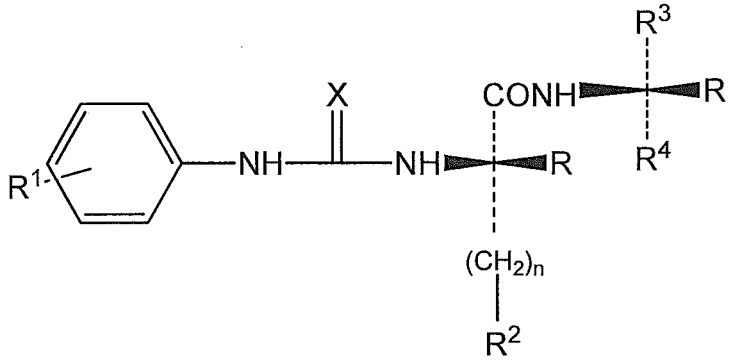
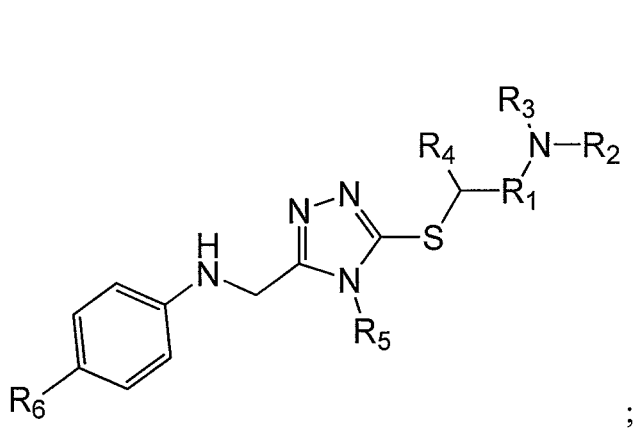
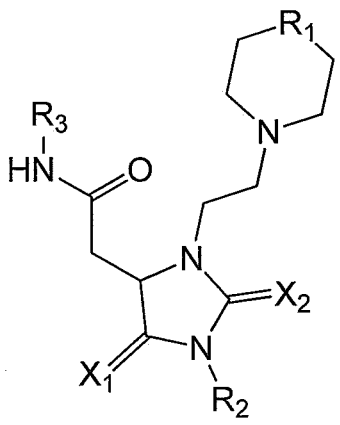
FR 2533210 discloses L-phenyl analine derivatives as synthetic sweeteners:



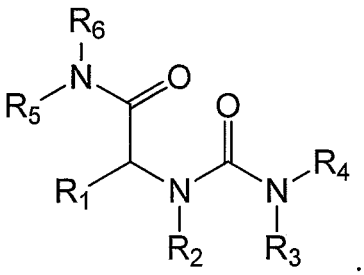
WO2005047899 discloses compounds which selectively activate the FPRL-1 receptor represented by the following scaffolds:



;



and



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SUMMARY OF THE INVENTION

A group of amide derivatives of N-urea substituted amino acids, which are potent and selective FPRL-1 modulators, has been discovered. As such, the compounds described herein are useful in treating a wide variety of disorders associated with modulation of FPRL-1 receptor. The term "modulator" as used herein, includes but is not limited to: receptor agonist, antagonist, inverse agonist, inverse antagonist, partial agonist, and partial antagonist.

In one aspect, the present invention provides a compound selected from:

{[2-{[(4-bromophenyl)carbamoyl]amino)-3-(1H-indol-3-yl)propanoyl]amino}acetic acid;

2-{[(2R)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-2-methylpropanoic acid;

{[2-{[(4-bromophenyl)carbamoyl]amino}-3-(1H-imidazol-4-yl)propanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfonyl)butanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfanyl)butanoyl]amino}acetic acid;

2-methyl-2-{[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}propanoic acid;

{[(2S)-4-methyl-2-({[4-(methylsulfonyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2S)-4-methyl-2-({[4-(methylsulfinyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-2-methylpropanoic acid;

({(2S)-4-methyl-2-({[4-[trifluoromethyl)sulfanyl]phenyl}carbamoyl)amino]pentanoyl}amino)acetic acid;

{[(2S)-4-methy1-2-({[4-(methylsulfanyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2R)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino)acetic acid;

{[(2R,3R)-2-{[(4-bromophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid; {[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2R)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino)-2-methylpropanoyl)amino]acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino}-2-ethylbutanoyl)amino]acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino}-2,4-dimethylpentanoyl)amino]acetic acid;

(2S)-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}(phenyl)ethanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}pentanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-3-methylbutanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}propanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}propanoic acid;

{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl)amino}acetic acid;

{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}pentanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}pentanoyl]amino}acetic acid;

{[(2S,3S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid;

{[(2S,3S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid;

3-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}propanoic acid; and

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3- phenylpropanoyl]amino}acetic acid.

In another aspect, the present invention provides a pharmaceutical composition including at least one compound or a pharmaceutically acceptable salt thereof disclosed herein in a pharmaceutically acceptable carrier.

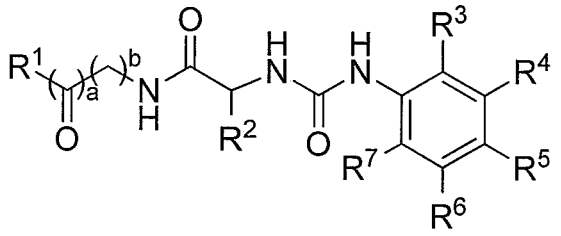
In yet another aspect, the present invention provides the compound or a pharmaceutically acceptable salt thereof disclosed herein or the pharmaceutical composition disclosed herein for use in treating a disease

In yet another aspect, the present invention provides use of a compound or a pharmaceutically acceptable salt thereof disclosed herein or a pharmaceutical composition disclosed herein in the manufacture of a medicament for treating an ocular inflammatory disease.

This invention describes compounds of **Formula I**, which have FPRL-1 receptor biological activity. The compounds in accordance with the present invention

are thus of use in medicine, for example in the treatment of humans with diseases and conditions that are alleviated by FPRL-1 modulation.

Disclosed is a compound represented by **Formula I** or the individual geometrical isomers, individual enantiomers, individual diastereoisomers, individual tautomers, individual zwitterions or a pharmaceutically acceptable salt thereof:



Formula I

wherein:

a is 0 or 1;

b is 0, 1, 2, 3 or 4;

R^1 is optionally substituted C_{1-8} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl, $-NH_2$, -OH, $-O(C_{1-8}$ alkyl),

R^2 is optionally substituted C_{1-8} alkyl, optionally substituted C_{6-10} aryl,

R^3 is H, optionally substituted C_{1-8} alkyl, halogen, -COOH, -OH, $-NH_2$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl;

