or 7-benzothienyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-benzopyrazolyl, 2-, 4-, 5-, 6- or 7-benzoxazolyl, 3-, 4-, 5-, 6- or 7-benzisoxazolyl, 2-, 4-, 5-, 6- or 7-benzothiazolyl, 2-, 4-, 5-, 6- or 7-benzisothiazolyl, 4-, 5-, 6- or 7-benz-2,1,3-oxadiazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl or 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl. The heterocyclic radicals can also be partially or completely hydrogenated. Het can consequently also, for example, be 2,3-dihydro-2-, -3-, -4- or -5-furyl, 2,5-dihydro-2-, -3-, -4- or -5-furyl, tetrahydro-2- or -3-thienyl, 1,3-dioxolan-4-yl, tetrahydro-2- or -3-thienyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 2,5-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 1-, 2- or

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3-pyrrolidinyl, tetrahydro-1-, -2- or -4-imidazolyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrazolyl, tetrahydro-1-, -3- or -4-pyrazolyl, 1,4-dihydro-1-, -2-, -3- or -4-pyridyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5- or -6-pyridyl, 1-, 2-, 3- or 4-piperidinyl, 2-, 3- or 4-morpholinyl, tetrahydro-2-, -3- or -4-pyranyl, 1,4-dioxanyl, 1,3-dioxan-2-, -4- or -5-yl, hexahydro-1-, -3- or -4-pyridazinyl, hexahydro-1-, -2-, -4- or -5-pyrimidinyl, 1-, 2- or 3-piperazinyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-quinolyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-isoquinolyl.

Amino-protecting group is preferably acetyl, propionyl, butyryl, phenylacetyl, benzoyl, toluy, POA, methoxycarbonyl, ethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, BOC, 2-iodoethoxycarbonyl, CBZ ("carbo-benzoyl"), 4-methoxybenzyloxycarbonyl, FMOC, Mtr or benzyl.

Fluorescent dye residue is preferably 7-acetoxycoumarin-3-yl, fluorescein-5-(and/or 6-)yl, 2',7'-dichlorofluorescein-5-(and 6-)yl, dihydrotetramethylrosamin-4-yl, tetramethylrhodamin-5-(and/or 6-)yl, 4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacen-3-ethyl or 4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-s-indacen-3-ethyl.

Suitable functionalized fluorescent dye residues which can be used as reagents for preparing the compounds according to the invention of the formula I are described, for example, in "Handbook of Fluorescent Probes and Research Chemicals, 5th Edition, 1992-1994" by R.P. Haughland, Molecular Probes, Inc.

m is preferably 1, with 2 also being preferred.

Hal is preferably F, Cl or Br, and also I.

The compounds of formula I may possess one or more chiral centres and therefore occur in different stereoisomeric forms. The formula I encompasses all these forms.

Accordingly, the invention relates, in particular, to those compounds of the formula I in

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which at least one of the said radicals has one of the abovementioned preferred meanings. Some preferred groups of compounds may be expressed by the following partial formulae Ia to Ih, which correspond to the formula I and in which the radicals which are not specifically named have the meaning given in formula I, but in which

- | | | | |
|----|-------|---|---|
| 10 | in a) | Q ¹ , Q ² and R ²
R ¹
X | are absent,
is cyclo-(Arg-Gly-Asp-Z), and
is alkanoyl; |
| 15 | in b) | Q ¹ , Q ² and R ²
R ¹
X | are absent,
is cyclo-(Arg-Gly-Asp-M), and
is alkanoyl; |
| 20 | in c) | Q ¹ , Q ² and R ²
R ¹
X | are absent,
is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and
is alkanoyl; |
| 25 | in d) | Q ¹ and Q ²
R ¹ and R ²
X | are absent,
are cyclo-(Arg-Gly-Asp-D-Phe-Lys), and
is -CO-(CH ₂) _n -CO-; |
| 30 | in e) | Q ² and R ²
Q ¹
R ¹
X | are absent,
is -NH-(CH ₂) ₅ -CO-,
is cyclo-(Arg-Gly-Asp-Z), and
is a fluorescent dye residue; |
| 35 | in f) | Q ² and R ²
Q ¹
R ¹
X | are absent,
is -NH-(CH ₂) ₅ -CO-,
is cyclo-(Arg-Gly-Asp-M), and
is fluoresceinoyl; |
| | in g) | Q ¹ and Q ²
R ¹ and R ²
X | are absent,
are cyclo-(Arg-Gly-Asp-M), and
is -CO-(CH ₂) ₈ -CO-; |

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in h) Q^1 , Q^2 and R^2 are absent,

R^1 is cyclo-(Arg-Gly-Asp-Z), and

X is $CH_3-(CH_2)_{16}-CO-$.

Particular preference is given to compounds of the
5 formula VII

Cyclo-(Arg-Gly-Asp-D-Phe-Lys(Q^1 -X)) VII

in which Q^1 has the meaning given in claim 1, and where Q^1 is
bonded to the side chain of the lysine, or, if Q^1 is absent,
X is bonded to the side chain of the lysine, and in which X
10 is preferably

alkanoyl having 1-18 carbon atoms which is
unsubstituted or substituted once by $COOH$, $COOA$, SR^{14} or
 $NR^{15}R^{15'}$, FCA or FTH ,

or aroyl having 7-11 carbon atoms which is
15 unsubstituted or substituted once or twice by alkyl having
1-6 carbon atoms, alkoxy having 1-4 carbon atoms, alkanoyl
having 1-8 carbon atoms, Hal, SR^{14} or $NR^{15}R^{15'}$, where R^{14} , R^{15}
and $R^{15'}$ have the meanings given above.

In one specific aspect, the invention provides a
20 compound of the formula I, wherein:

a) Q^1 , Q^2 and R^2 are absent,

R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is salicyloyl;

b) Q^1 and Q^2 are absent,

25 R^1 and R^2 are cyclo-(Arg-Gly-Asp-D-Phe-Lys),
and

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X is $-\text{CO}-(\text{CH}_2)_2-\text{CO}-$;

c) Q^2 and R^2 are absent,

Q^1 is $-\text{NH}-(\text{CH}_2)_5-\text{CO}-$,

R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

5 X is acetyl;

d) Q^2 and R^2 are absent,

Q^1 is $-\text{NH}-(\text{CH}_2)_5-\text{CO}-$,

R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is fluoresceinoyl; or

10 e) Q^2 and R^2 are absent,

Q^1 is $-\text{NH}-(\text{CH}_2)_5-\text{CO}-$,

R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is tert-butyloxycarbonyl;

and a physiologically harmless salt thereof.

15 Otherwise, the compounds of the formula I, and
also the starting compounds for preparing them, are prepared
by methods which are known per se, as described in the
literature (for example in the standard works such as
Houben-Weyl, Methoden der organischen Chemie, [Methods of
20 organic chemistry], Georg-Thieme-Verlag, Stuttgart);
specifically under reaction conditions which are known and
suitable for the said reactions. In this context, use can
also be made of variants which are known per se but which
are not detailed here.

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The starting compounds can, if desired, also be formed in situ, so that they are not isolated from the reaction mixture but, instead, immediately subjected to further reaction to give the compounds of the formula I.

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Compounds of the formula I may preferably be obtained by reacting compounds of the formula II with compounds of the formula III.

As a rule, the compounds of the formulae II and
5 III are known. If they are not known, they can be prepared by methods which are known per se.

In the compounds of the formula III, the radical L is preferably a preactivated carboxylic acid, preferably a carbonyl halide, symmetrical or mixed
10 anhydride or an active ester. Radicals of this nature for activating the carboxyl group in typical acylation reactions are described in the literature (for example in the standard works such as Houben-Weyl, Methoden der organischen Chemie [Methods of organic chemistry],
15 Georg-Thieme-Verlag, Stuttgart).

Activated esters are expediently formed in situ, for example by adding HOBt or N-hydroxysuccinimide.

L is preferably H, F, Cl, Br or -ON-succinimide.

20 As a rule, the reaction is carried out in an inert solvent in the presence of an acid-binding agent, preferably an organic base such as triethylamine, dimethylaniline, pyridine or quinoline, or of an excess of the carboxyl component of the formula III.

25 It can also be advantageous to add an alkali metal or alkaline earth metal hydroxide, carbonate or bicarbonate or another salt of a weak acid of the alkali metals or alkaline earth metals, preferably of potassium, sodium, calcium or caesium.

30 In each case depending on the conditions used, the reaction time is between a few minutes and 14 days, while the reaction temperature is between about -30° and 140°, normally between -10° and 90°, in particular between about 0° and about 70°.

35 Examples of suitable inert solvents are hydrocarbons such as hexane, petroleum ether, benzene, toluene or xylene; chlorinated hydrocarbons such as trichloroethylene, 1,2-dichloroethane, carbon tetrachloride, chloroform or dichloromethane; alcohols such

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as methanol, ethanol, isopropanol, n-propanol, n-butanol or tert-butanol; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran (THF) or dioxane; glycol ethers such as ethylene glycol monomethyl ether or ethylene glycol monoethyl ether (methyl glycol or ethyl glycol), ethylene glycol dimethyl ether (diglyme); ketones such as acetone or butanone; amides such as acetamide, dimethylacetamide or dimethylformamide (DMF); nitriles such as acetonitrile; sulphoxides such as dimethyl sulphoxide (DMSO); carbon disulphide; carboxylic acids such as formic acid or acetic acid; nitro compounds such as nitromethane or nitrobenzene; esters such as ethyl acetate, water, or mixtures of the said solvents.

15. In addition, compounds of the formula I can be obtained by reacting compounds of the formula IV with compounds of the formula V. As a rule, the starting compounds of the formula IV and V are known. If they are not known, they can be prepared by methods which are known per se.

20 In the compounds of the formula V, the radical L is preferably a preactivated carboxylic acid, preferably a carbonyl halide, symmetrical or mixed anhydride or an active ester. Radicals of this nature for activating the carboxyl group in typical acylation reactions are described in the literature (for example in the standard works such as Houben-Weyl, Methoden der organischen Chemie, [Methods of organic chemistry], Georg-Thieme-Verlag, Stuttgart).

30 L is preferably F, Cl, Br or -ON- succinimide.

The reaction of the compounds of the formula IV with compounds of the formula V is carried out under the same conditions, as regards the reaction time, the temperature and the solvent, as has been described for the reaction of the compounds of the formula II with compounds of the formula III.

