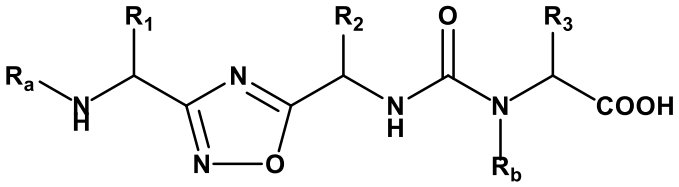
We claim:

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof;

wherein,

R_a is hydrogen or acyl; and R_1 represents hydrogen, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -CH_2COOH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -CH_2CONH_2, -$CH(CH_3)$-CH_2-CH_3, -CH_2-aryl, or -CH_2-heteroaryl; wherein the aryl and heteroaryl are unsubstituted; or R_a and R_1, together with the atoms to which they are attached form pyrrolidine ring optionally substituted with oxo group;

R_2 represents hydrogen, -CH_2-OH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -CH_2-aryl, or -CH_2-heteroaryl; wherein the aryl and heteroaryl are unsubstituted;

R_b is hydrogen; and R_3 represents hydrogen, -CH_2-aryl, -$(CH_2)_3NHC(=NH)NH_2$, -CH_2COOH, -$CH(CH_3)$-CH_2-CH_3, -CH_2-$CH(CH_3)_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -$(CH_2)_4NH_2$ or -CH_2-heteroaryl; wherein the aryl and heteroaryl are unsubstituted; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

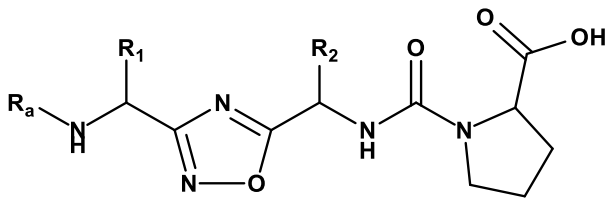
2. The compound of claim 1, wherein R_1 represents hydrogen, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -CH_2CONH_2, -$CH(CH_3)$-CH_2-CH_3, -CH_2-phenyl, -CH_2-indolyl, or -CH_2-imidazolyl.

3. The compound of any one of claims 1 to 2, wherein R_2 represents hydrogen, -CH_2-OH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -CH_2-phenyl, -CH_2-indolyl, or -CH_2-imidazolyl.

4. The compound of any one of claims 1 to 3, wherein R_3 represents hydrogen, -$(CH_2)_3NHC(=NH)NH_2$, -CH_2COOH, -$CH(CH_3)$-CH_2-CH_3, -CH_2-$CH(CH_3)_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -$(CH_2)_4NH_2$, -CH_2-phenyl, -CH_2-indolyl, or -CH_2-imidazolyl.

5. The compound of any one of claims 1 to 4, wherein R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

6. The compound of claim 1, represented by compound of formula (IA):



(IA)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_1, R_a and R_2 are as defined in claim 1.

7. The compound of claim 6, wherein R_1 represents hydrogen, $-CH_2-COOH$, $-CH_2-CONH_2$, $-CH(CH_3)-CH_2-CH_3$, $-(CH_2)_2CONH_2$, $-(CH_2)_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-CH_2$-phenyl, $-CH_2$-indolyl or $-CH_2$-imidazolyl.

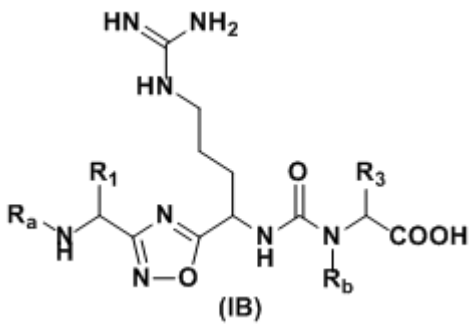
8. The compound of claim 6, wherein R_2 represents hydrogen, $-CH_2-OH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_2CONH_2$, $-(CH_2)_2COOH$, $-CH_2$-phenyl, or $-CH_2$-imidazolyl.

