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(54) Title: USE OF MELANOCORTINS TO TREAT DYSLIPIDEMIA

(57) Abstract: The present invention relates to peptide ligands of the melanocortin receptors, in particular the melanocortin-4 receptor, and as such, are useful in the treatment of dyslipidemia and associated complications such as alcoholic and non-alcoholic fatty liver disease.



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## USE OF MELANOCORTINS TO TREAT DYSLIPIDEMIA

### BACKGROUND OF THE INVENTION

Melanocortins are a family of regulatory peptides which are formed by post-translational processing of pro-hormone pro-opiomelanocortin (POMC; 131 amino acids in length). POMC is processed into three classes of hormones; the melanocortins, adrenocorticotropin hormone, and various endorphins (e.g. lipotropin) (Cone *et al.*, Recent Prog. Horm. Res., 51:287-317, (1996); Cone *et al.*, Ann. N.Y. Acad. Sci., 31:342-363, (1993)).

Five melanocortin receptors (MC-R) have been characterized to date. These include melanocyte-specific receptor (MC1-R), corticoadrenal-specific ACTH receptor (MC2-R), melanocortin-3 (MC3-R), melanocortin-4 (MC4-R) and melanocortin-5 receptor (MC5-R). All of the melanocortin receptors respond to the peptide hormone class of melanocyte stimulating hormones (MSH) (Cone *et al.*, Ann. N.Y. Acad. Sci., 680:342-363 (1993); Cone *et al.*, Recent Prog. Horm. Res., 51:287-318 (1996)).

There has been great interest in melanocortin (MC-R) receptors as targets for the design of novel therapeutics to treat disorders of body weight such as obesity and cachexia. One of the receptors, MC4-R, is a 332 amino acid transmembrane protein expressed in brain as well as placental and gut tissues (Cone *et al.*, Ann. N.Y. Acad. Sci., 680:342-363 (1993); Cone *et al.*, Recent Prog. Horm. Res., 51:287-318 (1996)). Recent pharmacological confirmation has established that central MC4-R receptors are the prime mediators of the anorexic and orexigenic effects reported for melanocortin agonists and antagonists, respectively (Giraudou *et al.*, Brain Res., 809:302-306 (1998); Farooqi *et al.*, NE J Med., 348:1085-1095 (2003); MacNeil *et al.*, Eu. J. Pharm., 44:141-157 (2002); MacNeil *et al.*, Eu. J. Pharm., 450:93-109 (2002); Kask *et al.*, NeuroReport, 10:707-711 (1999); Chen *et al.*, Transgenic Res., 9:145-54, (2000); Marsh *et al.*, Nat Genet., 21:119-22, (1999); Balthasar *et al.*, Cell, 123:493-505 (2005)).

In addition to the visible effects of body weight disorders, obese and overweight persons often develop a number of less-visible physiological

complications such as diabetes, dyslipidemia, atherosclerosis, hypertension and hepatic steatosis. Hepatic steatosis may also affect persons considered to be normal or even underweight. Left unaddressed, hepatic steatosis can progress into fatty liver disease, inflammation of the liver, lesions, fibrosis and cancer. Concurrent with the rising occurrence of obesity, fatty liver disease is quickly becoming a global health problem for both adults and children (see Reddy et al., Am. J. Physiol. Gastrointest. Liver Physiol., 290:G852-858, (2006) and references therein).

### SUMMARY OF THE INVENTION

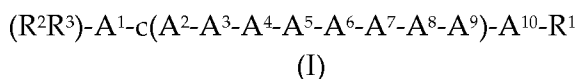
The present invention is directed to the use of peptides which are ligands of one or more of the melanocortin receptors (MC-R), or the pharmaceutically-acceptable salts thereof, to treat mammals suffering from dyslipidemia. In one embodiment, the ligands are agonists to the melanocortin 4 receptor. In a preferred embodiment, the melanocortin receptor ligands are according to the formulae described herein or are selected from particular peptides described herein.

The subject mammals suffering from dyslipidemia may be obese or overweight. The dyslipidemic subject mammals may also be normal weight or lean. In addition, the subject mammals may be human subjects of any age, such as an infant, a child, an adult or an elderly adult.

The subject mammals suffering from dyslipidemia may also suffer from increased levels of serum cholesterol, triglycerides, low-density lipoprotein cholesterol or free fatty acids or a decrease in high-density lipoprotein cholesterol concentration in the blood.

The subject mammals suffering from dyslipidemia may also suffer from hepatic steatosis. The hepatic steatosis may be non-alcoholic fatty acid liver disease or alcoholic fatty acid liver disease. The non-alcoholic fatty acid liver disease or alcoholic fatty acid liver disease may be accompanied by steatohepatitis, steatonecrosis, lobular inflammation, ballooning degeneration, fibrosis, cirrhosis or cancer or any combination thereof.

In the first embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor 4 ligand according to Formula (I) and pharmaceutically acceptable salts, hydrates, solvates or prodrugs thereof (see International Patent Application Publication Number WO 2007/008704, incorporated herein by reference in its entirety):



wherein:

$A^1$  is Acc,  $HN-(CH_2)_m-C(O)$ , L- or D-amino acid, or deleted;

$A^2$  is Cys, D-Cys, hCys, D-hCys, Pen, D-Pen, Asp, or Glu;

$A^3$  is Gly, Ala,  $\beta$ -Ala, Gaba, Aib, D-amino acid, or deleted;

$A^4$  is His, 2-Pal, 3-Pal, 4-Pal, Taz, 2-Thi, 3-Thi, or  $(X^1, X^2, X^3, X^4, X^5)Phe$ ;

$A^5$  is D-Phe, D-1-Nal, D-2-Nal, D-Trp, D-Bal, D- $(X^1, X^2, X^3, X^4, X^5)Phe$ , L-Phe or D-(Et)Tyr;

$A^6$  is Arg, hArg, Dab, Dap, Lys, Orn, or  $HN-CH((CH_2)_n-N(R^4R^5))-C(O)$ ;

$A^7$  is Trp, 1-Nal, 2-Nal, Bal, Bip, D-Trp, D-1-Nal, D-2-Nal, D-Bal or D-Bip;

$A^8$  is Gly, D-Ala, Acc, Ala,  $\beta$ -Ala, Gaba, Apn, Ahx, Aha,  $HN-(CH_2)_s-C(O)$ , or deleted;

$A^9$  is Cys, D-Cys, hCys, D-hCys, Pen, D-Pen, Dab, Dap, Orn, or Lys;

$A^{10}$  is Acc,  $HN-(CH_2)_t-C(O)$ , L- or D-amino acid, or deleted;

$R^1$  is OH or  $NH_2$ ;

each of  $R^2$  and  $R^3$  is, independently for each occurrence, selected from the group consisting of H,  $(C_1-C_{30})alkyl$ ,  $(C_1-C_{30})heteroalkyl$ ,  $(C_1-C_{30})acyl$ ,  $(C_2-C_{30})alkenyl$ ,  $(C_2-C_{30})alkynyl$ ,  $aryl(C_1-C_{30})alkyl$ ,  $aryl(C_1-C_{30})acyl$ , substituted  $(C_1-C_{30})alkyl$ , substituted  $(C_1-C_{30})heteroalkyl$ , substituted  $(C_1-C_{30})acyl$ , substituted  $(C_2-C_{30})alkenyl$ , substituted  $(C_2-C_{30})alkynyl$ , substituted  $aryl(C_1-C_{30})alkyl$ , and substituted  $aryl(C_1-C_{30})acyl$ ;

each of  $R^4$  and  $R^5$  is, independently for each occurrence, H,  $(C_1-C_{40})alkyl$ ,  $(C_1-C_{40})heteroalkyl$ ,  $(C_1-C_{40})acyl$ ,  $(C_2-C_{40})alkenyl$ ,  $(C_2-C_{40})alkynyl$ ,  $aryl(C_1-C_{40})alkyl$ ,  $aryl(C_1-C_{40})acyl$ , substituted  $(C_1-C_{40})alkyl$ , substituted  $(C_1-C_{40})heteroalkyl$ , substituted

(C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkynyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>1</sub>-C<sub>40</sub>)alkylsulfonyl, or -C(NH)-NH<sub>2</sub>;

m is, independently for each occurrence, 1, 2, 3, 4, 5, 6 or 7;

n is, independently for each occurrence, 1, 2, 3, 4 or 5;

s is, independently for each occurrence, 1, 2, 3, 4, 5, 6, or 7;

t is, independently for each occurrence, 1, 2, 3, 4, 5, 6, or 7;

X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, and X<sup>5</sup> each is, independently for each occurrence, H, F, Cl, Br, I, (C<sub>1-10</sub>)alkyl, substituted (C<sub>1-10</sub>)alkyl, (C<sub>2-10</sub>)alkenyl, substituted (C<sub>2-10</sub>)alkenyl, (C<sub>2-10</sub>)alkynyl, substituted (C<sub>2-10</sub>)alkynyl, aryl, substituted aryl, OH, NH<sub>2</sub>, NO<sub>2</sub>, or CN; provided that

(I). when R<sup>4</sup> is (C<sub>1</sub>-C<sub>40</sub>)acyl, aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>1</sub>-C<sub>40</sub>)acyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>1</sub>-C<sub>40</sub>)alkylsulfonyl, or -C(NH)-NH<sub>2</sub>, then R<sup>5</sup> is H or (C<sub>1</sub>-C<sub>40</sub>)alkyl, (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, (C<sub>2</sub>-C<sub>40</sub>)alkenyl, (C<sub>2</sub>-C<sub>40</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkynyl, or substituted aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl;

(II). when R<sup>2</sup> is (C<sub>1</sub>-C<sub>30</sub>)acyl, aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>1</sub>-C<sub>30</sub>)acyl, or substituted aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, then R<sup>3</sup> is H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, (C<sub>2</sub>-C<sub>30</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkynyl, or substituted aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl;

(III). either A<sup>3</sup> or A<sup>8</sup> or both must be present in said compound;

(IV). when A<sup>2</sup> is Cys, D-Cys, hCys, D-hCys, Pen, or D-Pen, then A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Pen, or D-Pen;

(V). when A<sup>2</sup> is Asp or Glu, then A<sup>9</sup> is Dab, Dap, Orn, or Lys;

(VI). when A<sup>8</sup> is Ala or Gly, then A<sup>1</sup> is not Nle; and

(VII). when A<sup>1</sup> is deleted, then R<sup>2</sup> and R<sup>3</sup> cannot both be H;

or pharmaceutically acceptable salts thereof.

In one aspect of the first embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically

effective amount of a subgroup of melanocortin receptor ligands of the immediate foregoing Formula I, wherein:

A<sup>1</sup> is A6c, Arg, D-Arg, Cha, D-Cha, hCha, Chg, D-Chg, Gaba, Ile, Leu, hLeu, Met,  $\beta$ -hMet, 2-Nal, D-2-Nal, Nip, Nle, Oic, Phe, D-Phe, hPhe, hPro, Val, or deleted;

A<sup>2</sup> is Asp, Cys, D-Cys, hCys, D-hCys, Glu, Pen, or D-Pen;

A<sup>3</sup> is D-Abu, Aib, Ala,  $\beta$ -Ala, D-Ala, D-Cha, Gaba, D-Glu, Gly, D-Ile, D-Leu, D-Tle, D-Val, or deleted;

A<sup>4</sup> is His or 3-Pal;

A<sup>5</sup> is D-Bal, D-1-Nal, D-2-Nal, D-Phe, D-Trp, or D-(Et)Tyr;

A<sup>6</sup> is Arg, or hArg;

A<sup>7</sup> is Bal, Bip, 1-Nal, 2-Nal, Trp, D-Trp;

A<sup>8</sup> is A6c, D-Ala, Aha, Ahx, Ala,  $\beta$ -Ala, Apn, Gaba, Gly or deleted;

A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Lys, Pen, or D-Pen;

A<sup>10</sup> is Thr, or deleted;

wherein at least one of A<sup>3</sup> or A<sup>8</sup> is deleted, but not both,  
or pharmaceutically acceptable salts thereof.

More preferred compounds of the immediately foregoing group of ligands according to Formula (I) useful to treat dyslipidemia in a mammalian subject are compounds of the formula:

Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp- $\beta$ -Ala-Lys)-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-A6c-Lys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-Phe-Arg-Trp-Ala-D-Cys)-Thr-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-Phe-Arg-Trp- $\beta$ -Ala-D-Cys)-Thr-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-NH<sub>2</sub>;

Ac-A6c-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;

Ac-D-2-Nal-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;

Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-β-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gaba-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Aib-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gly-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-β-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gaba-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Aib-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gly-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-β-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gaba-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Aib-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gly-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-D-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-β-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gaba-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Aib-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Oic-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nip-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hPro-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hLeu-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;

Ac-Phe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Phe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
n-butanoyl-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-β<sup>-</sup>-hMet-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Gaba-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Leu-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-hLeu-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Phe-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-D-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-β<sup>-</sup>-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Aha-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Apn-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-β<sup>-</sup>-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-D-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-NH<sub>2</sub>;  
n-butanoyl-Nle-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
n-butanoyl-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-1-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Bal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-D-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Trp-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-OH;  
Ac-Nle-c(Cys-D-Abu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Val-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ile-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Tle-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Leu-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Cha-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Ile-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Val-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-2-Nal-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;

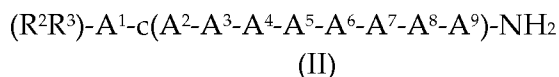
Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-3-Pal-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-His-Phe-Arg-D-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Ala-D-Cys)-Thr-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-OH;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-OH;  
Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-D-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Gaba-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-β-Ala-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-D-Ala-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-OH;

Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-OH;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-OH;  
Ac-Arg-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-D-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-β-Ala-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Trp-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-OH;  
Ac-Nle-c(Cys-D-Abu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Val-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ile-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Tle-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Leu-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Cha-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Ile-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Val-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-2-Nal-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-3-Pal-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-His-Phe-Arg-D-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
 Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;  
 Ac-hPhe-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
 Ac-Cha-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>; or  
 Ac-Arg-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
 or pharmaceutically acceptable salts thereof.

In the second embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor ligand according to Formula (II) and pharmaceutically acceptable salts, hydrates, solvates or prodrugs thereof (see International Patent Application Publication Number WO 2007/008704 incorporated herein by reference in its entirety):



wherein:

A<sup>1</sup> is Nle or deleted;

A<sup>2</sup> is Cys or Asp;

A<sup>3</sup> is Glu or D-Ala;

A<sup>4</sup> is His;

A<sup>5</sup> is D-Phe;

A<sup>6</sup> is Arg;

A<sup>7</sup> is Trp, 2-Nal or Bal;

A<sup>8</sup> is Gly, Ala, D-Ala, β-Ala, Gaba or Apn;

A<sup>9</sup> is Cys or Lys;

each of R<sup>2</sup> and R<sup>3</sup> is independently selected from the group consisting of H or (C<sub>1</sub>-C<sub>6</sub>)acyl;

provided that

(I). when R<sup>2</sup> is (C<sub>1</sub>-C<sub>6</sub>)acyl, then R<sup>3</sup> is H; and

(II). when A<sup>2</sup> is Cys, then A<sup>9</sup> is Cys,

or a pharmaceutically acceptable salt thereof.

More preferred of the immediately foregoing group of compounds which are useful to dyslipidemia in a mammalian subject are compounds of the formula:

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-D-Ala-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH<sub>2</sub>;

Ac-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;

Ac-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;

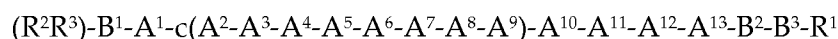
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>; or

Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Ala-Lys)-NH<sub>2</sub>;

or a pharmaceutically acceptable salt thereof.

In the third embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor compound according to Formula (III), and pharmaceutically acceptable salts, hydrates, solvates or prodrugs thereof (see International Application Publication Number WO 2007/008684, incorporated herein by reference in its entirety):



(III)

wherein:

B<sup>1</sup> is a peptide moiety which contains 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acids, wherein at least 5 amino acids are independently selected from the group consisting of L-Arg, D-Arg, L-hArg and D-hArg, or B<sup>1</sup> is optionally deleted;

A<sup>1</sup> is Acc, HN-(CH<sub>2</sub>)<sub>m</sub>-C(O), L- or D-amino acid or deleted;

A<sup>2</sup> is Cys, D-Cys, hCys, D-hCys, Pen, D-Pen, Asp or Glu;

A<sup>3</sup> is Gly, Glu, Ala, β-Ala, Gaba, Aib, D-amino acid or deleted;

A<sup>4</sup> is His, 2-Pal, 3-Pal, 4-Pal, Taz, 2-Thi, 3-Thi or (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe;

A<sup>5</sup> is D-Phe, D-1-Nal, D-2-Nal, D-Trp, D-Bal, D-(X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, D-(Et)Tyr, D-Dip, D-Bip or D-Bpa ;

A<sup>6</sup> is Arg, hArg, Dab, Dap, Lys, Orn or HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>4</sup>R<sup>5</sup>))-C(O);

A<sup>7</sup> is Trp, 1-Nal, 2-Nal, Bal, Bip, Dip, Bpa, D-Trp, D-1-Nal, D-2-Nal, D-Bal, D-Bip, D-Dip or D-Bpa;

A<sup>8</sup> is Gly, D-Ala, Acc, Ala, β-Ala, Gaba, Apn, Ahx, Aha, HN-(CH<sub>2</sub>)<sub>s</sub>-C(O) or deleted;

A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Pen, D-Pen, Dab, Dap, Orn or Lys;

A<sup>10</sup> is Acc, HN-(CH<sub>2</sub>)<sub>t</sub>-C(O), Pro, hPro, 3-Hyp, 4-Hyp, Thr, an L- or D-amino acid or deleted;

A<sup>11</sup> is Pro, hPro, 3-Hyp, 4-Hyp or deleted;

A<sup>12</sup> is Lys, Dab, Dap, Arg, hArg or deleted;

A<sup>13</sup> is Asp, Glu or deleted;

B<sup>2</sup> is a peptide moiety containing 1, 2, 3, 4, or 5 amino acids or deleted,

B<sup>3</sup> is a peptide moiety which contains 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 amino acids wherein at least 5 amino acids are independently selected from the group consisting of L-Arg, D-Arg, L-hArg and D-hArg, or is deleted;

R<sup>1</sup> is OH or NH<sub>2</sub>;

R<sup>2</sup> and R<sup>3</sup> each is , independently for each occurrence, selected from the group consisting of H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, (C<sub>2</sub>-C<sub>30</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl, aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkynyl, substituted aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl and substituted aryl(C<sub>1</sub>-C<sub>30</sub>)acyl;

R<sup>4</sup> and R<sup>5</sup> each is, independently for each occurrence, H, (C<sub>1</sub>-C<sub>40</sub>)alkyl, (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, (C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>2</sub>-C<sub>40</sub>)alkenyl, (C<sub>2</sub>-C<sub>40</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkynyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>1</sub>-C<sub>40</sub>)alkylsulfonyl or C(NH)-NH<sub>2</sub>;

n is, independently for each occurrence, 1, 2, 3, 4 or 5;

m is, independently for each occurrence, 1, 2, 3, 4, 5, 6 or 7;

s is, independently for each occurrence, 1, 2, 3, 4, 5, 6 or 7;

t is, independently for each occurrence, 1, 2, 3, 4, 5, 6 or 7;

X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup> and X<sup>5</sup> each is, independently for each occurrence, H, F, Cl, Br, I, (C<sub>1-10</sub>)alkyl, substituted (C<sub>1-10</sub>)alkyl, (C<sub>2-10</sub>)alkenyl, substituted (C<sub>2-10</sub>)alkenyl, (C<sub>2-10</sub>)alkynyl, substituted (C<sub>2-10</sub>)alkynyl, aryl, substituted aryl, OH, NH<sub>2</sub>, NO<sub>2</sub> or CN; provided that:

(I) when R<sup>4</sup> is (C<sub>1-C40</sub>)acyl, aryl(C<sub>1-C40</sub>)acyl, substituted (C<sub>1-C40</sub>)acyl, substituted aryl(C<sub>1-C40</sub>)acyl, (C<sub>1-C40</sub>)alkylsulfonyl or C(NH)-NH<sub>2</sub>, then R<sup>5</sup> is H, (C<sub>1-C40</sub>)alkyl, (C<sub>1-C40</sub>)heteroalkyl, (C<sub>2-C40</sub>)alkenyl, (C<sub>2-C40</sub>)alkynyl, aryl(C<sub>1-C40</sub>)alkyl, substituted (C<sub>1-C40</sub>)alkyl, substituted (C<sub>1-C40</sub>)heteroalkyl, substituted (C<sub>2-C40</sub>)alkenyl, substituted (C<sub>2-C40</sub>)alkynyl or substituted aryl(C<sub>1-C40</sub>)alkyl;

(II) when R<sup>2</sup> is (C<sub>1-C30</sub>)acyl, aryl(C<sub>1-C30</sub>)acyl, substituted (C<sub>1-C30</sub>)acyl or substituted aryl(C<sub>1-C30</sub>)acyl, then R<sup>3</sup> is H, (C<sub>1-C30</sub>)alkyl, (C<sub>1-C30</sub>)heteroalkyl, (C<sub>2-C30</sub>)alkenyl, (C<sub>2-C30</sub>)alkynyl, aryl(C<sub>1-C30</sub>)alkyl, substituted (C<sub>1-C30</sub>)alkyl, substituted (C<sub>1-C30</sub>)heteroalkyl, substituted (C<sub>2-C30</sub>)alkenyl, substituted (C<sub>2-C30</sub>)alkynyl or substituted aryl(C<sub>1-C30</sub>)alkyl;

(III) neither B<sup>1</sup> nor B<sup>2</sup> contains one or more of the following amino acid sequences: Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:1), Tyr-Ala-Arg-Lys-Ala-(Arg)<sub>2</sub>-Gln-Ala-(Arg)<sub>2</sub> (SEQ ID NO:2), Tyr-Ala-Arg-(Ala)<sub>2</sub>-(Arg)<sub>2</sub>-(Ala)<sub>2</sub>-(Arg)<sub>2</sub> (SEQ ID NO:3), Tyr-Ala-(Arg)<sub>9</sub> (SEQ ID NO:4), Tyr-(Ala)<sub>3</sub>-(Arg)<sub>7</sub> (SEQ ID NO:5), Tyr-Ala-Arg-Ala-Pro-(Arg)<sub>2</sub>-Ala-(Arg)<sub>3</sub> (SEQ ID NO:6) or Tyr-Ala-Arg-Ala-Pro-(Arg)<sub>2</sub>-Pro-(Arg)<sub>2</sub> (SEQ ID NO:7);

(IV) either B<sup>1</sup> or B<sup>2</sup> or both must be present in said compound;

(V) when A<sup>2</sup> is Cys, D-Cys, hCys, D-hCys, Pen or D-Pen, then A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Pen or D-Pen; and

(VI) when A<sup>2</sup> is Asp or Glu, then A<sup>9</sup> is Dab, Dap, Orn or Lys;

or pharmaceutically acceptable salts thereof.