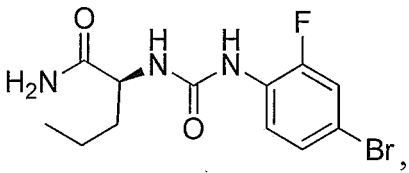
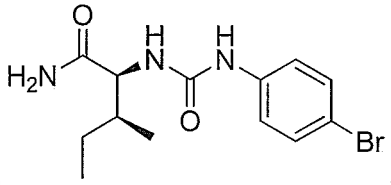
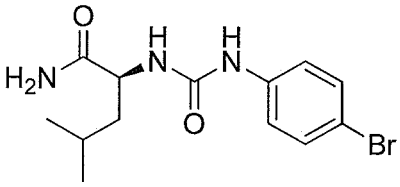
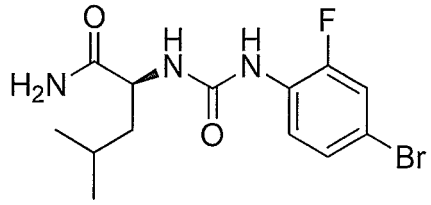
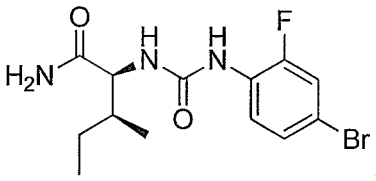
R^4 is H, optionally substituted C_{1-8} alkyl, halogen, -COOH, -OH, $-NH_2$, $-NO_2$, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl;

R^5 is optionally substituted C_{1-8} alkyl, halogen, -COOH, -OH, $-NH_2$, $-NO_2$, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl;

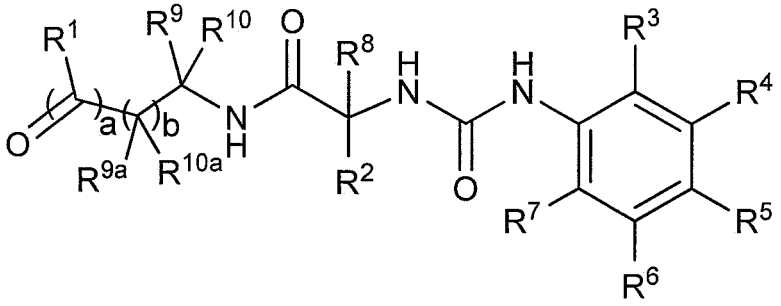
R^6 is H, optionally substituted C_{1-8} alkyl, halogen, -COOH, -OH, $-NH_2$, $-NO_2$, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl;

R^7 is H, optionally substituted C_{1-8} alkyl, halogen, -COOH, -OH, $-NH_2$, $-NO_2$, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl;

and compounds:


,

,

,

and

.

Also disclosed is a compound represented by **Formula II** or the geometrical isomers, enantiomers, diastereoisomers, tautomers, zwitterions, hydrates, cryslat forms, solvates or a pharmaceutically acceptable salt thereof:



Formula II

wherein:

a is 1 and b is 0;

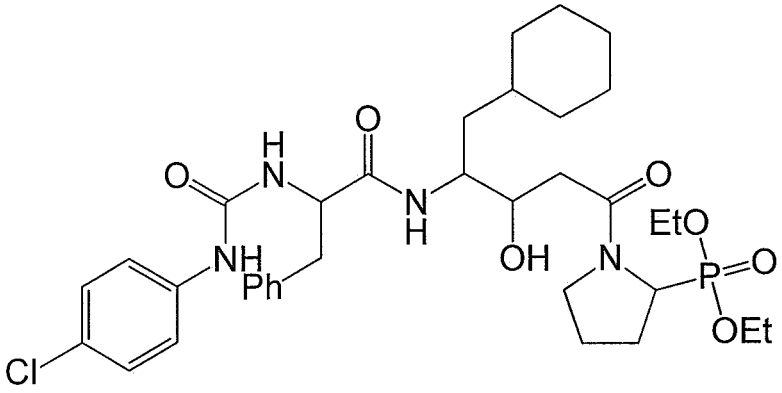
a is 0 and b is 1;

a is 1 and b is 1;

R^1 is optionally substituted C_{1-8} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

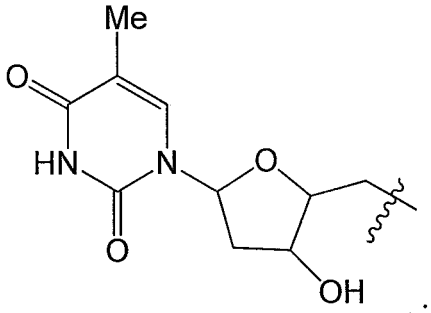
R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;



; and

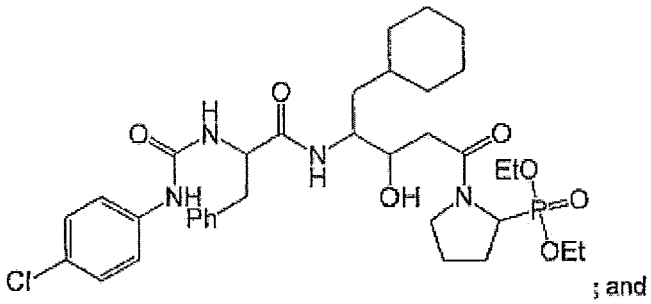
c). when a=1 and b=1 then:

R^{11} is not:



.

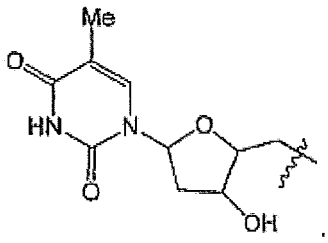
Also disclosed is a compound represented by Formula II, its enantiomers, diastereoisomers, tautomers, hydrates, solvates or a pharmaceutically acceptable salt thereof,



; and

c) when a=1 and b=1 then:

R^{11} is not:



Also disclosed is a compound represented by **Formula II**,

wherein:

a is 1 and b is 0 ;

R^1 is optionally substituted C_{1-8} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl, $-NR^{11}R^{12}$ or $-0R^{13}$;

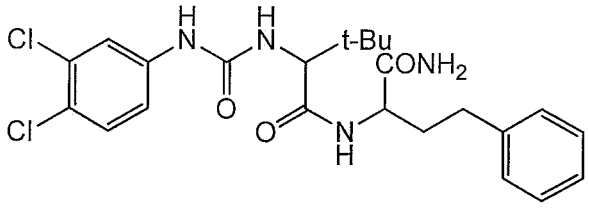
R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

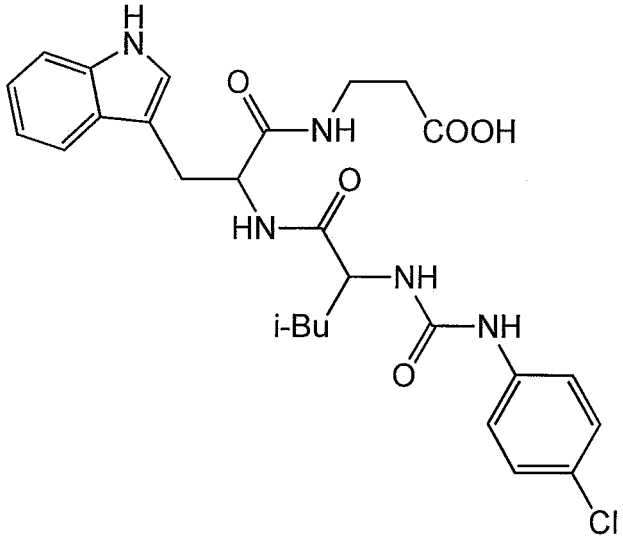
R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

