SUMMARY OF THE INVENTION

[0005] The subject application provides compositions, methods, and kits for treating hyperlipidemia in a subject. The compositions, methods, and kits can include leucine and/or leucine metabolites in combination with nicotinic acid. The present invention addresses the negative side effects of treating subjects with high doses of nicotinic acid.

[0006] The subject compositions can be administered orally or through other routes such as intravenous administration. Compositions for oral administration can include pills, tablets, capsules, and the like.

[0007] In one aspect, the current invention provides compositions comprising at least about 250 mg of leucine and/or about 25 mg of one or more leucine metabolites; and at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites.

[0007a] In another aspect, there is provided a composition comprising:

a. at least about 250 mg of leucine and/or at least about 25 mg of one or more leucine metabolites; and

b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the composition is free of isoleucine and valine.

[0007b] In another aspct, there is provided a kit comprising a multi-day supply of unit dosages of the composition as described herein, and instructions directing the administration of said multi-day supply over a period of multiple days.

[0007c] In another aspect, there is provided a composition comprising:

a. leucine and/or one or more leucine metabolites; and

b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the molar ratio of component (a) to (b) in said composition is greater than about 5, and

wherein the composition is free of isoleucine and valine.

[0007d] In another aspect, there is provided a use of the composition as described herein, in the manufacture of a medicament for lowering total cholesterol level in a subject in need thereof.

[0007e] In another aspect, there is provided a use of the composition as described herein, in the manufacture of a medicament for lowering total cholesterol level or total lipid content in a subject in need thereof

[0008] In another aspect of the invention, compositions are provided that comprise at least about 250 mg of leucine and/or about 25 mg of one or more leucine metabolites; and an amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites, wherein the composition is substantially free of each of alanine, glycine, glutamic acid, and proline.

[0009] In yet another aspect, the current invention also provides compositions comprising at least about 250 mg of leucine and/or about 25 mg of one or more leucine metabolites; and an amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites, wherein the amount of nicotinic acid and/or nicotinic acid metabolites is insufficient to reduce lipid content in the absence of component (a).

[0010] In still yet another aspect of the invention, compositions are provided that comprise an amount of leucine and/or one or more leucine metabolites; and an amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites, wherein the composition is administered to a subject in need thereof, further wherein the composition causes a reduced degree of cutaneous vasodilation in the subject administered as compared to a dose of nicotinic acid alone that has the same effectiveness as the composition in lowering lipid content in the subject.

[0011] In another aspect, current invention further provides compositions comprising leucine and/or one or more leucine metabolites; and at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites, wherein the molar ratio of component (a) to (b) in said composition is greater than about 20.

CLAIMS

What is claimed is:

1. A composition comprising:

a. at least about 250 mg of leucine and/or at least about 25 mg of one or more leucine metabolites; and

b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites.

2. The composition of claim 1, wherein the composition is substantially free of nicotinamide.

3. The composition of claim 1 wherein the composition is substantially free of nicotinic acid metabolites.

4. The composition of claim 1, wherein the composition is substantially free of each of nicotinyl CoA, nicotinuric acid, nicotinate mononucleotide, nicotinate adenine dinucleotide, and nicotinamide adenine dinucleotide

5. The composition of claim 1, wherein the component (b) in the composition is nicotinic acid.

6. The composition of claim 1, wherein the component (a) in the composition is leucine.

7. The composition of claim 1, wherein the amount of leucine and/or one or more leucine metabolites is less than about 1 g.

8. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 1g.

9. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 250 mg.

10. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is between about 1-100 mg.

11. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is less than about 100 nM.

12. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is about 10 nM.

13. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is between about 1-100 nM.

14. The composition of claim 1, wherein the composition is effective in lowering triglyceride level, total cholesterol or LDL level in the subject by at least about 5%.

15. The composition of claim 1, wherein the amount of component (a) and (b) synergistically reduces lipid content in said subject when administered to the subject.

16. The composition of claim 1, wherein component (a) and component (b) synergistically enhances a decrease in weight gain of the subject, an increase in fat oxidation of the subject, or an increase in activation of Sirt1 in the subject.

17. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is insufficient to reduce lipid content in the absence of the leucine and/or one or more leucine metabolites.

18. The composition of claim 1, wherein the composition is contained in a foodstuff.

19. The composition of claim 1, wherein a portion of the leucine and/or one or more leucine metabolites is in a free form.

20. The composition of claim 1, wherein a portion of the leucine and/or one or more leucine metabolites is in a salt form.