35 In addition, compounds of the formula I can be obtained by reacting compounds of the formula II with compounds of the formula VI. As a rule, the starting

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compounds of the formulae II and VI are known. If they are not known, they can be prepared by methods which are known per se.

The reaction of compounds of the formula II with
5 compounds of the formula III constitutes a typical addition to isothiocyanates. Additions of this nature are described in the literature (for example in the standard works such as Houben-Weyl, Methoden der organischen Chemie [Methods of organic chemistry],
10 Georg-Thieme-Verlag, Stuttgart).

Cyclic compounds of the formula R^1 and/or R^2 can be prepared by cyclizing the linear compounds as, for example, described in DE 43 10 643 or in Houben-Weyl, I.c., Volume 15/II, pages 1 to 806 (1974).

15 The compounds of the formula I can furthermore be obtained by liberating them from their functional derivatives by means of solvolysis, in particular hydrolysis, or by hydrogenolysis.

Starting compounds which are preferred for the
20 solvolysis or hydrogenolysis are those which, in place of one or more free amino and/or hydroxyl groups, contain corresponding, protected amino and/or hydroxyl groups, preferably those which carry an amino protecting group in place of an H atom which is bonded
25 to an N atom, for example those which conform to the formula I but which contain an NHR' group (in which R' is an amino protecting group, for example BOC or CBZ) in place of an NH_2 group.

In addition, starting compounds are preferred
30 which carry an hydroxyl-protecting group in place of the H atom of an hydroxyl group, for example those which conform to the formula I but which contain an $R''O$ -phenyl group (in which R'' is an hydroxyl-protecting group) in place of an hydroxyphenyl group.

35 Several - identical or different - protected amino and/or hydroxyl groups can also be present in the molecule of the starting compound. If the protecting groups which are present are different from each other, they can in many cases be eliminated selectively.

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The expression "amino-protecting group" is well known and relates to groups which are suitable for protecting (blocking) an amino group from chemical reactions but which can readily be removed after the
5 desired chemical reaction has been carried out at other sites in the molecule. Unsubstituted or substituted acyl, aryl, aralkoxymethyl or aralkyl groups are typical groups of this nature. Since the amino-protecting groups are removed after the desired
10 reaction (or reaction sequence), their nature and size is otherwise not critical; however, those having 1-20, in particular 1-8, carbon atoms are preferred. In connection with the present process, the expression "acyl group" is to be understood in the broadest
15 possible sense. It comprises acyl groups which are derived from aliphatic, araliphatic, aromatic or heterocyclic carboxylic acids or sulphonic acids, and also, in particular, alkoxycarbonyl, aryloxycarbonyl and, especially, aralkoxycarbonyl groups. Examples of
20 acyl groups of this nature are alkanoyl such as acetyl, propionyl and butyryl; aralkanoyl such as phenylacetyl; aroyl such as benzoyl or tolyl; aryloxyalkanoyl such as POA; alkoxycarbonyl such as methoxycarbonyl, ethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, BOC or
25 2-iodoethoxycarbonyl; aralkyloxycarbonyl such as CBZ ("carbobenzoxo"), 4-methoxybenzyloxycarbonyl or FMOC; arylsulphonyl such as Mtr. Those amino-protecting groups which are preferred are BOC and Mtr, and also CBZ, Fmoc, benzyl and acetyl.

30 The expression "hydroxyl-protecting group" is likewise well known and refers to groups which are suitable for protecting an hydroxyl group from chemical reactions but which can readily be removed after the
desired chemical reaction has been carried out at other
35 sites in the molecule. The abovementioned unsubstituted or substituted aryl, aralkyl or acyl groups, and also alkyl groups, are typical groups of this nature. The nature and size of the hydroxyl-protecting groups is not critical since the groups are removed once again

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after the desired chemical reaction or reaction sequence; groups having 1-20, in particular 1-10, carbon atoms are preferred. Examples of hydroxyl-protecting groups are, inter alia, benzyl, p-nitrobenzoyl, p-toluenesulphonyl, tert-butyl and acetyl, with benzyl and tert-butyl being particularly preferred. The COOH groups in aspartic acid and glutamic acid are preferably protected in the form of their tert-butyl esters (for example Asp(OBut)).

10 The compounds of the formula I are - depending on the protecting group employed - liberated from their functional derivatives using, for example, strong acids, expediently TFA or perchloric acid, but also other strong inorganic acids, such as hydrochloric acid or sulphuric acid, strong organic carboxylic acids, 15 such as trichloroacetic acid, or sulphonic acids, such as benzenesulphonic acid or p-toluenesulphonic acid. It is possible, but not always necessary, for an additional inert solvent to be present. Suitable inert solvents are preferably organic, for example carboxylic acids such as acetic acid, ethers such as tetrahydrofuran or dioxane, amides such as DMF, halogenated hydrocarbons such as dichloromethane, and also alcohols such as methanol, ethanol or isopropanol, 25 and also water. Mixtures of the previously mentioned solvents are also suitable. TFA is preferably used in excess without adding any other solvent, while perchloric acid is used in the form of a mixture of acetic acid and 70% perchloric acid in a ratio of 9:1. 30 The reaction temperatures for the cleavage are expediently between about - and about 50°, with the cleavage preferably being carried out at between 15 and 30° (room temperature).

35 The BOC, OBut and Mtr groups can preferably be eliminated, for example, using TFA in dichloromethane or using approximately 3 to 5n HCl in dioxane at 15-30°, while the FMOC group can preferably be eliminated using an approximately 5 to 50% solution of

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dimethylamine, diethylamine or piperidine in DMF at 15-30°.

The trityl group is employed for protecting the amino acids histidine, asparagine, glutamine and cysteine. Depending on the desired end product, it is eliminated using TFA/10% thiophenol, with the trityl group being eliminated from all the said amino acids; when TFA/anisole or TFA/thioanisole is used, the trityl group is only eliminated from His, Asn and Gln, whereas it remains on the Cys side chain.

Hydrogenolytically removable protecting groups (for example CBZ or benzyl) can, for example, be eliminated by treating with hydrogen in the presence of a catalyst (for example a precious metal catalyst such as palladium, expediently on a support such as carbon). Suitable solvents in this context are the abovementioned solvents, in particular, for example, alcohols such as methanol or ethanol or amides such as DMF. As a rule, the hydrogenolysis is carried out at temperatures of between about 0 and 100° and pressures of between 1 and 200 bar, preferably at 20-30° and 1-10 bar. The CBZ group is satisfactorily eliminated hydrogenolytically on 5 to 10% Pd/C in methanol or using ammonium formate (in place of hydrogen) on Pd/C in methanol/DMF at 20-30°.

A base of the formula I can be converted with an acid into the associated acid addition salt, for example by reacting equivalent quantities of the base and the acid in an inert solvent such as ethanol and then concentrating by evaporation. Suitable acids for this reaction are, in particular, those which give rise to physiologically harmless salts. Thus, use can be made of inorganic acids, for example sulphuric acid, nitric acid, hydrohalic acids such as hydrochloric acid or hydrobromic acid, phosphoric acids such as orthophosphoric acid, and sulphamic acid, and, in addition, organic acids, in particular aliphatic, alicyclic, araliphatic, aromatic or heterocyclic monobasic or polybasic carboxylic, sulphonic or

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5 sulphuric acids, for example formic acid, acetic acid, propionic acid, pivalic acid, diethylacetic acid, malonic acid, succinic acid, pimelic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, malic acid, citric acid, gluconic acid, ascorbic acid, nicotinic acid, isonicotinic acid, methanesulphonic acid, ethanesulphonic acid, ethanedisulphonic acid, 2-hydroxyethanesulphonic acid, benzenesulphonic acid, p-toluenesulphonic acid, naphthalenemonosulphonic acid, 10 naphthalenedisulphonic acid and lauryl sulphuric acid. Salts with acids which are not physiologically harmless, for example picrates, may be used for isolating and/or purifying the compounds of the formula I.

15 On the other hand, an acid of the formula I can be converted into one of its physiologically harmless metal or ammonium salts by reaction with a base. In this context, the sodium, potassium, magnesium, calcium and ammonium salts are particularly suitable as salts, 20 as are also substituted ammonium salts, for example the dimethyl-, diethyl- or diisopropylammonium salts, monoethanol-, diethanol- or diisopropylammonium salts, cyclohexyl- and dicyclohexylammonium salts, and dibenzylethylenediammonium salts, and also, for 25 example, salts with arginine or lysine.

The invention furthermore relates to the use of the compounds of the formula I and/or their physiologically harmless salts for producing pharmaceutical preparations, in particular by a non-chemical route. In this context, they can be brought 30 into a suitable dosage form together with at least one solid, liquid and/or semisolid carrier substance or auxiliary substance and, where appropriate, in combination with one or more additional active 35 compounds.

The invention furthermore relates to pharmaceutical preparations which contain at least one compound of the formula I and/or one of its physiologically harmless salts.

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These preparations may be used as pharmaceuticals in human and veterinary medicine. Suitable carrier substances are organic or inorganic substances which are suitable for enteral (for example oral), parenteral or topical administration or for administration in the form of an inhalation spray and which do not react with the novel compounds, for example water, vegetable oils, benzyl alcohols, alkylene glycols, polyethylene glycols, glycerol triacetate, gelatin, carbohydrates such as lactose or starch, magnesium stearate, talc or vaseline. For oral employment, use is made, in particular, of tablets, pills, coated tablets, capsules, powders, granules, syrups, juices or drops, for rectal employment of suppositories, for parenteral employment of solutions, preferably oily or aqueous solutions, and also suspensions, emulsions or implants, and, for topical employment, of ointment, creams or powders. The novel compounds can also be lyophilized and the resulting lyophilizates used, for example, for producing injection preparations. The preparations mentioned can be sterilized and/or contain auxiliary substances such as lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing the osmotic pressure, buffering substances, dyes, flavourings and/or several additional active compounds, for example one or more vitamins. For administration as an inhalation spray, sprays can be used which contain the active compound either dissolved or suspended in a propellant gas or propellant gas mixture (for example CO₂ or fluorochlorohydrocarbons). In this context, the active compound is expediently used in micronized form, with it being possible for one or more additional physiologically tolerated solvents, for example ethanol, to be present. Inhalation solutions can be administered using customary inhalers.