9. The compound of any one of claims 6 to 8, wherein,

R_a is hydrogen; and R_1 represents hydrogen, $-CH_2-COOH$, $-CH_2-CONH_2$, $-CH(CH_3)-CH_2-CH_3$, $-(CH_2)_2CONH_2$, $-(CH_2)_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-CH_2$-phenyl, $-CH_2$-indolyl or $-CH_2$-imidazolyl;

R_2 represents hydrogen, $-CH_2-OH$ $-(CH_2)_2CONH_2$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_2COOH$ or $-CH_2$-phenyl.

10. The compound of claim 1, represented by compound of formula (IB):



(IB)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_1, R_a, R_b and R_3 are as defined in claim 1.

11. The compound of claim 10, wherein, R_1 represents hydrogen, -CH_2-COOH, -CH_2-$CONH_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -CH_2-indolyl, -CH_2-imidazolyl or -CH_2-phenyl.

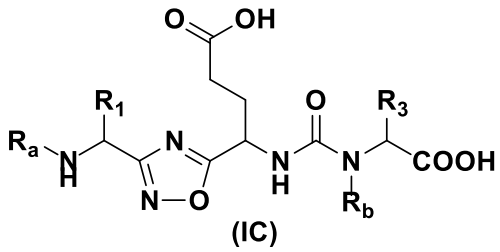
12. The compound of claim 10, wherein, R_b is hydrogen; R_3 represents hydrogen, -CH_2-COOH, -CH_2-$CH(CH_3)_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_4NH_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -CH_2-phenyl, CH_2-indolyl or CH_2-imidazolyl; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

13. The compound of any one of claims 10 to 12, wherein;

R_1 represents hydrogen, -CH_2-COOH, -CH_2-$CONH_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -CH_2-indolyl, -CH_2-imidazolyl or -CH_2-phenyl;

R_b is hydrogen; R_3 represents hydrogen, -CH_2-COOH, -CH_2-$CH(CH_3)_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_4NH_2$, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, -CH_2-phenyl, CH_2-imidazolyl or CH_2-imidazolyl; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

14. The compound of claim 1, represented by compound of formula (IC):



(IC)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_1, R_a, R_3 and R_b are as defined in claim 1.

15. The compound of claim 14, wherein R_a is hydrogen; R_1 represents -$(CH_2)_2COOH$, -$(CH_2)_2CONH_2$, -$(CH_2)_3NHC(=NH)NH_2$, or -$(CH_2)_4NH_2$; or R_a and R_1, together with the atoms to which they are attached form pyrrolidine ring.

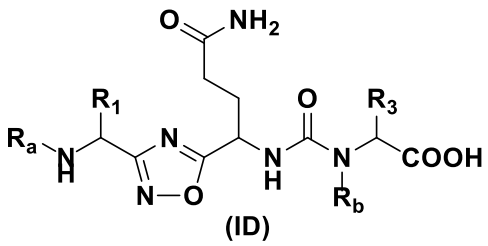
16. The compound of claim 14, wherein R_b is hydrogen; R_3 represents hydrogen, -CH_2-phenyl, -$(CH_2)_2CONH_2$, or -$(CH_2)_2COOH$; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

17. The compound of any one of claims 14 to 16, wherein;

R_a is hydrogen; R_1 represents -$(CH_2)_2COOH$, -$(CH_2)_2CONH_2$, -$(CH_2)_3NHC(=NH)NH_2$, or -$(CH_2)_4NH_2$; or R_a and R_1, together with the atoms to which they are attached form pyrrolidine ring;

R_b is hydrogen; R_3 represents hydrogen, -CH_2-phenyl, -$(CH_2)_2CONH_2$, or -$(CH_2)_2COOH$; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

18. The compound of claim 1, represented by compound of formula (ID):



(ID)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_1, R_a, R_3 and R_b are as defined in claim 1.

19. The compound of claim 18, wherein R_1 represents -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, or -CH_2CONH_2.