21. The composition of claim 1, wherein the composition further comprises resveratrol.

22. The composition of claim 1, wherein the composition is formulated for oral administration.

23. The composition of claim 1, wherein the composition is a tablet, a capsule, a pill, a granule, an emulsion, a gel, a plurality of beads encapsulated in a capsule, a powder, a suspension, a liquid, a semi-liquid, a semi-solid, a syrup, a slurry or a chewable form.

24. The composition of claim 1, wherein component (a) and component (b) are separately packaged.

25. The composition of claim 1, wherein component (a) and component (b) are mixed.

26. The composition of claim 1, wherein the composition is substantially free of each amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

27. The composition of claim 1, wherein the composition is substantially free of each free amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

28. The composition of claim 1, wherein the composition contains less than about 0.1% of each free amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

29. The composition of claim 1, wherein the composition contains less than about 10% of non-leucine amino acids.

30. The composition of claim 1, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and HMB.

31. The composition of claim 1, wherein the composition does not contain nicotinamide.

32. The composition of claim 1, further comprising one or more therapeutic agents that is capable of lowering lipid accumulation.

33. The composition of claim 32, wherein the one or more therapeutic agents is selected from the group consisting of HMG-CoA inhibitor, fibrate, bile acid sequestrant, ezetimibe, lomitapide, phytosterols, CETP antagonist, orlistat, and any combination thereof.

34. The composition of claim 1, wherein the molar ratio of component (a) to (b) in said composition is greater than about 20.

35. The composition of claim 1 wherein the composition is formulated in a unit dosage form.

36. A kit comprising a multi-day supply of unit dosages of the composition any of claims 1-35 and instructions directing the administration of said multi-day supply over a period of multiple days.

37. A method of lowering total cholesterol level in a subject in need thereof, comprising administering to said subject the composition of claim 1 to effect the total cholesterol level in the subject.

38. A method of lowering total lipid content in a subject in need thereof, comprising administering to said subject the composition of claim 1 to effect the total lipid content in the subject.

39. A composition comprising:

a. at least about 250 mg of leucine and/or at least about 25 mg of one or more leucine metabolites; and

b. an amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the composition is substantially free of each of alanine, glycine, glutamic acid, and proline.

40. A composition comprising:

a. at least about 250 mg of leucine and/or about at least 25 mg of one or more leucine metabolites; and

b. an amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites,

wherein the amount of nicotinic acid and/or nicotinic acid metabolites is insufficient to reduce lipid content in the absence of component (a).

41. A composition comprising:

a. an amount of leucine and/or one or more leucine metabolites; and

b. an amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the composition is administered to a subject in need thereof, further wherein the composition causes a reduced degree of cutaneous vasodilation in the subject administered as compared to a dose of nicotinic acid alone that has the same effectiveness as the composition in lowering lipid content in the subject.

42. A composition comprising:

a. leucine and/or one or more leucine metabolites; and

b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the molar ratio of component (a) to (b) in said composition is greater than about 20.

43. The composition of claims 41-42, wherein the composition comprises at least about 500 mg of leucine and/or at least about 200 mg of the one or more leucine metabolites.

44. The composition of claims 41-42, wherein the composition comprises at least about 250 mg of leucine and/or about 25 mg of one or more leucine metabolites.

45. The composition of claims 39-42, wherein the composition is substantially free of nicotinamide.

46. The composition of claims 39-42 wherein the composition is substantially free of nicotinic acid metabolites.

47. The composition of claims 39-42, wherein the composition is substantially free of each of nicotinyl CoA, nicotinuric acid, nicotinate mononucleotide, nicotinate adenine dinucleotide, and nicotinamide adenine dinucleotide.

48. The composition of claims 39-42, wherein the component (b) in the composition is nicotinic acid.

49. The composition of claims 39-42, wherein the component (a) in the composition is leucine.

50. The composition of claims 39-42, wherein the amount of leucine and/or one or more leucine metabolites is less than about 1 g.

51. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 1g.

52. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 250 mg.

53. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is between about 1-100 mg.

54. The composition of claims 39-41, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is at least about 1 mg. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is less than about 100 nM.

55. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is about 10 nM.

56. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of the nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is between about 1-100 nM.

57. The composition of claims 39-42, wherein the composition is effective in lowering triglyceride level, total cholesterol or LDL level in the subject by at least about 5%.

58. The composition of claims 39-42, wherein the amount of component (a) and (b) synergistically reduces lipid content in said subject when administered to the subject.

59. The composition of claims 39-42, wherein component (a) and component (b) synergistically enhances a decrease in weight gain of the subject, an increase in fat oxidation of the subject, or an increase in activation of Sirt1 in the subject.

60. The composition of claims 39-42, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is insufficient to reduce lipid content in the absence of the leucine and/or one or more leucine metabolites.

61. The composition of claims 39-42, wherein the composition is contained in a foodstuff.

62. The composition of claims 39-42, wherein a portion of the leucine and/or one or more leucine metabolites is in a free form.