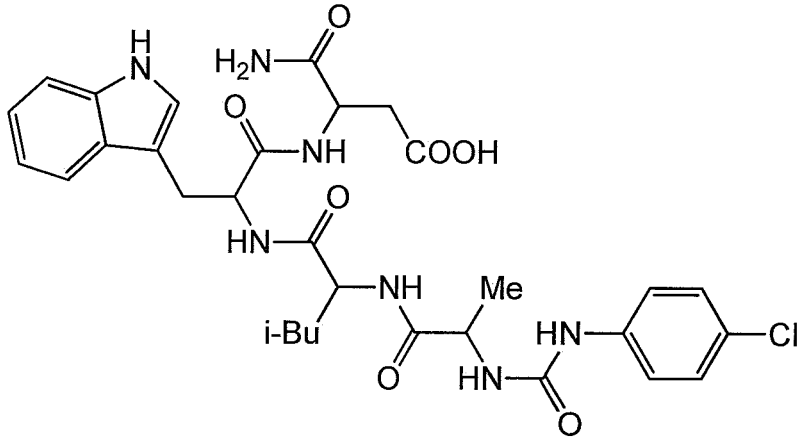
R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted 03-8 cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

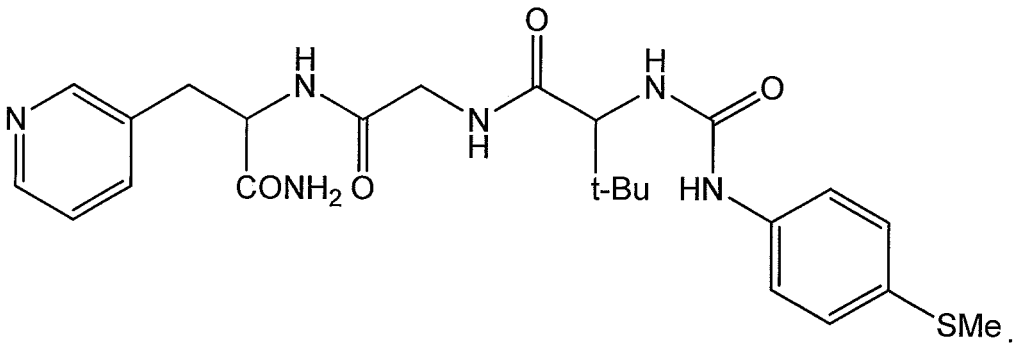
R^5 is halogen ,$-CF_3$ or $—S(O)_nR^{14}$;

n is 0, 1 or 2;


;



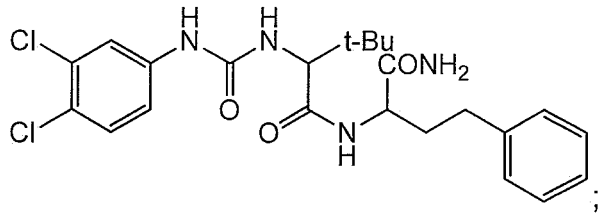

; or


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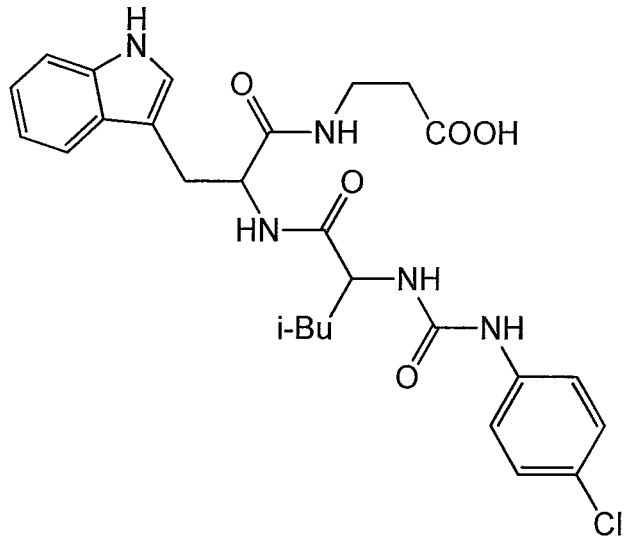
Also disclosed is a compound represented by **Formula II**,

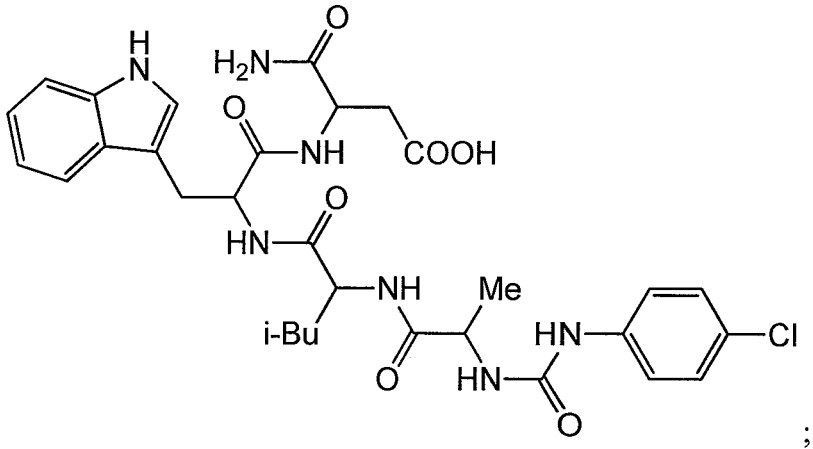
wherein:

a is 1 and b is 0 ;

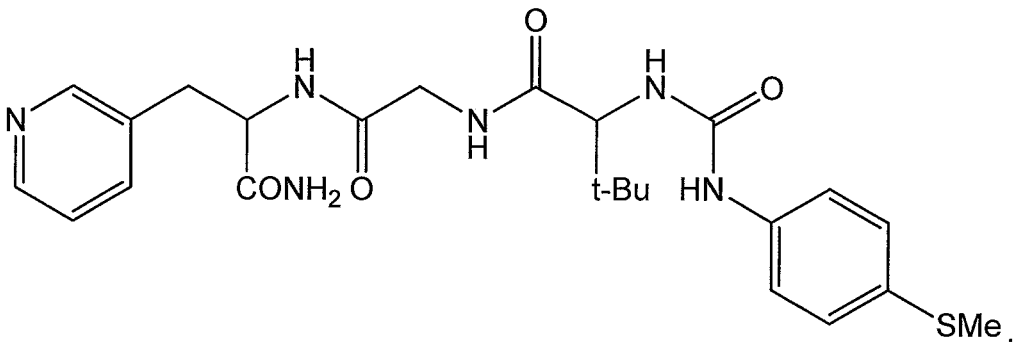


;