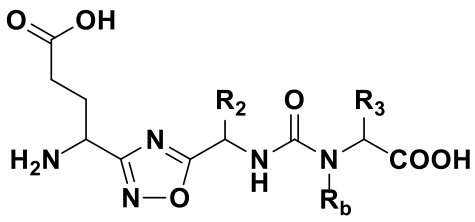
20. The compound of claim 18, wherein R_b is hydrogen; R_3 represents hydrogen, -$(CH_2)_3NHC(=NH)NH_2$, or -$(CH_2)_4NH_2$; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

21. The compound of any one of claims 18 to 20, wherein;

R_1 represents -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, or -CH_2CONH_2;

R_b is hydrogen; R_3 represents hydrogen, -$(CH_2)_3NHC(=NH)NH_2$, or -$(CH_2)_4NH_2$; or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

22. The compound of claim 1, represented by compound of formula (IE):



(IE)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_2, R_3 and R_b are as defined in claim 1.

23. The compound of claim 22, wherein R_2 represents hydrogen, -CH_2-OH, -$(CH_2)_2$COOH, -$(CH_2)_3$NHC(=NH)NH_2, -CH_2-phenyl or -CH_2- indolyl.

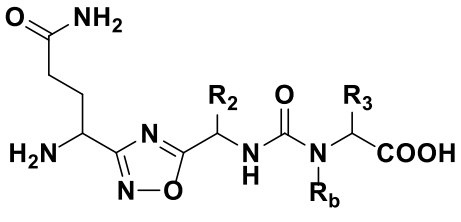
24. The compound of claim 22, wherein, R_3 represents hydrogen, -CH_2-COOH, -$(CH_2)_2$COOH, -CH_2-$CH(CH_3)_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_4$NH2, -CH_2-phenyl, -CH_2-indolyl, or -CH_2- imidazolyl or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

25. The compound of any one of claims 22 to 24, wherein;

R_2 represents hydrogen, -CH_2-OH, -$(CH_2)_2$COOH, -$(CH_2)_3$NHC(=NH)NH_2, -CH_2-phenyl or -CH_2- indolyl;

R_3 represents hydrogen, -CH_2-COOH, -$(CH_2)_2$COOH, -CH_2-$CH(CH_3)_2$, -$CH(CH_3)$-CH_2-CH_3, -$(CH_2)_4NH_2$, -CH_2-phenyl, -CH_2-indolyl, or -CH_2- imidazolyl or R_b and R_3, together with the atoms to which they are attached form pyrrolidine ring.

26. The compound of claim 1, represented by compound of formula (IF):



(IF)

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof; wherein, R_2, R_3 and R_b are as defined in claim 1.

27. The compound of claim 26, wherein R_2 represents hydrogen, -CH_2-phenyl, -$(CH_2)_3$NHC(=NH)NH_2, or -$(CH_2)_2$COOH.

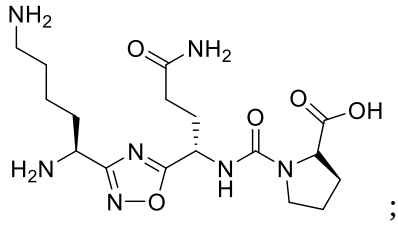
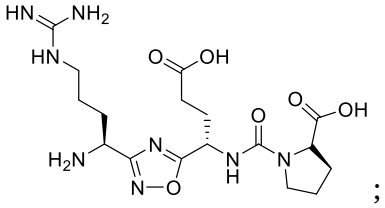
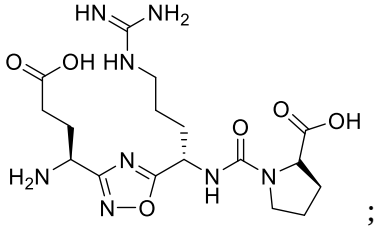
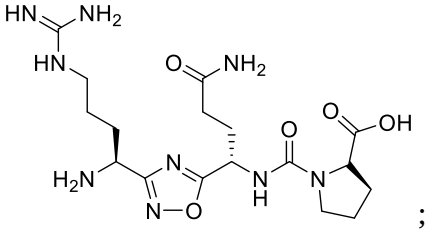
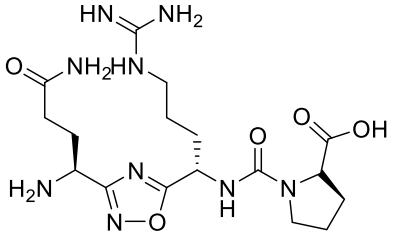
28. The compound of claim 26, wherein R_3 represents -CH_2-phenyl, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, or -$(CH_2)_4NH_2$.