In one aspect of the third embodiment, the invention is directed to the use of compounds of Formula (III) to treat dyslipidemia in a mammalian subject wherein B<sup>1</sup> is Arg-Lys-Gln-Lys-(Arg)<sub>5</sub> (SEQ ID NO:8), Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub> (SEQ ID NO:9), Arg-(Lys)<sub>2</sub>-(Arg)<sub>3</sub>-Gln-(Arg)<sub>2</sub> (SEQ ID NO:10), Arg-(Lys)<sub>2</sub>-(Arg)<sub>4</sub>-Gln-Arg (SEQ

ID NO:11), Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-Gln (SEQ ID NO:12), Arg-(Lys)<sub>2</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:13), Arg-Gln-(Lys)<sub>2</sub>-(Arg)<sub>5</sub> (SEQ ID NO:14), Arg-Gln-(Arg)<sub>7</sub> (SEQ ID NO:15), Arg-Gln-(Arg)<sub>8</sub> (SEQ ID NO:16), (Arg)<sub>2</sub>-Gln-(Arg)<sub>6</sub> (SEQ ID NO:17), (Arg)<sub>2</sub>-Gln-(Arg)<sub>7</sub> (SEQ ID NO:18), (Arg)<sub>3</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:19), (Arg)<sub>3</sub>-Gln-(Arg)<sub>6</sub> (SEQ ID NO:20), (Arg)<sub>4</sub>-Gln-(Arg)<sub>4</sub> (SEQ ID NO:21), (Arg)<sub>4</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:22), (Arg)<sub>5</sub> (SEQ ID NO:23), (Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:24), (Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub> (SEQ ID NO:25), (Arg)<sub>6</sub> (SEQ ID NO:26), (Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:27), (Arg)<sub>7</sub> (SEQ ID NO:28), (Arg)<sub>7</sub>-Gln-(Arg)<sub>2</sub> (SEQ ID NO:29), (Arg)<sub>8</sub> (SEQ ID NO:30), (Arg)<sub>8</sub>-Gln-Arg (SEQ ID NO:31), (Arg)<sub>9</sub> (SEQ ID NO:32), (Arg)<sub>9</sub>-Gln (SEQ ID NO:33), (D-Arg)<sub>5</sub>, (D-Arg)<sub>6</sub>, (D-Arg)<sub>7</sub>, (D-Arg)<sub>8</sub>, (D-Arg)<sub>9</sub>, Gln-Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub> (SEQ ID NO:34), Gln-(Arg)<sub>8</sub> (SEQ ID NO:35), Gln-(Arg)<sub>9</sub> (SEQ ID NO:36), Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:37), Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-Doc (SEQ ID NO:38); or deleted;

B<sup>2</sup> is  $\beta$ -Ala,  $\beta$ -Ala-Gly,  $\beta$ -Ala-Tyr,  $\beta$ -Ala-Tyr-Gly, ( $\beta$ -Ala)<sub>2</sub>, ( $\beta$ -Ala)<sub>2</sub>-Gly, ( $\beta$ -Ala)<sub>2</sub>-Tyr, ( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly (SEQ ID NO:39), Doc, Doc-Gly, Doc-Tyr, Doc-Tyr-Gly, (Doc)<sub>2</sub>, (Doc)<sub>2</sub>-Gly, (Doc)<sub>2</sub>-Tyr, (Doc)<sub>2</sub>-Tyr-Gly (SEQ ID NO:40), or deleted;

B<sup>3</sup> is Arg-Lys-Gln-Lys-(Arg)<sub>5</sub> (SEQ ID NO:8), Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:41), Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub> (SEQ ID NO:9), Arg-(Lys)<sub>2</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:13), Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:1), Arg-(Lys)<sub>2</sub>-(Arg)<sub>3</sub>-Gln-(Arg)<sub>2</sub> (SEQ ID NO:10), Arg-(Lys)<sub>2</sub>-(Arg)<sub>4</sub>-Gln-Arg (SEQ ID NO:11), Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-Gln (SEQ ID NO:12), Arg-Gln-(Lys)<sub>2</sub>-(Arg)<sub>5</sub> (SEQ ID NO:14), Arg-Gln-(Arg)<sub>7</sub> (SEQ ID NO:15), Arg-Gln-(Arg)<sub>8</sub> (SEQ ID NO:16), (Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:42), (Arg)<sub>2</sub>-Gln-(Arg)<sub>6</sub> (SEQ ID NO:17), (Arg)<sub>2</sub>-Gln-(Arg)<sub>7</sub> (SEQ ID NO:18), (Arg)<sub>3</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:19), (Arg)<sub>3</sub>-Gln-(Arg)<sub>6</sub> (SEQ ID NO:20), (Arg)<sub>4</sub>-Gln-(Arg)<sub>4</sub> (SEQ ID NO:21), (Arg)<sub>4</sub>-Gln-(Arg)<sub>5</sub> (SEQ ID NO:22), (Arg)<sub>5</sub> (SEQ ID NO:23), (Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:24), (Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub> (SEQ ID NO:25), (Arg)<sub>6</sub> (SEQ ID NO:26), (Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub> (SEQ ID NO:27), (Arg)<sub>7</sub> (SEQ ID NO:28), (Arg)<sub>7</sub>-Gln-(Arg)<sub>2</sub> (SEQ ID NO:29), (Arg)<sub>8</sub> (SEQ ID NO:30), (Arg)<sub>8</sub>-Gln-Arg (SEQ ID NO:31), (Arg)<sub>9</sub> (SEQ ID NO:32), (Arg)<sub>9</sub>-Gln (SEQ ID NO:33), (D-Arg)<sub>5</sub>, (D-Arg)<sub>6</sub>, (D-Arg)<sub>7</sub>, (D-Arg)<sub>8</sub>, (D-Arg)<sub>9</sub>, Gln-Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub> (SEQ ID NO:34), Gln-(Arg)<sub>8</sub> (SEQ ID NO:35), Gln-(Arg)<sub>9</sub> (SEQ ID NO:36), or deleted;

A<sup>1</sup> is A6c, Cha, hCha, Chg, D-Chg, hChg, Gaba, hLeu, Met,  $\beta$ -hMet, D-2-Nal, Nip, Nle, Oic, Phe, D-Phe, hPhe, hPro, or deleted;

A<sup>2</sup> is Cys

A<sup>3</sup> is D-Abu, Aib, Ala,  $\beta$ -Ala, D-Ala, D-Cha, Gaba, Glu, Gly, D-Ile, D-Leu, D-Met, D-Nle, D-Phe, D-Tle, D-Trp, D-Tyr, D-Val, or deleted;

A<sup>4</sup> is His;

A<sup>5</sup> is D-Bal, D-1-Nal, D-2-Nal, D-Phe, D-(X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, D-Trp, or D-(Et)Tyr;

A<sup>6</sup> is Arg or hArg;

A<sup>7</sup> is Bal, Bip, 1-Nal, 2-Nal, Trp, or D-Trp;

A<sup>8</sup> is A5c, A6c, Aha, Ahx, Ala,  $\beta$ -Ala, Apn, Gaba, Gly, or deleted;

A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Lys, Pen, or D-Pen;

A<sup>10</sup> is Pro, Thr or deleted;

A<sup>11</sup> is Pro or deleted;

A<sup>12</sup> is arg, Lys, or deleted;

A<sup>13</sup> is Asp or deleted;

each of R<sup>2</sup> and R<sup>3</sup> is, independently, H or acyl;

or pharmaceutically acceptable salts thereof.

Preferred ligands of the immediately foregoing group of compounds according to Formula (III), useful to treat dyslipidemia in a mammalian subject are compounds of the formula:

Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH<sub>2</sub>;

Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-Doc-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH<sub>2</sub>;

Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Pro)<sub>2</sub>-Lys-Asp-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Gln-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Gln-Lys-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>4</sub>-Gln-Arg-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Aib-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>3</sub>-Gln-(Arg)<sub>2</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Gln-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-  
(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala- (Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala- (Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-  
Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala- (Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-  
Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-  
Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala- (Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Gln-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-Gln-Lys-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Gln-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>3</sub>-Gln-(Arg)<sub>2</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>4</sub>-Gln-Arg-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-( $\beta$ -Ala)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp- $\beta$ -Ala-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp- $\beta$ -Ala-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-  
NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-  
NH<sub>2</sub>;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp- $\beta$ -Ala-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp- $\beta$ -Ala-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-( $\beta$ -Ala)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-Doc-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-(Doc)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp- $\beta$ -Ala-D-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

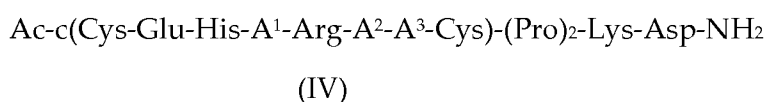
Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>; or  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>; ;  
 or pharmaceutically acceptable salts thereof.

In a fourth embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor compound according to Formula (IV), and pharmaceutically acceptable salts, hydrates, solvates and prodrugs thereof, with a compound having the following formula (formula (IV)):



wherein:

A<sup>1</sup> is the D-isomer of X-Phe or 2-Nal where X is halogen;

A<sup>2</sup> is Bal, 1-Nal, 2-Nal, or Trp; and

A<sup>3</sup> is Aib, Ala,  $\beta$ -Ala or Gly,

or pharmaceutically acceptable salts thereof.

Preferred compounds of the immediately foregoing formula discovered to treat dyslipidemia in a mammalian subject include the following:

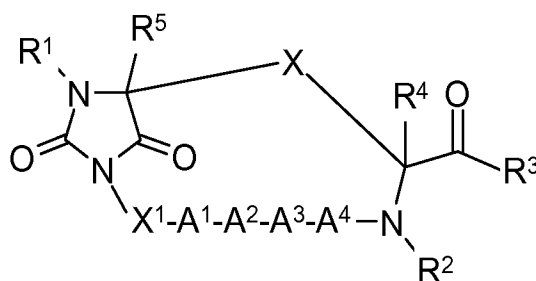
Ac-c(Cys-Glu-His-D-4-Br-Phe-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;  
 Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;  
 Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;  
 Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-β-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>; or  
 Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Aib-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;  
 or pharmaceutically acceptable salts thereof.

The invention additionally provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor compound modified with a hydantoin moiety according to Formula (V), (VI) or (VII), and pharmaceutically acceptable salts, hydrates, solvates or prodrugs thereof.

According to a fifth embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor ligand according to the following formula (Formula (V)), pharmaceutically-acceptable salts, hydrates, solvates and/or prodrugs thereof (see International Patent Application Number PCT/US08/06675 incorporated herein by reference in its entirety):



(V)

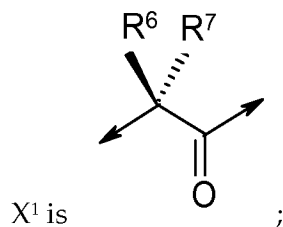
wherein

X is selected from the group consisting of -CH<sub>2</sub>-S-S-CH<sub>2</sub>-, -C(CH<sub>3</sub>)<sub>2</sub>-S-S-CH<sub>2</sub>-, -CH<sub>2</sub>-S-S-C(CH<sub>3</sub>)<sub>2</sub>-, -C(CH<sub>3</sub>)<sub>2</sub>-S-S-C(CH<sub>3</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-S-CH<sub>2</sub>-, -CH<sub>2</sub>-S-S-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-S-(CH<sub>2</sub>)<sub>2</sub>-, -C(CH<sub>3</sub>)<sub>2</sub>-S-S-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-S-C(CH<sub>3</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>t</sub>-C(O)-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>t</sub>- and -(CH<sub>2</sub>)<sub>t</sub>-NR<sup>8</sup>-C(O)-(CH<sub>2</sub>)<sub>t</sub>-;

R<sup>1</sup> and R<sup>2</sup> each is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl;

R<sup>3</sup> is -OH or -NH<sub>2</sub>;

R<sup>4</sup> and R<sup>5</sup> each is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl;



A<sup>1</sup> is His, 2-Pal, 3-Pal, 4-Pal, (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, Taz, 2-Thi, 3-Thi or is deleted;

A<sup>2</sup> is D-Bal, D-1-Nal, D-2-Nal, D-Phe or D-(X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe;

A<sup>3</sup> is Arg, hArg, Dab, Dap, Lys or Orn;

A<sup>4</sup> is Bal, 1-Nal, 2-Nal, (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe or Trp;

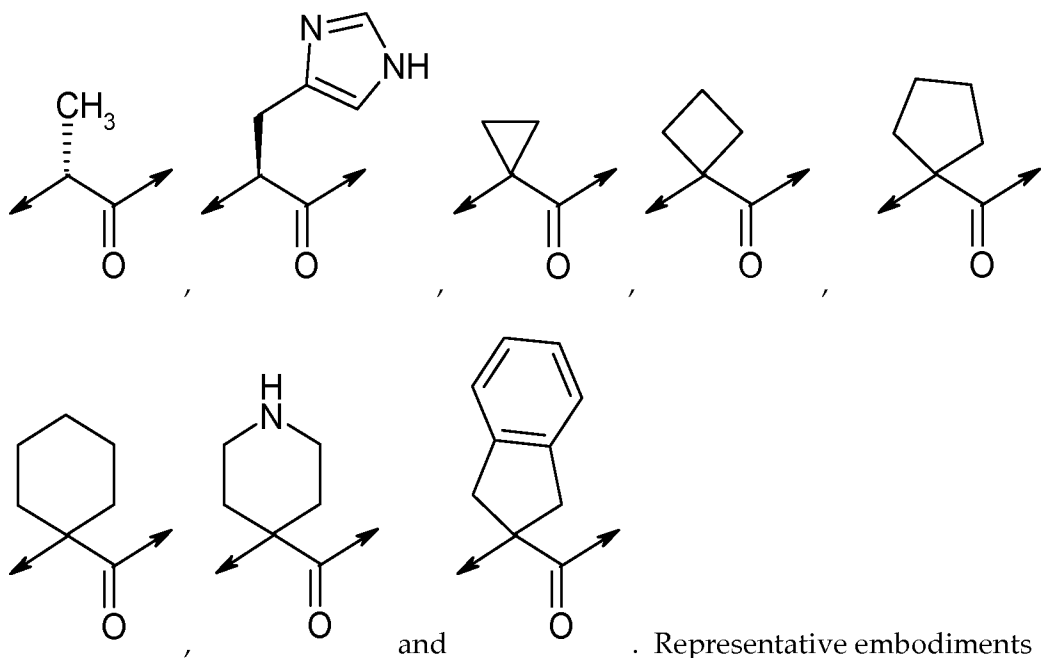
R<sup>6</sup> and R<sup>7</sup> each is, independently for each occurrence thereof, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl or substituted aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl provided that R<sup>6</sup> and R<sup>7</sup> may be joined together to form a ring;

R<sup>8</sup> is H, (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl;

r is, independently for each occurrence thereof, 1, 2, 3, 4 or 5; and

t is, independently for each occurrence thereof, 1 or 2.

Preferrably, a compound according the foregoing fourmula found useful to treat dyslipidemia in a mammalian subject include compounds wherein X<sup>1</sup> is selected from the group consisting of:

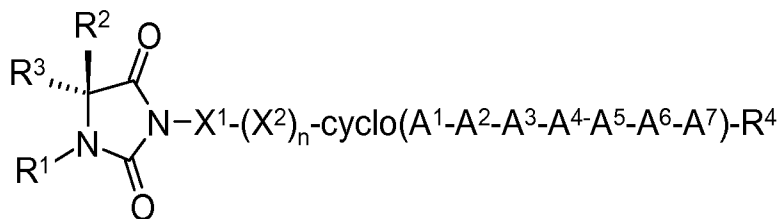


of the foregoing class of compounds useful to treat dyslipidemia in a mammalian subject are as follows:

c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(hCys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-2-Nal-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(hCys-D-Ala))-His-D-2-Nal-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dab]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-His))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-His))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A3c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A5c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A6c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A3c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A5c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-A6c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Aic))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Apc))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Aic))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Apc))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Aic))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Asp-Apc))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dab]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>, or  
 c[Hydantoin(C(O)-(Glu-His))-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>.

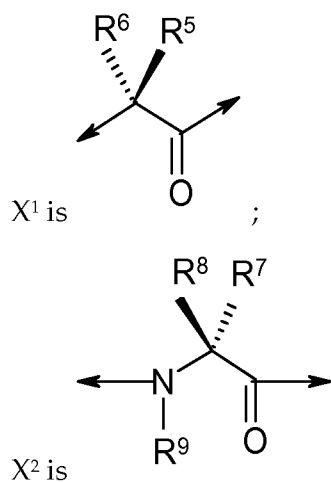
According to a sixth embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor compound according to Formula (VI),

pharmaceutically-acceptable salts, hydrates, solvates and/or prodrugs thereof (see International Patent Application Number PCT/US08/06675 which is incorporated herein by reference in its entirety):



(VI)

wherein



A<sup>1</sup> is Asp, Cys, D-Cys, Dab, Dap, Glu, Lys, Orn, Pen or D-Pen;

A<sup>2</sup> is an L- or D-amino acid;

A<sup>3</sup> is His, 2-Pal, 3-Pal, 4-Pal, (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, Taz, 2-Thi or 3-Thi;

A<sup>4</sup> is D-Bal, D-1-Nal, D-2-Nal, D-Phe or D-(X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe;

A<sup>5</sup> is Arg, hArg, Dab, Dap, Lys or Orn;

A<sup>6</sup> is Bal, 1-Nal, 2-Nal, (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe or Trp,

A<sup>7</sup> is Asp, Cys, D-Cys, Dab, Dap, Glu, Lys, Orn, Pen or D-Pen;

R<sup>1</sup> is H, (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl;

R<sup>2</sup> and R<sup>3</sup> each is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl or substituted aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl or R<sup>2</sup> and R<sup>3</sup> may be fused together form a cyclic moiety;

R<sup>4</sup> is CO<sub>2</sub>H or C(O)NH<sub>2</sub>;

R<sup>5</sup> and R<sup>6</sup> each is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl or substituted aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl or R<sup>5</sup> and R<sup>6</sup> may be fused together form a cyclic moiety;

R<sup>7</sup> and R<sup>8</sup> each is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl or substituted aryl(C<sub>1</sub>-C<sub>5</sub>)alkyl; or R<sup>7</sup> and R<sup>8</sup> may be fused together form a cyclic moiety;

R<sup>9</sup> is H, (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl; and

n is, independently for each occurrence thereof, 1, 2, 3, 4, 5, 6 or 7;

or a pharmaceutically acceptable salt thereof.

A preferred class of compounds according to Formula (VI) useful to treat dyslipidemia in a mammalian subject are those compounds wherein:

A<sup>1</sup> is Cys;

A<sup>2</sup> is D-Ala, Asn, Asp, Gln, Glu or D-Phe;

A<sup>3</sup> is His;

A<sup>4</sup> is D-2-Nal or D-Phe;

A<sup>5</sup> is Arg;

A<sup>6</sup> is Trp; and

A<sup>7</sup> is Cys or Pen;

each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>9</sup> is, independently, H;

R<sup>4</sup> is C(O)NH<sub>2</sub>;

each of R<sup>5</sup> and R<sup>6</sup> is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl or R<sup>5</sup> and R<sup>6</sup> may be fused together form a cyclic moiety; and

each of R<sup>7</sup> and R<sup>8</sup> is, independently, H, (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>10</sub>)alkyl or substituted (C<sub>1</sub>-C<sub>10</sub>)heteroalkyl; or pharmaceutically acceptable salts thereof.

Preferred compounds of the immediately foregoing formula (Formula (VI)) useful to treat dyslipidemia in a mammalian subject include:

Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

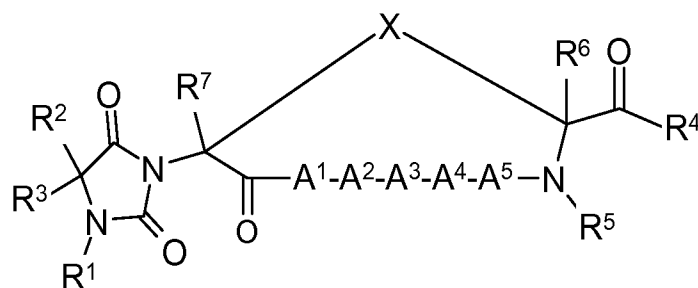
Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Aib-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Val-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ile-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Leu-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Aib-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Val-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ile-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Leu-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Ala-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Val-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(A6c-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(D-Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Val-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Leu-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Cha-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Aib-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>; or  
 Hydantoin(C(O)-(Nle-Ala))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

or pharmaceutically acceptable salts thereof.