; or

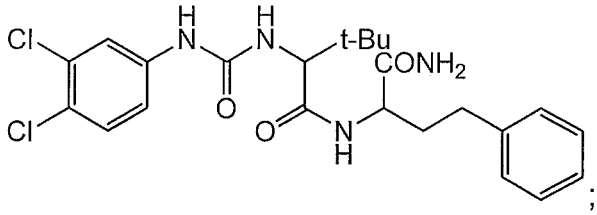


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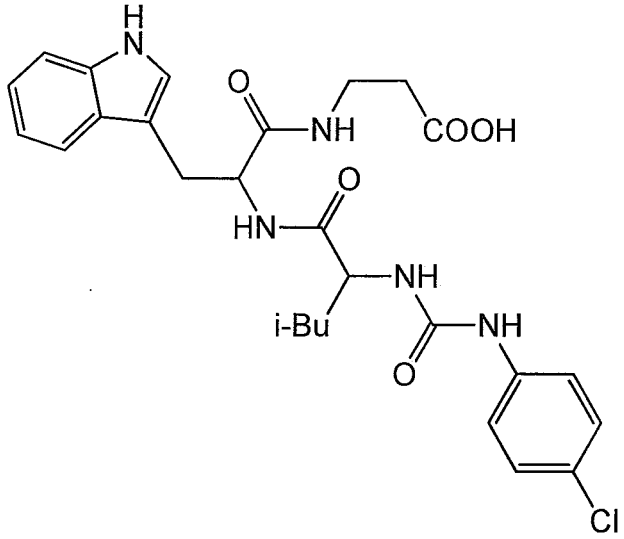
Also disclosed is a compound represented by **Formula II**,

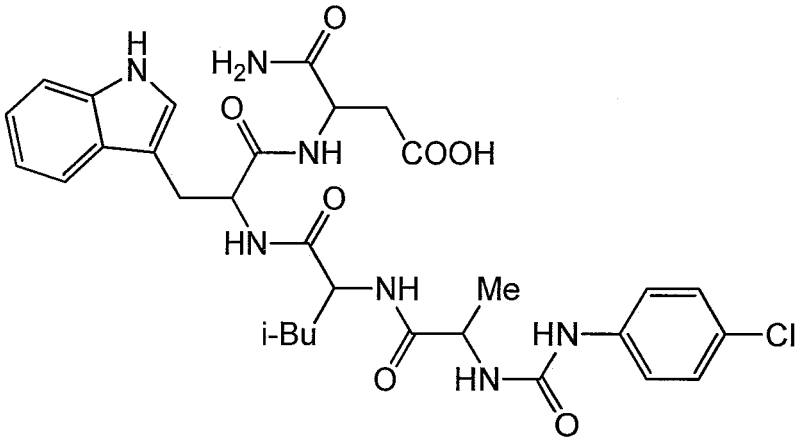
wherein:

a is 1 and b is 0 ;

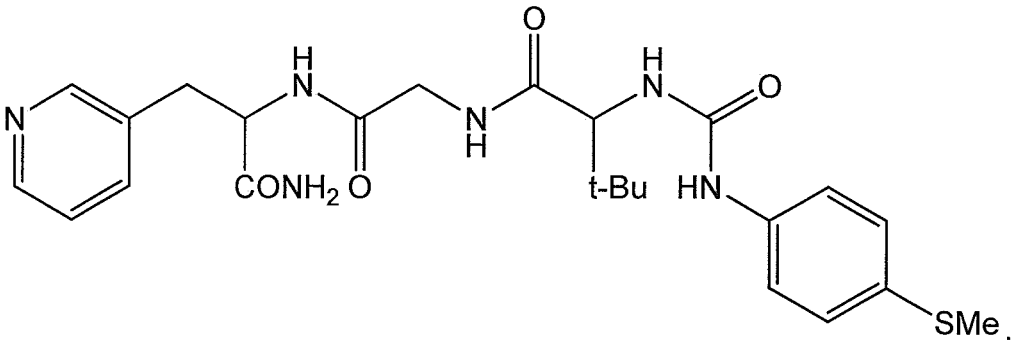


;





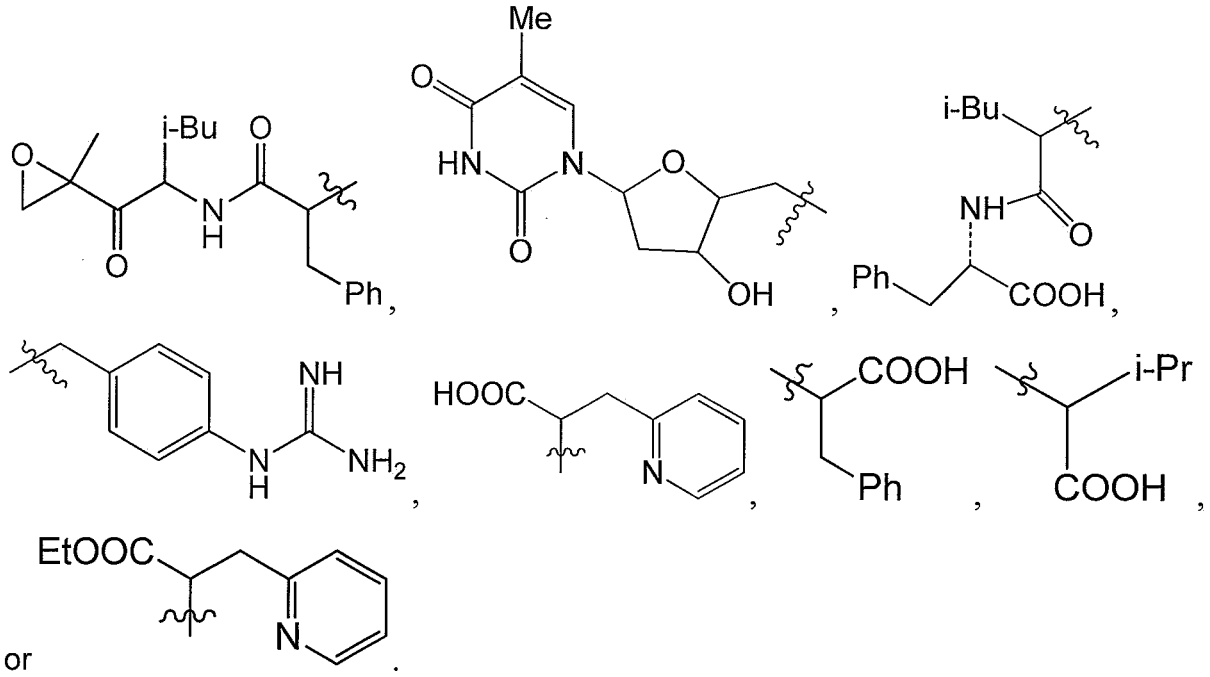
; or



.