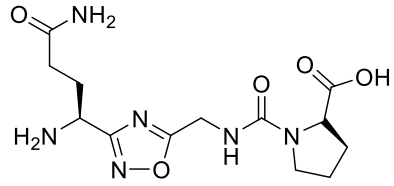
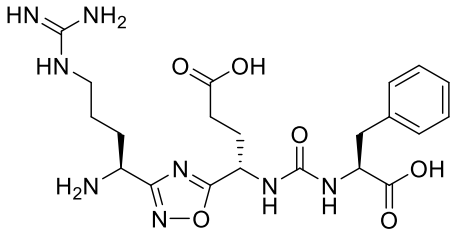
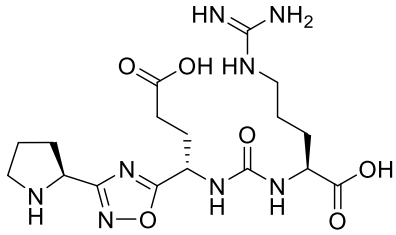
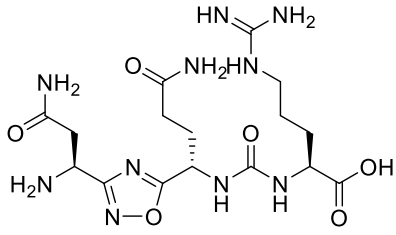
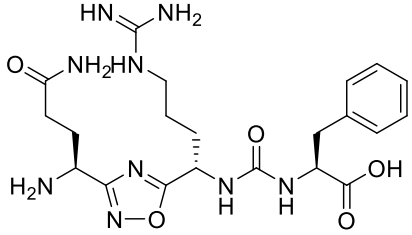
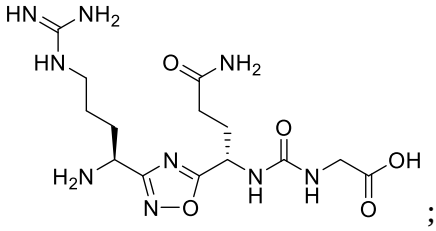
29. The compound of any one of claims 26 to 28, wherein,

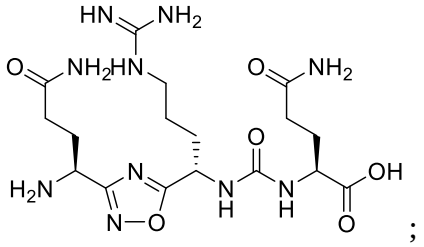
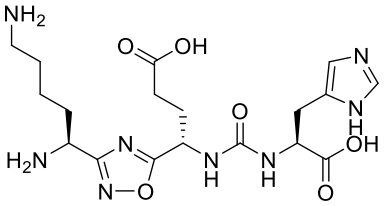
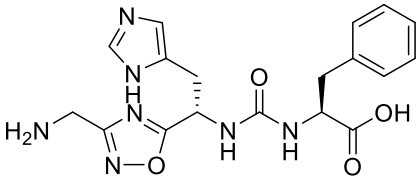
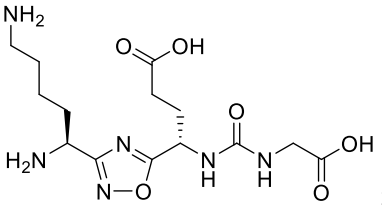
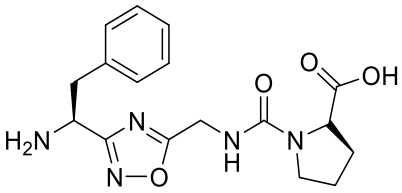
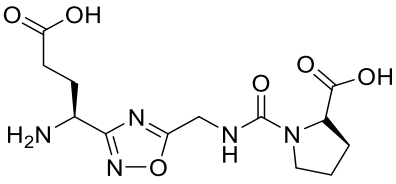
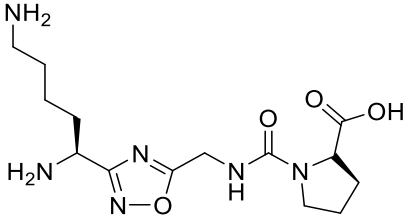
R_2 represents hydrogen, -CH_2-phenyl, -$(CH_2)_3NHC(=NH)NH_2$, or -$(CH_2)_2COOH$; and