The compounds of the formula I and their physiologically harmless salts may be used as integrin inhibitors in the control of diseases, in particular

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pathologically angiogenic diseases, thromboses, cardiac infarct, coronary heart diseases, arteriosclerosis, tumours, osteoporosis, inflammations and infections.

In this connection, the substances according to the invention can, as a rule, be administered in analogy with other known, commercially available peptides, in particular, however, in analogy with the compounds described in US-A-4 472 305, preferably in dosages of between 0.05 and 500 mg, in particular between 0.5 and 100 mg per dosage unit. The daily dose is preferably between about 0.01 and 2 mg/kg of body weight. However, the special dose for each patient depends on a very wide variety of factors, for example on the activity of the special compound employed, on age, body weight, general state of health, sex, diet, time and route of administration, the excretion rate, pharmaceutical combination and severity of the particular disease to which the therapy applies. Parenteral administration is preferred.

In addition, the novel compounds of the formula I can be used in analytical biology and molecular biology.

The novel compounds of the formula I, in which X is a fluorescent dye residue which is linked by way of a - CONH-, -COO-, -NH-C(=S)-NH-, -NH-C(=O)-NH-, -SO₂NH- or -NHCO- bond, can be used as diagnostic markers in FACS (fluorescence activated cell sorter) analysis and fluorescence microscopy.

The use of labelled compounds in fluorescence microscopy is described, for example, by Y.-L. Wang and D.L. Taylor in "Fluorescence Microscopy of Living Cells in Culture, Part A + B, Academic Press, Inc. 1989".

The novel compounds of the formula I may also be used in affinity chromatography for eluting bound proteins.

In particular, they may be used as integrin ligands for eluting integrins.

Both in the above text and in that which follows all temperatures are given in °C. In the

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following examples, "customary working-up" denotes:
water is added, if required, the pH is adjusted, if
required and depending on the constitution of the end
product, to values of between 2 and 10, the mixture is
5 extracted with ethyl acetate or dichloromethane, the
phases are separated, the organic phase is dried over
sodium sulphate and evaporated, and the residue is
purified by chromatography on silica gel and/or by
crystallization. Rf values on silica gel; mobile phase:
10 ethyl acetate/methanol 9:1.
RT = retention time (minutes) in HPLC in the following
systems:

[A]

15 Column: Nucleosil[™] 7C 18 250 x 4 mm
Eluent A: 0.1% TFA in water
Eluent B: 0.1% TFA in acetonitrile
Flow rate: 1 ml/min
Gradient: 20-50% B/30 min.

20

[B]

50 minute gradient of 0-80% 2-propanol in water
containing 0.3% TFA at 1 ml/min on a Lichrosorb® RP
Select B (7 µm) 250 x 4 mm column

25

[C]

Column: Lichrospher[™] (5 µm) 100 RP8 125 x 4 mm
Eluent A: 0.1 M Na phosphate pH 7.0
Eluent B: 0.005 M Na phosphate, pH 7.0/60 vol % of 2-
30 propanol
Flow rate: 0.7 ml/min
Gradient: 1-99% B/50 min.

35

Mass spectrometry (MS): EI (electron collision
ionization) M⁺
FAB (fast atom bombardment)
(M+H)⁺

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The invention also provides a commercial package comprising a compound of formula I or a physiologically harmless salt thereof, or a pharmaceutical preparation thereof, and associated therewith instructions for use
5 thereof in preventing, controlling or treating a disease.

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Example 1

1.0 g of O-acetyl salicylic acid N-succinimidyl ester [obtainable by reacting acetylsalicylic acid with
 5 HONSu in ethyl acetate, DMF and 1.2 equivalents of diisopropylcarbodiimide, FAB 278] and 0.5 g of triethylamine are added to a solution of 3.05 g of cyclo-(Arg-Gly-Asp-D-Phe-Lys) [obtainable by cyclizing
 H-Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Lys(BOC)-OH to give
 10 cyclo-(Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Lys(BOC)) and then eliminating the protecting groups] in 100 ml of DMF. The mixture is stirred at room temperature for 5 hours, and cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Sal)) × TFA; RT[B]
 22.0; FAB 724 is obtained after the customary working-
 15 up and with the concomitant elimination of the acetyl group.

The following are obtained in an analogous manner by reacting cyclo-(Arg-Gly-Asp-D-Phe-Lys)

20 with phenylpropionic acid N-succinimidyl ester (PhEtCO-ONSu):

cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-PhEtCo)) × TFA;
 RT [C] 28.2; FAB 736;

25 with 3,3,3-tris-(4-chlorophenyl)-propionic acid N-succinimidyl ester (TCPP-ONSu)

cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-TCPP)) × TFA;
 RT [B] 33.19; FAB 992;

30 with S-tritylmercaptopropionic acid N-succinimidyl ester (TrtSEtCO-ONSu):

cyclo-(Arg-Gly-Asp-D-Phe)Lys(N^εTrtSEtCO)) × TFA;
 RT [B] 33.4; FAB 934;

35 with benzyloxycarbonyl chloride
 cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-CBZ))

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with octanoyl anhydride:

cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Oct)) × TFA; RT
[B] 27.58; FAB 730;

5 with acetic anhydride:

cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Ac)) × TFA; RT
[B] 17.02; FAB 646;

with FCA-N-succinimidyl ester:

10 cyclo-((Arg-Gly-Asp-D-Phe-Lys(N^ε-FCA)) RT [B]
24.18; FAB 962;

with FITC:

15 cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-FTH)) × TFA; RT
[B] 27.3; FAB 994; inner Salt with NH₄HCO₃; RT
[B] 22.26.

The following compound is obtained in an
analogous manner by reacting cyclo-(Arg-Gly-Asp-D-Phe-
20 N(Me)-Lys) with FITC:

cyclo-(Arg-Gly-Asp-D-Phe-N(Me)-Lys(N^ε-FTH)); RG
22.64; FAB 1007;

25 with benzyloxycarbonyl chloride (CBZ-Cl)

cyclo-(Arg-Gly-Asp-D-Phe-N(Me)-Lys(N^ε-CBZ)); RT
23,35 FAB 752.

Example 2

30

6 g of BOC-Aha-N-succinimidyl ester are added
to a solution of 3.05 g of cyclo-(Arg-Gly-Asp-D-Phe-
Lys) in 40 ml of 5% aqueous NaHCO₃ and 40 ml of THF. The
mixture is stirred for 4 hours and worked-up in the
35 customary manner, affording cyclo-(Arg-Gly-Asp-D-Phe-
Lys(BOC-Aha)); RT [C] 27.7; FAB 817. After the BOC
group has been eliminated in HCl/dioxane, cyclo-(Arg-
Gly-Asp-D-Phe-Lys(N^ε-Aha)) × 2 TFA; RT [C] 14.76;
FAB 717 is obtained after the customary working-up.

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Cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-FCA-Aha)) × TFA; RT [B] 23.8; FAB 1075 is obtained, in analogy with Example 1, by subsequent reaction with FCA-N-succinimidyl ester.

The following are obtained in an analogous
5 manner by reacting cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Aha))

with FITC:

cyclo-(Arg-Gly-Asp-D-Phe-Lys (N^ε-FTH-Aha))

10 with acetic anhydride:

cyclo-(Arg-Gly-Asp-D-Phe-Lys (N^ε-Ac-Aha)) × TFA;
RT [B] 17.1; FAB 759;

Example 3

15

In analogy with Example 2, cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-BOC-Aha)-Gly) is obtained from cyclo-(Arg-Gly-Asp-D-Phe-Lys-Gly) [obtainable by cyclizing H-Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Lys(BOC)-Gly-OH to give
20 cyclo-(Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Lys(BOC)-Gly) and then eliminating the protecting groups] and BOC-Aha-N-succinimidyl ester;

After eliminating the BOC group in HCl/dioxane, cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Aha)-Gly) × 2 TFA is obtained
25 after the customary working-up.

The following is obtained, in analogy with Example 1, by subsequently reacting cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Aha)-Gly × 2 TFA with phenylpropionic acid N-succinimidyl ester:

30

Cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-PhEtCO-Aha)-Gly).

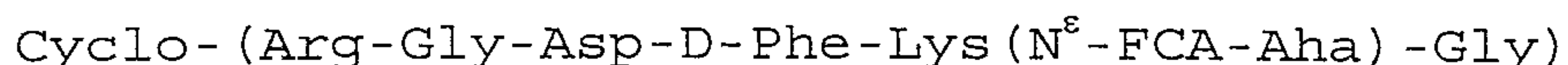
The following are obtained in an analogous manner by reacting cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Aha)-
35 Gly)

with octanoyl anhydride:

Cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-Oct-Aha)-Gly)

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with FCA-N-succinimidyl ester:



with FITC:



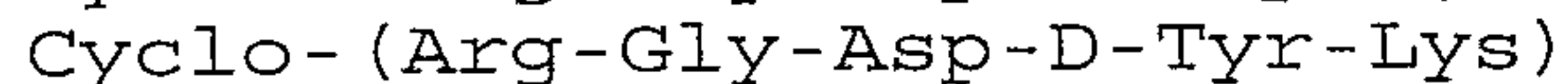
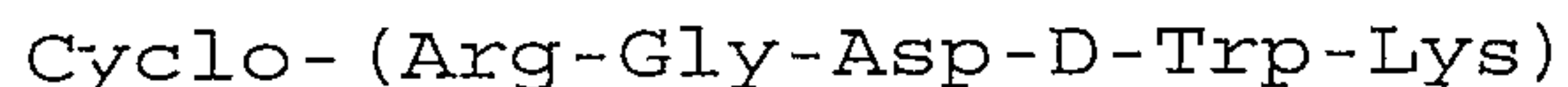
In analogy with Example 2, cyclo-(Arg-Gly-Asp-D-Phe-Val-Lys-(N^ε-BOC-Aha)) × TFA is obtained from cyclo-(Arg-Gly-Asp-D-Phe-Val-Lys) [obtainable by
10 cyclizing H-Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Val-Lys(BOC)-OH to give cyclo-(Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Val-Lys(BOC)) and then eliminating the protecting groups] and BOC-Aha-N-succinimidyl ester.

After the BOC group is eliminated in HCl/dioxane,
15 cyclo-(Arg-Gly-Asp-D-Phe-Val-Lys(N^ε-Aha)) × 2 TFA is obtained after the customary working-up.

