R^1 and R2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

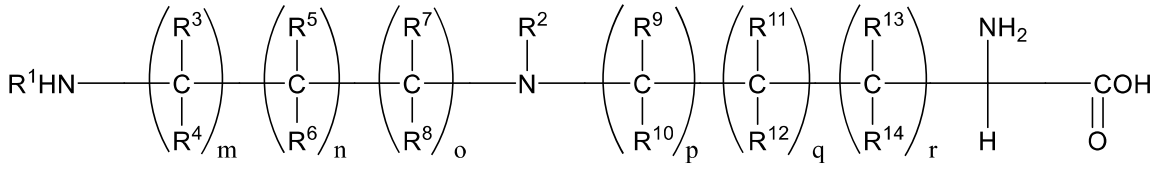
R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;
n is 0, 1, 2, 3 or 4;
o is 0, 1, 2, 3 or 4;
p is 1, 2, 3 or 4;
q is 0, 1, 2, 3 or 4; and
r is 0, 1, 2, 3 or 4;

wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

[0003b] In another aspect, the present disclosure refers to the use of a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



Formula I

in the manufacture of a medicament for preventing or treating pre-diabetes in a subject in need thereof,

wherein:

R^1 and R2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

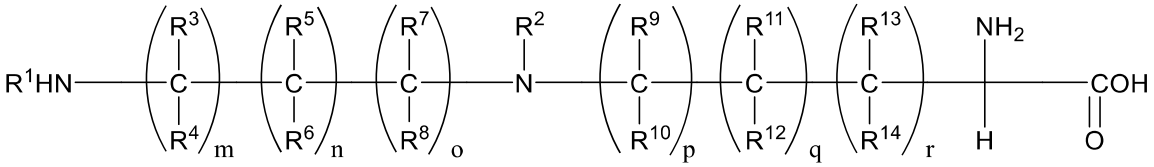
R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;
o is 0, 1, 2, 3 or 4;
p is 1, 2, 3 or 4;
q is 0, 1, 2, 3 or 4; and
r is 0, 1, 2, 3 or 4;

wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

[0003c] In yet another aspect, the present disclosure refers to the use of a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



Formula I

in the manufacture of a medicament for preventing or treating a condition in a subject in need thereof,

wherein:

R^1 and R2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;
n is 0, 1, 2, 3 or 4;
o is 0, 1, 2, 3 or 4;
p is 1, 2, 3 or 4;
q is 0, 1, 2, 3 or 4; and
r is 0, 1, 2, 3 or 4, and

wherein the condition is characterized by an increase in a measurement selected from the group consisting of A1C, glucose, insulin, homeostasis model of assessment of insulin resistance (HOMA-IR), oxidative stress in adipose tissue, and carbonylation of GLUT4;

wherein the condition is selected from obesity, metabolic syndrome, insulin resistance, insulin resistance syndromes, syndrome X, dyslipidernia, hyperlipidemia, atherosclerotic disease, hyperglycemia, hyperinsulinemia and/or hyperproinsulinemia, impaired glucose tolerance, and delayed insulin release; and
wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

DESCRIPTION OF THE DRAWINGS

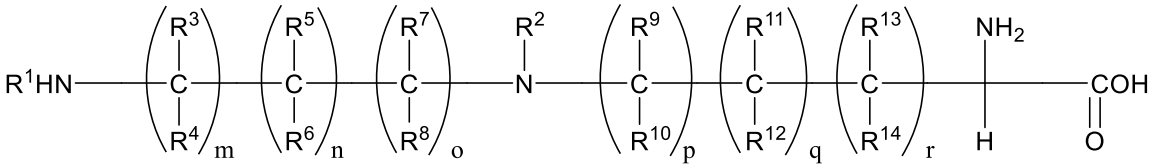
[0001] FIG. 1 demonstrated the stoichiometry of GLUT4 carbonylation in adipose tissue from obese non-diabetic (n=4), obese pre-diabetic (n=4), and obese diabetic (n=12) subjects (* $p< 0.005$).

[0002] FIG. 2 provides a graphical depiction of the correlation between adipose tissue GLUT4 carbonylation and HbA1C.

[0003] FIG. 3 provides typical MRM data showing an increase in the transitions of HNE-induced K264-HNE adduct (left panel) which were used to calculate the amounts of carbonylated GLUT4 (right panel). Four transitions of the GLUT4 peptide found in humans are shown. The sequence of the carbonylated GLUT4 peptide LTGWADVSGVLAELKDEK-4HNE (SEQ ID NO:1) is depicted.