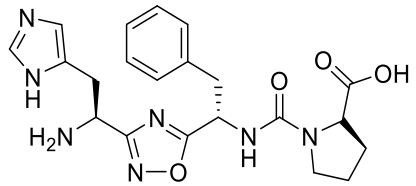
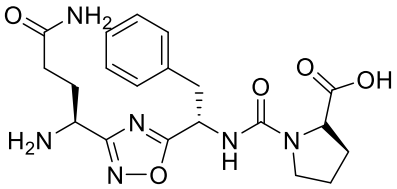
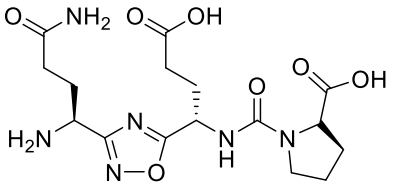
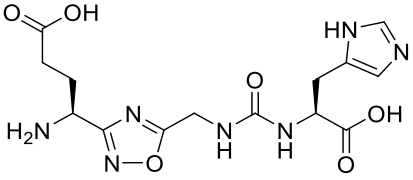
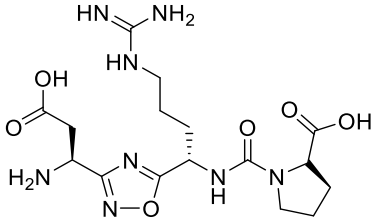
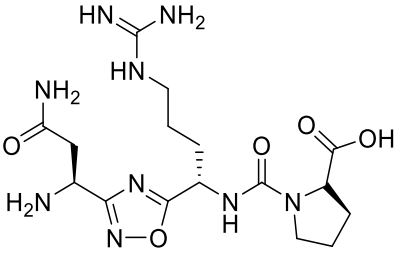
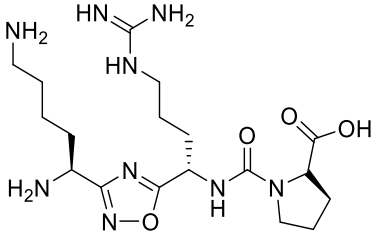
R_3 represents -CH_2-phenyl, -$(CH_2)_2CONH_2$, -$(CH_2)_2COOH$, or -$(CH_2)_4NH_2$.