In analogy with Example 1, cyclo-(Arg-Gly-Asp-D-Phe-Val-Lys(N^ε-PhEtCo-Aha)) is obtained by subsequently reacting cyclo-(Arg-Gly-Asp-D-Phe-Val-Lys
20 (N^ε-Aha)) × 2 TFA with phenylpropionic acid N-succinimidyl ester.

Example 4

In analogy with Example 2, reaction of
25 BOC-aminocaproic acid N-succinimidyl ester with the following cyclic compounds



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Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys)
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys)
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab)
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys)
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys)
 Cyclo-(Arg-Gly-Asp-Phe-D-Lys)
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys)
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys)
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys)
 Cyclo-(Arg-Gly-Asp-Phe-Dab)
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys)
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys)
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn)
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn)
 Cyclo-(Arg-Gly-Asp-D-Phe-Orn)
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn)
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn)
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn)
 Cyclo-(Arg-Gly-Asp-D-Trp-Dab)
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab)
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap)
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap)
 Cyclo-(Arg-Gly-Asp-D-Phe-Dap)
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap)
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap)
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap)

gives the following peptides:

Cyclo-(Arg-Gly-Asp-D-Trp-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys(S-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab(N^γ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys(S-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys(S-BOC-Aha))

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Cyclo-(Arg-Gly-Asp-Phe-D-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys(N^ε-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys(S-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-Dab(N^γ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys(S-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys(S-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn(N^δ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dab(N^γ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab(N^γ-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap(N^β-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap(N^β-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dap(N^β-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap(N^β-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap(N^β-BOC-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap(N^β-BOC-Aha)).

After eliminating the BOC group in HCl/dioxane, the following compounds ("A") are obtained:

5

Cyclo-(Arg-Gly-Asp-D-Trp-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys(S-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab(N^γ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys(S-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys(S-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys(N^ε-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys(S-Aha))

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Cyclo-(Arg-Gly-Asp-Phe-Dab(N^γ-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys(S-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys(S-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn(N^δ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dab(N^γ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab(N^γ-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap(N^β-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap(N^β-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dap(N^β-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap(N^β-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap(N^β-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap(N^β-Aha)).

The following are obtained by reaction with octanoyl anhydride:

Cyclo-(Arg-Gly-Asp-D-Trp-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab(N^γ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys(N^ε-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-Dab(N^γ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys(S-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn(N^δ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn(N^δ-Oct-Aha))

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Cyclo-(Arg-Gly-Asp-D-Phe-Orn(N^δ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn(N^δ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn(N^δ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn(N^δ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dab(N^γ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab(N^γ-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap(N^β-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap(N^β-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dap(N^β-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap(N^β-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap(N^β-Oct-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap(N^β-Oct-Aha)).

The following are obtained by analogous
 reaction of the "A" compounds with FCA-N-succinimidyl
 5 ester:

Cyclo-(Arg-Gly-Asp-D-Trp-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab(N^γ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys(N^ε-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-Dab(N^γ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys(S-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn(N^δ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn(N^δ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Orn(N^δ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn(N^δ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn(N^δ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn(N^δ-FCA-Aha))

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Cyclo-(Arg-Gly-Asp-D-Trp-Dab(N^γ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab(N^γ-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap(N^β-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap(N^β-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dap(N^β-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap(N^β-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap(N^β-FCA-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap(N^β-FCA-Aha)).

The following are obtained by analogous
 reaction of "A" compounds with O-acetylsalicylic acid
 5 N-succinimidyl ester:

Cyclo-(Arg-Gly-Asp-D-Trp-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Dab(N^γ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Lys(N^ε-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-D-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Phe-Dab(N^γ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Trp-D-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-Tyr-D-Cys(S-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Orn(N^δ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dab(N^γ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dab(N^γ-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-Dap(N^β-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-Dap(N^β-Ac-Sal-Aha))

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Cyclo-(Arg-Gly-Asp-D-Phe-Dap(N^β-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Trp-D-Dap(N^β-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Tyr-D-Dap(N^β-Ac-Sal-Aha))
 Cyclo-(Arg-Gly-Asp-D-Phe-D-Dap(N^β-Ac-Sal-Aha)),

with the deacetylated compounds, which are separated
 off under customary chromatographic conditions, also
 5 resulting at the same time.

Example 5

Cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-HSEtCO)) × TFA;
 10 RT [B] 18.54; FAB 692 is obtained, after the customary
 working-up, by eliminating the trityl group from cyclo-
 (Arg-Gly-Asp-D-Phe-Lys(N^ε-TrtSEtCO)) using TFA/thiophenol.

Example 6

2.0 g of succinic acid N-succinimidyl ester
 15 monomethyl ester and 0.5 g of triethylamine are added
 to a solution of 3.05 g of cyclo-(Arg-Gly-Asp-D-Phe-
 Lys) in 100 ml of dichloromethane. The mixture is
 stirred at room temperature for 5 hours, and cyclo-
 (Arg-Gly-Asp-D-Phe-Lys(N^ε-H₃COCO(CH₂)₂CO)) is obtained
 20 after the customary working-up. Cyclo-(Arg-Gly-Asp-D-
 Phe-Lys(N^ε-HOCO(CH₂)₂CO)) is obtained by hydrolysing the
 ester with aqueous potassium hydroxide. Cyclo-(Arg-Gly-
 Asp-D-Phe-Lys(N^ε-SuN-O-CO(CH₂)₂CO)) is obtained by
 subsequent reaction with HONSu in ethyl acetate. The
 25 following compound is obtained, in analogy with Example
 1, by reaction with cyclo-(Arg-Gly-Asp-D-Phe-Lys-Gly):
 cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-CO(CH₂)₂CO-R²)), in which
 R² is cyclo-(Arg-Gly-Asp-D-Phe-Lys(N^ε-)-Gly).

30 Example 7

0.5 ml of acetic acid and 0.5 g of palladium on
 active carbon are added to a solution of 1.17 g of
 cyclo-(Arg(Mtr)-Gly-Asp(OBut)-D-Phe-Lys(CBZ)) in 50 ml
 35 of dimethylacetamide, and the mixture is stirred for
 2 hours under a hydrogen atmosphere. Cyclo-

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(Arg(Mtr)Gly-Asp(OMe)-D-Phe-Lys) ("B"); RT [A, 30-80% acetonitrile] 18.6 is obtained after separating off the catalyst and after the customary working-up.

0.075 g of succinic anhydride are added to a solution of 0.3 g of "B" in 15 ml of DMF and the mixture is stirred at room temperature for 12 hours. 0.26 g of cyclo-(Arg(Mtr)-Gly-Asp(OMe)-D-Phe-Lys (N^ε-CO-(CH₂)₂-COOH)) ("C"); RT [A, 30-80% acetonitrile] 19.2; FAB 972 is obtained after the customary working-up.

0.1 g of EDCI × HCl, 0.075 g of HOBt and a solution of 0.3 g of "B" in 15 ml of DMF are added to a solution of 0.23 g of "B" in 20 ml of DMF, and the mixture is stirred for 12 hours. Cyclo-(Arg(Mtr)-Gly-Asp(OMe)-D-Phe-Lys)₂(COCH₂CH₂CO) ("D"); RT [A, 30-80% acetonitrile] 26.6; FAB 1826 is obtained after the customary working-up.

A solution consisting of 85.5% TFA, 2% water, 2.5% ethanedithiol, 5% phenol, 5% thioanisole and 0.25 g of "D" is stirred at room temperature for 24 hours. Cyclo-(Arg-Gly-Asp-D-Phe-Lys)₂(COCH₂CH₂CO); RT [A, 10-50% acetonitrile] 20.2; FAB 1289 is obtained after the customary working-up.

The following compound is obtained in an analogous manner by reacting

cyclo (Arg(Mtr)-Gly-Asp(OMe)-D-Phe-Lys(CBZ)) with the anhydride of dithiodipropionic acid (DTDB-OH) bis -N^ε-cyclo-(Arg-Gly-Asp-DPhe-Lys)-DtDP; RT 20.73; FAB 1382.

The following examples relate to pharmaceutical preparations:

Example A: Injection vials

A solution of 100 g of an active compound of the formula I and 5 g of disodium hydrogen phosphate is adjusted, in 3 l of double distilled water, to pH 6.5

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with 2 n hydrochloric acid, sterilized by filtration and used to fill injection vials; the solution is lyophilized, and the vials sealed, under sterile conditions. Each injection vial contains 5 mg of active compound.

Example B: Suppositories

A mixture of 20 g of an active compound of the formula I with 100 g of soya bean lecithin and 1400 g of cocoa butter is melted, poured into moulds and allowed to cool. Each suppository contains 20 mg of active compound.

Example C: Solution

A solution is prepared from 1 g of an active compound of the formula I, 9.38 g of $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$, 28.48 g of $\text{Na}_2\text{HPO}_4 \cdot 12 \text{H}_2\text{O}$ and 0.1 g of benzalkonium chloride in 940 ml of double distilled water. The solution is adjusted to pH 6.8, made up to 1 l and sterilized by irradiation. This solution can be used in the form of eyedrops.

Example D: Ointment

500 mg of an active compound of the formula I is mixed with 99.5 g of vaseline under aseptic conditions.

Example E: Tablets

A mixture of 1 kg of active compound of the formula I, 4 kg of lactose, 1.2 kg of potato starch, 0.2 kg of talc and 0.1 kg of magnesium stearate is compressed into tablets in a customary manner, such that each tablet contains 10 mg of active compound.

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Example F: Coated tablets

Tablets are compressed in analogy with Example E, with the tablets then being coated, in a customary manner, with a coating composed of sucrose, potato starch, talc, tragacanth and dye.

Example G: Capsules

Hard gelatine capsules are filled, in a customary manner, with 2 kg of active compound of the formula I such that each capsule contains 20 mg of the active compound.

Example H: Ampoules

A solution of 1 kg of active compound of the formula I in 60 l of double distilled water is sterilized by filtration and used to fill ampoules; the solution is lyophilized, and the ampoules are sealed, under sterile conditions. Each ampoule contains 10 mg of active compound.