CLAIMS

1. Use of a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



Formula I

in the manufacture of a medicament for preventing or treating type 2 diabetes in a subject in need thereof,

wherein:

R^1 and R^2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

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

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

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

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

wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

2. The use of claim 1, wherein a symptom of type 2 diabetes is treated.

3. The use of claim 2, wherein the symptom is selected from the group consisting of increased A1C level, increased fasting blood glucose, impaired glucose tolerance increased blood pressure, and increased blood glucose level.

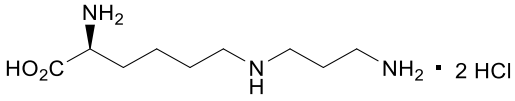
4. The use of claim 1, wherein the therapeutically effective amount of a compound of Formula I is 300 mg/day to 500 mg/day.

5. The use of claim 1, wherein the therapeutically effective amount of a compound of Formula I is 500 mg/day to 1000 mg/day.

6. The use of claim 1, wherein the compound of Formula I is to be administered with one or more additional therapeutic agent.

7. The use of claim 1, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

8. The use of claim 7, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid dihydrochloride,

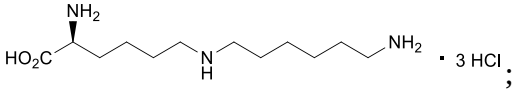


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9. The use of claim 1, wherein the compound of Formula I is selected from (S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid, (S)-2-amino-5-((6-aminopentyI)amino)pentanoic acid, and (S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

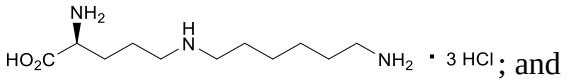
10. The use as claimed in claim 9, wherein the pharmaceutically active salt of the compound of Formula I is selected from the group consisting of:

(S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid trihydrochloride,



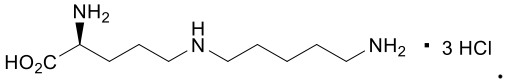
;

(S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid trihydrochloride



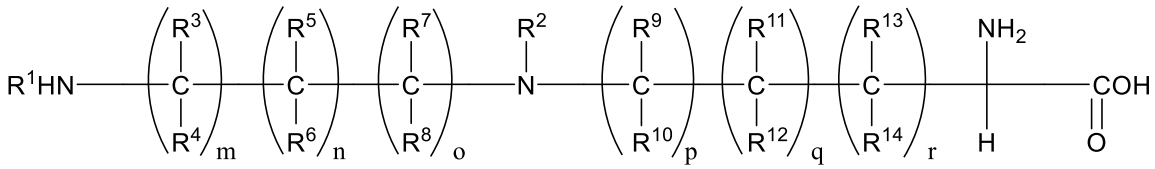
; and

(S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid trihydrochloride



.

11. Use of a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



Formula I

in the manufacture of a medicament for preventing or treating pre-diabetes in a subject in need thereof,

wherein:

R^1 and R^2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

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

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

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

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

wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

12. The use of claim 11, wherein the subject has been diagnosed with impaired glucose tolerance, impaired fasting glucose, or insulin resistance.

13. The use of claim 11, wherein a risk of developing diabetes is reduced.

14. The use of claim 11, wherein a risk of developing a disease selected from the group consisting of kidney disease, diabetic retinopathy, heart attack and stroke, is reduced.

15. The use of claim 11, wherein a symptom of pre-diabetes is treated.

16. The use of claim 11, wherein the symptom is selected from the group consisting of increased A1C level, increased fasting blood glucose, impaired glucose tolerance, increased blood pressure, and increased blood glucose level.

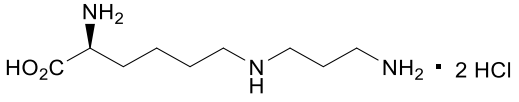
17. The use of claim 11, wherein the therapeutically effective amount of a compound of Formula I is 300 mg/day to 500 mg/day.

18. The use of claim 11, wherein the therapeutically effective amount of a compound of Formula I is 500 mg/day to 1000 mg/day.

19. The use of claim 11, wherein the compound of Formula I is to be administered with one or more additional therapeutic agent.

20. The use of claim 11, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

21. The use of claim 20, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid dihydrochloride,

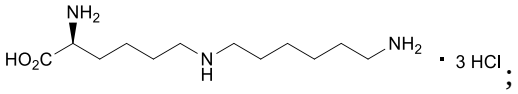


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22. The use of claim 11, wherein the compound of Formula I is selected from (S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid, (S)-2-amino-5-((6-aminopentyI)amino)pentanoic acid, and (S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

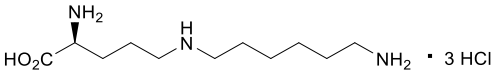
23. The use as claimed in claim 22, wherein the pharmaceutically active salt of the compound of Formula I is selected from the group consisting of:

(S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid trihydrochloride,



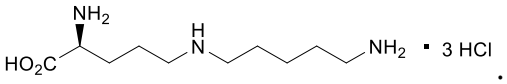
;