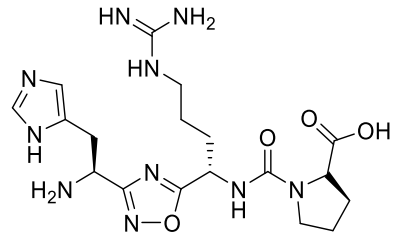
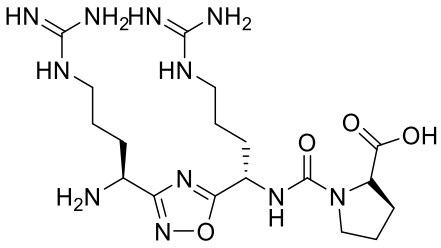
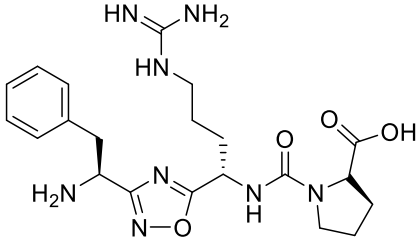
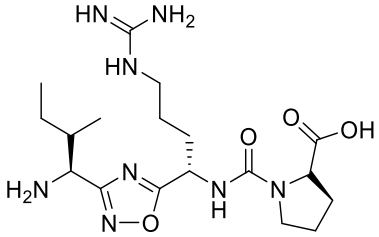
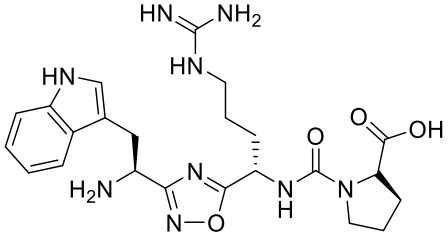
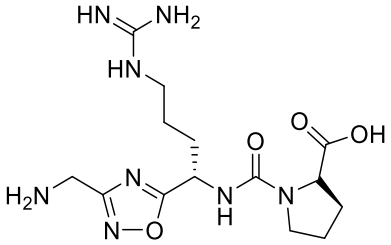
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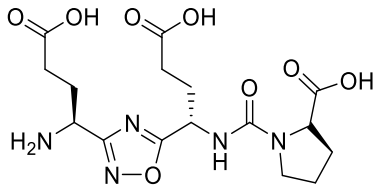
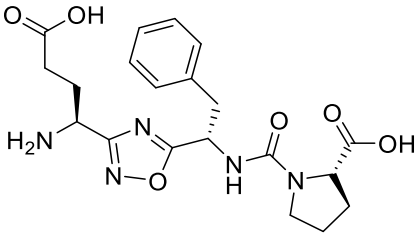
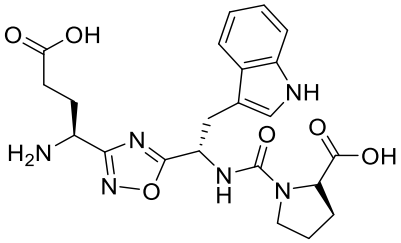
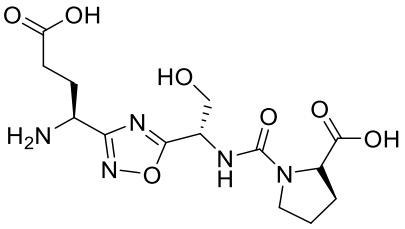
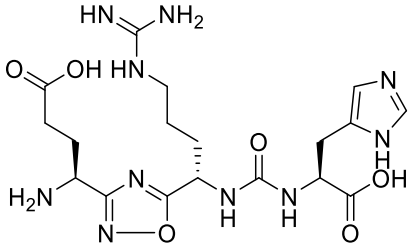
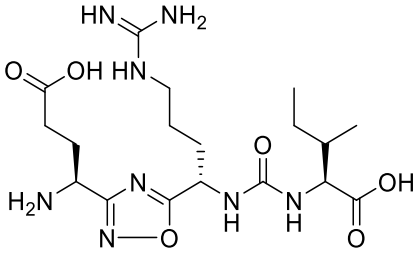
Compound	Structure
1	 ;
2	 ;
3	 ;
4	 ;
5	 ;

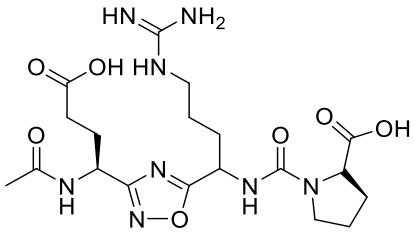
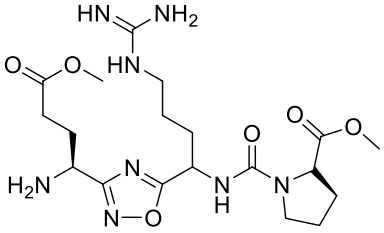
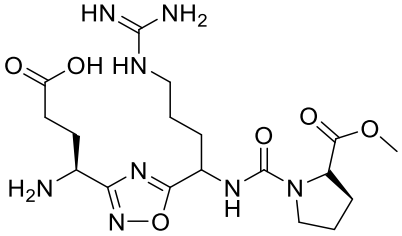
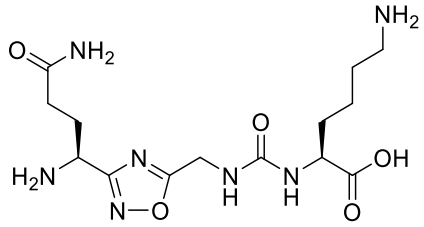
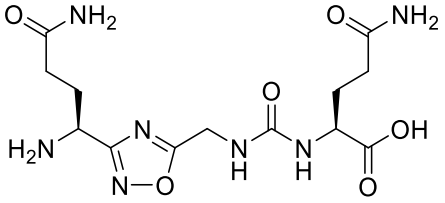
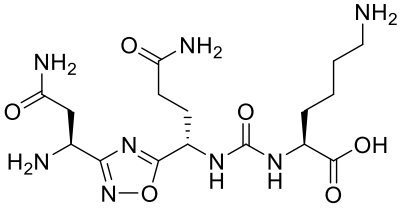
Compound	Structure
6	 ;
7	 ;
8	 ;
9	 ;
10	 ;
11	 ;