Example I: Inhalation spray

25

14 g of active compound of the formula I are dissolved in 10 l of isotonic NaCl solution and the solution is used to fill commercially available spraying vessels which have a pumping mechanism. The solution can be sprayed into the mouth or nose. One spray burst (approximately 0.1 ml) corresponds to a dose of about 0.14 mg.

- 40 -

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: MERCK PATENT GESELLSCHAFT MIT BESCHRANKTER HAFTUNG
- (ii) TITLE OF INVENTION: CYCLOPEPTIDE DERIVATIVES
- (iii) NUMBER OF SEQUENCES: 171
- (iv) CORRESPONDENCE ADDRESS:
- (A) ADDRESSEE: FETHERSTONHAUGH & CO.
- (B) STREET: P.O. BOX 2999, STATION D
- (C) CITY: OTTAWA
- 10 (D) STATE: ONT
- (E) COUNTRY: CANADA
- (F) ZIP: K1P 5Y6
- (v) COMPUTER READABLE FORM:
- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: ASCII (text)
- (vi) CURRENT APPLICATION DATA:
- (A) APPLICATION NUMBER: CA 2,234,980
- 20 (B) FILING DATE: 14-OCT-1996
- (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
- (A) APPLICATION NUMBER: DE 195 38 741.4
- (B) FILING DATE: 18-OCT-1995
- (viii) ATTORNEY/AGENT INFORMATION:
- (A) NAME: FETHERSTONHAUGH & CO.
- (B) REGISTRATION NUMBER:
- (C) REFERENCE/DOCKET NUMBER: 26474-409
- (ix) TELECOMMUNICATION INFORMATION:
- 30 (A) TELEPHONE: (613)-235-4373
- (B) TELEFAX: (613)-232-8440

(2) INFORMATION FOR SEQ ID NO: 1:

- (i) SEQUENCE CHARACTERISTICS:

26474-409

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- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (v) FRAGMENT TYPE: internal
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /product= "Xaa"
/label= D-Phe
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /product= "Xaa"
/label= Lys-N-eps-Sal
/note= "epsilon amino group modified with salicyloyl"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Arg	Gly	Asp	Xaa	Xaa
1			5	
- (2) INFORMATION FOR SEQ ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: circular
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (v) FRAGMENT TYPE: internal
 - (ix) FEATURE:

- 42 -

(A) NAME/KEY: Modified-site
 (B) LOCATION:4
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= Lys-N-PhEtCO

10 /note= "epsilon amino group modified with Ph-Et-CO"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Arg Gly Asp Xaa Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular

20

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:4
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Phe

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= Lys-N-eps-TCP
 /note= "epsilon amino group modified with

- 43 -

3,3,3-tris-(4-chlorophenyl)-propionyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

20 (B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-TrtSEtCO

/note= "epsilon amino group modified with

S-tritylmercaptopropionyl"

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

40 (C) STRANDEDNESS: single

- 44 -

(D) TOPOLOGY: circular
(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTI-SENSE: NO
(v) FRAGMENT TYPE: internal
(ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION:4
(D) OTHER INFORMATION:/product= "Xaa"

10

/label= D-Phe

(ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION:5
(D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-eps-CBZ
/note= "epsilon amino group modified with
benzyloxycarbonyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

20

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: circular

30

(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTI-SENSE: NO
(v) FRAGMENT TYPE: internal
(ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION:4

- 45 -

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-eps-Oct

/note= "epsilon amino group modified with octanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

10 Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

20 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

30 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-eps-Ac

/note= "epsilon amino group modified with acetyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

- 46 -

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

20 /label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-eps-FCA

/note= "epsilon amino group modified with
fluoresceincarbonyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

30 Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

40 (ii) MOLECULE TYPE: peptide

- 47 -

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-eps-FTH

/note= "epsilon amino group modified with

fluorescein-NH-C(=S) -"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

- 48 -

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= N-Me-Lys

/note= "N-methyl-lysine"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Arg Gly Asp Xaa Xaa
 1 5

10

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

20

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

30

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= NMe-Lys-N-FTH

/note=

"N-methyl-lysine-N-epsilon-(fluorescein-NH-C(=S)-)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

Arg Gly Asp Xaa Xaa
 1 5

- 49 -

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20

(D) OTHER INFORMATION:/product= "Xaa"

/label= NMe-Lys-N-CBZ

/note= "N-methyl-lysine-N-epsilon-(benzyloxycarbonyl-)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 13:

30

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

- 50 -

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"

10

/label= Lys-N-Boc-Aha
/note= "epsilon amino group modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Arg Gly Asp Xaa Xaa
1 5

20

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-eps-Aha

/note= "epsilon amino group modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Arg	Gly	Asp	Xaa	Xaa
1			5	

10 (2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

30 /label= Lys-N-FCA-Aha

/note= "epsilon amino group modified with

fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

Arg	Gly	Asp	Xaa	Xaa
1			5	

40 (2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:

- 52 -

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

10

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-FTH-Aha

/note= "epsilon amino group modified with

20

fluorescein-NH-C(=S)-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

- 53 -

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"

10

/label= Lys-N-Ac-Aha

/note= "epsilon amino group modified with

acetyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 18:

20

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-BOC-Aha

/note= "epsilon amino group modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

Arg Gly Asp Xaa Xaa Gly
1 5

10

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-Aha

/note= "epsilon amino group modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

Arg Gly Asp Xaa Xaa Gly
1 5

40

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

- 55 -

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

10

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-PhEtCOAha

/note= "epsilon amino group modified with

20

phenylpropionyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Arg Gly Asp Xaa Xaa Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-Oct-Aha
/note= "epsilon amino group modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

Arg Gly Asp Xaa Xaa Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-FCA-Aha

/note= "epsilon amino group modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Arg Gly Asp Xaa Xaa Gly
1 5

10

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-FTH-Aha

/note= "epsilon amino group modified with
fluorescein-NH-C(=S)-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

Arg Gly Asp Xaa Xaa Gly
1 5

40

(2) INFORMATION FOR SEQ ID NO: 24:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:6

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-BOC-Aha

20 /note= "epsilon amino group modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

Arg Gly Asp Xaa Val Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 25:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:6

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-Aha
/note= "epsilon amino group modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

Arg Gly Asp Xaa Val Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 26:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:6

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-PhEtCOAha

/note= "epsilon amino group modified with
phenylpropionylamino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

Arg Gly Asp Xaa Val Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-BOC-Aha

/note= "epsilon amino group modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

Arg Gly Asp Xaa Xaa
1 5

40

(2) INFORMATION FOR SEQ ID NO: 28:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-BOC-Aha

20

/note= "epsilon amino group modified with
tert.-butoxycarbonyl-aminohexa..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 29:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Lys-N-BOC-Aha
/note= "epsilon amino group of D-Lys modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

Arg Gly Asp Xaa Xaa
1 5

20 (2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Cys-S-BOC-Aha

/note= "thiol group modified with

tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

Arg	Gly	Asp	Xaa	Xaa
1				5

10

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= DbU-N-BOC-Aha

/note= "gamma amino group of DbU (2,4-diaminobutyric
acid)

modified with ter.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

Arg	Gly	Asp	Xaa	Xaa
1				5

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(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-BOC-Aha

/note= "thiol group of D-Cys modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-BOC-Aha

/note= "thiol group of D-Cys modified with

tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-BOC-Aha

/note= "epsilon amino group of D-Lys modified with

- 66 -

tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

Arg	Gly	Asp	Phe	Xaa
1				5

(2) INFORMATION FOR SEQ ID NO: 35:

10 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

20 (A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-BOC-Aha

/note= "epsilon amino group of D-lysine modified with

tert.-butyloxy-carbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

Arg	Gly	Asp	Trp	Xaa
1				5

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-BOC-Aha

/note= "epsilon amino group of D-Lys modified with
tert.-butyloxy-carbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

10 Arg Gly Asp Tyr Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

20 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

30 /label= D-Cys-S-BOC-Aha
/note= "thiol group of D-Cys modified with
tert.-butyloxycarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

Arg Gly Asp Phe Xaa
1 5

40 (2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

10

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-BOC-Aha

/note= "gamma amino group of Dbu modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

Arg Gly Asp Phe Xaa
1 5

20

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

30

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-BOC-Aha

/note= "thiol group of D-Cys modified with

- 69 -

tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

Arg	Gly	Asp	Trp	Xaa
1				5

(2) INFORMATION FOR SEQ ID NO: 40:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

20

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-BOC-Aha

/note= "thiol group of D-Cys modified with

tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

Arg	Gly	Asp	Tyr	Xaa
1				5

30

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

40

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= Orn-N-BOC-Aha/note= "delta amino group of Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-BOC-Aha

/note= "delta amino group of Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-BOC-Aha

/note= "delta amino group of Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

Arg Gly Asp Xaa Xaa
1 5

40

(2) INFORMATION FOR SEQ ID NO: 44:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-BOC-Aha

20

/note= "delta amino group of D-Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 45:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Orn-N-BOC-Aha
/note= "delta amino group of D-Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

Arg	Gly	Asp	Xaa	Xaa
1			5	

20 (2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-BOC-Aha

/note= "delta amino group of D-Orn modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30 (B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-BOC-Aha

/note= "gamma amino group of Dbu modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

Arg Gly Asp Xaa Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-BOC-Aha

/note= "gamma amino group of Dbu modified with

tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

Arg	Gly	Asp	Xaa	Xaa
1			5	

30 (2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-BOC-Aha

/note= "beta amino group of Dpr modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"
 /label= Dpr-N-BOC-Aha
 /note= "beta amino group of Dpr modified with
 tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

10 Arg Gly Asp Xaa Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Tyr

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"
 /label= Dpr-N-BOC-Aha
 /note= "beta amino group of Dpr modified with
 tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

30 Arg Gly Asp Xaa Xaa
 1 5

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(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-BOC-Aha

/note= "beta amino group of D-Dpr modified with

tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

Arg	Gly	Asp	Xaa	Xaa
1			5	

30 (2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-BOC-Aha

/note= "beta amino group of D-Dpr modified with

tert.-butyloxycarbonyl-amino hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

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(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-BOC-Aha

/note= "beta amino group of D-Dpr modified with
tert.-butyloxycarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-Aha