Also disclosed is a compound represented by **Formula II**, wherein:

a is 1 and b is 0;



Also disclosed is a compound represented by **Formula II**, wherein

a is 1 and b is 0;

R^1 is optionally substituted C_{1-8} alkyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

n is 0, 1 or 2;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$;

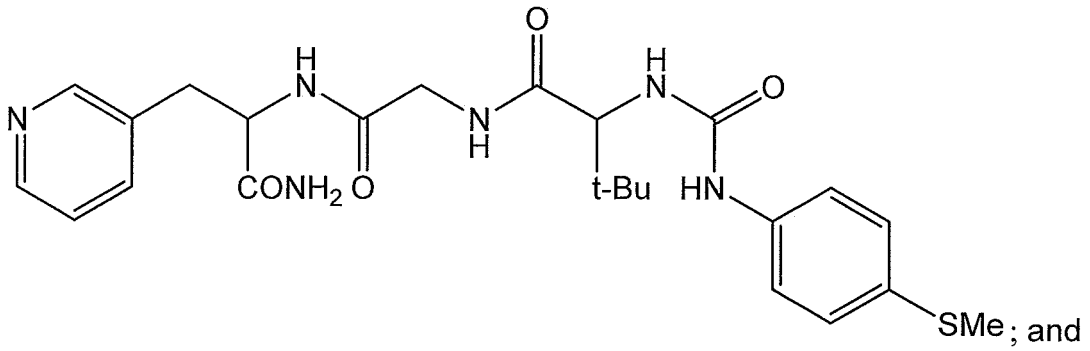
R^8 is hydrogen or optionally substituted C_{1-8} alkyl;

R^9 is hydrogen , optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10} is hydrogen or optionally substituted C_{1-8};

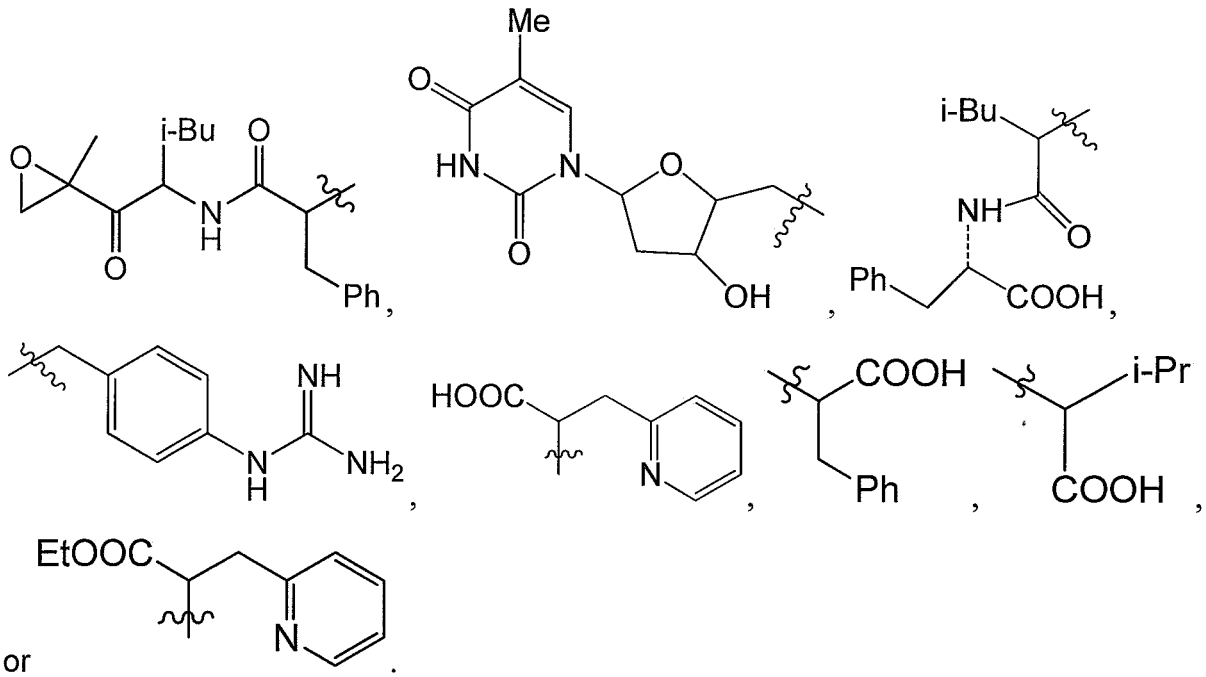
R^{11} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{12} is hydrogen or optionally substituted C_{1-8} alkyl;



; and

R^{11} is not:



or

Also disclosed is a compound represented by **Formula II**, wherein

a is 1 and b is 0;

R^1 is optionally substituted C_{1-8} alkyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

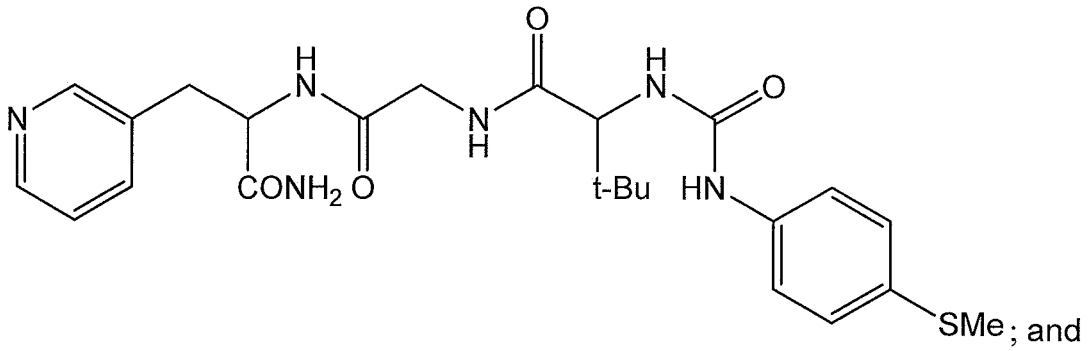
n is 0, 1 or 2;

R^6 is hydrogen;

R^7 is hydrogen;

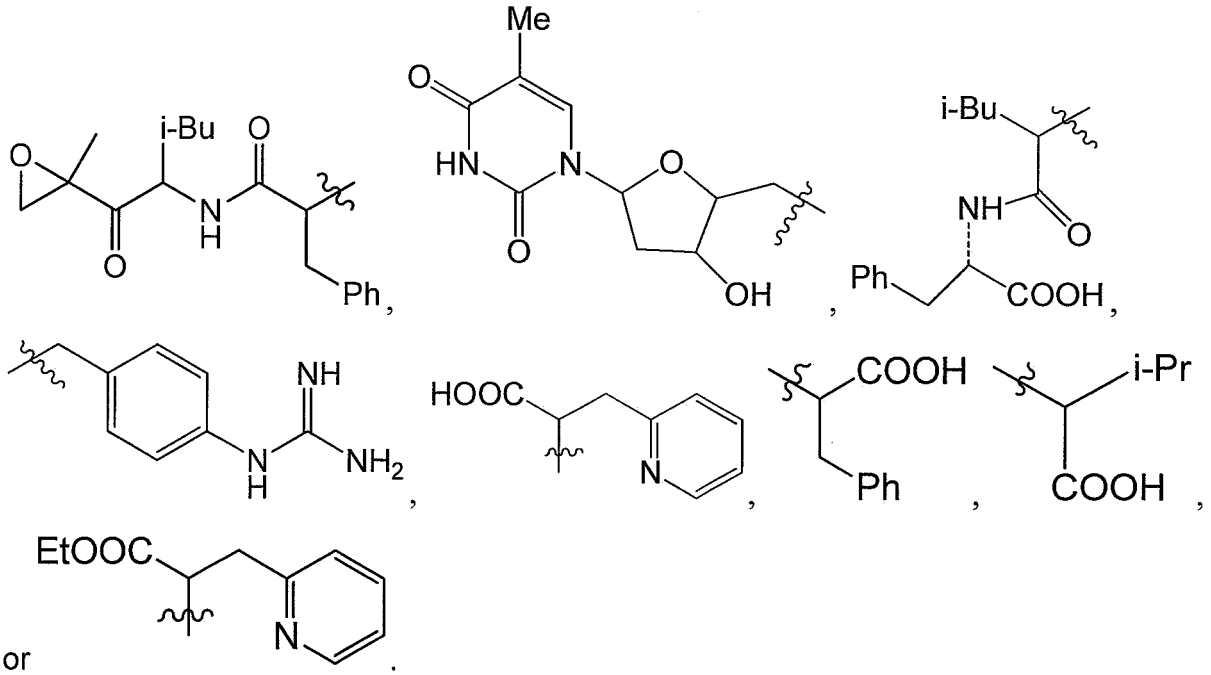
R^8 is hydrogen, optionally substituted C_{1-8} alkyl;