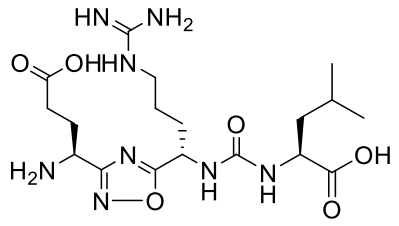
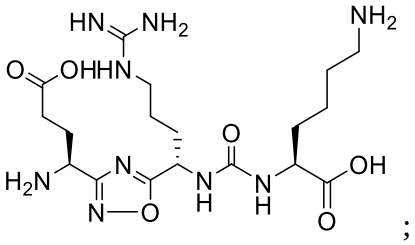
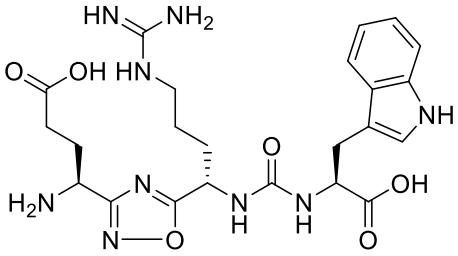
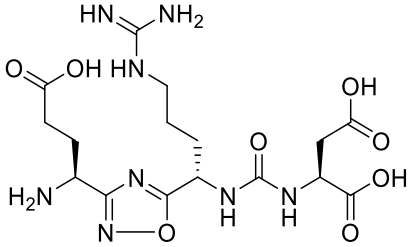
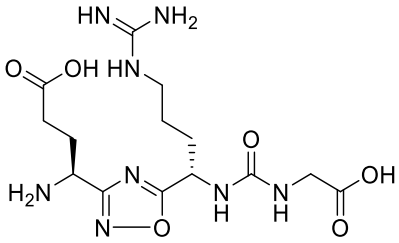
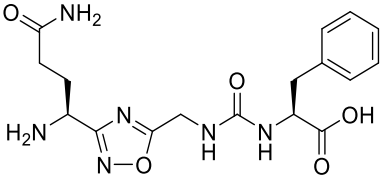
Compound	Structure
12	 ;
13	 ;
14	 ;
15	 ;
16	 ;
17	 ;
18	 ;

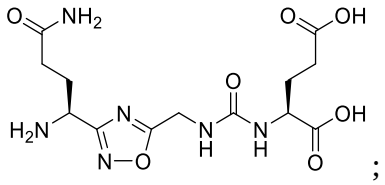
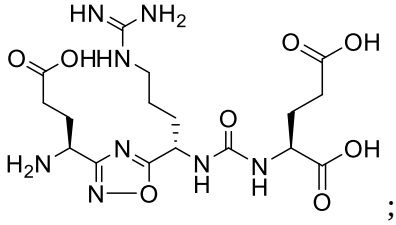
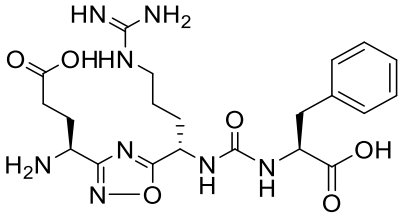
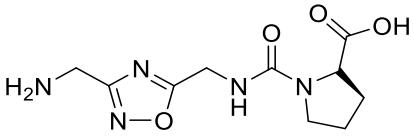
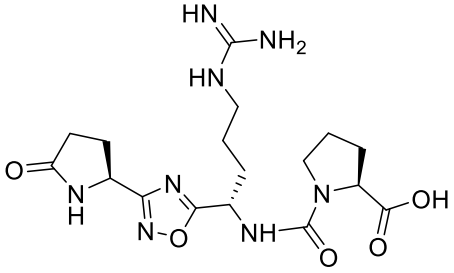
Compound	Structure
19	 ;
20	 ;
21	 ;
22	 ;
23	 ;
24	 ;
25	 ;