/note= "epsilon amino group of Lys modified with

aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

Arg Gly Asp Xaa Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-Aha

/note= "epsilon amino group of Lys modified with

aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

Arg	Gly	Asp	Xaa	Xaa
1			5	

30 (2) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Lys-N-Aha
/note= "epsilon amino group of D-Lys modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

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(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Cys-S-Aha

/note= "thiol group of Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

Arg	Gly	Asp	Xaa	Xaa
1			5	

10

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Aha

/note= "gamma amino group of Dbu modified with

aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

Arg	Gly	Asp	Xaa	Xaa
1			5	

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(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Aha

/note= "thiol group of D-Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 61:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Cys-S-Aha
/note= "thiol group of D-Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 62:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Lys-N-Aha/note= "epsilon amino group of D-Lys modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

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Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

10 (B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-Aha

/note= "epsilon amino group of D-Lys modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

Arg Gly Asp Trp Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 64:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

40 (ix) FEATURE:

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(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-Aha

/note= "epsilon aminogroup of D-Lys modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

Arg Gly Asp Tyr Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Aha

/note= "thiol group of D-Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 66:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

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(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

10 /label= DbU-N-Aha

/note= "gamma amino group of DbU modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 67:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Aha

/note= "thiol group of D-Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

Arg Gly Asp Trp Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Aha

/note= "thiol group of D-Cys modified with aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

20 Arg Gly Asp Tyr Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

30 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

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/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-Aha

/note= "delta amino group of Orn modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

10 Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 70:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

20 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

30 /label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-Aha

/note= "delta amino group of Orn modified with
aminohexanoyl"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

20

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-Aha

/note= "delta amino group of Orn modified with
aminohexanoyl"

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 72:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

40

(B) TYPE: amino acid

(C) STRANDEDNESS: single

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(D) TOPOLOGY: circular
(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTI-SENSE: NO
(v) FRAGMENT TYPE: internal
(ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION:4
(D) OTHER INFORMATION:/product= "Xaa"

10 /label= D-Trp
(ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION:5
(D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Orn-N-Aha
 /note= "delta amino group of D-Orn modified with
 aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

20 Arg Gly Asp Xaa Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: circular

30 (ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTI-SENSE: NO
(v) FRAGMENT TYPE: internal
(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION:4

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(D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Orn-N-Aha

/note= "delta amino group of D-Orn modified with
 aminohexanoyl"

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

Arg Gly Asp Xaa Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

20 (B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

30 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Orn-N-Aha

/note= "delta amino group of D-Orn modified with

- 94 -

aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 75:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

20

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Aha

/note= "gamma amino group of Dbu modified with
aminohexanoyl"

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

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(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Aha

/note= "beta amino group of Dpr modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

20 Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Aha

/note= "beta amino group of Dpr modified with

aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 78:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Aha

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/note= "beta amino group of Dpr modifies with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

Arg Gly Asp Xaa Xaa
1 5

10 (2) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

20 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-Aha

30 /note= "beta amino group of D-Dpr modified with
aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 80:

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

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(B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular
 (ii) MOLECULE TYPE: peptide
 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 (v) FRAGMENT TYPE: internal
 (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION:4
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Tyr
 (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Dpr-N-Aha
 /note= "beta amino group of D-Dpr modified with
 aminohexanoyl"
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:
 Arg Gly Asp Xaa Xaa
 1 5
 (2) INFORMATION FOR SEQ ID NO: 81:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular
 (ii) MOLECULE TYPE: peptide
 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 (v) FRAGMENT TYPE: internal
 (ix) FEATURE:

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(A) NAME/KEY: Modified-site
 (B) LOCATION:4
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Dpr-N-Aha

10 /note= "beta amino group of D-Dpr modified with
 aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

Arg Gly Asp Xaa Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 82:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

30 (A) NAME/KEY: Modified-site
 (B) LOCATION:4
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"

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/label= Lys-N-Oct-Aha

/note= "epsilon amino group of Lys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

Arg Gly Asp Xaa Xaa
1 5

10 (2) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

30 /label= Lys-N-Oct-Aha

/note= "epsilon amino group of Lys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

Arg Gly Asp Xaa Xaa
1 5

40 (2) INFORMATION FOR SEQ ID NO: 84:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

10

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Lys-N-Oct-Aha

/note= "epsilon amino group of D-Lys modified with

20

octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 85:

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"
/label= Cys-S-Oct-Aha
/note= "thiol group of Cys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Oct-Aha

/note= "gamma amino group of Dbu modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Oct-Aha

/note= "thiol group of D-Cys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

Arg Gly Asp Xaa Xaa
1 5

40

(2) INFORMATION FOR SEQ ID NO: 88:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Oct-Aha

20

/note= "thiol group of D-Cys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 89:

30

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-Oct-Aha

/note= "epsilon amino group of D-Lys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

10 Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

20 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-Oct-Aha

30 /note= "epsilon amino group of D-Lys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

Arg Gly Asp Trp Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 91:

40 (i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular
 (ii) MOLECULE TYPE: peptide
 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 (v) FRAGMENT TYPE: internal
 (ix) FEATURE:

10 (A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Lys-N-Oct-Aha
 /note= "epsilon amino group of D-Lys modified with
 octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

Arg	Gly	Asp	Tyr	Xaa
1				5

20 (2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: circular
 (ii) MOLECULE TYPE: peptide

30 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 (v) FRAGMENT TYPE: internal
 (ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION:5
 (D) OTHER INFORMATION:/product= "Xaa"
 /label= D-Cys-S-Oct-Aha

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/note= "thiol group of D-Cys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

Arg Gly Asp Phe Xaa
1 5

10 (2) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

20 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Oct-Aha

/note= "gamma amino group of Dbu modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

Arg Gly Asp Phe Xaa
1 5

30

(2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

40 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Oct-Aha

/note= "thiol group of D-Cys modified with
octanoyl-amino-hexanoyl"

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

Arg Gly Asp Trp Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

20 (B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-Oct-Aha

/note= "thiol group of D-Cys modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

Arg Gly Asp Tyr Xaa
1 5

40 (2) INFORMATION FOR SEQ ID NO: 96:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-Oct-Aha

20 /note= "delta amino group of Orn modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 97:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= Orn-N-Oct-Aha
/note= "delta amino group of Orn modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

Arg	Gly	Asp	Xaa	Xaa
1			5	

20 (2) INFORMATION FOR SEQ ID NO: 98:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-Oct-Aha

/note= "delta amino group of Orn modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-Oct-Aha

/note= "delta amino group of D-Orn modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

Arg Gly Asp Xaa Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 100:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

10 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

20 /label= D-Orn-N-Oct-Aha

/note= "delta amino group of D-Orn modified with

octanoyl-amino-hexanyol"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 101:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

30

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-Oct-Aha

/note= "delta amino group of D-Orn modified with

octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

Arg Gly Asp Xaa Xaa
1 5

20 (2) INFORMATION FOR SEQ ID NO: 102:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Oct-Aha

/note= "gamma amino group of Dbu modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-Oct-Aha

/note= "gamma amino group of Dbu modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

Arg Gly Asp Xaa Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Oct-Aha

/note= "beta amino group of Dpr modified with

octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 105:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Oct-Aha

/note= "beta amino group of Dpr modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 106:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

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(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-Oct-Aha

/note= "beta amino group of Dpr modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 107:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

20

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

30

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-Oct-Aha

/note= "beta amino group of D-Dpr modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

Arg Gly Asp Xaa Xaa
1 5

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(2) INFORMATION FOR SEQ ID NO: 108:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:4
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Tyr

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION:5
- (D) OTHER INFORMATION:/product= "Xaa"
/label= D-Dpr-N-Oct-Aha
/note= "beta amino group of D-Dpr modified with
octanoyl-amino-hexanoyl"

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

Arg Gly Asp Xaa Xaa
1 5

30

(2) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 119 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Dpr-N-Oct-Aha
/note= "beta amino group of D-Dpr modified with
octanoyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

- 120 -

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-FCA-Aha

/note= "epsilon amino group of Lys modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-FCA-Aha

/note= "epsilon amino group of Lys modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

Arg Gly Asp Xaa Xaa
1 5

- 121 -

(2) INFORMATION FOR SEQ ID NO: 112:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-FCA-Aha

/note= "epsilon amino group of D-Lys modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 122 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= Cys-S-FCA-Aha/note= "thiol group of Cys modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 114:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

- 123 -

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-FCA-Aha

/note= "gamma amino group of Dbu modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 115:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-FCA-Aha

/note= "thiol group of D-Cys modified with
fluoresceincarbonyl-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

Arg Gly Asp Xaa Xaa
1 5

- 124 -

(2) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-FCA-Aha

/note= "thiol group of D-Cys modified with

fluoresceincarbonyl-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

Arg	Gly	Asp	Xaa	Xaa
1			5	

30 (2) INFORMATION FOR SEQ ID NO: 117:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 125 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-FCA-Aha

/note= "epsilon amino group of D-Lys modified with
fluoresceincarbonyl-amino-hexanoyl"

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

20 (B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-FCA-Aha

/note= "epsilon amino group of D-Lys modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

Arg Gly Asp Trp Xaa
1 5

40 (2) INFORMATION FOR SEQ ID NO: 119:

- 126 -

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-FCA-Aha

/note= "epsilon amino group of D-Lys modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

Arg Gly Asp Tyr Xaa
1 5

20

(2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

30

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

- 127 -

/label= D-Cys-S-FCA-Aha

/note= "thiol group of D-Cys modified with
fluoresceincarbonyl-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

Arg Gly Asp Phe Xaa
1 5

10 (2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-FCA-Aha

/note= "gamma amino group of Dbu modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

30 Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

40 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

- 128 -

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-FCA-Aha

/note= "thiol group of D-Cys modified with

10 fluoresceincarbonyl-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

Arg Gly Asp Trp Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

30 (B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-FCA-Aha

/note= "thiol group of D-Cys modified with

fluoresceincarbonyl-amino-hexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

Arg Gly Asp Tyr Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 124:

- 129 -

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-FCA-Aha

20

/note= "delta amino group of Orn modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

- 130 -

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

10

/label= Orn-N-FCA-Aha

/note= "delta amino group of Orn modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 126:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

- 131 -

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-FCA-Aha

/note= "delta amino group of Orn modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 127:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-FCA-Aha

/note= "delta amino group of D-Orn modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