In a seventh embodiment, the invention provides a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor ligand belonging to a class of cyclic peptide analogs that are ligands for the melanocortin receptors having a structure according to Formula (VII) as depicted below (see International Patent Application Number PCT/US08/06675 which is incorporated herein by reference in its entirety):



(VII)

wherein

X is selected from the group consisting of  $-\text{CH}_2\text{-S-S-CH}_2-$ ,  $-\text{C}(\text{CH}_3)_2\text{-S-S-CH}_2-$ ,  $-\text{CH}_2\text{-S-S-C}(\text{CH}_3)_2-$ ,  $-\text{C}(\text{CH}_3)_2\text{-S-S-C}(\text{CH}_3)_2-$ ,  $-(\text{CH}_2)_2\text{-S-S-CH}_2-$ ,  $-\text{CH}_2\text{-S-S-}(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-S-S-}(\text{CH}_2)_2-$ ,  $-\text{C}(\text{CH}_3)_2\text{-S-S-}(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-S-S-C}(\text{CH}_3)_2-$ ,  $-(\text{CH}_2)_t\text{-C(O)-NR}^8-$ ,  $(\text{CH}_2)_r-$  and  $-(\text{CH}_2)_r\text{-NR}^8\text{-C(O)-}(\text{CH}_2)_t-$ ;

each of  $\text{R}^1$  and  $\text{R}^5$  is, independently, H,  $(\text{C}_1\text{-C}_{10})$ alkyl or substituted  $(\text{C}_1\text{-C}_{10})$ alkyl;

each of  $\text{R}^2$  and  $\text{R}^3$  is, independently, H,  $(\text{C}_1\text{-C}_{10})$ alkyl,  $(\text{C}_1\text{-C}_{10})$ heteroalkyl, aryl $(\text{C}_1\text{-C}_5)$ alkyl, substituted  $(\text{C}_1\text{-C}_{10})$ alkyl, substituted  $(\text{C}_1\text{-C}_{10})$ heteroalkyl or substituted aryl $(\text{C}_1\text{-C}_5)$ alkyl or  $\text{R}^2$  and  $\text{R}^3$  may be fused together to form a ring;

$\text{R}^4$  is OH or  $\text{NH}_2$ ;

each of  $\text{R}^6$  and  $\text{R}^7$  is, independently, H,  $(\text{C}_1\text{-C}_{10})$ alkyl or substituted  $(\text{C}_1\text{-C}_{10})$ alkyl;

$\text{A}^1$  is an L- or D-amino acid or deleted;

$\text{A}^2$  is His, 2-Pal, 3-Pal, 4-Pal,  $(\text{X}^1, \text{X}^2, \text{X}^3, \text{X}^4, \text{X}^5)$ Phe, Taz, 2-Thi or 3-Thi;

$\text{A}^3$  is D-Bal, D-1-Nal, D-2-Nal, D-Phe or D- $(\text{X}^1, \text{X}^2, \text{X}^3, \text{X}^4, \text{X}^5)$ Phe;

$\text{A}^4$  is Arg, hArg, Dab, Dap, Lys or Orn,;

$\text{A}^5$  is Bal, 1-Nal, 2-Nal,  $(\text{X}^1, \text{X}^2, \text{X}^3, \text{X}^4, \text{X}^5)$ Phe or Trp,;

r is, independently for each occurrence thereof, 1, 2, 3, 4 or 5; and

t is, independently for each occurrence thereof, 1 or 2;

or pharmaceutically acceptable salts thereof.

In the preferred aspect of the compounds according to Formula (VII) useful to treat dyslipidemia in a mammalian subject,

$\text{A}^1$  is Ala, D-Ala, Asn, Asp, Gln, Glu or Gly;

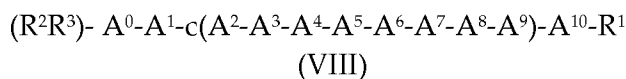
or pharmaceutically acceptable salts thereof.

Preferred compounds according to Formula (VII) useful in the treatment of dyslipidemia in a mammalian subject, include the following compounds:

c[Hydantoin(C(O)-(Nle-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Ala-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(D-Ala-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Aib-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Val-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Abu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Leu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Ile-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Cha-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(A6c-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Phe-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Gly-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Gly-Cys))-Glu-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>; or  
 c[Hydantoin(C(O)-(Gly-Cys))-Glu-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;

or pharmaceutically acceptable salts thereof.

In an eighth embodiment, the present invention is directed to a method to treat dyslipidemia in a mammalian subject by the administration of a therapeutically effective amount of a melanocortin receptor ligand according to Formula (VIII) (see International Patent Application Number PCT/US08/07411, incorporated herein by reference in its entirety):



wherein:

A<sup>0</sup> is an aromatic amino acid

A<sup>1</sup> is Acc, HN-(CH<sub>2</sub>)<sub>m</sub>-C(O), an L- or D-amino acid;

A<sup>2</sup> is Asp, Cys, D-Cys, hCys, D-hCys, Glu, Pen, or D-Pen;

A<sup>3</sup> is Aib, Ala, β-Ala, Gaba, Gly or a D-amino acid;

A<sup>4</sup> is His, 2-Pal, 3-Pal, 4-Pal, (X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, Taz, 2-Thi, or 3-Thi;

A<sup>5</sup> is D-Bal, D-1-Nal, D-2-Nal, D-Phe, L-Phe, D-(X<sup>1</sup>,X<sup>2</sup>,X<sup>3</sup>,X<sup>4</sup>,X<sup>5</sup>)Phe, L-Phe,

D-Trp or D-(Et)Tyr;

A<sup>6</sup> is Arg, hArg, Dab, Dap, Lys, Orn, or HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>4</sup>R<sup>5</sup>))-C(O);

A<sup>7</sup> is Bal, D-Bal, Bip, D-Bip, 1-Nal, D-1-Nal, 2-Nal, D-2-Nal, or D-Trp;

A<sup>8</sup> is Acc, Aha, Ahx, Ala, D-Ala, β-Ala, Apn, Gaba, Gly, HN-(CH<sub>2</sub>)<sub>s</sub>-C(O), or deleted;

A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Dab, Dap, Lys, Orn, Pen, or D-Pen;

A<sup>10</sup> is Acc, HN-(CH<sub>2</sub>)<sub>t</sub>-C(O), L- or D-amino acid, or deleted;

R<sup>1</sup> is OH, or NH<sub>2</sub>;

each of R<sup>2</sup> and R<sup>3</sup> is, independently for each occurrence selected from the group consisting of H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, (C<sub>2</sub>-C<sub>30</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl, aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkynyl, substituted aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl, and substituted aryl(C<sub>1</sub>-C<sub>30</sub>)acyl;

each of R<sup>4</sup> and R<sup>5</sup> is, independently for each occurrence, H, (C<sub>1</sub>-C<sub>40</sub>)alkyl, (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, (C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>2</sub>-C<sub>40</sub>)alkenyl, (C<sub>2</sub>-C<sub>40</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkynyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>1</sub>-C<sub>40</sub>)alkylsulfonyl, or -C(NH)-NH<sub>2</sub>;

m is, independently for each occurrence, 1, 2, 3, 4, 5, 6 or 7;

n is, independently for each occurrence, 1, 2, 3, 4 or 5;

s is, independently for each occurrence, 1, 2, 3, 4, 5, 6, or 7;

t is, independently for each occurrence, 1, 2, 3, 4, 5, 6, or 7;

X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, and X<sup>5</sup> each is, independently for each occurrence, H, F, Cl, Br, I, (C<sub>1-10</sub>)alkyl, substituted (C<sub>1-10</sub>)alkyl, (C<sub>2-10</sub>)alkenyl, substituted (C<sub>2-10</sub>)alkenyl, (C<sub>2-10</sub>)alkynyl, substituted (C<sub>2-10</sub>)alkynyl, aryl, substituted aryl, OH, NH<sub>2</sub>, NO<sub>2</sub>, or CN; provided that

(I). when R<sup>4</sup> is (C<sub>1</sub>-C<sub>40</sub>)acyl, aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, substituted (C<sub>1</sub>-C<sub>40</sub>)acyl, substituted aryl(C<sub>1</sub>-C<sub>40</sub>)acyl, (C<sub>1</sub>-C<sub>40</sub>)alkylsulfonyl, or -C(NH)-NH<sub>2</sub>, then R<sup>5</sup> is H or (C<sub>1</sub>-C<sub>40</sub>)alkyl, (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, (C<sub>2</sub>-C<sub>40</sub>)alkenyl, (C<sub>2</sub>-C<sub>40</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl,

substituted (C<sub>1</sub>-C<sub>40</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>40</sub>)heteroalkyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>40</sub>)alkynyl, or substituted aryl(C<sub>1</sub>-C<sub>40</sub>)alkyl;

(II). when R<sup>2</sup> is (C<sub>1</sub>-C<sub>30</sub>)acyl, aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, substituted (C<sub>1</sub>-C<sub>30</sub>)acyl, or substituted aryl(C<sub>1</sub>-C<sub>30</sub>)acyl, then R<sup>3</sup> is H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, (C<sub>2</sub>-C<sub>30</sub>)alkynyl, aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)alkyl, substituted (C<sub>1</sub>-C<sub>30</sub>)heteroalkyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkenyl, substituted (C<sub>2</sub>-C<sub>30</sub>)alkynyl, or substituted aryl(C<sub>1</sub>-C<sub>30</sub>)alkyl;

(III). when A<sup>2</sup> is Cys, D-Cys, hCys, D-hCys, Pen, or D-Pen, then A<sup>9</sup> is Cys, D-Cys, hCys, D-hCys, Pen, or D-Pen;

(IV). when A<sup>2</sup> is Asp or Glu, then A<sup>9</sup> is Dab, Dap, Orn, or Lys;

(V). when A<sup>8</sup> is Ala or Gly, then A<sup>1</sup> is not Nle; or  
pharmaceutically acceptable salts thereof.

A preferred group of compounds of the immediate foregoing formula useful to treat dyslipidemia in a mammalian subject is wherein

A<sup>0</sup> is 1-Nal, 2-Nal, His, Pff, Phe, Trp, or Tyr;

A<sup>1</sup> is Arg;

A<sup>2</sup> is Cys;

A<sup>3</sup> is D-Ala;

A<sup>4</sup> is His;

A<sup>5</sup> is D-Phe;

A<sup>6</sup> is Arg;

A<sup>7</sup> is Trp;

A<sup>8</sup> is deleted;

A<sup>9</sup> is Cys; and

A<sup>10</sup> is deleted;

or pharmaceutically acceptable salts thereof.

Preferred compounds of the immediately foregoing group of compounds is which are useful to treat dyslipidemia in a mammalian subject of the formula:

Ac-Tyr-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Ac-2-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Ac-1-Nal-Arg-c(Cys-D-Ala-His-DPhe-Arg-Trp-Cys)-NH<sub>2</sub>;

Ac-Phe-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Trp-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Pff-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
H-His-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>; or  
Ac-His-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
or pharmaceutically acceptable salts thereof.

In yet another preferred embodiment, the compound or compounds of Formula (I), (II), (III), (IV), (V), (VI), (VII) or (VIII) as defined hereinabove, which are useful to treat dyslipidemia in a mammalian subject or a pharmaceutically acceptable salt thereof, are provided to said subject in need in a composition with a pharmaceutically acceptable carrier or diluent.

In preferred embodiment, the invention provides a method of treating dyslipidemia in a subject in need thereof, comprising peripheral administration of an effective amount of a melanocortin receptor 4 agonist to treat the dyslipidemic subject in need thereof.

In one aspect, the melanocortin receptor 4 agonist according to any one of the compound or compounds of Formula (I), (II), (III), (IV), (V), (VI), (VII) or (VIII), or a pharmaceutically acceptable salt thereof, as defined herein are useful to treat dyslipidemia in the subject in need thereof.

In one preferred aspect, the melanocortin receptor 4 agonist useful to treat dyslipidemia in the subject in need thereof, is Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub> or a pharmaceutically acceptable salt thereof.

In one preferred aspect, the melanocortin receptor 4 agonist useful to treat dyslipidemia in the subject in need thereof, Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub> or a pharmaceutically acceptable salt thereof.

Other melanocortin ligands suitable for use in the practice of the invention include compounds, compositions or combinations thereof disclosed in:

U.S. Patent No. 7,517,854 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,501,525 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,495,009 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,473,760 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,456,184 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,419,990 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,417,027 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,414,057 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,368,453 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,354,923 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,345,144 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,342,089 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,329,673 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,326,707 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,314,879 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,307,063 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,291,619 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,276,520 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,189,755 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,189,727 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,186,715 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,169,777 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,160,886 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,157,463 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,115,607 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,049,398 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 7,034,033 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 6,977,264 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 6,960,582 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 6,794,489 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 6,699,873 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 6,579,968 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent No. 5,731,408 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20090069224 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20080234289 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20080070921 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20070155670 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060287332 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060287331 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060287330 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060281784 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060173036 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060111281 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060014676 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20060014194 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20050176728 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20050164914 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20050124636 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20050038230 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20050037951 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040106682 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040224957 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040167201 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040157264 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040152134 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20040024211 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within);

U.S. Patent Application Publication No. 20020143141 (incorporated herein by reference in its entirety, particularly for compounds, compositions or combinations thereof disclosed within).

In other aspects of the invention, administration of a compound or composition comprising a compound or pharmaceutical salt of a compound of the invention useful to treat dyslipidemia, is continuous, hourly, four times daily, three times daily, twice daily, once daily, once every other day, twice weekly, once weekly, once every two weeks, once a month, or once every two months, or longer.

The dyslipidemic subject in need of treatment may be obese, overweight, of normal weight or lean. The obese, overweight, normal weight or lean subject may suffer from type II diabetes. The preferred administration of a compound or composition comprising a compound or pharmaceutical salt of a compound of the invention useful to treat dyslipidemia is peripheral administration. Examples of peripheral administration include oral, subcutaneous, intraperitoneal, intramuscular, intravenous, rectal, transdermal or intranasal forms of administration.

**BRIEF DESCRIPTION OF THE DRAWINGS:**

Figure 1: Dose-related decrease in body weight gain induced by sub-cutaneous (sc) infusion of Compound A in obese Zucker rats. Data is presented as the difference in mean body weight gain from vehicle treated group (g)  $\pm$  standard error of the mean (shaded area is the mean standard error of the vehicle group).

Figure 2. Dose-related decrease in food intake induced by sc infusion of Compound A in obese Zucker rats. Data is presented as the difference in mean body weight gain from vehicle treated group (g)  $\pm$  standard error of the mean (shaded area is the mean standard error of the vehicle group).

Figure 3. Dose-related decrease in triglycerides induced by sc infusion of Compound A. Data is presented as serum triglyceride level (mg/dL)  $\pm$  standard error of the mean.

Figure 4. Dose-related decrease in cholesterol induced by sc infusion of Compound A. Data is presented as serum cholesterol level (g/dL)  $\pm$  standard error of the mean.

Figure 5. Decrease in free fatty acids induced by sc infusion of Compound A. Data is presented as serum free fatty acid level (mmole/L)  $\pm$  standard error of the mean.

### DETAILED DESCRIPTION OF THE INVENTION

Recent studies have reported that staggering numbers of people world wide are overweight and suffering a wide variety of serious and expensive health problems. According the World Health Organization (as reported in Kouris-Blazos *et al.*, Asia Pac. J. Clin. Nutr., 2007, 16:329-338), an estimated 1 billion people throughout the world are overweight and an estimated 300 million of these are obese. An estimated 22 million children under the age of 5 are severely overweight and in the European Union alone, the number of children who are overweight is expected to rise by 1.3 million children per year (Kosti *et al.*, 2006, Cent. Eur. J. Public Health, 14:151-159). Obesity, as defined by the Statistical Bulletin provided by the Metropolitan Life Insurance Co., (1959, 40:1), is a condition in which a person is approximately 20-25% over normal body weight. Alternatively, an individual is considered obese if the person has a body mass index of greater than 25% over normal or greater than 30% over normal with risk factors (see Bray *et al.*, Diabetes/Metabolism Review, 1988, 4:653-679 or Flynn *et al.*, Proc. Nutritional Society, 1991, 50:413). One of the main causes for obesity is the consumption of a high caloric diet (Riccardi *et al.*, Clin. Nutr., 2004, 23:447-456).

Diabetes is a chronic, debilitating disease afflicting many overweight and obese people. It is estimated that 20.8 million people in the United States alone have diabetes and more than 6 million more additional cases remain undiagnosed (Cornell, Manag. Care Pharm., 2007, 13:S11-5). Type 2 diabetes (also referred to herein as type II diabetes) is a chronic disease characterized by insulin resistance, impaired insulin secretion and hyperglycemia. Worldwide, type II diabetes is believed to affect approximately 171 million people, imparting numerous microvascular and macrovascular complications resulting in morbidity and mortality (Mudaliar, Indian J. Med. Res., 2007, 125:275-296). Mudaliar further notes that despite the availability of anti-hyperglycaemic agents available, control of glucose remains elusive in many patients.

Dyslipidemia is a condition in which may also result when energy consumption far exceeds the expenditure of energy. The unused energy is conserved in the form of fat (*i.e.*, triacylglycerol (TG)) which accumulates in adipose tissue leading to the accumulation of excess body weight. Often times, the excess TGs accumulate in large vacuoles in the liver cells, a condition known as fatty liver disease (FLD) or hepatic steatosis. In the early stages of FLD, the vesicles are small (microvesicular) but can enlarge and crowd the cell (macrovesicular). In the past, the majority of FLD cases were associated with alcohol consumption but FLD is becoming more common without this factor (non-alcoholic fatty liver disease or NAFLD). FLD is now categorized into two broad groups ALFD (alcoholic FLD) and NAFLD, typically associated with overweight and obese subjects (see Reddy *et al.*, *Am. J. Physiol. Gastrointest. Liver Physiol.*, 2006, 290:G852-G858).

It is estimated that 20-35% of the general adult population in the US have hepatic steatosis and that approximately 10% of these cases will advance to NAFLD. In contrast, in the obese population, it is estimated that 75% have steatosis and that about 35% or more of this population will advance to full NAFLD. Other causes of NAFLD include parenteral nutrition, gastric bypass surgery and certain disorders associated with fatty acid metabolism. NAFLD typically worsens and progresses from the early stages of simple fat accumulation in the liver (hepatic steatosis) to nonalcoholic steatohepatitis (NASH) to steatonecrosis to steatonecrosis complicated by fibrosis leading to cirrhosis of the liver.

Additional complications of NAFLD or AFLD include but are not limited to, cell death, inflammation, lobular inflammation, ballooning degeneration of liver tissue, hepatocellular regeneration, stellate cell activation, fibrogenesis, cirrhosis and hepatocellular carcinoma. In essence, excess energy consumption coupled with reduced energy combustion (due, for example, to defective fatty acid oxidation in the liver), can trigger hepatic steatosis which can ultimately lead to cirrhosis, liver cancer and death.

Melanocortins are proposed to play a large role in energy metabolism and homeostasis. Melanocortins cleaved from the POMC precursor exert their effects by binding to members of the melanocortin receptor family located in the brain. The

major effect of melanocortin in the brain is to reduce food intake however, it has also been shown that melanocortin agonists or antagonists injected directly into the cerebral ventricle affect insulin actions in the periphery while food was withdrawn or while food intake was kept constant (see Schwartz *et al.*, Nature, 2000, 404:661-671; Seeley *et al.*, Ann. Rev. Nutr., 2004, 24:133-149; Cone *et al.*, Recent Prog. Horm. Res., 1996, 51:287-317; Heijbor *et al.*, Diabetologia, 2005, 48:1621-1626; Obici *et al.*, J. Clin. Inv., 2001, 108:1079-1085). Banno *et al.*, (FEBS letters, 2007, 581:1131-1136) demonstrated that intracerebral injections of a melanocortin agonist to DIO rats decreased the size of and increased the number of adipocytes in white adipose tissue and decreased triglycerides content in the liver.

Considering the large numbers of overweight subjects in need of treatment, intracerebral administration is an unlikely means to disperse medicaments to patients. There is a need in the art, therefore, to identify melanocortin agonists and antagonists suitable for peripheral administration to affect parameters of insulin action and energy metabolism such as cellular characteristics of white adipose tissue, triglyceride levels and the like.

### ***Nomenclature and Abbreviations***

As used herein, an "obese subject" or mammal is characterized as having a body weight approximately 20% or greater than the normal body weight for said subject. Normal body weight may be determined by a comparison of the weight of the subject at a prior point in time or by a comparison of the weight of the subject as compared to averages of other subjects of a similar age and/or condition.

As used herein, an "overweight subject" or mammal is characterized as having a body weight approximately 5% greater to approximately 20% greater than the normal body weight for said subject. Normal body weight may be determined by a comparison of the weight of the subject at a prior point in time or by a comparison of the weight of the subject as compared to averages of other subjects of a similar age and/or condition.

As used herein, a "normal subject" or mammal is characterized as having a body weight up to approximately 5% greater than to approximately 5% less than the

normal body weight for said subject. Normal body weight may be determined by a comparison of the weight of the subject at a prior point in time or by a comparison of the weight of the subject as compared to averages of other subjects of a similar age and/or condition.

As used herein, a "lean subject" or mammal is characterized as having a body weight approximately 5% to 30% or even to 50% less than the normal body weight for said subject. Normal body weight may be determined by a comparison of the weight of the subject at a prior point in time or by a comparison of the weight of the subject as compared to averages of other subjects of a similar age and/or condition.

As used herein, the terms "treat", "treating" and "treatment" include palliative, curative and prophylactic treatment.

As used herein, "measurable" means the biologic effect is both reproducible and significantly different from the baseline variability of the assay.

As used herein, "dyslipidemia" refers to a biological condition in which lipid metabolism is abnormal, including lipoprotein overproduction or underproduction. Dyslipidemia in which lipoproteins are over-produced typically results in an elevation of total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides concentrations, with a concomitant decrease in high-density lipoprotein (HDL) cholesterol concentration in the blood.

As used herein, "fatty liver disease" or "hepatic steatosis" refers to a condition in which the liver has accumulated greater than normal levels of triglycerides in the hepatocytes of the liver. The triglycerides are contained in either or both micro- or macrovesicular vacuoles within the hepatocyte cells. The diagnosis is made when the lipid content of the liver exceeds 5010% by weight. FLD may or may not be associated with consumption of alcohol (see Reddy *et al.*, Am. J. Physiol. Gastrointest. Liver Physiol., 2006, 290:G852-G858).

As used herein, "alcoholic fatty liver disease" refers to a condition of fatty liver disease in which the subject consumes on average, greater than 20 grams per day of alcohol. AFLD develops in essentially all individuals who consume approximately 60 or more grams of alcohol per day. AFLD can occur after the

ingestion of moderate to large amounts of alcohol for even a short period of time. The subject may or may not be overweight or obese.