Compound	Structure
26	 ;
27	 ;
28	 ;
29	 ;
30	 ;
31	 ;

Compound	Structure
32	 ;
33	 ;
34	 ;
35	 ;
36	 ;
37	 ;

Compound	Structure
38	 ;
39	 ;
40	 ;
41	 ;
42	 ;
43	 ;

Compound	Structure
44	 ;
45	 ;
46	 ;
47	 ;
48	 ;
49	 ;

Compound	Structure
50	 ;
51	 ;
52	 ;
53	 ; and
54	

or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof.

31. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1-30, and a pharmaceutically acceptable carrier.

32. A compound of any one of claims 1 to 30 for use as a medicament.

33. Use of a compound according to any one of claims 1 to 30, in the manufacture of a medicament for modulating macrophage phagocytic activity towards a cancer cell or tumor cell.

34. The use of claim 33, wherein the cancer cell is the cell of cancer selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone

cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia (AML), chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), non-small cell lung cancer (NSCLC), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, B-cell lymphomas, environmentally induced cancers including those induced by asbestos (e.g., mesothelioma), and combinations of said cancers.

35. The use of claim 33, wherein the cancer cell is an AML cell.

36. Use of a compound according to any one of claims 1 to 30, in the manufacture of a medicament for treating or delaying progression of diseases or disorders mediated by CD47.

37. The use of claim 36, wherein the disease or disorder mediated by CD47 is cancer.

38. The use of claim 37, wherein the cancer is selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the

bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), non-small cell lung cancer (NSCLC), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, B-cell lymphomas, environmentally induced cancers including those induced by asbestos (e.g., mesothelioma), and combinations of said cancers.

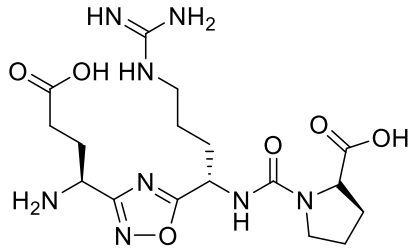
39. The use of claim 36, wherein the disease or disorder mediated by CD47 is bacterial, viral and fungal infection.

40. The use of claim 39, wherein infectious disease is HIV, Influenza, Herpes, Giardia, Malaria, Leishmania, the pathogenic infection by the virus Hepatitis (A, B, & C), herpes virus (e.g., VZV, HSV-I, HAV-6, HSV-II, and CMV, Epstein Barr virus), adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, coronavirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus and arboviral encephalitis virus, pathogenic infection by the bacteria chlamydia, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci and conococci, klebsiella, proteus, serratia, pseudomonas, E. coli, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lyme's disease bacteria, pathogenic infection by the fungi Candida (albicans, krusei, glabrata, tropicalis, etc.), Cryptococcus neoformans, Aspergillus (fumigatus, niger, etc.), Genus Mucorales (mucor, absidia, rhizophus), Sporothrix schenkii, Blastomyces dermatitidis, Paracoccidioides brasiliensis, Coccidioides immitis and Histoplasma capsulatum, and pathogenic infection by the parasites Entamoeba histolytica, Balantidium coli, Naegleriafowleri, Acanthamoeba sp., Giardia lambia, Cryptosporidium sp., Pneumocystis carinii, Plasmodium vivax, Babesia microti, Trypanosoma brucei, Trypanosoma cruzi, Leishmania donovani, Toxoplasma gondi, or Nippostrongylus brasiliensis.

41. Use of a compound according to any one of claims 1 to 30, in the manufacture of a medicament for treating or delaying progression of atherosclerosis and multiple sclerosis mediated by CD47.

42. Use of a compound according to any one of claims 1 to 30, in the manufacture of a medicament for the treatment of cancer.

43. A compound of the formula:



or a pharmaceutically acceptable salt or an amide or an ester, or a stereoisomer thereof.

44. A pharmaceutical composition comprising a compound according to claim 43, and a pharmaceutically acceptable carrier.