R^9 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;



; and

R^{11} is not:



or

Also disclosed is a compound represented by **Formula II**, wherein

a is 0 and b is 1;

R^1 is $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

n is 0, 1 or 2;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, - $COOR^{15}$, - OR^{13}, - $NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, - $COOR^{15}$, - OR^{13}, - $NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^8 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^9 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{9a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{11} is hydrogen or optionally substituted C_{1-8} alkyl;

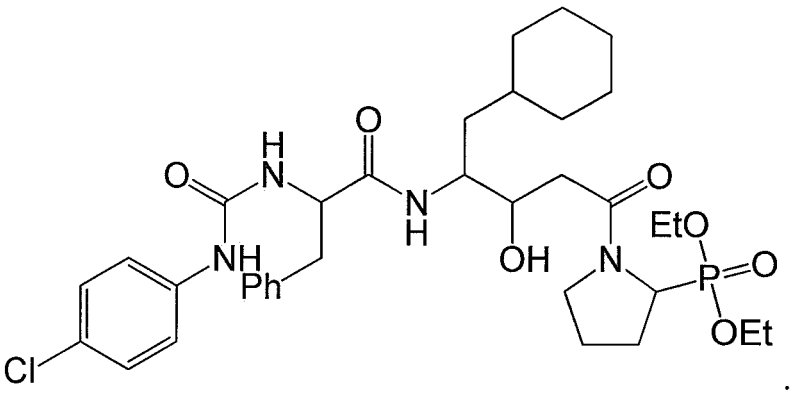
R^{12} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{13} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{14} is hydrogen, CF_3 or optionally substituted C_{1-8} alkyl;

R^{15} is hydrogen or optionally substituted C_{1-8} alkyl; and

the compound of Formula II is not of structure:



.

Also disclosed is a compound represented by **Formula II**,

wherein

a is 0 and b is 1;

R^1 is -OR^{13};

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

Also disclosed is a compound represented by **Formula II**, wherein:

a is 0 and b is 1;

R^1 is $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

n is 0, 1 or 2;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^8 is hydrogen;

R^9 is hydrogen;

R^{10} is hydrogen, optionally substituted C_{1-8} alkyl;

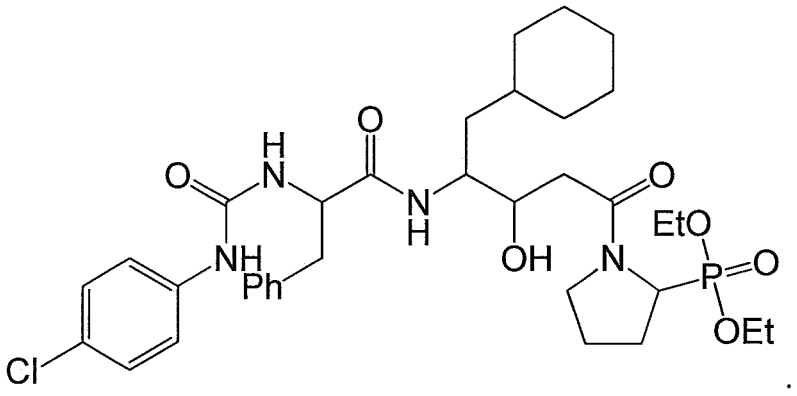
R^{9a} is hydrogen, optionally substituted C_{1-8} alkyl;

R^{10a} is hydrogen, optionally substituted C_{1-8} alkyl;

R^{13} is hydrogen or optionally substituted C_{1-8} alkyl; and

R^{14} is hydrogen, CF_3 or optionally substituted C_{1-8} alkyl; and

the compound of Formula II is not of structure:



Also disclosed is a compound represented by **Formula II**, wherein:

a is 0 and b is 1;

R^1 is $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen;

R^5 is halogen;

R^6 is hydrogen;

R^7 is hydrogen;

R^8 is hydrogen;

R^9 is hydrogen;

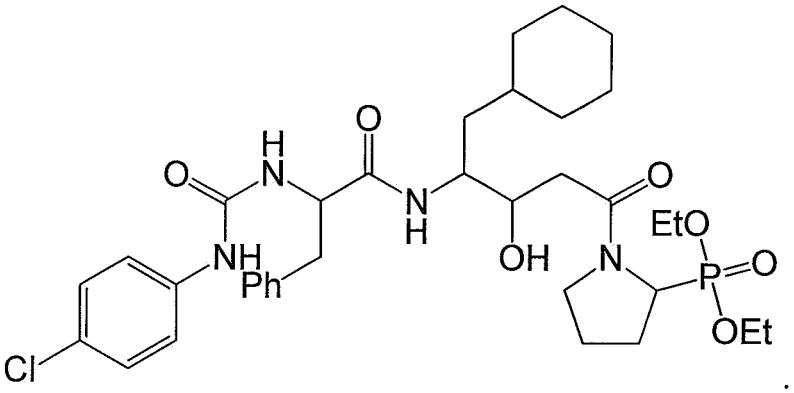
R^{10} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{9a} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{10a} is hydrogen or optionally substituted C_{1-8} alkyl; and

R^{13} is hydrogen; and

the compound of Formula II is not of structure:



.

Also disclosed is a compound represented by **Formula II**, wherein:

a is 0 and b is 1;

R^1 is $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen;

R^5 is halogen;

R^6 is hydrogen;

R^7 is hydrogen;

R^8 is hydrogen;

R^9 is hydrogen;

R^{10} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{9a} is optionally substituted C_{1-8} alkyl;

R^{10a} is optionally substituted C_{1-8} alkyl; and

R^{13} is hydrogen.