As used herein, "non-alcoholic fatty liver disease" refers to a condition of fatty liver disease in which the subject consumes on average, less than 20 grams per day of alcohol. The subject may or may not be overweight or obese.

As used herein, "nonalcoholic steatohepatitis" or NASH refers to that stage of the development of NA fatty liver disease in which macrovesicles of fat have developed accompanied by lobular inflammation in the liver. Steatohepatitis, in which macrovesicles of fat have developed accompanied by lobular inflammation in the liver, may also occur in alcoholic fatty liver disease.

As used herein, "steatonecrosis" refers to that stage of NA fatty liver disease in which macrovesicles of fat have developed accompanied by lobular inflammation and ballooning degeneration in the liver. Further development of NAFLD from the level of steatonecrosis includes the development of fibrosis in addition to the presence of macrovesicles of fat, inflammation and ballooning degeneration in the liver. Steatonecrosis, in which macrovesicles of fat have developed accompanied by lobular inflammation and ballooning degeneration in the liver, as well as the development of fibrosis in addition to the presence of macrovesicles of fat, inflammation and ballooning degeneration in the liver may also occur in alcoholic fatty liver disease.

As used herein, peripheral administration includes all forms of administration of a compound or a composition comprising a compound of the instant invention which excludes intracranial administration. Examples of peripheral administration include, but are not limited to, oral, parenteral (*e.g.*, intramuscular, intraperitoneal, intravenous or subcutaneous injection, implant and the like), nasal, vaginal, rectal, sublingual or topical routes of administration, including transdermal patch applications and the like.

A "subject", as used herein and throughout this application, refers to a mammalian or non-mammalian animal including, for example and without limitation, a human, a rat, a mouse or farm animal. Reference to a subject does not necessarily indicate the presence of a disease or disorder. The term "subject"

includes, for example, a mammalian or non-mammalian animal being dosed with a melanocortin analog as part of an experiment, a mammalian or non-mammalian animal being treated to help alleviate a disease or disorder, and a mammalian or non-mammalian animal being treated prophylactically to retard or prevent the onset of a disease or disorder. Subject mammals may be human subjects of any age, such as an infant, a child, an adult or an elderly adult.

A “therapeutically acceptable amount” of a compound or composition of the invention, regardless of the formulation or route of administration, is that amount which elicits a desired biological response in a subject. The biological effect of the therapeutic amount may occur at and be measured at many levels in an organism. For example, the biological effect of the therapeutic amount may occur at and be measured at the cellular level by measuring the response at a receptor which binds melanocortin and/or a melanocortin analog, or the biological effect of the therapeutic amount may occur at and be measured at the system level, such as effecting an increase/decrease in the levels of insulin. The biological effect of the therapeutic amount may occur at and be measured at the organism level, such as the alleviation of a symptom(s) or progression of a disease or condition in a subject. A therapeutically acceptable amount of a compound or composition of the invention, regardless of the formulation or route of administration, may result in one or more biological responses in a subject. In the event that the compound or composition of the invention is subject to testing in an *in vitro* system, a therapeutically acceptable amount of the compound or composition may be viewed as that amount which gives a measurable response in the *in vitro* system of choice.

The nomenclature used to define the peptides is that typically used in the art wherein the amino group at the N-terminus appears to the left and the carboxyl group at the C-terminus appears to the right. Where the amino acid has D and L isomeric forms, it is the L form of the amino acid that is represented unless otherwise explicitly indicated.

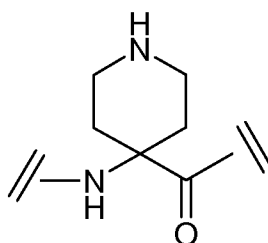
The compounds of the invention useful for the treatment of dyslipidemia may possess one or more chiral centers and so exist in a number of stereoisomeric forms. All stereoisomers and mixtures thereof are included in the scope of the

present invention. Racemic compounds may either be separated using preparative HPLC and a column with a chiral stationary phase or resolved to yield individual enantiomers utilizing methods known to those skilled in the art. In addition, chiral intermediate compounds may be resolved and used to prepare chiral compounds of the invention.

The compounds of the invention useful for the treatment of dyslipidemia may exist in one or more tautomeric forms. All tautomers and mixtures thereof are included in the scope of the present invention. For example, a claim to 2-hydroxypyridinyl would also cover its tautomeric form,  $\alpha$ -pyridonyl.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Also, all publications, patent applications, patents and other references mentioned herein are incorporated by reference in their entirety.

| Symbol       | Meaning                                                               |
|--------------|-----------------------------------------------------------------------|
| Abu          | $\alpha$ -aminobutyric acid                                           |
| Ac           | acyl group                                                            |
| Acc          | 1-amino-1-cyclo(C <sub>3</sub> -C <sub>9</sub> )alkyl carboxylic acid |
| A3c          | 1-amino-1-cyclopropanecarboxylic acid                                 |
| A4c          | 1-amino-1-cyclobutanecarboxylic acid                                  |
| A5c          | 1-amino-1-cyclopentanecarboxylic acid                                 |
| A6c          | 1-amino-1-cyclohexanecarboxylic acid                                  |
| Aha          | 7-aminoheptanoic acid                                                 |
| Ahx          | 6-aminohexanoic acid                                                  |
| Aib          | $\alpha$ -aminoisobutyric acid                                        |
| Aic          | 2-aminoindan-2-carboxylic acid                                        |
| Ala or A     | alanine                                                               |
| $\beta$ -Ala | $\beta$ -alanine                                                      |



Apc denotes the structure:

Apn 5-aminopentanoic acid ( $\text{HN}-(\text{CH}_2)_4-\text{C}(\text{O})$ )

Arg or R arginine

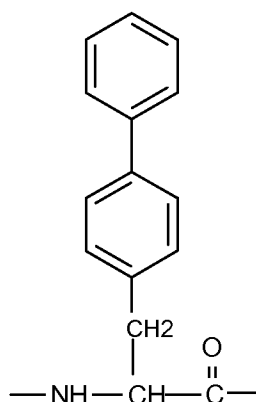
hArg homoarginine

Asn or N asparagine

Asp or D aspartic acid

Bal 3-benzothienylalanine

Bip 4,4'-biphenylalanine, represented by the structure



Bpa 4-benzoylphenylalanine

4-Br-Phe 4-bromo-phenylalanine

Cha  $\beta$ -cyclohexylalanine

hCha homo-cyclohexylalanine

Chg cyclohexylglycine

Cys or C cysteine

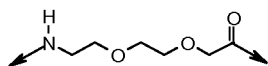
hCys homocysteine

Dab 2,4-diaminobutyric acid

Dap 2,3-diaminopropionic acid

Dip  $\beta,\beta$ -diphenylalanine

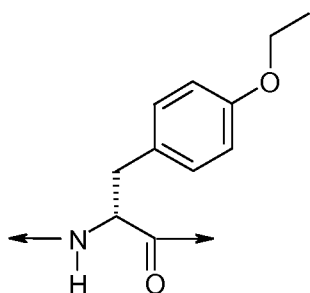
Doc 8-amino-3,6-dioxaoctanoic acid with the structure of:



|               |                                                                                          |
|---------------|------------------------------------------------------------------------------------------|
| 2-Fua         | $\beta$ -(2-furyl)-alanine                                                               |
| Gaba          | 4-aminobutyric acid                                                                      |
| Gln or Q      | glutamine                                                                                |
| Glu or E      | glutamic acid                                                                            |
| Gly or G      | glycine                                                                                  |
| His or H      | histidine                                                                                |
| 3-Hyp         | trans-3-hydroxy-L-proline, <i>i.e.</i> , (2S, 3S)-3-hydroxypyrrolidine-2-carboxylic acid |
| 4-Hyp         | 4-hydroxyproline, <i>i.e.</i> , (2S, 4R)-4-hydroxypyrrolidine-2-carboxylic acid          |
| Ile or I      | isoleucine                                                                               |
| Leu or L      | leucine                                                                                  |
| hLeu          | homoleucine                                                                              |
| Lys or K      | lysine                                                                                   |
| Met or M      | methionine                                                                               |
| $\beta$ -hMet | $\beta$ -homomethionine                                                                  |
| 1-Nal         | $\beta$ -(1-naphthyl)alanine:                                                            |
| 2-Nal         | $\beta$ -(2-naphthyl)alanine                                                             |
| Nip           | nipecotic acid                                                                           |
| Nle           | norleucine                                                                               |
| Oic           | octahydroindole-2-carboxylic acid                                                        |
| Orn           | ornithine                                                                                |
| 2-Pal         | $\beta$ -(2-pyridiyl)alanine                                                             |
| 3-Pal         | $\beta$ -(3-pyridiyl)alanine                                                             |
| 4-Pal         | $\beta$ -(4-pyridiyl)alanine                                                             |
| Pen           | penicillamine                                                                            |
| Pff           | (S)-pentafluorophenylalanine                                                             |
| Phe or F      | phenylalanine                                                                            |
| hPhe          | homophenylalanine                                                                        |
| Pro or P      | proline                                                                                  |
| hPro          | homoproline                                                                              |

|          |                               |
|----------|-------------------------------|
| Ser or S | serine                        |
| Tle      | tert-Leucine                  |
| Taz      | $\beta$ -(4-thiazolyl)alanine |
| 2-Thi    | $\beta$ -(2-thienyl)alanine   |
| 3-Thi    | $\beta$ -(3-thienyl)alanine   |
| Thr or T | threonine                     |
| Trp or W | tryptophan                    |
| Tyr or Y | tyrosine                      |

D-(Et)Tyr has a structure of



Val or V valine

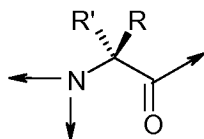
Certain other abbreviations used herein are defined as follows:

|       |                                                                              |
|-------|------------------------------------------------------------------------------|
| Boc:  | <i>tert</i> -butoxycarbonyl                                                  |
| Bzl:  | benzyl                                                                       |
| DCM:  | dichloromethane                                                              |
| DIC:  | N, N-diisopropylcarbodiimide                                                 |
| DIEA: | diisopropylethyl amine                                                       |
| Dmab: | 4-[N-(1-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3-methylbutyl)-amino] benzyl |
| DMAP: | 4-(dimethylamino)pyridine                                                    |
| DMF   | dimethylformamide                                                            |
| DNP:  | 2,4-dinitrophenyl                                                            |
| Fm:   | fluorenylmethyl                                                              |
| Fmoc: | fluorenylmethyloxycarbonyl                                                   |

|        |                                                                              |
|--------|------------------------------------------------------------------------------|
| For:   | formyl                                                                       |
| HBTU:  | 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium<br>hexafluorophosphate  |
| cHex   | cyclohexyl                                                                   |
| HOAT:  | O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium<br>hexafluorophosphate |
| HOBt:  | 1-hydroxy-benzotriazole                                                      |
| MBHA   | 4-methylbenzhydramine                                                        |
| Mmt:   | 4-methoxytrityl                                                              |
| NMP:   | N-methylpyrrolidone                                                          |
| O-tBu  | oxy-tert-butyl                                                               |
| Pbf:   | 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl                            |
| PyBroP | bromo-tris-pyrrolidino-phosphonium hexafluorophosphate                       |
| tBu:   | tert-butyl                                                                   |
| TIS:   | triisopropylsilane                                                           |
| TOS:   | tosyl                                                                        |
| Trt    | trityl                                                                       |
| TFA:   | trifluoro acetic acid                                                        |
| TFFH:  | tetramethylfluoroformidinium hexafluorophosphate                             |
| Z:     | benzyloxycarbonyl                                                            |

Unless otherwise indicated, with the exception of the N-terminal amino acid, all abbreviations (e.g. Ala) of amino acids in this disclosure stand for the structure of -NH-C(R)(R')-CO-, wherein R and R' each is, independently, hydrogen or the side chain of an amino acid (e.g., R = CH<sub>3</sub> and R' = H for Ala), or R and R' may be joined to form a ring system.

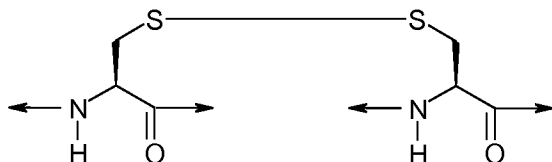
For the N-terminal amino acid, the abbreviation stands for the structure of:



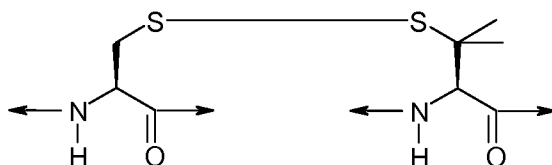
The designation "NH<sub>2</sub>" in e.g., Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>, indicates that the C-terminus of the peptide is amidated. Ac-Nle-c(Cys-D-Ala-

His-D-Phe-Arg-Trp-Cys) , or alternatively Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH , indicates that the C-terminus is the free acid.

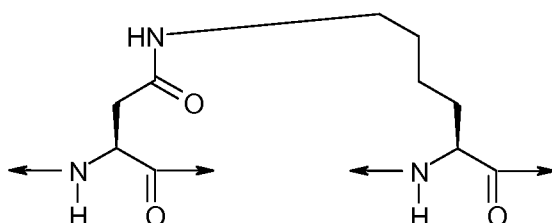
“-c(Cys-Cys)-“ or “-cyclo(Cys-Cys)-“ denotes the structure:



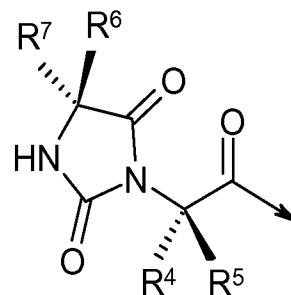
“-c(Cys-Pen)-“ or “-cyclo(Cys-Pen)-“ denotes the structure:



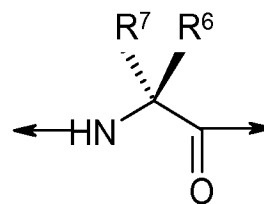
“-c(Asp-Lys)-“ or “-cyclo(Asp-Lys)-“ denotes the structure:



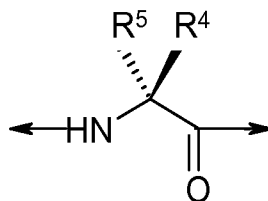
Applicants have devised the following shorthand used in naming the specific embodiments and/or species:



“HydantoinC(O)-(A<sup>a</sup>-A<sup>b</sup>)” denotes the structure:

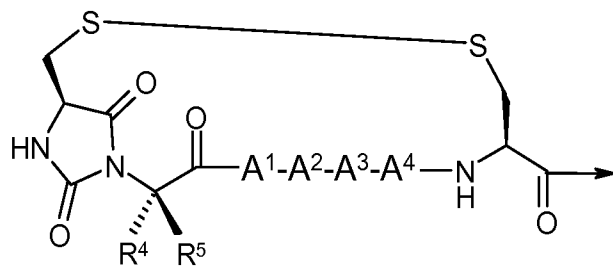


and

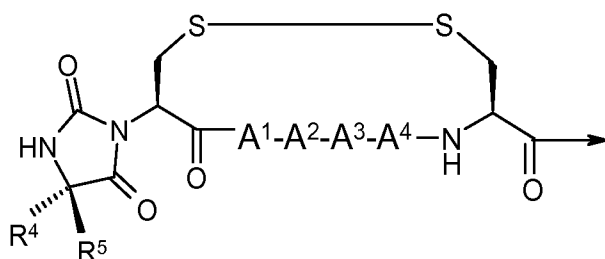


amino acid “A<sup>b</sup>” the structure:

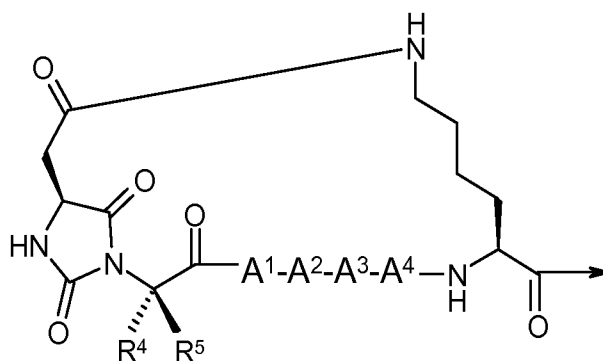
For example, a compound represented as “c[Hydantoin(C(O)-(Cys-A<sup>b</sup>))-A<sup>1</sup>-A<sup>2</sup>-A<sup>3</sup>-A<sup>4</sup>-Cys]-” would have the following the structure:



whereas a compound represented as “c[Hydantoin(C(O)-(A<sup>b</sup>-Cys))-A<sup>1</sup>-A<sup>2</sup>-A<sup>3</sup>-A<sup>4</sup>-Cys]-” would have the structure:



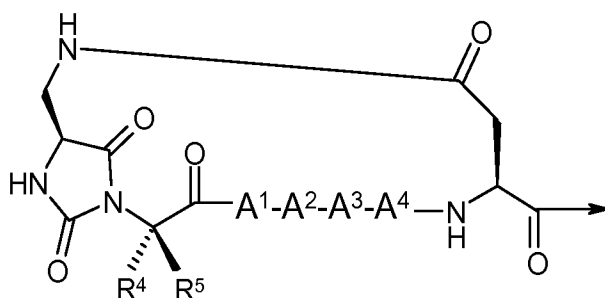
For further guidance, “c[Hydantoin(C(O)-(Asp-A<sup>b</sup>))-A<sup>1</sup>-A<sup>2</sup>-A<sup>3</sup>-A<sup>4</sup>-Lys]-” represents



the following compound:

, whereas

“c[Hydantoin(C(O)-(Dap-A<sup>b</sup>))-A<sup>1</sup>-A<sup>2</sup>-A<sup>3</sup>-A<sup>4</sup>-Asp]-” has the following formula:



“Acyl” refers to R<sup>''</sup>-C(O)-, where R<sup>''</sup> is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, alkylaryl, or substituted alkylaryl, and is indicated in the general formula of a particular embodiment as

"Ac".

"Alkyl" refers to a hydrocarbon group containing one or more carbon atoms, where multiple carbon atoms if present are joined by single bonds. The alkyl hydrocarbon group may be straight-chain or contain one or more branches or cyclic groups.

"Hydroxyalkyl" refers to an alkyl group wherein one or more hydrogen atoms of the hydrocarbon group are substituted with one or more hydroxy radicals, such as hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, hydroxypentyl, hydroxyhexyl and the like.

"Substituted alkyl" refers to an alkyl wherein one or more hydrogen atoms of the hydrocarbon group are replaced with one or more substituents selected from the group consisting of halogen, (i.e., fluorine, chlorine, bromine, and iodine), -OH, -CN, -SH, -NH<sub>2</sub>, -NHCH<sub>3</sub>, -NO<sub>2</sub>, and -C<sub>1-20</sub> alkyl, wherein said -C<sub>1-20</sub> alkyl optionally may be substituted with one or more substituents selected, independently for each occurrence, from the group consisting of halogens, -CF<sub>3</sub>, -OCH<sub>3</sub>, -OCF<sub>3</sub>, and -(CH<sub>2</sub>)<sub>0-20</sub>-COOH. In different embodiments 1, 2, 3 or 4 substituents are present. The presence of -(CH<sub>2</sub>)<sub>0-20</sub>-COOH results in the production of an alkyl acid. Non-limiting examples of alkyl acids containing, or consisting of, -(CH<sub>2</sub>)<sub>0-20</sub>-COOH include 2-norbornane acetic acid, tert-butyric acid, 3-cyclopentyl propionic acid, and the like.

The term "halo" encompasses fluoro, chloro, bromo and iodo.

"Heteroalkyl" refers to an alkyl wherein one or more of the carbon atoms in the hydrocarbon group is replaced with one or more of the following groups: amino, amido, -O-, -S- or carbonyl. In different embodiments 1 or 2 heteroatoms are present.

"Substituted heteroalkyl" refers to a heteroalkyl wherein one or more hydrogen atoms of the hydrocarbon group are replaced with one or more substituents selected from the group consisting of halogen, (i.e., fluorine, chlorine, bromine, and iodine), -OH, -CN, -SH, -NH<sub>2</sub>, -NHCH<sub>3</sub>, -NO<sub>2</sub>, and -C<sub>1-20</sub> alkyl, wherein said -C<sub>1-20</sub> alkyl optionally may be substituted with one or more substituents selected, independently for each occurrence, from the group consisting of halogens, -CF<sub>3</sub>, -OCH<sub>3</sub>, -OCF<sub>3</sub>, and -(CH<sub>2</sub>)<sub>0-20</sub>-COOH. In different embodiments 1, 2, 3 or 4 substituents are present.

"Alkenyl" refers to a hydrocarbon group made up of two or more carbons where one or more carbon-carbon double bonds are present. The alkenyl hydrocarbon group may be straight-chain or contain one or more branches or cyclic groups.

"Substituted alkenyl" refers to an alkenyl wherein one or more hydrogens are replaced with one or more substituents selected from the group consisting of halogen (i.e., fluorine, chlorine, bromine, and iodine), -OH, -CN, -SH, -NH<sub>2</sub>, -NHCH<sub>3</sub>, -NO<sub>2</sub>, and -C<sub>1-20</sub> alkyl, wherein said -C<sub>1-20</sub> alkyl optionally may be substituted with one or more substituents selected, independently for each occurrence, from the group consisting of halogens, -CF<sub>3</sub>, -OCH<sub>3</sub>, -OCF<sub>3</sub>, and -(CH<sub>2</sub>)<sub>0-20</sub>-COOH. In different embodiments 1, 2, 3 or 4 substituents are present.

"Aryl" refers to an optionally substituted aromatic group with at least one ring having a conjugated pi-electron system, containing up to three conjugated or fused ring systems. Aryl includes carbocyclic aryl, heterocyclic aryl and biaryl groups. Preferably, the aryl is a 5- or 6-membered ring. Preferred atoms for a heterocyclic aryl are one or more sulfur, oxygen, and/or nitrogen. Non-limiting examples of aryl include phenyl, 1-naphthyl, 2-naphthyl, indole, quinoline, 2-imidazole, 9-anthracene, and the like. Aryl substituents are selected from the group consisting of -C<sub>1-20</sub> alkyl, -C<sub>1-20</sub> alkoxy, halogen (i.e., fluorine, chlorine, bromine, and iodine), -OH, -CN, -SH, -NH<sub>2</sub>, -NO<sub>2</sub>, -C<sub>1-20</sub> alkyl substituted with halogens, -CF<sub>3</sub>, -OCF<sub>3</sub>, and -(CH<sub>2</sub>)<sub>0-20</sub>-COOH. In different embodiments the aryl contains 0, 1, 2, 3, or 4 substituents.