(S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid trihydrochloride



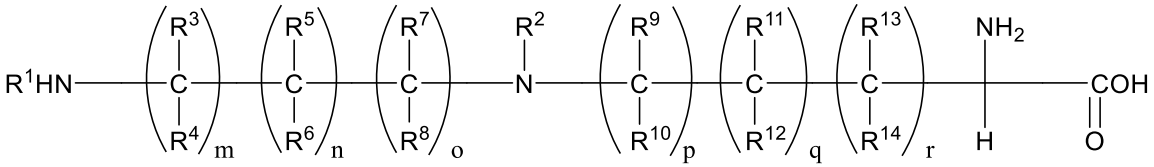
; and

(S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid trihydrochloride



.

24. Use of a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



Formula I

in the manufacture of a medicament for preventing or treating a condition in a subject in need thereof,

wherein:

R^1 and R^2 are hydrogen;

R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13}, and R^{14} are independently selected from the group consisting of hydrogen and -(C_1-C_6)alkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, -(C_1-C_6)alkyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;
n is 0, 1, 2, 3 or 4;
o is 0, 1, 2, 3 or 4;
p is 1, 2, 3 or 4;
q is 0, 1, 2, 3 or 4; and
r is 0, 1, 2, 3 or 4, and

wherein the condition is characterized by an increase in a measurement selected from the group consisting of A1C, glucose, insulin, homeostasis model of assessment of insulin resistance (HOMA-IR), oxidative stress in adipose tissue, and carbonylation of GLUT4;
wherein the condition is selected from obesity, metabolic syndrome, insulin resistance, insulin resistance syndromes, syndrome X, dyslipidernia, hyperlipidemia, atherosclerotic disease, hyperglycemia, hyperinsulinemia and/or hyperproinsulinemia, impaired glucose tolerance, and delayed insulin release; and
wherein the therapeutically effective amount of the compound of Formula I is 1 mg/day to 1,000 mg/day.

25. The use of claim 24, wherein the subject has been diagnosed with impaired glucose tolerance, impaired fasting glucose, insulin resistance, pre-diabetes, or type 2 diabetes.

26. The use of claim 24, wherein a risk of developing pre-diabetes or type 2 diabetes is reduced.

27. The use of claim 24, wherein a risk of developing a disease selected from the group consisting of kidney disease, diabetic retinopathy, heart attack and stroke, is reduced.

28. The use of claim 24, wherein a symptom of the condition is treated.

29. The use of claim 28, wherein the symptom is selected from the group consisting of increased A1C level, increased fasting blood glucose, impaired glucose tolerance, increased blood pressure, and increased blood glucose level.

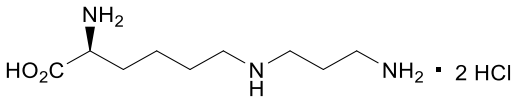
30. The use of claim 24, wherein the therapeutically effective amount of a compound of Formula I is 300 mg/day to 500 mg/day.

31. The use of claim 24, wherein the therapeutically effective amount of a compound of Formula I is 500 mg/day to 1,000 mg/day.

32. The use of claim 24, wherein the compound of Formula I is to be administered with one or more additional therapeutic agent.

33. The use of claim 24, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

34. The use of claim 33, wherein the compound of Formula I is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid dihydrochloride,

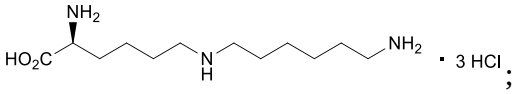


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35. The use of claim 24, wherein the compound of Formula I is selected from (S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid, (S)-2-amino-5-((6-aminopentyI)amino)pentanoic acid, and (S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid, or a pharmaceutically acceptable salt thereof.

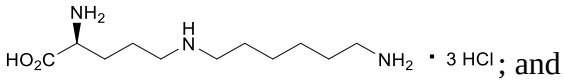
36. The use as claimed in claim 35, wherein the pharmaceutically active salt of the compound of Formula I is selected from the group consisting of:

(S)-2-amino-6-((6-aminohexyl)amino)hexanoic acid trihydrochloride,



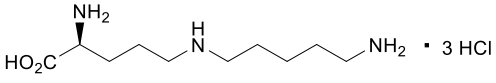
;

(S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid trihydrochloride



; and

(S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid trihydrochloride



.

37. The use of claim 7, wherein the pharmaceutically acceptable salt is an acid addition salt of hydrochloric acid.

38. The use of claim 20, wherein the pharmaceutically acceptable salt is an acid addition salt of hydrochloric acid.

39. The use of claim 33, wherein the pharmaceutically acceptable salt is an acid addition salt of hydrochloric acid.