Also disclosed is a compound represented by **Formula II**, wherein

a is 1 and b is 1;

R^1 is optionally substituted C_{1-8} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

n is 0, 1 or 2;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^8 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^9 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{9a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{11} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{12} is hydrogen or optionally substituted C_{1-8} alkyl;

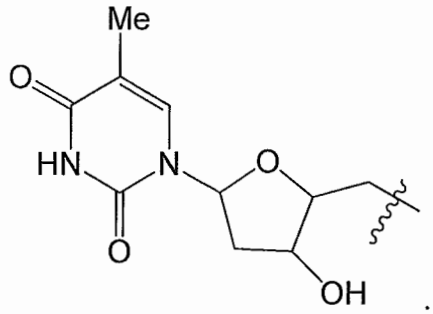
R^{13} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{14} is hydrogen or optionally substituted C_{1-8} alkyl; and

R^{15} is hydrogen or optionally substituted C_{1-8} alkyl; and

with the proviso:

that R^{11} is not:



Also disclosed is a compound represented by **Formula II**, wherein

a is 1 and b is 1;

R^1 is optionally substituted C_{1-8} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{3-8} cycloalkenyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^5 is halogen;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen, $-COOR^{15}$, $-OR^{13}$, $-NR^{11}R^{12}$, NO_2, optionally substituted heterocycle, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{6-10} aryl or optionally substituted C_{3-8} cycloalkenyl;

R^8 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^9 is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{9a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{10a} is hydrogen, optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^{11} is hydrogen or optionally substituted C_{1-8} alkyl;

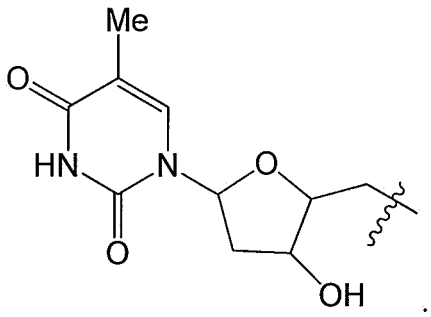
R^{12} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{13} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{15} is hydrogen or optionally substituted C_{1-8} alkyl; and

with the proviso:

that R^{11} is not:



Also disclosed is a compound represented by **Formula II**, wherein

a is 1 and b is 1;

R^1 is optionally substituted C_{1-8} alkyl, $-NR^{11}R^{12}$ or $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^3 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^4 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^5 is halogen, $-CF_3$ or $-S(O)_nR^{14}$;

n is 0, 1 or 2;

R^6 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^7 is hydrogen, optionally substituted C_{1-8} alkyl, halogen;

R^8 is hydrogen;

R^9 is hydrogen, optionally substituted C_{1-8} alkyl;

R^{10} is hydrogen, optionally substituted C_{1-8} alkyl;

R^{9a} is hydrogen, optionally substituted C_{1-8} alkyl;

R^{10a} is hydrogen, optionally substituted C_{1-8} alkyl;

R^{11} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{12} is hydrogen or optionally substituted C_{1-8} alkyl;

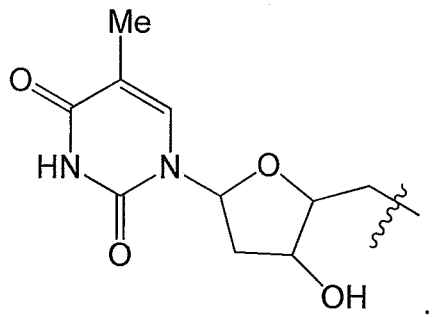
R^{13} is hydrogen or optionally substituted C_{1-8} alkyl;

R^{14} is hydrogen or optionally substituted C_{1-8} alkyl; and

R^{15} is hydrogen or optionally substituted C_{1-8} alkyl;

with the proviso:

that R^{11} is not:



Also disclosed is a compound represented by **Formula II**,

wherein

a is 1 and b is 1;

R^1 is $-OR^{13}$;

R^2 is optionally substituted C_{1-8} alkyl or optionally substituted C_{6-10} aryl;

R^3 is hydrogen;

R^4 is hydrogen;

R^5 is halogen;

R^6 is hydrogen;

R^7 is hydrogen;

R^8 is hydrogen;

R^9 is hydrogen;

R^{10} is hydrogen;

R^{9a} is hydrogen;

R^{10a} is hydrogen; and

R^{13} is hydrogen or optionally substituted C_{1-8} alkyl; and

with the proviso:

that R^{11} is not:

3-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}propanoic acid;
tert-butyl 3-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}propanoate;
{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}acetic acid;
tert-butyl {[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}acetate.

Also disclosed is compounds:
{[2-{[(4-bromophenyl)carbamoyl]amino}-3-(1H-imidazol-4-yl)propanoyl]amino}acetic acid;
tert-butyl {[2-{[(4-bromophenyl)carbamoyl]amino}-3-(1H-imidazol-4-yl)propanoyl]amino}acetate;
{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfonyl)butanoyl]amino}acetic acid;
tert-butyl {[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfonyl)butanoyl]amino}acetate;
{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfanyl)butanoyl]amino}acetic acid;
tert-butyl {[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfanyl)butanoyl]amino}acetate;
2-methyl-2-{[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}propanoic acid;
tert-butyl 2-methyl-2-{[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}propanoate;
{[(2S)-4-methyl-2-({[4-(methylsulfonyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;
tert-butyl {[(2S)-4-methyl-2-({[4-(methylsulfonyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetate;
{[(2S)-4-methyl-2-({[4-(methylsulfinyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;
tert-butyl {[(2S)-4-methyl-2-({[4-(methylsulfinyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetate;

salts" according to the invention include therapeutically active, non-toxic base or acid salt forms, which the compounds of Formula I and of Formula II are able to form.

The acid addition salt form of a compound of Formula I and of Formula II that occurs in its free form as a base can be obtained by treating the free base with an appropriate acid such as an inorganic acid, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid and the like; or an organic acid such as for example, acetic acid, hydroxyacetic acid, propanoic acid, lactic acid, pyruvic acid, malonic acid, fumaric acid, maleic acid, oxalic acid, tartaric acid, succinic acid, malic acid, ascorbic acid, benzoic acid, tannic acid, pamoic acid, citric acid, methylsulfonic acid, ethanesulfonic acid, benzenesulfonic acid, formic and the like (Handbook of Pharmaceutical Salts, P. Heinrich Stahal & Camille G. Wermuth (Eds), Verlag Helvetica Chemica Acta- Zürich, 2002, 329-345).

The base addition salt form of a compound of Formula I and of Formula II that occurs in its acid form can be obtained by treating the acid with an appropriate base such as an inorganic base, for example, sodium hydroxide, magnesium hydroxide, potassium hydroxide, Calcium hydroxide, ammonia and the like; or an organic base such as for example, L-Arginine, ethanolamine, betaine, benzathine, morpholine and the like. (Handbook of Pharmaceutical Salts, P.Heinrich Stahal& Camille G. Wermuth (Eds), Verlag Helvetica Chemica Acta- Zürich, 2002, 329-345).

Compounds of Formula I and of Formula II and their salts can be in the form of a solvate, which is included within the scope of the present invention. Such solvates include for example hydrates, alcoholates and the like.

Compounds according to the present invention may exist in different polymorphic forms. Although not explicitly indicated in the above formula, such forms are intended to be included within the scope of the present invention.

The compounds of the invention are indicated for use in treating or preventing conditions in which there is likely to be a component involving the N-formyl peptide receptor like-1 receptor.