"Alkylaryl" refers to an "alkyl" joined to an "aryl".

The term "(C<sub>1</sub>-C<sub>12</sub>)hydrocarbon moiety" encompasses alkyl, alkenyl and alkynyl and in the case of alkenyl and alkynyl there is C<sub>2</sub>-C<sub>12</sub>.

For the avoidance of doubt, unless otherwise indicated, the term substituted means substituted by one or more defined groups. In the case where groups may be selected from a number of alternative groups, the selected groups may be the same or different. For the avoidance of doubt, the term independently means that where more than one substituent is selected from a number of possible substituents, those substituents may be the same or different.

The pharmaceutically acceptable salts of the compounds of the invention which contain a basic center are, for example, non-toxic acid addition salts formed with inorganic acids such as hydrochloric, hydrobromic, hydroiodic, sulfuric and phosphoric acid, with carboxylic acids or with organo-sulfonic acids. Examples include the HCl, HBr, HI, sulfate or bisulfate, nitrate, phosphate or hydrogen phosphate, acetate, benzoate, succinate, saccharate, fumarate, maleate, lactate, citrate, tartrate, gluconate, camsylate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate salts. Compounds of the invention can also provide pharmaceutically acceptable metal salts, in particular non-toxic alkali and alkaline earth metal salts, with bases. Examples include the sodium, potassium, aluminum, calcium, magnesium, zinc and diethanolamine salts (Berge, S. M. *et al.*, *J. Pharm. Sci.*, 66:1-19 (1977); Gould, P.L., *Int'l J. Pharmaceutics*, 33:201-17 (1986); and Bighley, L.D. *et al.*, *Encyclo. Pharma. Tech.*, Marcel Dekker Inc, New York, 13:453-97 (1996).

The pharmaceutically acceptable solvates of the compounds of the invention include the hydrates thereof. Also included within the scope of the invention and various salts of the invention are polymorphs thereof. Hereinafter, compounds their pharmaceutically acceptable salts, their solvates or polymorphs, defined in any aspect of the invention (except intermediate compounds in chemical processes) are referred to as "compounds of the invention".

## **EXAMPLES**

### **In vitro studies**

Compounds of the present invention can be and were tested for activity as ligands of one or more of the melanocortin receptors according to the following procedures. One skilled in the art would know that procedures similar to those described herein may be used to assay the binding activities of the compounds of the invention to melanocortin receptor molecules.

### *Radioligand Binding Assays*

Cellular membranes used for the *in vitro* receptor binding assays were obtained from transgenic CHO-K1 cells stably expressing hMC-R receptor subtypes 1, 3, 4 or 5. The CHO-K1 cells expressing the desired hMC-R receptor type were sonicated (Branson® setting 7, approximately 30 sec) in ice-cold 50 mM Tris-HCl at pH 7.4 and then centrifuged at 39,000 g for 10 minutes at approximately 4°C. The pellets were resuspended in the same buffer and centrifuged at 50,000 g for 10 minutes at approximately 4°C. The washed pellets containing the cellular membranes were stored at approximately -80°C.

Competitive inhibition of [<sup>125</sup>I](Tyr<sup>2</sup>)-(Nle<sup>4</sup>-D-Phe<sup>7</sup>)α-MSH ([<sup>125</sup>I]-NDP-α-MSH, Amersham Biosciences®) binding was carried out in polypropylene 96 well plates. Cell membranes (1-10 µg protein/well) prepared as described above were incubated in 50 mM Tris-HCl at pH 7.4 containing 0.2% bovine serum albumin (BSA), 5 mM MgCl<sub>2</sub>, 1 mM CaCl<sub>2</sub> and 0.1 mg/mL bacitracin, with increasing concentrations of the test compound and 0.1-0.3 nM [<sup>125</sup>I]-NDP-α-MSH for approximately 90-120 minutes at approximately 37°C. Bound [<sup>125</sup>I]-NDP-α-MSH ligand was separated from free [<sup>125</sup>I]-NDP-α-MSH by filtration through GF/C glass fiber filter plates (Unifilter®; Packard) presoaked with 0.1 % (w/v) polyethylenimine (PEI), using a Packard Filtermate® harvester. Filters were washed three times with 50 mM Tris-HCl at pH 7.4 at a temperature of approximately 0-4°C and then assayed for radioactivity using a Packard Topcount® scintillation counter. Binding data were analyzed by computer-assisted non-linear regression analysis (XL fit; IDBS). A selection of the preferred embodiments was tested using the above-discussed assay and the binding constants (K<sub>i</sub> in nM) are reported in Tables 5, 6, 7 and 8.

TABLE 5 - Radioligand Binding Assay Data for Selected Compounds

Table 5A

| Compound (according to Formula I)                           | Ki hMC1-R | Ki hMC3-R | Ki hMC4-R | Ki hMC5-R | Ki hMC1-R/MC4-R |
|-------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------------|
| Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 3.87      | 10.1      | 2.09      | 430       | 1.9             |
| Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 4.01      | 12.1      | 1.76      | 352       | 2.3             |
| Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub> | 8.29      | 13.3      | 2.78      | 816       | 3.0             |
| Ac-D-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>  | 3.93      | 172       | 11.0      | 538       | 0.36            |
| Ac-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>    | 1.81      | 20.5      | 4.57      | 502       | 0.4             |
| Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>   | 9.67      | 22.0      | 4.2       | 1900      | 2.3             |
| Ac-D-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH <sub>2</sub>   | 0.79      | 45.5      | 1.21      | 493       | 0.6             |
| Ac-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH <sub>2</sub>     | 0.68      | 20.7      | 1.01      | 783       | 0.7             |

Table 5B

| Compound (according to Formula I)                                  | Ki hMC1-R | Ki hMC3-R | Ki hMC4-R | Ki hMC5-R | Ki hMC1-R/MC4-R |
|--------------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------------|
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-NH <sub>2</sub>      | 114       | 63.9      | 3.07      | 1657      | 37.1            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>          | 11        | 26        | 7.6       | 1800      | 1.4             |
| D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.05      | 9.3       | 1.1       | 2.9       | 0.0             |
| Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH <sub>2</sub>               | 0.07      | 4.1       | 0.85      | 8.8       | 0.1             |
| Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>           | 0.12      | 10        | 0.43      | 0.42      | 0.3             |
| Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>              | 0.05      | 1.3       | 0.47      | 0.2       | 0.1             |
| Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-NH <sub>2</sub>          | 0.0996    | 9318      | 0.617     | 10.9      | 0.16            |
| Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-NH <sub>2</sub>            | .0132     | 16.1      | 1.23      | 0.359     | 0.11            |

| Compound (according to Formula I)                                           | Ki<br>hMC1-R | Ki<br>hMC3-R | Ki<br>hMC4-R | Ki<br>hMC5-R | Ki<br>hMC1-R<br>/MC4-R |
|-----------------------------------------------------------------------------|--------------|--------------|--------------|--------------|------------------------|
| D-Phe-c(Cys-His-D-Phe-Arg-Trp- $\beta$ -Ala-D-Cys)-Thr-NH <sub>2</sub>      | 0.207        | 43.2         | 2.58         | 344          | 0.08                   |
| D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-NH <sub>2</sub>               | 0.420        | 106          | 4.75         | 1260         | 0.09                   |
| Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH <sub>2</sub>                     | 0.0951       | 9.33         | 0.894        | 13.4         | 0.11                   |
| Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-NH <sub>2</sub>                     | 0.999        | 300          | 11.1         | 431          | 0.09                   |
| Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                    | 0.106        | 11.8         | 1.49         | 110          | 0.07                   |
| Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                    | 0.0506       | 9.89         | 1.04         | 16.3         | 0.05                   |
| Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                    | 0.884        | 223          | 22.5         | 609          | 0.04                   |
| Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                   | 0.721        | 93.5         | 56.0         | 747          | 0.01                   |
| Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                  | 0.227        | 14.5         | 2.99         | 164          | 0.08                   |
| Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>                   | 0.277        | 25.2         | 3.37         | 203          | 0.08                   |
| Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp- $\beta$ -Ala-Cys)-NH <sub>2</sub>         | 0.323        | 14.1         | 1.96         | 24.0         | 0.16                   |
| Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                   | 34.1         | 118          | 17.0         | 5560         | 2.01                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>                   | 29.1         | 22.8         | 3.84         | 2550         | 7.58                   |
| D-Phe-c(Cys-His-D-Phe-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-NH <sub>2</sub>     | 0.442        | 123          | 10.3         | 521          | 0.04                   |
| D-Phe-c(Cys-His-D-Phe-Arg-Bip- $\beta$ -Ala-D-Cys)-Thr-NH <sub>2</sub>      | 5.80         | 3370         | 583          | 1130         | 0.01                   |
| D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.0567       | 31.4         | 14.7         | 9.27         | 0                      |
| D-Phe-c(Cys-His-D-Phe-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-NH <sub>2</sub>     | 1.68         | 1260         | 172          | 1220         | 0.01                   |

| Compound (according to Formula I)                                   | Ki<br>hMC1-R | Ki<br>hMC3-R | Ki<br>hMC4-R | Ki<br>hMC5-R | Ki<br>hMC1-R<br>/MC4-R |
|---------------------------------------------------------------------|--------------|--------------|--------------|--------------|------------------------|
| D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip-β-Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.128        | 85.6         | 36.9         | 38.0         | 0                      |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)-NH <sub>2</sub>       | 0.352        | 149          | 3.01         | 339          | 0.12                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-D-Ala-Cys)-NH <sub>2</sub>     | 3.93         | 876          | 48.0         | 4940         | 0.08                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH <sub>2</sub>     | 0.995        | 287          | 4.80         | 766          | 0.21                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.848        | 184          | 3.76         | 956          | 0.23                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Apn-Cys)-NH <sub>2</sub>       | 1.10         | 228          | 7.58         | 859          | 0.15                   |
| Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Trp-Lys)-NH <sub>2</sub>           | 0.659        | 98.9         | 2.55         | 4.19         | 0.26                   |
| Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Lys)-NH <sub>2</sub>           | 4.12         | 445          | 50.6         | 4300         | 0.08                   |
| Ac-c(Cys-Glu-His-D-Phe-Arg-Trp-Ala-Cys)-NH <sub>2</sub>             | 111          | 1710         | 47.7         | 694          | 2.33                   |
| Ac-c(Cys-Glu-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH <sub>2</sub>           | 262          | 2500         | 96.4         | 1460         | 2.72                   |
| Ac-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH <sub>2</sub>           | 199          | 5990         | 96.7         | > 10000      | 2.06                   |
| Ac-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH <sub>2</sub>         | 132          | 4560         | 40.7         | 8810         | 3.24                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH <sub>2</sub>       | 9.12         | 1130         | 22.1         | 2860         | 0.41                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH <sub>2</sub>     | 1.00         | 227          | 5.55         | 496          | 0.18                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.536        | 169          | 3.12         | 358          | 0.17                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-OH                        | 32.1         | 330          | 17.4         | 165          | 1.84                   |
| Ac-Nle-c(Cys-D-Abu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>           | 10.6         | 41.1         | 7.69         | 54.9         | 1.38                   |
| Ac-Nle-c(Cys-D-Val-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>           | 13.0         | 104          | 10.1         | 40           | 1.29                   |

| Compound (according to Formula I)                             | Ki<br>hMC1-R | Ki<br>hMC3-R | Ki<br>hMC4-R | Ki<br>hMC5-R | Ki<br>hMC1-R<br>/MC4-R |
|---------------------------------------------------------------|--------------|--------------|--------------|--------------|------------------------|
| Ac-Nle-c(Cys-D-Ile-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 4.28         | 38.5         | 9.0          | 12.5         | 0.48                   |
| Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 1.60         | 6.82         | 4.13         | 5.57         | 0.39                   |
| Ac-Nle-c(Cys-D-Tle-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 12.0         | 85.8         | 11.2         | 40           | 1.07                   |
| Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 0.353        | 2.08         | 1.41         | 0.857        | 0.25                   |
| Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.537        | 86.1         | 5.89         | 2.56         | 0.09                   |
| Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>      | 0.744        | 178          | 3.51         | 2.69         | 0.21                   |
| Ac-Leu-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.216        | 17.4         | 0.995        | 0.486        | 0.22                   |
| Ac-Cha-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.107        | 9.11         | 0.884        | 0.354        | 0.12                   |
| Ac-Ile-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.148        | 13.9         | 1.06         | 0.423        | 0.14                   |
| Ac-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.254        | 18.5         | 2.13         | 0.714        | 0.12                   |
| Ac-Val-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>      | 0.256        | 29.9         | 1.98         | 0.864        | 0.13                   |
| Ac-2-Nal-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>    | 0.560        | 39.2         | 2.94         | 2.73         | 0.19                   |
| Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>         | 0.186        | 15.2         | 4.93         | 0.537        | 0.04                   |
| Ac-Nle-c(Cys-3-Pal-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>    | 21.1         | 151          | 10.4         | 92.6         | 2.03                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH                  | 30.7         | 152          | 15.6         | 114          | 1.97                   |
| Ac-Nle-c(Cys-His-Phe-Arg-D-Trp-Gaba-Cys)-NH <sub>2</sub>      | 5.20         | 150          | 138          | 20.3         | 0.04                   |
| Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Ala-Lys)-NH <sub>2</sub> | 4.89         | 290          | 21.3         | 11.1         | 0.23                   |
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub>   | 25.5         | 3.82         | 7.61         | 102          | 3.35                   |
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-NH <sub>2</sub> | 32.5         | 5.85         | 2.53         | 94.6         | 12.85                  |
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-NH <sub>2</sub>   | 22.2         | 12.7         | 16.6         | 125          | 1.34                   |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Ala-Lys)-NH <sub>2</sub>     | 1.17         | 1.56         | 0.277        | 3.24         | 4.22                   |

| Compound (according to Formula I)                                   | Ki hMC1-R | Ki hMC3-R | Ki hMC4-R | Ki hMC5-R | Ki hMC1-R /MC4-R |
|---------------------------------------------------------------------|-----------|-----------|-----------|-----------|------------------|
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp- $\beta$ -Ala-Lys)-NH <sub>2</sub> | 0.648     | 2.78      | 0.329     | 1.4       | 1.97             |
| Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>          | 0.393     | 1.86      | 0.375     | 1.11      | 1.05             |
| Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Ahx-Cys)-NH <sub>2</sub>           | 0.333     | 2.91      | 0.998     | 0.366     | 0.33             |
| Ac-hPhe-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>         | 0.461     | 2.45      | 0.931     | 1.37      | 0.50             |
| Ac-Cha-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>          | 0.576     | 3.98      | 2.82      | 3.91      | 0.20             |

Table 5C

| Compound (according to Formula I)                           | Ki hMC1-R | Ki hMC3-R | Ki hMC4-R | Ki hMC5-R | Ki hMC1-R /MC4-R |
|-------------------------------------------------------------|-----------|-----------|-----------|-----------|------------------|
| Ac-Arg-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub> | 17.9      | 1.68      | 0.256     | 23.4      | 69.9             |

TABLE 6 - Radioligand Binding Assay Data for Selected Compounds

Table 6A

| Compound (according to Formula III)                                                                             | Ki hMC1-R | Ki hMC3-R | Ki hMC4-R | Ki hMC5-R |
|-----------------------------------------------------------------------------------------------------------------|-----------|-----------|-----------|-----------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                       | 49.9      | 9.00      | 0.569     | 218       |
| Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH <sub>2</sub>                  | 11.9      | 38.1      | 5.70      | 11.8      |
| Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Doc-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH <sub>2</sub>              | 3.46      | 16.6      | 6.65      | 4.88      |
| Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>    | 0.614     | 5.09      | 2.31      | 3.23      |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.56      | 14.1      | 5.17      | 7.12      |

| Compound (according to Formula III)                                                                                                   | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|---------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| H-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-Doc-<br>Doc-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-<br>Arg-Arg-NH <sub>2</sub>                      | 1.10             | 1.58             | 6.00             | 0.629            |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-<br>Pro-Pro-Lys-Asp-Tyr-Gly-Arg-Lys-Lys-Arg-<br>Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>             | 0.0868           | 0.751            | 0.0944           | 0.147            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-<br>Cys)-Pro-Pro-Lys-Asp-Tyr-Gly-Arg-Lys-Lys-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 1.66             | 4.80             | 0.250            | 9.62             |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-β-<br>Ala-β-Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-<br>Gln-Arg-Arg-Arg-NH <sub>2</sub>                 | 0.0452           | 0.298            | 0.169            | 0.386            |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-<br>Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-Lys-Lys-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 0.0808           | 0.396            | 0.0747           | 0.311            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-<br>Cys)-Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-Lys-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 4.41             | 4.23             | 0.455            | 12.9             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 1.25             | 0.661            | 0.292            | 5.94             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-Lys-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 1.89             | 0.546            | 0.166            | 6.06             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                       | 87.8             | 9.08             | 1.20             | 359              |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                       | 124              | 17.8             | 1.11             | 348              |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                         | 163              | 23.0             | 0.586            | 844              |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-<br>Doc-Doc-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-<br>Arg-Arg-Arg-NH <sub>2</sub>                     | 0.144            | 0.352            | 0.0845           | 0.415            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.74             | 0.590            | 0.170            | 4.38             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-Arg-<br>Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>           | 3.86             | 4.97             | 0.192            | 38.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 12.8             | 15.9             | 0.950            | 165              |

| Compound (according to Formula III)                                                                                                 | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Arg-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 3.07             | 4.05             | 0.498            | 31.1             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Gln-Arg-Arg-Arg-Arg-NH <sub>2</sub> | 0.792            | 0.570            | 0.162            | 4.18             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Gln-Arg-Arg-Arg-Arg-Arg-NH <sub>2</sub> | 0.726            | 0.474            | 0.209            | 5.12             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Gln-Lys-Arg-Arg-Arg-Arg-Arg-NH <sub>2</sub> | 0.857            | 0.580            | 0.209            | 4.42             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Arg-Arg-Gln-Arg-NH <sub>2</sub> | 0.813            | 0.675            | 0.269            | 4.20             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Tyr-Aib-Arg-Lys-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 7.84             | 10.2             | 0.783            | 91.8             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 2.93             | 9.07             | 0.293            | 59.0             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 2.42             | 6.56             | 0.238            | 41.7             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 6.66             | 19.3             | 0.819            | 88.8             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 2.63             | 2.09             | 0.0737           | 11.6             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 2.48             | 1.21             | 0.209            | 9.17             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 3.65             | 2.26             | 0.261            | 12.1             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 7.32             | 11.0             | 0.659            | 78.0             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-Arg-<br>Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 4.11             | 7.26             | 0.302            | 48.3             |

| Compound (according to Formula III)                                                                                                              | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>          | 6.77             | 14.3             | 0.781            | 84.0             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Arg-Gln-Arg-Arg-NH <sub>2</sub> (85) | 3.04             | 3.22             | 0.230            | 3.85             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-<br>Gln-Lys-Lys-Arg-Arg-Arg-Arg-Arg-NH <sub>2</sub>      | 3.24             | 2.66             | 0.208            | 5.96             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Arg-Arg-Arg-Gln-NH <sub>2</sub>      | 1.58             | 1.43             | 0.275            | 2.97             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>    | 4.59             | 6.28             | 0.588            | 22.6             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Lys-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>      | 6.46             | 5.22             | 0.380            | 15.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Arg-Lys-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>            | 4.62             | 5.68             | 0.505            | 45.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Lys-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>            | 2.12             | 3.99             | 0.352            | 27.5             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Arg-Lys-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>            | 3.41             | 0.975            | 0.549            | 11.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-<br>Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>    | 4.18             | 1.12             | 0.223            | 15.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Gly-Arg-Arg-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>        | 2.71             | 0.732            | 0.202            | 5.53             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Gly-Arg-Lys-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>        | 5.66             | 1.40             | 0.446            | 6.23             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-(Doc)2-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-<br>Gln-Arg-Arg-Arg-NH <sub>2</sub>                             | 0.211            | 0.665            | 0.635            | 118              |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Gln-<br>Arg-Arg-Arg-Arg-NH <sub>2</sub>                      | 0.351            | 0.891            | 0.503            | 102              |

| Compound (according to Formula III)                                                                         | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-NH <sub>2</sub>       | 0.209            | 0.699            | 0.596            | 137              |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 0.439            | 1.52             | 0.476            | 115              |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 0.821            | 2.50             | 0.700            | 148              |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 0.406            | 1.11             | 0.602            | 131              |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 1.27             | 4.63             | 1.51             | 220              |

Table 6B

| Compound (according to Formula IV)                                                                                            | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-β-Ala-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                 | 2058             | 113              | 10.7             | 239              |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Aib-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                   | 1818             | 306              | 5.87             | 979              |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.75             | 1.74             | 0.15             | 16.8             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.50             | 1.61             | 0.301            | 10.4             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 1.81             | 2.08             | 0.305            | 19.3             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 2.69             | 2.59             | 0.243            | 19.2             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 2.25             | 0.62             | 0.303            | 2.77             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.49             | 0.604            | 0.865            | 3.13             |

| Compound (according to Formula IV)                                                                                                  | Ki<br>hMC1-<br>R | Ki<br>hMC3-<br>R | Ki<br>hMC4-<br>R | Ki<br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|------------------|------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Arg-Lys-Arg-Arg-<br>Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 3.28             | 1.95             | 0.575            | 15.5             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Arg-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 2.24             | 1.57             | 0.437            | 16.4             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 2.14             | 1.12             | 0.624            | 11.9             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Arg-Lys-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 2.50             | 1.59             | 0.573            | 15.7             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Lys-Arg-<br>Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 3.00             | 1.70             | 0.442            | 15.5             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-<br>Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Lys-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 4.29             | 2.15             | 0.425            | 15.5             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-<br>Gln-Arg-Arg-Arg-NH <sub>2</sub>                 | 0.410            | 0.837            | 0.246            | 56.3             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-<br>Gln-Arg-Arg-Arg-NH <sub>2</sub>                 | 0.572            | 1.07             | 0.210            | 63.6             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-<br>Arg-Arg-Arg-NH <sub>2</sub>                     | 0.475            | 0.800            | 0.196            | 53.8             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-<br>Arg-Arg-Arg-NH <sub>2</sub>                     | 0.779            | 1.21             | 0.293            | 56.0             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Arg-Arg-Lys-Arg-Arg-Gln-Arg-<br>Arg-Arg-NH <sub>2</sub>                         | 0.212            | 1.23             | 0.484            | 58.5             |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-<br>Cys)-β-Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-<br>Arg-Arg-NH <sub>2</sub>                         | 0.778            | 1.22             | 0.468            | 47.0             |