Arg Gly Asp Xaa Xaa
1 5

40

(2) INFORMATION FOR SEQ ID NO: 128:

- 132 -

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-FCA-Aha

20

/note= "delta amino group of D-Orn modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 129:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 133 -

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Orn-N-FCA-Aha/note= "delta amino group of D-Orn modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

Arg Gly Asp Xaa Xaa
1 5

20 (2) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

- 134 -

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= DbU-N-FCA-Aha

/note= "gamma amino group of DbU modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= DbU-N-FCA-Aha

/note= "gamma amino group of DbU modified with
fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

Arg Gly Asp Xaa Xaa
1 5

- 135 -

(2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-FCA-Aha

/note= "beta amino group of Dpr modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 133:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 136 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-FCA-Aha

/note= "beta amino group of Dpr modified with

fluoresceincarbonyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

- 137 -

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-FCA-Aha

/note= "beta amino group of Dpr modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 135:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-FCA-Aha

/note= "beta amino group of D-Dpr modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

Arg Gly Asp Xaa Xaa
1 5

- 138 -

(2) INFORMATION FOR SEQ ID NO: 136:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-FCA-Aha

/note= "beta amino group of D-Dpr modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 137:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 139 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-FCA-Aha

/note= "beta amino group of D-Dpr modified with
fluoresceincarbonyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

- 140 -

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-AcSal-Aha

/note= "epsilon amino group of Lys modified with
acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 139:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-AcSal-Aha

/note= "epsilon amino group of Lys modified with
Acetylsalicyloyl-amino-hexanoyl "

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

Arg Gly Asp Xaa Xaa
1 5

- 141 -

(2) INFORMATION FOR SEQ ID NO: 140:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-AcSalAh

/note= "epsilon amino group of D-Lys modified with
acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 141:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 142 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Cys-S-AcSal-Aha

/note= "thiol group of Cys modified with

acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 142:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

- 143 -

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-AcSal-Aha

/note= "gamma amino group of Dbu modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

Arg Gly Asp Xaa Xaa

1

5

10

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

20

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site

- 144 -

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-AcSal-A

/note= "thiol group of D-Cys modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 144:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-AcSal-A

/note= "thiol group of D-Cys modified with
acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

Arg Gly Asp Xaa Xaa
1 5

- 145 -

(2) INFORMATION FOR SEQ ID NO: 145:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-AcSal-A

/note= "epsilon amino group of D-Lys modified with
acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

20 Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 146:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

- 146 -

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-AcSal-A

/note= "epsilon amino group of D-Lys modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

Arg Gly Asp Trp Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 147:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Lys-N-AcSal-A

/note= "epsilon amino group of D-Lys modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

30

Arg Gly Asp Tyr Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 148:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

40

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

- 147 -

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-AcSal-A

10 /note= "thiol group of D-Cys modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

Arg Gly Asp Phe Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 149:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

30 (A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-AcSal-Aha

/note= "gamma amino group of Dbu modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

Arg Gly Asp Phe Xaa
1 5

- 148 -

(2) INFORMATION FOR SEQ ID NO: 150:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-AcSal-A

/note= "thiol group of D-cys modified with
acetylsalicyloyl-amino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

20 Arg Gly Asp Trp Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 151:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

- 149 -

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Cys-S-AcSal-A

/note= "thiol group of D-Cys modified with
acetylsalicyloylamino-hexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

Arg Gly Asp Tyr Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 152:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-AcSal-Aha

/note= "delta amino group of Orn modified with
acteylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

Arg Gly Asp Xaa Xaa
1 5

40

(2) INFORMATION FOR SEQ ID NO: 153:

- 150 -

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Orn-N-AcSal-Aha

20 /note= "delta amino group of Orn modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 154:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 151 -

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= Orn-N-AcSal-Aha
/note= "delta amino group of Orn modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

Arg	Gly	Asp	Xaa	Xaa
1			5	

20 (2) INFORMATION FOR SEQ ID NO: 155:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

- 152 -

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-AcSal-A

/note= "delta amino group of D-Orn modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

Arg Gly Asp Xaa Xaa
1 5

10

(2) INFORMATION FOR SEQ ID NO: 156:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-AcSal-A

/note= "delta amino group of D-Orn modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

Arg Gly Asp Xaa Xaa
1 5

- 153 -

(2) INFORMATION FOR SEQ ID NO: 157:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Orn-N-AcSal-A

/note= "delta amino group of D-Orn modified with

acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 158:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

- 154 -

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-AcSal-Aha

/note= "gamma amino group of Dbu modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 159:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

- 155 -

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dbu-N-AcSal-Aha

/note= "gamma amino group of Dbu modified with
acetylsalicyloyl-aminohexan..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 160:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-AcSal-Aha

/note= "beta amino group of Dpr modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

Arg Gly Asp Xaa Xaa
1 5

- 156 -

(2) INFORMATION FOR SEQ ID NO: 161:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-AcSal-Aha

/note= "beta amino group of Dpr modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

Arg Gly Asp Xaa Xaa
1 5

30 (2) INFORMATION FOR SEQ ID NO: 162:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Dpr-N-AcSal-Aha

/note= "beta amino group of Dpr modified with
acetylsalicyloyl-aminohexanoyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 163:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Trp

(ix) FEATURE:

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(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-AcSal-A

/note= "beta amino group of D-Dpr modified with
acetylsalicyloyl-aminohexa..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 164:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Tyr

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-AcSal-A

/note= "beta amino group of D-Dpr modified with
acetylsalicyloyl-aminohexa..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

Arg Gly Asp Xaa Xaa
1 5

- 159 -

(2) INFORMATION FOR SEQ ID NO: 165:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

10 (iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

20 (D) OTHER INFORMATION:/product= "Xaa"

/label= D-Dpr-N-AcSal-A

/note= "beta amino group of D-Dpr modified with
acetylsalicyloyl-aminohexa..."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 166:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-HSEtCO/note= "epsilon amino group of Lys modified with
mercaptopropionyl"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

Arg Gly Asp Xaa Xaa
1 5

20 (2) INFORMATION FOR SEQ ID NO: 167:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-CO-sucOMe

/note= "epsilon amino group of Lys modified with

MeO-CO-(CH2)2-CO"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

Arg	Gly	Asp	Xaa	Xaa
1			5	

10

(2) INFORMATION FOR SEQ ID NO: 168:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

30

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-CO-suc-OH

/note= "epsilon amino group of Lys modified with

HOOC-(CH2)2-CO-"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

Arg	Gly	Asp	Xaa	Xaa
1			5	

(2) INFORMATION FOR SEQ ID NO: 169:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

10 (ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"

/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-R1

20 /note= "epsilon amino group of Lys modified with
R2-CO-(CH2)2-CO-, wherein R2 is
cyclo-(Arg-Gly-Asp-D-Phe-Lys-(N-epsilon-)-Gly) "

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 170:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(v) FRAGMENT TYPE: internal

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:5

10 (D) OTHER INFORMATION:/product= "Xaa"
/label= Lys-N-R1
/note= "epsilon amino group of Lys modified with
cyclo(Arg-Gly-Asp-D-Phe-Lys)-CO-CH2-CH2-CO-"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

Arg Gly Asp Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO: 171:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: circular

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(v) FRAGMENT TYPE: internal

30

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION:4

(D) OTHER INFORMATION:/product= "Xaa"
/label= D-Phe

(ix) FEATURE:

(A) NAME/KEY: Peptide

(B) LOCATION:5

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(D) OTHER INFORMATION:/product= "Xaa"

/label= Lys-N-R1

/note= "epsilon amino group of Lys modified with

cyclo(Arg-Gly-Asp-D-Phe-Lys(N-epsilon)-CO-(CH₂)₂-S-S-(CH₂)₂-CO-)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

Arg	Gly	Asp	Xaa	Xaa
1			5	

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CLAIMS:

1. A compound of the general formula I:



wherein:

5 Q^1, Q^2 are, in each case independently of each other, either absent or $-NH-(CH_2)_n-CO-$;

R^1, R^2 are, in each case independently of each other, either absent or cyclo-(Arg-Gly-Asp-Z), wherein Z is bonded in the side chain to Q^1 or Q^2 or, if Q^1, Q^2 or Q^1 and Q^2 is/are absent, to X, and wherein at least one of the radicals R^1 or R^2 must always be present;

X is $-CO-R^{18}-CO-$, and if R^1-Q^1- or R^2-Q^2- is absent, $R^{10}, R^{13}, R^{16},$ Het-CO or a fluorescent dye residue which is linked by way of a $-CONH-, -COO-, -NH-C(=S)-NH-, -NH-C(=O)-NH-, -SO_2NH-$ or $-NHCO-$ bond;

Z is, in each case for R^1 and R^2 independently of each other, an amino acid residue or a di-, tri- or tetra-peptide residue, wherein the amino acids are selected, independently of each other, from the group consisting of Ala, Asn, Asp, Arg, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, Val and M, wherein the amino acids can also be derivatized to N-methyl, N-ethyl, N-propyl, N-benzyl or C_α -methyl derivatives, and the amino acid residues are linked to each other, in peptide manner, by way of the α -amino and α -carboxyl groups;