CLAIMS

1). A compound selected from:

{[2-{[(4-bromophenyl)carbamoyl]amino)-3-(1H-indol-3-yl)propanoyl]amino}acetic acid;

2-{[(2R)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-2-methylpropanoic acid;

{[2-{[(4-bromophenyl)carbamoyl]amino}-3-(1H-imidazol-4-yl)propanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfonyl)butanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-(methylsulfanyl)butanoyl]amino}acetic acid;

2-methyl-2-{[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}propanoic acid;

{[(2S)-4-methyl-2-({[4-(methylsulfonyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2S)-4-methyl-2-({[4-(methylsulfinyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-2-methylpropanoic acid;

({(2S)-4-methyl-2-({[4-[trifluoromethyl)sulfanyl]phenyl}carbamoyl)amino]pentanoyl}amino)acetic acid;

{[(2S)-4-methy1-2-({[4-(methylsulfanyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2R)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino)acetic acid;

{[(2R,3R)-2-{[(4-bromophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid;

{[(2S)-4-methyl-2-({[4-(trifluoromethyl)phenyl]carbamoyl}amino)pentanoyl]amino}acetic acid;

{[(2R)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino)-2-methylpropanoyl)amino]acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino}-2-ethylbutanoyl)amino]acetic acid;

[(2-{[(4-bromophenyl)carbamoyl]amino}-2,4-dimethylpentanoyl)amino]acetic acid;

(2S)-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}(phenyl)ethanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}pentanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}-3-methylbutanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}propanoic acid;

(2S)-2-{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}propanoic acid;

{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl)amino}acetic acid;

{[(2S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}pentanoyl]amino}acetic acid;

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}pentanoyl]amino}acetic acid;

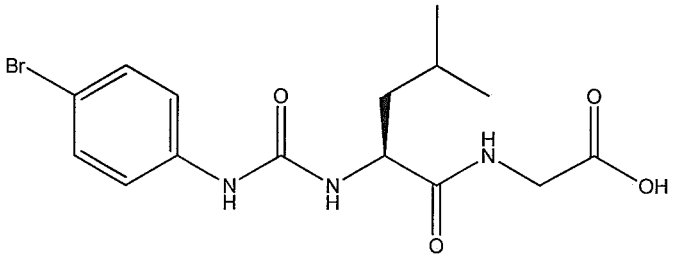
{[(2S,3S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid;

{[(2S,3S)-2-{[(4-bromo-2-fluorophenyl)carbamoyl]amino}-3-methylpentanoyl]amino}acetic acid;

3-{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3-phenylpropanoyl]amino}propanoic acid; and

{[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-3- phenylpropanoyl]amino}acetic acid.

2). The compound according to claim 1: {[(2S)-2-{[(4-bromophenyl)carbamoyl]amino}-4-methylpentanoyl]amino}acetic acid, which has the following structure:



or a pharmaceutically acceptable salt thereof.

3). A pharmaceutical composition including at least one compound or a pharmaceutically acceptable salt thereof according to claims 1 or 2 in a pharmaceutically acceptable carrier.

4). The compound or a pharmaceutically acceptable salt thereof according to claims 1 or 2 or the pharmaceutical composition according to claim 3 for use in treating a disease.

5). Use of a compound or a pharmaceutically acceptable salt thereof according to claims 1 and 2 or a pharmaceutical composition according to claim 3 in the manufacture of a medicament for treating an ocular inflammatory disease.

6). The use according to claim 5, wherein the disease is selected from wet and dry age-related macular degeneration (ARMD), uveitis, dry eye, Keratitis, allergic eye disease and conditions affecting the posterior part of the eye, such as maculopathies and retinal degeneration including non-exudative age related macular degeneration, exudative age related macular degeneration, choroidal neovascularization, diabetic retinopathy (proliferative), retinopathy of prematurity (ROP), acute macular neuroretinopathy, central serous chorioretinopathy, cystoid macular edema, and diabetic macular edema; infectious keratitis, uveitis, herpetic keratitis, corneal angiogenesis, lymphangiogenesis, uveitis, retinitis, and choroiditis such as acute multifocal placoid pigment epitheliopathy, Behcet's disease, birdshot retinochoroidopathy, infectious (syphilis, lyme, tuberculosis, toxoplasmosis), intermediate uveitis (pars planitis), multifocal choroiditis, multiple evanescent white dot syndrome (mewds), ocular sarcoidosis, posterior scleritis, serpiginous choroiditis, subretinal fibrosis and uveitis syndrome, Vogt-Koyanagi-and Harada syndrome; vascular diseases/ exudative diseases such as retinal arterial occlusive disease, central retinal vein occlusion, cystoids macular edema, disseminated intravascular coagulopathy, branch retinal vein occlusion, hypertensive fundus changes, ocular ischemic syndrome, retinal arterial microaneurysms, Coat's disease, parafoveal telangiectasis, hemi-retinal vein occlusion, papillophlebitis, central retinal artery occlusion, branch retinal artery occlusion, carotid artery disease (CAD), frosted branch angiitis, sickle cell retinopathy and other hemoglobinopathies, angioid streaks, familial exudative vitreoretinopathy, and Eales disease; traumatic/ surgical conditions such as sympathetic ophthalmia, uveitic retinal disease, retinal detachment, trauma, post surgical corneal wound healing, conditions caused by laser, conditions caused by photodynamic therapy, photocoagulation, hypoperfusion during surgery, radiation retinopathy, and bone marrow transplant retinopathy; proliferative disorders such as proliferative vitreal retinopathy and epiretinal membranes, and proliferative diabetic retinopathy; infectious disorders such as ocular histoplasmosis, ocular toxocariasis, presumed ocular histoplasmosis syndrome (POHS), endophthalmitis, toxoplasmosis, retinal diseases associated with HIV infection,

choroidal disease associate with HIV infection, uveitic disease associate with HIV infection, viral retinitis, acute retinal necrosis, progressive outer retinal necrosis, fungal retinal diseases, ocular syphilis, ocular tuberculosis, diffuse unilateral subacute neuroretinitis, and myiasis; genetic disorders such as retinitis pigmentosa, systemic disorders with accosiated retinal dystrophies, congenital stationary night blindness, cone dystrophies, Stargardt's disease and fundus flavimaculatus, Best's disease, pattern dystrophy of the retinal pigmented epithelium, X-linked retinoschisis, Sorsby's fundus dystrophy, benign concentric maculopathy, Bietti's crystalline dystrophy, and pseudoxanthoma elasticum; retinal tears/ holes such as retinal detachment, macular hole, and giant retinal tear; tumors such as retinal disease associated with tumors, congenital hypertrophy of the retinal pigmented epithelium, posterior uveal melanoma, choroidal hemangioma, choroidal osteoma, choroidal metastasis, combined hamartoma of the retina and retinal pigmented epithelium, retinoblastoma, vasoproliferative tumors of the ocular fundus, retinal astrocytoma, and intraocular lymphoid tumors; and miscellaneous other diseases affecting the posterior part of the eye such as punctate inner choroidopathy, acute posterior multifocal placoid pigment epitheliopathy, myopic retinal degeneration, and acute retinal pigement epitheliitis, systemic inflammatory diseases such as stroke, coronary artery disease, obstructive airway diseases, HIV-mediated retroviral infections, cardiovascular disorders including coronary artery disease, neuroinflammation, neurological disorders, pain and immunological disorders, asthma, allergic disorders, inflammation, systemic lupus erythematosus, psoriasis, CNS disorders such as Alzheimer's disease, arthritis, sepsis, inflammatory bowel disease, cachexia, angina pectoris, post-surgical corneal inflammation, blepharitis, MGD, dermal wound healing, burns, rosacea, atopic dermatitis, acne, psoriasis, seborrheic dermatitis, actinic keratoses, viral warts, photoaging rheumatoid arthritis and related inflammatory disorders, alopecia, glaucoma, branch vein occlusion, Best's vitelliform macular degeneration, retinitis pigmentosa, proliferative vitreoretinopathy (PVR), and any other degenerative disease of either the photoreceptors or the RPE.