TABLE 7 - Binding Constants for Formula (V) Examples

Table 7A

| Formula (V) Compounds                                                | Ki<br>hMC1 | Ki<br>hMC3 | Ki<br>hMC4 | Ki<br>hMC5 |
|----------------------------------------------------------------------|------------|------------|------------|------------|
| c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 230        | 7590       | 126        | 7020       |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Lys]-NH <sub>2</sub> | 72.6       | 1920       | 45.2       | >10000     |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH <sub>2</sub> | 60.4       | 2840       | 52.4       | >10000     |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dab]-NH <sub>2</sub> | 28         | 90.5       | 12.7       | 877        |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH <sub>2</sub> | 16.4       | 863        | 4.97       | >10000     |
| c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH <sub>2</sub> | 37.7       | 576        | 7.81       | 6400       |
| c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH <sub>2</sub> | 66.6       | 1820       | 19.9       | >10000     |
| c[Hydantoin(C(O)-(Asp-His))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 200        | 68.8       | 6.63       | 142        |
| c[Hydantoin(C(O)-(Asp-Aic))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 9028       | 2628       | 35.8       | 1156       |
| c[Hydantoin(C(O)-(Asp-A5c))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 9938       | 2390       | 44.6       | 1103       |
| c[Hydantoin(C(O)-(Asp-A6c))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 2170       | 1479       | 16.5       | 451        |
| c[Hydantoin(C(O)-(Asp-Apc))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 1276       | 2756       | 266        | 1096       |
| c[Hydantoin(C(O)-(Asp-A3c))-D-2-Nal-Arg-Trp-Lys]-NH <sub>2</sub>     | 7567       | 1922       | 420        | 2879       |

TABLE 7B - Binding Constants for Formula (VI) Examples

| Formula (VI) Compounds                                                         | Ki<br>hMC1 | Ki<br>hMC3 | Ki<br>hMC4 | Ki<br>hMC5 |
|--------------------------------------------------------------------------------|------------|------------|------------|------------|
| Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 14.3       | 198        | 5.76       | 67.8       |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 11.9       | 311        | 5.41       | 73.9       |
| Hydantoin(C(O)-(A6c-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 31.6       | 224        | 19.6       | 2500       |
| Hydantoin(C(O)-(D-Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 16.0       | 63.9       | 8.64       | 1820       |
| Hydantoin(C(O)-(Val-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 33.7       | 132        | 40.2       | 3210       |

| Formula (VI) Compounds                                                                        | Ki<br>hMC1 | Ki<br>hMC3 | Ki<br>hMC4 | Ki<br>hMC5 |
|-----------------------------------------------------------------------------------------------|------------|------------|------------|------------|
| Hydantoin(C(O)-(Leu-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 48.3       | 534        | 74.1       | 3290       |
| Hydantoin(C(O)-(Cha-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 40.8       | 870        | 137        | 3560       |
| Hydantoin(C(O)-(Aib-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 17.7       | 73.6       | 8.40       | 2120       |
| Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 7.92       | 46.4       | 6.70       | 21.3       |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 20.9       | 69.7       | 8.32       | 50.0       |
| Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>                  | 12.9       | 38.5       | 3.53       | 27.1       |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>                  | 127        | 811        | 10.4       | 381        |
| Hydantoin(C(O)-(Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 13.9       | 38.4       | 5.73       | 18.9       |
| Hydantoin(C(O)-(D-Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                | 11.7       | 73.1       | 4.28       | 34.7       |
| Hydantoin(C(O)-(Aib-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 36.8       | 290        | 13.7       | 133        |
| Hydantoin(C(O)-(Val-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 15.3       | 160        | 8.66       | 33.4       |
| Hydantoin(C(O)-(Ile-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 11.6       | 194        | 11.5       | 28.9       |
| Hydantoin(C(O)-(Leu-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 19.3       | 331        | 26.7       | 44.6       |
| Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 9.49       | 124        | 2.95       | 2260       |
| Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 4.30       | 78.0       | 1.77       | 4540       |
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                    | 8.59       | 94.1       | 2.44       | 7760       |
| Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                    | 5.68       | 55.5       | 2.44       | 4220       |
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 2.65       | 41.3       | 4.17       | 650        |
| Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                | 3.52       | 48.7       | 5.78       | 872        |
| Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> (SEQ ID NO288) | 3.51       | 29.2       | 6.04       | 914        |
| Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>                  | 1.14       | 01.7       | 4.53       | 783        |

| Formula (VI) Compounds                                                         | Ki<br>hMC1 | Ki<br>hMC3 | Ki<br>hMC4 | Ki<br>hMC5 |
|--------------------------------------------------------------------------------|------------|------------|------------|------------|
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub> | 11.9       | 7.43       | 0.195      | 14.6       |

TABLE 7C - Binding Constants for Formula (VII) Examples

| Formula (VII) Compounds                                                  | Ki<br>hMC1 | Ki<br>hMC3 | Ki<br>hMC4 | Ki<br>hMC5 |
|--------------------------------------------------------------------------|------------|------------|------------|------------|
| c[Hydantoin(C(O)-(Aib-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 47.6       | 1100       | 47.1       | >10000     |
| c[Hydantoin(C(O)-(Val-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 21.2       | 730        | 34.5       | >10000     |
| c[Hydantoin(C(O)-(Leu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 47.4       | 1550       | 27.9       | >10000     |
| c[Hydantoin(C(O)-(Ile-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 53.4       | 1760       | 41.6       | >10000     |
| c[Hydantoin(C(O)-(A6c-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | 38.5       | 1760       | 53.2       | 9270       |
| c[Hydantoin(C(O)-(Gly-Cys))-Glu-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub>   | 15.6       | 305        | 8.92       | 3070       |

TABLE 8 - Radioligand Binding Assay Data for Selected Compounds

| Compound                                                        | Ki<br>hMC1-R | Ki<br>hMC3-R | Ki<br>hMC4-R | Ki<br>hMC5-R |
|-----------------------------------------------------------------|--------------|--------------|--------------|--------------|
| Ac-Tyr-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 8.53         | 21.2         | 3.72         | 714          |
| Ac-2-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 6.09         | 34.9         | 2.02         | 864          |
| Ac-1-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 6.27         | 36.4         | 1.53         | 888          |
| Ac-Phe-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 1.48         | 14.8         | 2.34         | 491          |
| Ac-Trp-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 4.7          | 42           | 2.25         | 1470         |
| Ac-Pff-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 0.323        | 1.33         | 1.95         | 786          |

### *Melanocortin Functional Activity and Selectivity*

The compounds of the present invention will interact preferentially (i.e., selectively) to MC-4 relative to the other melanocortin receptors. Selectivity is particularly important when the compounds are administered to humans or other animals to minimize the number of side effects associated with their administration. MC-4 selectivity of a compound is defined herein as the ratio of the EC<sub>50</sub> of the compound for an MC-1 receptor (EC<sub>50</sub> -MC-1) over the EC<sub>50</sub> of the compound for the MC-3 (EC<sub>50</sub> -MC-3)/MC-4 (EC<sub>50</sub> -MC-4) receptor, the EC<sub>50</sub> values being measured as described above. The formulas are as follows:

$$MC-3 \text{ selectivity} = [EC_{50}\text{-MC-1}]/[EC_{50}\text{-MC-3}]$$

$$MC-4 \text{ selectivity} = [EC_{50}\text{-MC-1}]/[EC_{50}\text{-MC-4}]$$

A compound is defined herein as being "selective for the MC-3 receptor" when the above mentioned ratio "MC-3-selectivity" is at least about 10, preferably at least about 100, and more preferably at least about 500.

A compound is defined herein as being "selective for the MC-4 receptor" when the above mentioned ratio "MC-4-selectivity" is at least about 10, preferably at least about 100, and more preferably at least about 500.

One skilled in the art would know that procedures similar to those described herein may be used to assay the binding activities of the compounds of the invention to melanocortin receptor molecules.

### *cyclic AMP Bioassay*

Intracellular cyclic AMP (cAMP) levels were determined by an electrochemiluminescence (ECL) assay (Meso Scale Discovery®, Gaithersburg, MD; referred to hereinafter as MSD). CHO-K1 cells stably expressing the hMC receptor subtypes were suspended in RMPI 1640® assay buffer (RMPI 1640 buffer contains 0.5 mM isobutylmethylxanthine (IBMX), and 0.2% protein cocktail (MSD blocker A)). Transgenic CHO-K1 cells stably expressing hMC receptor subtypes 1, 3, 4 or 5 were dispensed at a density of approximately 7,000 cells/well in 384-well Multi-Array®

plates (MSD) containing integrated carbon electrodes and coated with anti-cAMP antibody. Increasing concentrations of the test compounds were added and the cells were incubated for approximately 40 minutes at approximately 37°C. Following this incubation, lysis buffer (HEPES-buffered saline solution with MgCl<sub>2</sub> and Triton X-100® at pH 7.3) containing 0.2% protein cocktail and 2.5 nM TAG™ ruthenium-labeled cAMP (MSD) was added and the cells were incubated for approximately 90 minutes at room temperature. At the end of the second incubation period read buffer (Tris-buffered solution containing an ECL co-reactant and Triton X-100 at pH 7.8) was added and the cAMP levels in the cell lysates were immediately determined by ECL detection with a Sector Imager 6000 reader® (MSD). Data were analyzed using a computer-assisted non-linear regression analysis (XL fit; IDBS) and reported as either an EC<sub>50</sub> value or a Kb value.

EC<sub>50</sub> represents the concentration of an agonist compound needed to obtain 50% of the maximum reaction response, *e.g.*, 50% of the maximum level of cAMP as determined using the assay described above. The Kb value reflects the potency of an antagonist and is determined by Schild analysis. In brief, concentration-response curves of an agonist are carried out in the presence of increasing concentrations of an antagonist. The Kb value is the concentration of antagonist which would produce a 2-fold shift in the concentration-response curve for an agonist. It is calculated by extrapolating the line on a Schild plot to zero on the y-axis.

A selection of compounds was tested using the above-discussed assays and the results are reported in Tables 9, 10, 11, and 12.

TABLE 9 - cAMP Bioassay Data for Selected Compounds

Table 9A

| Compound<br>(according to<br>Formula I)                   | EC <sub>50</sub><br>hMC1-R | EC <sub>50</sub><br>hMC3-R | EC <sub>50</sub><br>hMC4-R | EC <sub>50</sub><br>hMC5-R | EC <sub>50</sub><br>hMC1-R<br>/MC4-R |
|-----------------------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|--------------------------------------|
| Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 5.79                       | 5.25                       | 0.313                      | 1630                       | 18.0                                 |

| Compound<br>(according to<br>Formula I)                     | EC <sub>50</sub><br>hMC1-R | EC <sub>50</sub><br>hMC3-R | EC <sub>50</sub><br>hMC4-R | EC <sub>50</sub><br>hMC5-R | EC <sub>50</sub><br>hMC1-R<br>/MC4-R |
|-------------------------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|--------------------------------------|
| Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 6.17                       | 5.6                        | 0.397                      | 1020                       | 16.0                                 |
| Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub> | 26.5                       | 10.5                       | 0.493                      | 2440                       | 54.0                                 |
| Ac-D-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>  | 8.43                       | 32.4                       | 0.959                      | 2140                       | 9.0                                  |
| Ac-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>    | 4.23                       | 8.09                       | 0.719                      | 23.2                       | 6.0                                  |
| Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>   | 48.3                       | 13.3                       | 0.79                       | 10000                      | 61.0                                 |
| Ac-D-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH <sub>2</sub>   | 1.48                       | 5.76                       | 0.078                      | 297                        | 19.0                                 |
| Ac-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH <sub>2</sub>     | 1.39                       | 2.89                       | 0.055                      | 467                        | 25.0                                 |

ND = not determined

Table 9B

| Compound<br>(according to Formula I)                               | EC <sub>50</sub><br>hMC1-R | EC <sub>50</sub><br>hMC3-R | EC <sub>50</sub><br>hMC4-R | EC <sub>50</sub><br>hMC5-R | EC <sub>50</sub><br>hMC1-R<br>/MC4-R |
|--------------------------------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|--------------------------------------|
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>          | 2.4                        | 0.33                       | 0.078                      | 420                        | 31                                   |
| D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.35                       | 1.1                        | 0.11                       | 0.37                       | 3                                    |
| Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH <sub>2</sub>               | 0.31                       | 0.27                       | 0.018                      | 3.1                        | 17                                   |
| Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH <sub>2</sub>           | 0.28                       | 0.24                       | 0.028                      | 3.9                        | 10                                   |
| Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>              | 0.37                       | 0.1                        | 0.021                      | 1.7                        | 18                                   |
| Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-NH <sub>2</sub>          | 0.834                      | 0.145                      | 0.128                      | 2.79                       | 6.52                                 |

| Compound<br>(according to Formula I)                                | EC <sub>50</sub><br>hMC1-<br>R | EC <sub>50</sub><br>hMC3-<br>R | EC <sub>50</sub><br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R | EC <sub>50</sub><br>hMC1-R<br>/MC4-R |
|---------------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------------|
| Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH <sub>2</sub>             | 0.76                           | 0.199                          | 0.0492                         | 1.73                           | 15.45                                |
| Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>            | 3.26                           | 0.189                          | 0.0949                         | 30.2                           | 34.35                                |
| Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>            | 1.37                           | 0.628                          | 0.131                          | 3.48                           | 10.46                                |
| Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>           | 2.27                           | 3.32                           | 7.24                           | 415                            | 0.31                                 |
| Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>           | ND                             | 1.89                           | 0.531                          | ND                             | ND                                   |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>           | 14.3                           | 2.03                           | 0.183                          | 2240                           | 78.14                                |
| D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.345                          | 2.71                           | 5376                           | 2.38                           | 0.06                                 |
| D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip-β-Ala-D-Cys)-Thr-NH <sub>2</sub> | 0.685                          | 81.8                           | 86.9                           | 31.8                           | 0.01                                 |
| Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Lys)-NH <sub>2</sub>           | 0.931                          | 3.22                           | 1.65                           | >10000                         | 0.56                                 |
| Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>           | 3.24                           | 0.465                          | 0.0915                         | 78.5                           | 35.41                                |
| Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>           | 0.819                          | 0.541                          | 0.453                          | 45.3                           | 1.81                                 |

ND = not determined

Table 9C

| Compound<br>(according to Formula I)                        | EC <sub>50</sub><br>hMC1-R | Kb<br>hMC3-R | Kb<br>MC4-R | EC <sub>50</sub><br>hMC5-R |
|-------------------------------------------------------------|----------------------------|--------------|-------------|----------------------------|
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub> | 17.6                       | 12.4         | 38.8        | 11.8                       |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Ala-Lys)-NH <sub>2</sub>   | 0.619                      | 2.98         | 0.109       | 0.189                      |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-β-Ala-Lys)-NH <sub>2</sub> | 0.913                      | 0.536        | 0.346       | 0.489                      |
| Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Gaba-Cys)-NH <sub>2</sub>  | 0.231                      | 18.4         | 0.782       | 0.153                      |
| Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Ahx-Cys)-NH <sub>2</sub>   | 0.581                      | 10.8         | 0.967       | 0.126                      |
| Ac-hPhe-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH <sub>2</sub> | 0.413                      | 9.32         | 0.824       | 0.307                      |

| Compound<br>(according to Formula I)                          | EC50<br>hMC1-R | Kb<br>hMC3-R | Kb<br>MC4-R | EC50<br>hMC5-R |
|---------------------------------------------------------------|----------------|--------------|-------------|----------------|
| Ac-Cha-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH <sub>2</sub>    | 1.27           | 3.02         | 0.442       | 0.736          |
| Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-NH <sub>2</sub> | 383            | 61.5         | 53.6        | 2842           |

Table 9D

| Compound<br>(according to Formula I)                        | EC50<br>hMC1-R | Kb<br>hMC3-R | Kb<br>MC4-R | EC50<br>hMC5-R |
|-------------------------------------------------------------|----------------|--------------|-------------|----------------|
| Ac-Arg-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub> | 193            | 5.72         | 1.58        | 1111           |

Table 10A

| Compound (according to Formula III)                                                                                           | EC <sub>50</sub><br>hMC1-R | Kb<br>hMC3-R | Kb<br>hMC4-R | EC <sub>50</sub><br>hMC5-R |
|-------------------------------------------------------------------------------------------------------------------------------|----------------------------|--------------|--------------|----------------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                     | 66.1                       | 33.4         | 0.687        | 6.84                       |
| Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH <sub>2</sub>                                | ND                         | 4500         | 105          | ND                         |
| Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Doc-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH <sub>2</sub>                            | ND                         | 395          | 16.8         | ND                         |
| Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-NH <sub>2</sub>                      | ND                         | 207          | 18.5         | ND                         |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>               | ND                         | 220          | 4.07         | ND                         |
| H-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-Doc-Doc-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>                      | ND                         | 261          | 3.11         | ND                         |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-Pro-Pro-Lys-Asp-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>             | ND                         | 14.1         | 22.8         | ND                         |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-Cys)-Pro-Pro-Lys-Asp-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | ND                         | 233          | 26.0         | ND                         |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 1.39                       | 16.2         | 7.94         | 0.839                      |

| Compound (according to Formula III)                                                                                                 | EC <sub>50</sub><br>hMC1-<br>R | Kb<br>hMC3-<br>R | Kb<br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------|--------------------------------|
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-<br>Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-Lys-<br>Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 3.65                           | 19.4             | 3.73             | 1.61                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-<br>Cys)-Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | ND                             | 17.7             | 1.49             | ND                             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 6.3                            | 70.0             | 1.66             | 38.2                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-<br>Cys)-Pro-Pro-Lys-Asp-Doc-Tyr-Gly-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 12.1                           | 30.3             | 1.81             | 70.0                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                     | 33.6                           | 140              | 12.2             | 66.9                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                     | 269                            | 105              | 5.92             | 104                            |
| Ac-c Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                       | 690                            | 70.7             | 4.56             | 177                            |
| Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-<br>Doc-Doc-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-<br>Gln-Arg-Arg-Arg-NH <sub>2</sub>                   | 3.23                           | 8.97             | 4.61             | 2.86                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 52.0                           | 170              | 6.14             | 328                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Arg-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 146                            | 104              | 32.0             | 1400                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-<br>Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 114                            | 44.6             | 28.4             | 879                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Aib-Arg-<br>Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 67.1                           | 439              | 46.5             | 582                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 144                            | 116              | 8.93             | 819                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 36.0                           | 46.5             | 11.4             | 56.1                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-<br>Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-<br>Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 93.0                           | 71               | 15.9             | > 10000                        |

| Compound (according to Formula III)                                                                                           | EC <sub>50</sub><br>hMC1-<br>R | Kb<br>hMC3-<br>R | Kb<br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------|--------------------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 39.7                           | 30.9             | 6.66             | 501                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 35.2                           | 22.9             | 12.6             | 199                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 29.1                           | 13.6             | 13.4             | 204                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 86.1                           | 41.7             | 19.4             | 2360                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Arg-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 38.3                           | 20.2             | 21.2             | > 10000                        |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 68.6                           | 153              | 33.2             | > 10000                        |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 70.4                           | 286              | 18.6             | > 10000                        |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 33.1                           | 65.1             | 15.3             | 1720                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 88.2                           | 10.6             | 17.4             | 514                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 58.7                           | 39.3             | 10.3             | 460                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 45.4                           | 12.7             | 12.7             | 162                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 309                            | 22.8             | 17.1             | 570                            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>                   | 7.86                           | 10.5             | 0.843            | 4900                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 29.7                           | 25.6             | 7.37             | 82.9                           |

| Compound (according to Formula III)                                                                                        | EC <sub>50</sub><br>hMC1-<br>R | Kb<br>hMC3-<br>R | Kb<br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|----------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------|--------------------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 15.2                           | 14.6             | 4.52             | 36.8                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Gln-Arg-Arg-Arg-Arg-NH <sub>2</sub>     | 6.7                            | 9.38             | 11.7             | 46.2                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Gln-Lys-Arg-Arg-Arg-Arg-NH <sub>2</sub>     | 7.9                            | 41.7             | 10.9             | 62.4                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Arg-Arg-Gln-Arg-NH <sub>2</sub> | 16.9                           | 36.0             | 7.12             | 58.9                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Arg-Gln-Arg-NH <sub>2</sub>     | 16.4                           | 20.8             | 7.31             | 44.2                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Gln-Lys-Lys-Arg-Arg-Arg-Arg-NH <sub>2</sub>     | 12.0                           | 13.7             | 9.38             | 54.2                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Arg-Arg-Gln-NH <sub>2</sub>     | 7.5                            | 12.2             | 7.61             | 51.7                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-NH <sub>2</sub>   | 43.3                           | 215              | 5.87             | 1286                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-NH <sub>2</sub>     | 37.9                           | 112              | 41.1             | 1798                           |

ND = not determined

Table 10B

| Compound (according to Formula III)                                                                          | EC <sub>50</sub><br>hMC1-<br>R | EC <sub>50</sub><br>hMC3-<br>R | EC <sub>50</sub><br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|--------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)2-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 4.70                           | 4.56                           | 0.634                          | 147                            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-βAla-Tyr-Gly-Arg-Lys-Lys-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 5.90                           | 7.73                           | 1.02                           | 2890                           |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-βAla-Gly-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>           | 0.481                          | 7.32                           | 0.964                          | 2010                           |

|                                                                                                         |      |      |      |      |
|---------------------------------------------------------------------------------------------------------|------|------|------|------|
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Arg-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 7.15 | 9.37 | 1.25 | 1570 |
|---------------------------------------------------------------------------------------------------------|------|------|------|------|