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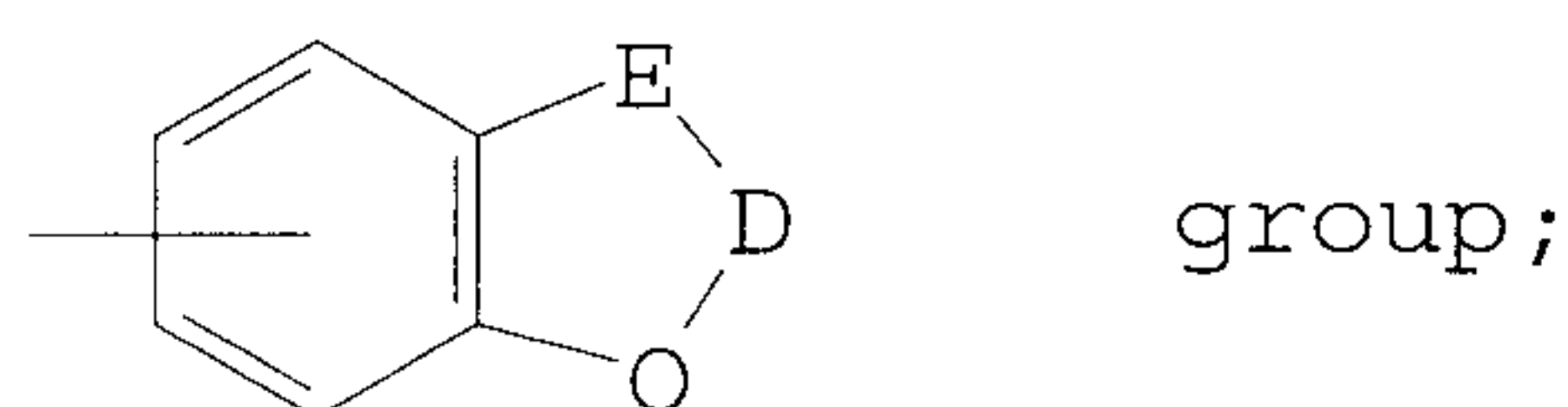
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- M is always present and is $\text{NH}(\text{R}^8)-\text{CH}(\text{R}^3)-\text{COOH}$;
- R^3 is $-\text{R}^5-\text{R}^4$, $-\text{R}^6-\text{R}^4$ or $-\text{R}^7-\text{R}^4$;
- R^4 is OH, NH_2 , SH or COOH;
- R^5 is alkylene having 1-6 carbon atoms;
- 5 R^6 is alkylenephenylene having 7-14 carbon atoms;
- R^7 is alkylenephenylalkylene having 8-15 carbon atoms;
- R^8 is H, A or alkylenephenyl having 7-12 carbon atoms;
- 10 A is alkyl having 1-6 carbon atoms;
- R^{10} is alkanoyl having 1-18 carbon atoms which is substituted once by COOH, COOA, SR^{11} or $\text{NR}^{12'}$;
- R^{11} is trityl, pyridyl-2-thio or alkylthio having 1-6 carbon atoms;
- 15 R^{12} is H, alkyl having 1-8 carbon atoms or an amino-protecting group;
- $\text{R}^{12'}$ is alkyl having 1-8 carbon atoms or an amino-protecting group;
- R^{13} is aroyl having 7-11 carbon atoms which is
20 unsubstituted or substituted once or twice by alkyl having 1-6 carbon atoms, alkoxy having 1-4 carbon atoms, alkanoyl having 1-8 carbon atoms, Hal, SR^{14} or $\text{NR}^{15}\text{R}^{15'}$;
- R^{14} is H or A;
- 25 R^{15} , $\text{R}^{15'}$ are, in each case independently of each other, H or A;

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R^{16} is aralkanoyl having 7-19 carbon atoms which is unsubstituted or substituted once, twice or three times in the aryl moiety by Hal, alkoxy having 1-6 carbon atoms or OH, and wherein the aryl moiety can also be a:



E is CH_2 or O;

10 D is carbonyl or $[\text{C}(\text{R}^{17}\text{R}^{17'})]_m$;

R^{17} , $\text{R}^{17'}$ are, in each case independently of each other, H or A;

15 R^{18} is absent, or is R^{19} , R^{20} , $\text{R}^{19}-\text{R}^{20}-\text{R}^{19}$, or phenylene which is unsubstituted or substituted once or twice by R^5 , wherein the chain length of R^5 is in each case independent of each other;

R^{19} is alkylene having 1-8 carbon atoms, wherein 1 or 2 methylene groups can be replaced by S, $-\text{CH}=\text{CH}-$ or $-\text{C}\equiv\text{C}-$;

20 R^{20} is cycloalkylene having 3-7 carbon atoms;

Hal is F, Cl, Br or I;

25 Het is a mononuclear or binuclear saturated, unsaturated or aromatic heterocycle having from 1 to 4 N, O, S atoms or a mixture thereof, bonded via N or C, which can be unsubstituted or substituted once, twice or three times by Hal, A,

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R^3 , $NR^{15}R^{15'}$, CN, NO_2 , carbonyl oxygen or a mixture thereof;

n is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10; and

m is 1 or 2;

5 wherein, provided that the residues are residues of optically active amino acids and amino acid derivatives, both the D and the L forms are included; or a salt thereof.

2. A compound of the general formula I according to
10 claim 1, wherein:

a) Q^1 , Q^2 and R^2 are absent,

R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is salicyloyl;

b) Q^1 and Q^2 are absent,

15 R^1 and R^2 are cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is $-CO-(CH_2)_2-CO-$;

c) Q^2 and R^2 are absent,

Q^1 is $-NH-(CH_2)_5-CO-$,

20 R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is fluoresceinoyl; or

d) Q^2 and R^2 are absent,

Q^1 is $-NH-(CH_2)_5-CO-$,

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R^1 is cyclo-(Arg-Gly-Asp-D-Phe-Lys), and

X is tert-butyloxycarbonyl;

or a physiologically harmless salt thereof.

3. A process for preparing a compound of the general
5 formula I according to claim 1, and a salt thereof,
comprising:

a) reacting a compound of the general formula II:

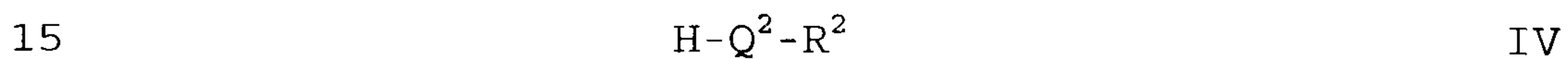


wherein Q^1 and R^1 are as defined in claim 1, in an acylation
10 reaction, with a compound of the general formula III:



wherein X is as defined in claim 1, and L is Cl, Br, I or a
free or reactive functionally modified OH group; or

b) reacting a compound of the general formula IV:



wherein Q^2 and R^2 are as defined in claim 1, in an acylation
reaction, with a compound of the general formula V:



wherein R^1 , Q^1 , X are as defined in claim 1, and L is as
20 defined above; or

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c) reacting a compound of the general formula II as defined above, in an addition reaction, with a compound of the general formula VI:

X-U

VI

5 wherein X is as defined in claim 1, and U is $-N=C=O$, $-N=C=S$ or maleimidyl; or

d) liberating a compound of the general formula I from a functional derivative thereof by treatment under solvolysing or hydrogenolysing conditions; or

10 e) converting a basic or acidic compound of the general formula I into a salt thereof by treatment with an acid or base.

4. A process for producing a pharmaceutical preparation, comprising bringing into a suitable dosage form
15 a compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof together with at least one solid, liquid or semisolid carrier substance or auxiliary substance.

5. A pharmaceutical preparation comprising at least
20 one compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof and at least one solid, liquid or semisolid carrier substance or auxiliary substance.

6. Use of a compound of the general formula I
25 according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, for the prevention, control or treatment of a disease for which integrin receptor inhibition is indicated.

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7. Use according to claim 6, wherein the disease is thrombosis, myocardial infarct, arteriosclerosis, an inflammation, stroke, angina pectoris, a tumour, an osteolytic disease, a pathologically angiogenic disease, an ophthalmological disease, diabetic retinopathy, macular degeneration, myopia, ocular histoplasmosis, rheumatic arthritis, osteoarthritis, rubeotic glaucoma, ulcerative colitis, Crohn's disease, atherosclerosis, psoriasis, restenosis following angioplasty, a viral infection, a bacterial infection, a fungal infection or acute liver failure.
8. Use according to claim 7, wherein the osteolytic disease is osteoporosis.
9. Use of a compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, for supporting the healing processes in wound healing.
10. Use of a compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, as an integrin inhibitor.
11. Use according to claim 10, for inhibiting the interaction of an α_v -, β_3 - or β_5 -integrin receptor with a ligand.
12. Use according to claim 11, for inhibiting the binding of fibrogen to the β_3 -integrin receptor.
13. Use according to claim 11, wherein the integrin is $\alpha_v\beta_3$, $\alpha_v\beta_5$, $\alpha_{11b}\beta_3$, $\alpha_v\beta_1$, $\alpha_v\beta_6$ or $\alpha_v\beta_8$.
14. Use of a compound of the general formula I

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according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, for preparing a medicament for the prevention, control or treatment of a disease for which integrin receptor
5 inhibition is indicated.

15. Use according to claim 14, wherein the disease is thrombosis, myocardial infarct, arteriosclerosis, an inflammation, stroke, angina pectoris, a tumour, an osteolytic disease, a pathologically angiogenic disease, an
10 ophthalmological disease, diabetic retinopathy, macular degeneration, myopia, ocular histoplasmosis, rheumatic arthritis, osteoarthritis, rubeotic glaucoma, ulcerative colitis, Crohn's disease, atherosclerosis, psoriasis, restenosis following angioplasty, a viral infection, a
15 bacterial infection, a fungal infection or acute liver failure.

16. Use according to claim 15, wherein the osteolytic disease is osteoporosis.

17. Use of a compound of the general formula I
20 according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, for preparing a medicament for supporting the healing processes in wound healing.

18. Use of a compound of the general formula I
25 according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, for preparing a medicament as an integrin inhibitor.

19. Use according to claim 18, for inhibiting the interaction of an α_v -, β_3 - or β_5 -integrin receptor with a
30 ligand.

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20. Use according to claim 19, for inhibiting the binding of fibrogen to the β_3 -integrin receptor.

21. Use according to claim 19, wherein the integrin is $\alpha_v\beta_3$, $\alpha_v\beta_5$, $\alpha_{11b}\beta_3$, $\alpha_v\beta_1$, $\alpha_v\beta_6$ or $\alpha_v\beta_8$.

5 22. A commercial package comprising a compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, and associated therewith instructions for use thereof in preventing, controlling or treating a
10 disease as defined in claim 6, 7 or 8.

23. A commercial package comprising a compound of the general formula I according to claim 1 or 2, or a physiologically harmless salt thereof, or a preparation according to claim 5, and associated therewith instructions
15 for use thereof for supporting the healing processes in wound healing.

24. Use of a compound of the general formula I according to claim 1, wherein X is a fluorescent dye residue which is linked by way of a -CONH-, -COO-, -NH-C(=S)-NH-,
20 -NH-C(=O)-NH-, -SO₂NH- or -NHCO- bond, as a diagnostic marker in FACS analysis and fluorescence microscopy.

25. Use of a compound of the general formula I according to claim 1 or 2, in affinity chromatography.

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OTTAWA, CANADA

PATENT AGENTS