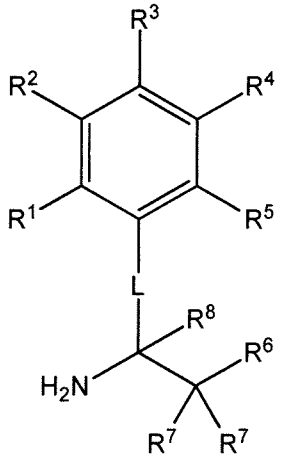
Claims

1. A compound of Formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from $C_{1\text{-}6}$ alkyl and $C_{1\text{-}6}$ alkoxy;

R^4 is $-N(-CH_2-CH_2-R^9)_2$, wherein each R^9 is independently selected from –Cl, –Br, –I, $-OSO_2CH_3$, and $-OSO_2CF_3$;

each of R^2, R^3, and R^5 is independently selected from hydrogen and deuterio;

R^6 is ~~selected from –COOH and $-CO(-OCH_3)$~~;

each R^7 is independently selected from hydrogen and deuterio;

R^8 is selected from hydrogen and deuterio; and

L is selected from a bond ("–") and $-CH_2-$.

2. The compound of claim 1, wherein,

L is $-CH_2-$;

R^1 is $C_{1\text{-}6}$ alkyl;

R^4 is $-N(-CH_2-CH_2-Cl)_2$;

each of R^2, R^3, and R^5 is hydrogen;

each R^7 is hydrogen; and

R^8 is hydrogen.

3. The compound of claim 1, wherein,

L is $-CH_2-$;

R^1 is C_{1-6} alkoxy;

R^4 is $-N(-CH_2-CH_2-Cl)_2$;

each of R^2, R^3, and R^5 is hydrogen;

each R^7 is hydrogen; and

R^8 is hydrogen.

4. The compound of claim 1, wherein L is a bond.

5. The compound of claim 1, wherein L is $-CH_2-$.

6. The compound of any one of claims 1, 2, 4 and 5, wherein R^1 is selected from methyl and ethyl.

7. The compound of any one of claims 1 and 3 to 5, wherein R^1 is selected from methoxy and ethoxy.

~~8. The compound of claim 1, wherein R^6 is –COOH.~~

~~9. The compound of claim 1, wherein R^6 is $-CO(-OCH_3)$.~~

~~10~~8. The compound of any one of claims 1 to 7, wherein, the compound of Formula (1) is selected from:

3-amino-3-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]propanoic acid (1);

3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]butanoic acid (3);

(3S)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]butanoic acid (5);

(3R)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]butanoic acid (6);

(3S)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methoxy-phenyl]butanoic acid (7);

(3R)-3-amino-4-[5-(2-methylsulfonyloxyethyl(propyl)amino)-2-methyl-phenyl]butanoic acid (11);

(3R)-3-amino-4-[5-(bis(2-bromoethyl)amino)-2-methyl-phenyl]butanoic acid (12)

(3R)-3-amino-4-[5-(2-chloroethyl(2-methylsulfonyloxyethyl)amino)-2-methyl-phenyl]butanoic acid (13);

(3R)-3-amino-4-[5-(2-bromoethyl(2-chloroethyl)amino)-2-methyl-phenyl]butanoic acid (14); and

(3R)-3-amino-4-[5-(2-bromoethyl(2-methylsulfonyloxyethyl)amino)-2-methyl-phenyl]butanoic acid (15);

or a pharmaceutically acceptable salt of any of the foregoing.

~~11~~9. The compound of any one of claims 1 to 8, wherein the compound of Formula (1) exhibits:

a LAT1/4F2hc-dependent uptake of at least 10% that of gabapentin measured at an extracellular concentration of 1 mM (1 mmol/L); and

a system A-, system N-, a system ASC-, and a LAT2/4F2hc-dependent uptake of less than 50% that of L-leucine measured at an extracellular concentration of 1 mM (1 mmol/L).

~~12~~10. A pharmaceutical composition comprising the compound of any one of claims 1 to 9 and a pharmaceutically acceptable vehicle.

~~13~~11. A pharmaceutical composition comprising the compound of claim 8~~10~~ and a pharmaceutically acceptable vehicle.

~~14~~12. The use of the compound of any of claims 1-9~~11~~ in the manufacture of a medicament for the treatment of cancer in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of the compound of any of claims 1-9~~11~~.

15~~3~~. The use of the pharmaceutical composition of any of claims 10~~2~~-11~~3~~ in the manufacture of a medicament for the treatment of cancer in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of the composition of claim 10~~2~~ or claim 11~~3~~.

16~~4~~. A compound selected from the group consisting of:

3-amino-3-[4-[bis(2-chloroethyl)amino]-2-methyl-phenyl]propanoic acid (2);

3-amino-4-[4-[bis(2-chloroethyl)amino]-2-methyl-phenyl]butanoic acid (4);

(3S)-3-amino-4-[3-[bis(2-chloroethyl)amino]-2,6-dimethyl-phenyl]butanoic acid (8);

(3S)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]-3-methyl-butanoic acid (9);

[(2R)-2-amino-3-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]propyl]phosphinic acid (10);

(3S)-3-amino-4-[[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]amino]-4-oxo-butanoic acid (16);

(3R)-3-amino-5-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]pentanoic acid (18);

(3R)-3-amino-4-[5-(2-chloroethyl(chloromethyl)carbamoyl)oxy-2-methyl-phenyl]butanoic acid (19);

(3R)-3-amino-4-[5-[bis(2-chloroethyl)carbamoyloxymethyl]-2-nitro-phenyl]butanoic acid (20);

(3R)-3-amino-4-[5-(2-chloroethoxy(2-chloroethyl)amino)-2-methyl-phenyl]butanoic acid (21); and

3-[(2R)-2-amino-4-hydroxy-4-oxo-butyl]-*N,N*-bis(2-chloroethyl)-4-methyl-benzeneamine oxide (22);

or a pharmaceutically acceptable salt of any of the foregoing.

1~~7~~5. A pharmaceutical composition comprising the compound of claim 1~~4~~6 and a pharmaceutically acceptable vehicle.

16. The compound of claim 1, wherein the compound is (3S)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methyl-phenyl]butanoic acid (5) or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1, wherein the compound is (3S)-3-amino-4-[5-[bis(2-chloroethyl)amino]-2-methoxy-phenyl]butanoic acid (7) or a pharmaceutically acceptable salt thereof.