Table 10C

| Compound (according to Formula IV)                                                                                                    | EC <sub>50</sub><br>hMC1-<br>R | Kb<br>hMC3-<br>R | Kb<br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|---------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------|--------------------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal- $\beta$ -Ala-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                 | ND                             | ND               | ND               | ND                             |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Aib-Cys)-Pro-Pro-Lys-Asp-NH <sub>2</sub>                                                           | 770                            | 221              | 4.52             | 869                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 29                             | 22.6             | 16.7             | 173                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 102                            | 26.3             | 14.6             | 261                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 26.6                           | 101              | 9.34             | 351                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 45.5                           | 181              | 6.35             | 149                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 23.7                           | 9.22             | 5.87             | 39.7                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 34.7                           | 15.0             | 8.68             | 28.2                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>           | 19.1                           | 106              | 4.59             | 100                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 19.8                           | 37.8             | 8.43             | 158                            |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>   | 11.2                           | 52.1             | 9.45             | 95.7                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>       | 33.8                           | 93.6             | 4.42             | 89.5                           |
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp- $\beta$ -Ala-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>           | 232                            | 68.8             | 10.0             | 250                            |

| Compound (according to Formula IV)                                                                                      | EC <sub>50</sub><br>hMC1-<br>R | Kb<br>hMC3-<br>R | Kb<br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------|--------------------------------|
| Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-Pro-Pro-Lys-Asp-β-Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 32.2                           | 98.3             | 5.23             | 194                            |

ND = not determined

Table 10D

| Compound (according to Formula IV)                                                                          | EC <sub>50</sub><br>hMC1-<br>R | EC <sub>50</sub><br>hMC3-<br>R | EC <sub>50</sub><br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|-------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 5.66                           | 4.70                           | 0.422                          | 1551                           |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub> | 7.57                           | 4.18                           | 0.600                          | 1792                           |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 2.36                           | 2.74                           | 0.260                          | 500                            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>     | 2.81                           | 3.29                           | 0.298                          | 566                            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Arg-Arg-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 1.86                           | 1.39                           | 0.367                          | 165                            |
| Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Arg-Lys-Arg-Arg-Arg-Gln-Arg-Arg-Arg-NH <sub>2</sub>         | 2.06                           | 1.61                           | 0.394                          | 199                            |

TABLE 11 - Intracellular Cyclic AMP (cAMP) Levels for Formula (I) Examples

Table 11A

| Formula (V) Compounds                                                | EC <sub>50</sub><br>hMC1 | EC <sub>50</sub><br>hMC3 | EC <sub>50</sub><br>hMC4 | EC <sub>50</sub><br>hMC5 |
|----------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 218                      | 5.42                     | -                        |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Lys]-NH <sub>2</sub> | -                        | 22.3                     | 3.62                     | -                        |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH <sub>2</sub> | -                        | 39.2                     | 4.94                     | -                        |
| c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH <sub>2</sub> | 56.7                     | 18.2                     | 0.182                    | >10000                   |

| Formula (V) Compounds                                                | EC <sub>50</sub><br>hMC1 | EC <sub>50</sub><br>hMC3 | EC <sub>50</sub><br>hMC4 | EC <sub>50</sub><br>hMC5 |
|----------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH <sub>2</sub> | 56.6                     | 88.6                     | 4.50                     | 9300                     |
| c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH <sub>2</sub> | -                        | 49.3                     | 2.12                     | -                        |

TABLE 11B -

| Formula (VI) Compounds                                                         | EC <sub>50</sub><br>hMC1 | EC <sub>50</sub><br>hMC3 | EC <sub>50</sub><br>hMC4 | EC <sub>50</sub><br>hMC5 |
|--------------------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 54.3                     | 12.2                     | 0.177                    | >10000                   |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 124                      | 8.05                     | 0.214                    | >10000                   |
| Hydantoin(C(O)-(A6c-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | -                        | 4.89                     | 1.80                     | -                        |
| Hydantoin(C(O)-(D-Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | -                        | 2.56                     | 1.47                     | -                        |
| Hydantoin(C(O)-(Val-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | -                        | 4.61                     | 0.977                    | -                        |
| Hydantoin(C(O)-(Leu-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | -                        | 9.68                     | 1.83                     | -                        |
| Hydantoin(C(O)-(Cha-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | -                        | 9.97                     | 13.9                     | -                        |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 14.2                     | 2.46                     | 0.336                    | 201                      |
| Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>   | 17.0                     | 21.5                     | 0.584                    | 352                      |
| Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH <sub>2</sub>   | 40.2                     | 8.90                     | 0.495                    | 8300                     |
| Hydantoin(C(O)-(Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 17.6                     | 2.23                     | 0.241                    | 516                      |
| Hydantoin(C(O)-(D-Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 4.70                     | 2.22                     | 0.309                    | 355                      |
| Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 18.0                     | 17.1                     | 0.160                    | 2710                     |
| Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 12.9                     | 10.3                     | 0.125                    | 7440                     |
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 8.83                     | 7.86                     | 0.0979                   | 4010                     |
| Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>     | 9.97                     | 3.63                     | 0.0687                   | 335                      |
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 8.81                     | 18.2                     | 0.503                    | 3560                     |

| Formula (VI) Compounds                                                         | EC <sub>50</sub><br>hMC1 | EC <sub>50</sub><br>hMC3 | EC <sub>50</sub><br>hMC4 | EC <sub>50</sub><br>hMC5 |
|--------------------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 11.5                     | 23.2                     | 0.513                    | 3950                     |
| Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 7.53                     | 11.6                     | 0.435                    | 9840                     |
| Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 8.85                     | 5.17                     | 0.599                    | 3610                     |
| Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH <sub>2</sub> | 96.6                     | 13.1                     | 21.2                     | 103                      |

TABLE 11C

| Formula (VII) Compounds                                                  | EC <sub>50</sub><br>hMC1 | EC <sub>50</sub><br>hMC3 | EC <sub>50</sub><br>hMC4 | EC <sub>50</sub><br>hMC5 |
|--------------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| c[Hydantoin(C(O)-(Aib-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 6.28                     | 0.407                    | -                        |
| c[Hydantoin(C(O)-(Val-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 3.77                     | 0.214                    | -                        |
| c[Hydantoin(C(O)-(Leu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 4.72                     | 0.428                    | -                        |
| c[Hydantoin(C(O)-(Ile-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 8.51                     | 1.85                     | -                        |
| c[Hydantoin(C(O)-(A6c-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub> | -                        | 5.66                     | 1.72                     | -                        |
| c[Hydantoin(C(O)-(Gly-Cys))-Glu-His-D-Phe-Arg-Trp-Cys]-NH <sub>2</sub>   | 14.5                     | 21.8                     | 0.576                    | 1780                     |

TABLE 12-cAMP Bioassay Data for Selected Compounds

| Compound                                                        | EC <sub>50</sub><br>hMC1-<br>R | EC <sub>50</sub><br>hMC3-<br>R | EC <sub>50</sub><br>hMC4-<br>R | EC <sub>50</sub><br>hMC5-<br>R |
|-----------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Ac-Tyr-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 6.42                           | 2.39                           | 0.194                          | 1540                           |
| Ac-2-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 9.66                           | 6.11                           | 0.275                          | 1730                           |
| Ac-1-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> | 8.67                           | 4.21                           | 0.363                          | 1320                           |
| Ac-Trp-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub>   | 5.78                           | 3.95                           | 0.219                          | 2580                           |

### In vivo studies

Compounds of the present invention can be and were tested for an effect upon dyslipidemia, insulin resistance and/or body weight according to the following procedures. One skilled in the art would know that procedures similar to those described herein may be used to assay the effect of the compounds of the invention upon insulin resistance and/or body weight.

Ligand compounds activating melanocortin receptors tested in the *in vivo* studies were as follows (Table 13):

Table 13

| Ligand Code | Structure                                                 |
|-------------|-----------------------------------------------------------|
| Compound A  | Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH <sub>2</sub> |

Compound A was used at a dose of either 50 or 500 nmole/kg/day dissolved at the appropriate concentration in 0.9% NaCl containing 5% DMA, 2% tween-80 and 2% heat inactivated normal rat serum. Sub-cutaneous (sc) infusion pumps (Alzet 2002) were implanted into the rats and used to dose Compound A or the carrier vehicle. The dosage forms were prepared prior to the start of the experiment and used to fill the pumps under sterile conditions. Pumps were primed overnight at 37°C in sterile saline and implanted on the starting day of the experiment.

Obese Zucker rats were used to study the effects of Compound A upon dyslipidemia, food consumption and body weight. The Zucker rats are obese due to a spontaneous mutation in the leptin gene. In addition to the visible phenotype of obesity, these *lep<sup>-/-</sup>* animals also exhibit hyperinsulinemia, hypertriglyceridemia, hypercholesterolemia and elevated blood pressure..

Three groups of eight obese male Zucker rats (350-400g) were housed in individual cages and maintained under 12:12 hour light:dark conditions with both food (Harlan Teklad Sterilized Rodent Diet LM-485) and water available *ad libitum*. Prior to day 1 of the experiment, pumps were primed overnight at 37°C in sterile saline and Compound A was dissolved at the appropriate concentration in 0.9% NaCl containing 5% DMA, 2% tween-80 and 2% heat inactivated normal rat serum.

On the morning of day 1, the rats were anesthetized using chlorohydrate anesthetic and implanted with a sub-cutaneous infusion pump (Alzet® 2002) just under the skin. Pumps were filled with either Compound A at either 50 or 500 nmole/kg/day, or vehicle (0.9% NaCl containing 5% DMA, 2% tween-80 and 2% heat inactivated normal rat serum). Individual body weight and food and water consumption were measured daily at 0800 hours for 7 days.

On day 7 a right atrial cannula was implanted in the jugular vein under chlorohydrate anesthesia. The animals were fasted overnight and an intravenous (iv) glucose tolerance test was performed. Glucose (1g/kg) was injected at time 0 and blood samples were taken via the cannula at 0, 2.5, 5, 10, 20 and 40 minutes post-injection. Plasma was collected and assayed for glucose (Glucose (Trinder) Assay; Diagnostic Chemicals Limited, Charlottetown, P.E.I., Canada; Cat # 220-32) and insulin (Mercodia Rat Insulin ELISA; Mercodia, Uppsala, Sweden; ALPCO 10-1124-10) content. At the conclusion of the glucose tolerance test and additional serum samples were collected and assayed for triglycerides (Triglyceride L-Type TG H kit: Wako Diagnostics, Richmond, VA), cholesterol (Cholesterol E assay kit: Wako Diagnostics, Richmond, VA) and free fatty acids (Fatty Acid HR series NEFA-HR2 kit: Wako Diagnostics, Richmond, VA).

By day 7, treatment with Compound A at a low dose of 50 and a high dose of 500 nmole/kg/day induced a dose-related decrease in body weight gain of 35 g and 60 g, respectively (Figure 1). A similar dose-related decrease in food intake was also observed by the end of the 7 day treatment period; the low dose group reduced its food intake by 60 g and the high dose group by 100 g (Figure 2).

Treatment with 500 nmole/kg/day of Compound A decreased basal fasted plasma glucose. Both the low and the high doses of Compound A decreased plasma glucose levels after a glucose challenge (Figure 3). As shown in Figure 4, a 7 day infusion of Compound A decreased the amount of insulin required to clear the glucose challenge of the glucose tolerance test.

Figures 5, 6 and 7 show the dose-related decreases in triglycerides, cholesterol and free fatty acids which resulted from treatment with Compound A.

### *Histology studies*

Progression of AFLD and NAFLD through the various stages of fat accumulation (in both micro and macro vesicles), cell death, lobular inflammation, ballooning degeneration, cirrhosis, formation of tumors and cancers, inflammation, and fibrosis may be monitored via tissue examination.

Development and progression of AFLD and NAFLD may be made at the gross tissue level. Livers, *in situ* or dissected from control or test animals, are inspected for appearance, weight, color, odor and other visually observable characteristics at various stages prior to and following administration of Compound A or vehicle control.

Development and progression of AFLD and NAFLD may also be made at the microscopic tissue level. Liver tissues are extracted from test and control animals at various stages prior to and following administration of Compound A. The tissues are flash frozen or otherwise preserved for fixation, microtoming and staining procedures, and the like.

The skilled artisan would know and appreciate that a variety of methods are available to study the tissue samples (see for example Matteoni CA *et al.* Gastroenterology 116:1413, 1999) and that a variety of visualization aids may be employed such as, but not limited to, oil red staining, immunohistochemical staining for visualization of macrophages, fibroblasts, collagen and the like, NAFLD activity scores, AFLD activity scores, visualization of glutamine synthesis, detection of eosinophilic cells, detection of HE or endogenous ALP, appearance of infiltrating cells, incorporation of BrdU to measure cellular proliferation, hematoxylin-eosin staining, Masson's trichome staining and gene expression analysis for tumor necrosis factors such as TNF- $\alpha$ , for interleukins such as IL-6 or IL-10 and for interferons such as IFN- $\gamma$  and the like.

### *Administration and Use*

The peptides of this invention can be provided in the form of pharmaceutically acceptable salts. Examples of such salts include, but are not limited to, those formed with organic acids (e.g., acetic, lactic, maleic, citric, malic, ascorbic, succinic, benzoic, methanesulfonic, toluenesulfonic, or pamoic acid), inorganic acids (e.g., hydrochloric acid, sulfuric acid, or phosphoric acid), and polymeric acids (e.g., tannic acid, carboxymethyl cellulose, polylactic, polyglycolic, or copolymers of polylactic-glycolic acids). A typical method of making a salt of a peptide of the present invention is well known in the art and can be accomplished by standard methods of salt exchange. Accordingly, the TFA salt of a peptide of the present invention (the TFA salt results from the purification of the peptide by using preparative HPLC, eluting with TFA containing buffer solutions) can be converted into another salt, such as an acetate salt, by dissolving the peptide in a small amount of 0.25 N acetic acid aqueous solution. The resulting solution is applied to a semi-prep HPLC column (Zorbax®, 300 SB, C-8). The column is eluted with: (1) 0.1N ammonium acetate aqueous solution for 0.5 hours; (2) 0.25N acetic acid aqueous solution for 0.5 hours; and (3) a linear gradient (20% to 100% of solution B over 30 minutes) at a flow rate of 4 ml/min (solution A is 0.25N acetic acid aqueous solution; solution B is 0.25N acetic acid in acetonitrile/water, 80:20). The fractions containing the peptide are collected and lyophilized to dryness.

As is well known to those skilled in the art, the known and potential uses of peptides with melanocortin receptor (MC-R) agonist or antagonist activity is varied and multitudinous, thus the administration of the compounds of this invention for purposes of eliciting an agonist effect can have the same effects and uses as melanocortin itself.

Accordingly, the present invention includes within its scope pharmaceutical compositions comprising, as an active ingredient, at least one of the compounds of formula (I) in association with a pharmaceutically acceptable carrier.

The dosage of active ingredient in the compositions of this invention may be varied; however, it is necessary that the amount of the active ingredient be such that a suitable dosage form is obtained. The selected dosage depends upon the desired

therapeutic effect, on the route of administration, and on the duration of the treatment. In general, an effective dosage for the activities of this invention is in the range of  $1 \times 10^{-7}$  to 200 mg/kg/day, preferably  $1 \times 10^{-4}$  to 100 mg/kg/day which can be administered as a single dose or divided into multiple doses.

The compounds of this invention can be administered by oral, parenteral (e.g., intramuscular, intraperitoneal, intravenous or subcutaneous injection, or implant), nasal, vaginal, rectal, sublingual or topical routes of administration and can be formulated with pharmaceutically acceptable carriers to provide dosage forms appropriate for each route of administration.

Solid dosage forms for oral administration include capsules, tablets, pills, powders and granules. In such solid dosage forms, the active compound is admixed with at least one inert pharmaceutically acceptable carrier such as sucrose, lactose, or starch. Such dosage forms can also comprise, as is normal practice, additional substances other than such inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, the elixirs containing inert diluents commonly used in the art, such as water. Besides such inert diluents, compositions can also include adjuvants, such as wetting agents, emulsifying and suspending agents, and sweetening, flavoring and perfuming agents.

Preparations according to this invention for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, or emulsions. Examples of non-aqueous solvents or vehicles are propylene glycol, polyethylene glycol, vegetable oils, such as olive oil and corn oil, gelatin, and injectable organic esters such as ethyl oleate. Such dosage forms may also contain adjuvants such as preserving, wetting, emulsifying, and dispersing agents. Preparations may be sterilized by, for example, filtration through a bacteria-retaining filter, by incorporating sterilizing agents into the compositions, by irradiating the compositions, or by heating the compositions. Preparations can also be

manufactured in the form of sterile solid compositions which can be dissolved in sterile water or some other sterile injectable medium immediately before use.

Compositions for rectal or vaginal administration are preferably suppositories which may contain, in addition to the active substance, excipients such as cocoa butter or a suppository wax.

Compositions for nasal or sublingual administration are also prepared with standard excipients well known in the art.

Further, a compound of this invention can be administered in a sustained release composition such as those described in the following patents and patent applications. U.S. Patent No. 5,672,659 teaches sustained release compositions comprising a bioactive agent and a polyester. U.S. Patent No. 5,595,760 teaches sustained release compositions comprising a bioactive agent in a gelable form. U.S. Patent No. 5,821,221 teaches polymeric sustained release compositions comprising a bioactive agent and chitosan. U.S. Patent No. 5,916,883 teaches sustained release compositions comprising a bioactive agent and cyclodextrin. The teachings of the foregoing patents and applications are incorporated herein by reference.

What is claimed is:

1. A method of treating dyslipidemia in a subject in need thereof, comprising peripheral administration of an effective amount of a melanocortin receptor 4 agonist to treat said dyslipidemia in said subject in need thereof.
2. A method according to claim 1, wherein said treatment of dyslipidemia results in decreased levels of serum cholesterol, triglycerides, low-density lipoprotein cholesterol, free fatty acids, or increased levels of high-density lipoprotein cholesterol, or any combination thereof.
3. A method according to claim 1 wherein said subject is suffering from hepatic steatosis.
4. A method according to claim 3, wherein said hepatic steatosis is non-alcoholic fatty acid liver disease or alcoholic fatty acid liver disease.
5. A method according to claim 4, wherein said non-alcoholic fatty acid liver disease or alcoholic fatty acid liver disease is accompanied by steatohepatitis, steatonecrosis, lobular inflammation, ballooning degeneration, fibrosis, cirrhosis or cancer or any combination thereof.
6. The method according to claim 1, where in said melanocortin receptor 4 agonist useful to treat dyslipidemia is selected from the group consisting of:  
Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-A6c-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-NH<sub>2</sub>;  
Ac-A6c-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-2-Nal-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-β-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gaba-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Aib-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gly-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-β-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gaba-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Aib-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gly-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-β-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gaba-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Aib-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-Gly-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-D-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-β-Ala-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Gaba-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(D-Cys-Aib-His-D-Phe-Arg-Trp-D-Cys)-NH<sub>2</sub>;  
Ac-Oic-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;

Ac-Nip-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hPro-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hLeu-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Phe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Phe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
n-butanoyl-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-β-hMet-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Gaba-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-hCha-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Leu-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-hLeu-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Phe-c(Asp-His-D-Phe-Arg-D-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-D-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Aha-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-D-Trp-Apn-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-β-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-D-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-NH<sub>2</sub>;  
n-butanoyl-Nle-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Cys)-NH<sub>2</sub>;  
n-butanoyl-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Cys)-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-1-Nal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Bal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-D-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-Arg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-Phe-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip-β-Ala-D-Cys)-Thr-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Trp-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-OH;  
Ac-Nle-c(Cys-D-Abu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Val-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ile-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Tle-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Nle-c(Pen-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Leu-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Cha-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Ile-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;

Ac-Val-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-2-Nal-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-3-Pal-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-His-Phe-Arg-D-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-β-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-2-Nal-Arg-Trp-Ahx-Cys)-NH<sub>2</sub>;  
Ac-hPhe-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Cha-c(Asp-His-D-2-Nal-Arg-Trp-Gaba-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Ala-D-Cys)-Thr-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-OH;  
D-Phe-c(Cys-His-D-Phe-Arg-Trp-Gaba-D-Cys)-Thr-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-OH;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Apn-Lys)-OH;  
Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-D-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Gaba-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-β-Ala-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-D-Ala-Cys)-OH;

Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-2-Nal-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-1-Nal-Cys)-OH;  
Ac-Nle-c(Cys-D-Ala-His-D-2-Nal-Arg-Bal-Cys)-OH;  
Ac-Nle-c(Pen-D-Ala-His-D-Phe-Arg-Trp-Cys)-OH;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-OH;  
Ac-Arg-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-D-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Arg-c(Cys-His-D-Phe-Arg-Trp-Gaba-Pen)-NH<sub>2</sub>;  
Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Ac-D-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Arg-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-3-Pal-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-D-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gaba-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Apn-Cys)-NH<sub>2</sub>;  
Ac-c(Cys-Glu-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;  
Ac-c(Cys-Glu-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH<sub>2</sub>;  
Ac-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;  
Ac-c(Cys-D-Ala-His-D-Phe-Arg-2-Nal-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-β-Ala-Cys)-NH<sub>2</sub>;  
Ac-Nle-c(Asp-D-Ala-His-D-Phe-Arg-Bal-Ala-Lys)-NH<sub>2</sub>;  
Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH<sub>2</sub>;  
Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-Doc-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-NH<sub>2</sub>;

Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Pro)<sub>2</sub>-Lys-Asp-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-2-Nal-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Gln-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-Gln-Lys-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>4</sub>-Gln-Arg-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Aib-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>3</sub>-Gln-(Arg)<sub>2</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Gln-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>2</sub>-Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-  
Lys-(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Arg-Lys-(Arg)<sub>3</sub>-  
Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>2</sub>-  
Lys-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-(Arg)<sub>2</sub>-Lys-  
(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Gly-Arg-Lys-  
(Arg)<sub>3</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-  
(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-  
(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-  
Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-  
Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-  
(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-  
(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-  
Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Arg-Asp-β-Ala-Tyr-Gly-(Arg)<sub>6</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-Arg-(Lys)<sub>2</sub>-Arg-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-Arg-(Lys)<sub>2</sub>-(Arg)<sub>2</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>2</sup>-Lys-(Arg)<sup>2</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-Arg-Lys-(Arg)<sup>3</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Gly-(Arg)<sup>2</sup>-Lys-(Arg)<sup>2</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Gly-Arg-Lys-(Arg)<sup>3</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>2</sup>-Lys-(Arg)<sup>2</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Arg-Lys-(Arg)<sup>3</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sup>2</sup>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-β-Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-β-Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-β-Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Ala-Lys)-β-Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-β-Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(β-Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Lys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-β-Ala-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Ahx-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-Phe-Arg-Trp-β-Ala-D-Cys)-Thr-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Cha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(β-Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(β-Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-hCha-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-D-Chg-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-hPhe-c(Asp-His-D-Phe-Arg-Trp-Gaba-Lys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp-Ahx-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp- $\beta$ -Ala-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-His-D-Phe-Arg-D-Trp- $\beta$ -Ala-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-β-Ala-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(β-Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(β-Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(β-Ala)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(β-Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Doc-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(Doc)<sub>2</sub>-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-Arg-Trp-β-Ala-D-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-β-Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-β-Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp-β-Ala-D-Cys)-Thr-(β-Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Trp- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 D-Phe-c(Cys-His-D-(Et)Tyr-hArg-Bip- $\beta$ -Ala-D-Cys)-Thr-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Gly-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Nle-c(Cys-His-D-Phe-Arg-Trp-Apn-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;  
 Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Leu-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sup>5</sup>-Gln-(Arg)<sup>3</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;  
Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)- $\beta$ -Ala-(Arg)<sup>5</sup>-Gln-(Arg)<sup>4</sup>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-Nle-c(Cys-D-Cha-His-D-Phe-Arg-Trp-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)- $\beta$ -Ala-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-( $\beta$ -Ala)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>3</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-Doc-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-Tyr-Gly-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Nle-c(Cys-His-D-Phe-Arg-Trp-Gaba-Cys)-(Doc)<sub>2</sub>-(Arg)<sub>5</sub>-Gln-(Arg)<sub>4</sub>-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-4-Br-Phe-Arg-Trp-Gly-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-1-Nal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-Bal-Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal- $\beta$ -Ala-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

Ac-c(Cys-Glu-His-D-2-Nal-Arg-2-Nal-Aib-Cys)-(Pro)<sub>2</sub>-Lys-Asp-NH<sub>2</sub>;

c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(hCys-D-Ala))-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Cys-D-Ala))-His-D-2-Nal-Arg-Trp-Cys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(hCys-D-Ala))-His-D-2-Nal-Arg-Trp-Cys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dab]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-His))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-His))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A3c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A5c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A6c))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A3c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A5c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A6c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-A5c))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Aic))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Apc))-D-Phe-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Aic))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Apc))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Aic))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Asp-Apc))-D-2-Nal-Arg-Trp-Lys]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Orn]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dab]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Glu-D-Ala))-His-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>;  
c[Hydantoin(C(O)-(Glu-His))-D-Phe-Arg-Trp-Dap]-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;

Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Pen)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Ala-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Aib-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Val-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ile-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Leu-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Gly))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Nle-Gly))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Arg-Gly))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ala-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Val-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Nle))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(A6c-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(D-Ala-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Val-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Leu-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Cha-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Aib-Nle))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Arg))-c(Cys-Glu-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
Hydantoin(C(O)-(Gly-Arg))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;

Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Gly-D-Arg))-c(Cys-D-Ala-His-D-2-Nal-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Hydantoin(C(O)-(Nle-Ala))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Ala-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Nle-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(D-Ala-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Aib-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Val-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Abu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Leu-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Ile-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Cha-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(A6c-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Phe-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Gly-Cys))-D-Ala-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 c[Hydantoin(C(O)-(Gly-Cys))-Glu-His-D-Phe-Arg-Trp-Cys]-NH<sub>2</sub>;  
 Ac-Tyr-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-2-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-1-Nal-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-Phe-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-Trp-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-Pff-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 H-His-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>;  
 Ac-His-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>; and  
 Ac-D-Arg-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>  
 or a pharmaceutically acceptable salt thereof.

7. The method according to claim 6, wherein said compound is Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub> or a pharmaceutically acceptable salt thereof.

8. The method according to claim 6, wherein said compound is Hydantoin(C(O)-(Arg-Gly))-c(Cys-Glu-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub> or a pharmaceutically acceptable salt thereof.
9. The method according to any one of claims 1-8, wherein said subject is obese, overweight, normal weight or lean.
10. The method according to claim 9, wherein said subject suffers from type II diabetes.
11. The method according to claim 1, wherein said peripheral administration is oral, subcutaneous, intraperitoneal, intramuscular, intravenous, rectal, transdermal or intranasal.
12. The method according to claim 11, wherein said administration is continuous, hourly, four times daily, three time daily, twice daily, once daily, once every other day, twice weekly, once weekly, once every two weeks, once a month, or once every two months.

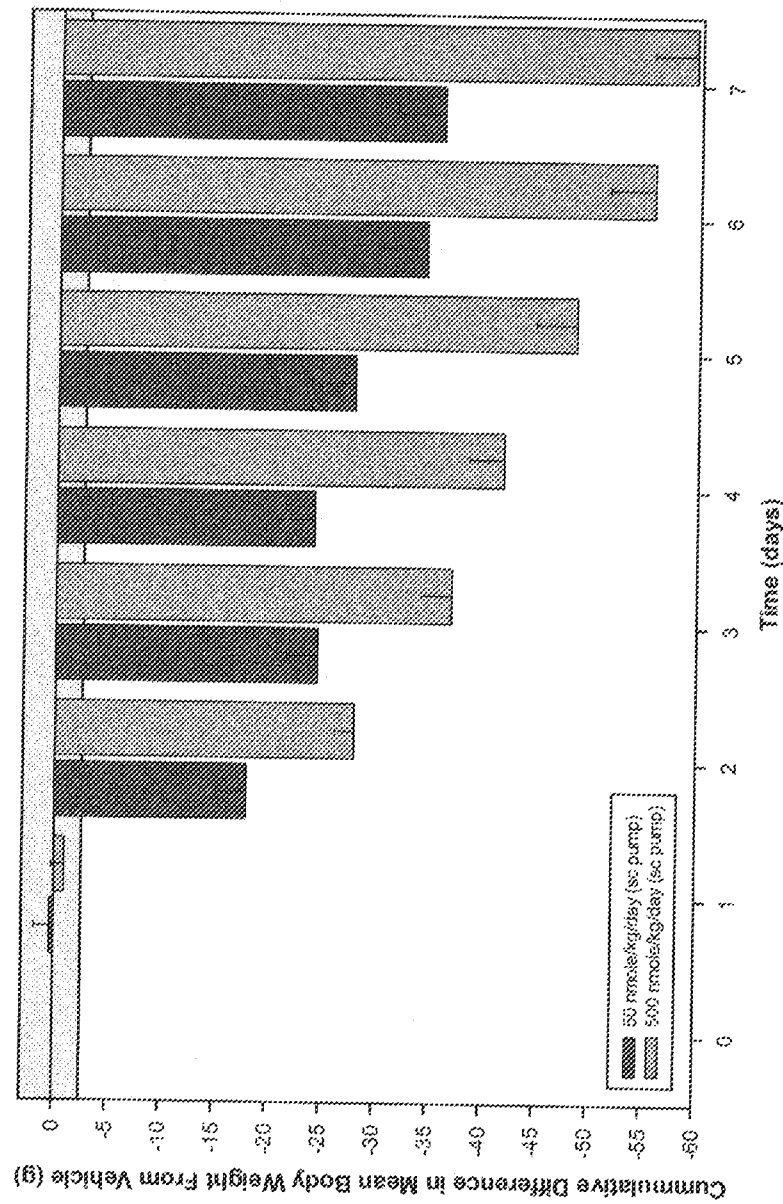


Figure 1

Figure 2

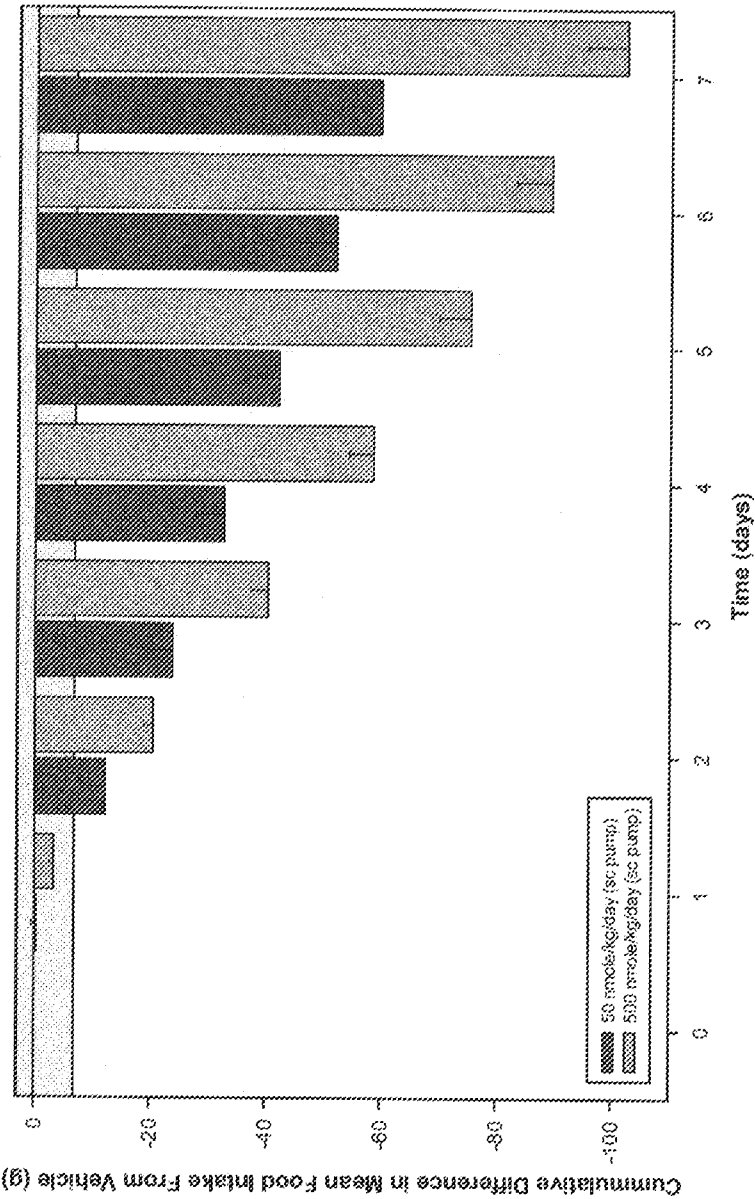
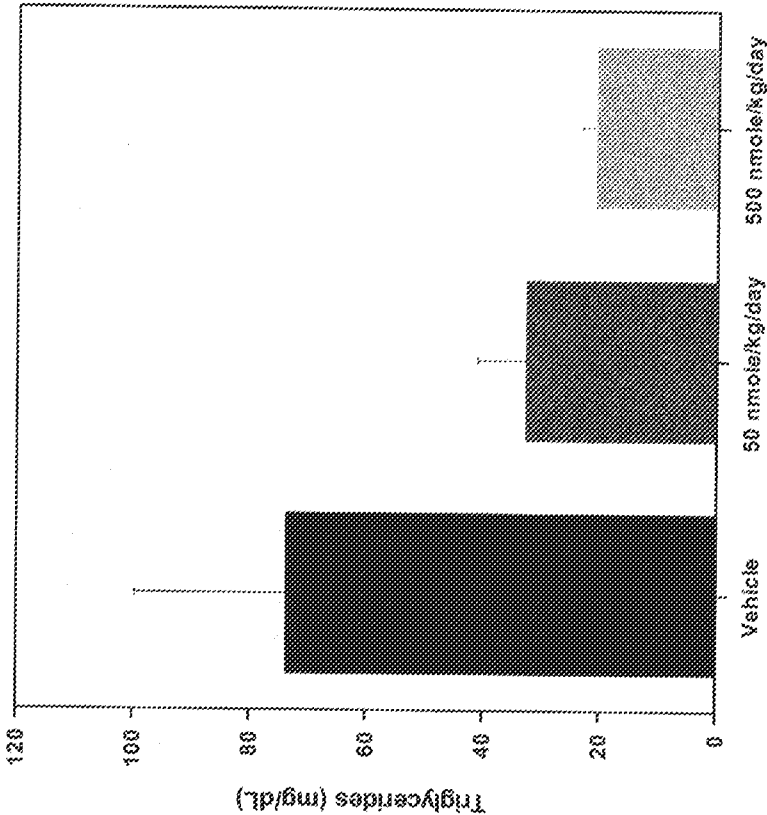


Figure 3



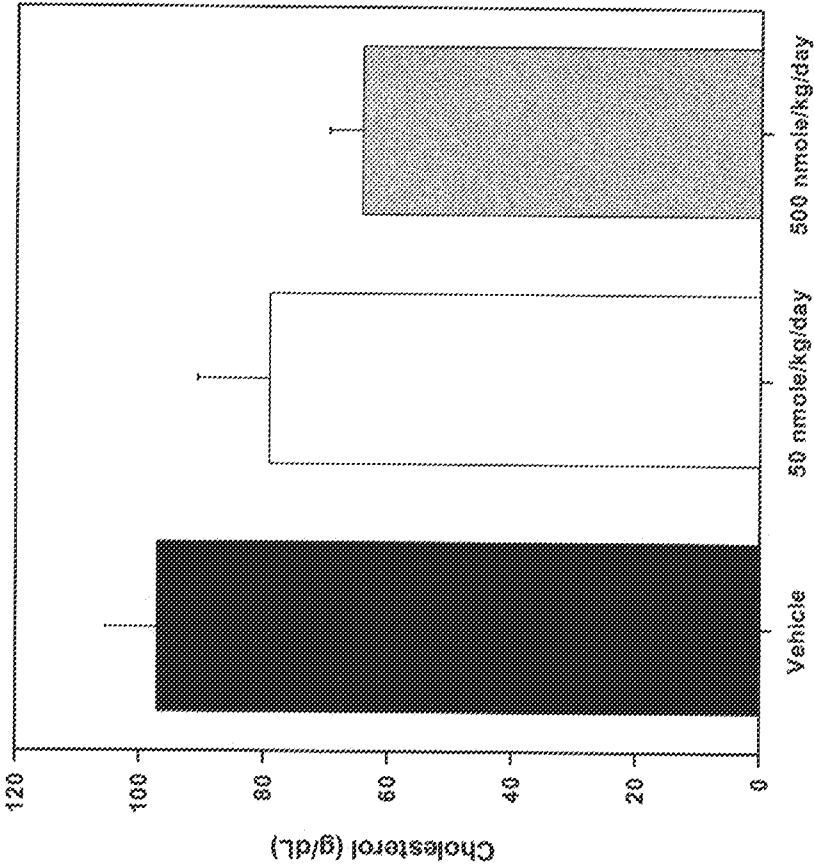
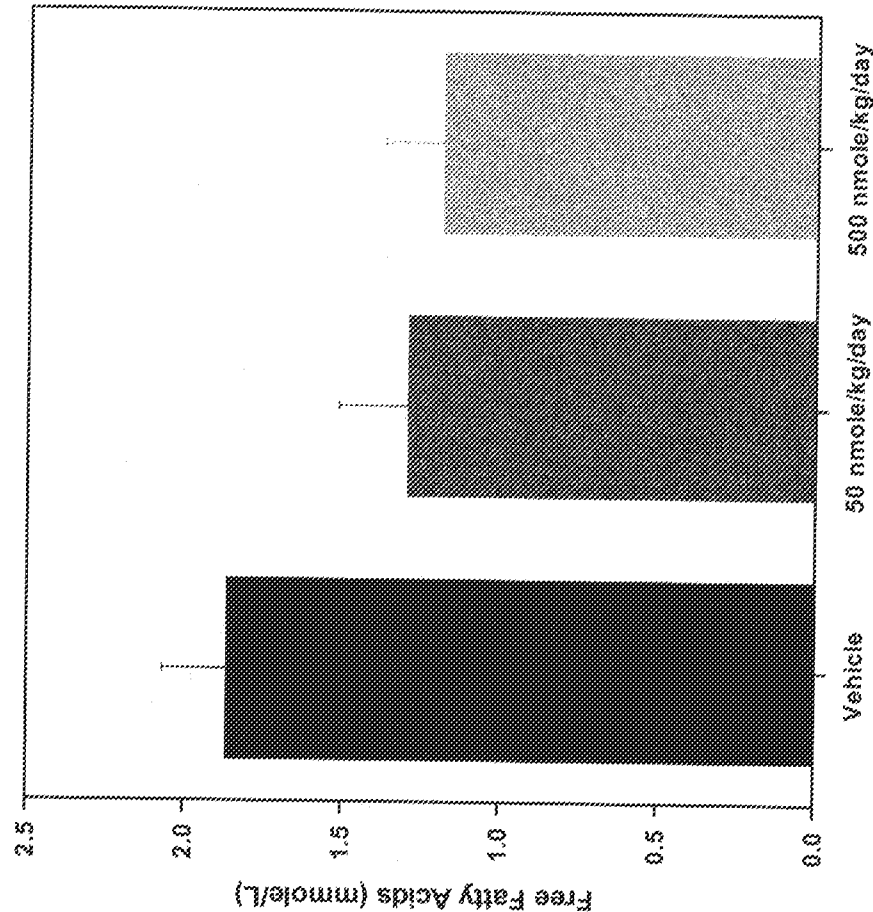


Figure 4

Figure 5



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/43832

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A01N 37/18; A61K 38/00 (2010.01)

USPC - 514/2

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC- 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
USPC- 514/1; 530/328; 424/185.1; 424/184.1

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(PGPB,USPT,USOC,EPAB,JPAB), Google, Google Scholar: melanocortin receptor 4 agonist dyslipidemia, hepatic steatosis, rimonabant

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category*   | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                   | Relevant to claim No.             |
|-------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|
| X<br>—<br>Y | US 2008/0306008 A1 (SENSFUSS et al.) 11 December 2008 (11.12.2008) para [0082], [0096], [0102]                                                                                                                       | 1-2, 9, 11-12<br>-----<br>3-7, 10 |
| A           | KUMAR et al., Analysis of the therapeutic functions of novel melanocortin receptor agonists in MC3R- and MC4R- deficient C57BL/6J mice. Peptides 29 July 2009, 30:1892-1900; pg 1894, right col, para 5              | 2                                 |
| Y           | TOLEDO et al. Influence of Hepatic Steatosis (Fatty Liver) on Severity and Composition of Dyslipidemia in Type 2 Diabetes. Diabetes Care 2006, 29:1845-1850; pg 1845, right col, para 1; pg 1847, right col, para 3  | 3-5                               |
| Y           | WO 2007/008704 A2 (DONG et al.), 18 January 2007 (18.01.2007) pg 15, ln 1-19; pg 21, para 4                                                                                                                          | 6-7                               |
| Y           | US 2006/0148721 A1 (ERONDU et al.); 6 July 2006 (06.07.2006) para [0003]                                                                                                                                             | 10                                |
| Y           | UEKI et al. Central role of suppressors of cytokine signaling proteins in hepatic steatosis, insulin resistance, and the metabolic syndrome in the mouse. PNAS 2004, 101(28):10422-10427; pg 10442, left col, para 1 | 5                                 |

☐ Further documents are listed in the continuation of Box C.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;" document member of the same patent family

Date of the actual completion of the international search

16 November 2010 (16.11.2010)

Date of mailing of the international search report

24 NOV 2010

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/43832

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I+: claims 1-12, drawn to a method of treating dyslipidemia in a subject in need thereof, comprising peripheral administration of an effective amount of a melanocortin receptor 4 agonist to treat said dyslipidemia in said subject in need thereof. The first invention encompasses the first agonist of claim 6, i.e. Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub>. Due to the number of sequences in this application, an additional invention(s) of Group I+ will be defined as necessary depending on Applicant's ultimate payment of additional fees. The additional sequences will be searched if applicant pays for each additional sequence or shows that the sequences share a special technical feature, i.e. a common structure or feature that defines a contribution over the prior art. Note that each additional sequence to be searched must be specified by the Applicant in the response to this invitation and must either (1) have an additional invention fee paid or (2) have a showing that the sequences share a common structure or feature that defines a contribution over the prior art. The exact claims searched will depend on the specifically elected antagonist(s).

[NOTE: Claim 8 was excluded from the search, because it is drawn to a non-elected subject matter.]

\*\*\*\*\* See Supplemental Box to continue \*\*\*\*\*

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-7, 9-12, first agonist of claim 6

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/43832

\*\*\*\*\* Supplemental Box \*\*\*\*\*

Continuation of Box III. LoU:

The inventions listed as Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions of Group I+ share the technical feature of a method of treating dyslipidemia in a subject in need thereof, comprising peripheral administration of an effective amount of a melanocortin receptor 4 agonist to treat said dyslipidemia in said subject in need thereof. However, this shared technical feature does not represent a contribution over prior art. Specifically, US 2003/0109556 A1 to MAZUR et al. (hereinafter 'Mazur') teaches a method of treating dyslipidemia in a subject in need thereof, comprising peripheral administration of an effective amount of a melanocortin receptor 4 agonist to treat said dyslipidemia in said subject in need thereof (para [0555]-[0556]). As said agent was known at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Another technical feature of the inventions listed as Group I+ is the specific antagonist of the specific amino acid sequence recited therein. The inventions do not share a special technical feature because 1) WO 2007/008704 to Dong et al. discloses melanocortin receptors agonists similar to the claimed agonists (Abstract), and further specifically discloses the first agonist of claim 6, i.e. Ac-Arg-c(Cys-D-Ala-His-D-Phe-Arg-Trp-Cys)-NH<sub>2</sub> (claim 5, last compound). Thus, no significant novel and non-obvious structural similarities can readily be ascertained among the agonists. Without a shared special technical feature, the inventions lack unity with one another.

The inventions Group I+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.