63. The composition of claims 39-42, wherein a portion of the leucine and/or one or more leucine metabolites is in a salt form.

64. The composition of claims 39-42, wherein the composition further comprises resveratrol.

65. The composition of claims 39-42, wherein the composition is formulated for oral administration.

66. The composition of claims 39-42, wherein the composition is a tablet, a capsule, a pill, a granule, an emulsion, a gel, a plurality of beads encapsulated in a capsule, a powder, a suspension, a liquid, a semi-liquid, a semi-solid, a syrup, a slurry or a chewable form.

67. The composition of claims 39-42, wherein component (a) and component (b) are separately packaged.

68. The composition of claims 39-42, wherein component (a) and component (b) are mixed.

69. The composition of claims 39-42, wherein the composition is substantially free of each amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

70. The composition of claims 39-42, wherein the composition is substantially free of each free amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

71. The composition of claims 39-42, wherein the composition contains less than about 0.1% of each free amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.

72. The composition of claim 39-42, wherein the composition contains less than about 10% of non-leucine amino acids.

73. The composition of claims 39-42, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and HMB.

74. The composition of claims 39-42, wherein the composition does not contain nicotinamide.

75. The composition of claims 39-42, further comprising one or more therapeutic agents that is capable of lowering lipid accumulation.

76. The composition of claim 75, wherein the one or more therapeutic agents is selected from the group consisting of HMG-CoA inhibitor, fibrate, bile acid sequestrant, ezetimibe, lomitapide, phytosterols, CETP antagonist, orlistat, and any combination thereof.

77. The composition of claims 39-42, wherein the molar ratio of component (a) to (b) in said composition is greater than about 20.

78. The composition of claims 39-42 wherein the composition is formulated in a unit dosage form.

79. A kit comprising a multi-day supply of unit dosages of the composition any of claims 39-78 and instructions directing the administration of said multi-day supply over a period of multiple days.

80. A method of lowering total cholesterol level in a subject in need thereof, comprising administering to said subject the composition of claims 39-42 to effect the total cholesterol level in the subject.

81. A method of lowering total lipid content in a subject in need thereof, comprising administering to said subject the composition of claims 39-42 to effect the total lipid content in the subject.

82. A method of lowering total cholesterol level in a subject in need thereof, comprising administering to said subject a dose of a composition comprising leucine and/or one or more leucine metabolites and an amount of nicotinic acid and/or nicotinic acid metabolites to effect the total cholesterol level in the subject.

83. The method of claim 82, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 250 mg.

84. The method of claim 82, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 100 mg.

85. The method of claim 82, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 25 mg.

86. The method of claim 82, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 10 mg

87. The method of claim 82, wherein the dose is a unit dose.

88. A method of reducing a side effect of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites wherein the side effect is characterized by an increase in cutaneous vasodilation in a subject administered with nicotinic acid and/or nicotinamide riboside and/or the one or more nicotinic acid metabolites, comprising administering a composition comprising an effective amount of leucine and/or one or more leucine metabolites to said subject that is administered with nicotinic acid and/or the one or more nicotinic acid metabolites.

89. The method of claim 88, wherein the composition is administered orally.

90. The method of claim 88, wherein the effective amount comprises at least about 500 mg of leucine and/or at least about 200 mg of the one or more leucine metabolites.

91. The method of claim 88, wherein the effective amount comprises at least about 250 mg of leucine and/or at least about 25 mg of the one or more leucine metabolites.

92. The method of claim 88, wherein nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is in a sub-therapeutic amount if administered alone.

93. The method of claim 88, wherein nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is in an amount that is less than about 1 g.

94. The method of claim 88, wherein nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is in an amount that is less than about 250 mg.

95. The method of claim 88, wherein the amount of nicotinic acid and or nicotinamide riboside and/or one or more nicotinic acid metabolites is between about 1-100 mg.

96. The method of claim 88, wherein the amount of nicotinic acid and or nicotinamide riboside and/or one or more nicotinic acid metabolites is capable of achieving a serum level of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites that is between about 1-100 nM.

97. A method of reducing atherosclerotic plaque size in a subject in need thereof, comprising administering to said subject a dose of a composition comprising leucine and/or one or more leucine metabolites and an amount of nicotinic acid and/or nicotinic acid metabolites to effect the total atherosclerotic plaque size in the subject.

98. The method of claim 97, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 250 mg.

99. The method of claim 97, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is between about 1-100 mg.

100. The method of claim 97, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is less than about 25 mg.

101. The method of claim 97, wherein the composition is administered to the subject for at least about 1 year.

102. The method of claim 97, wherein the dose is a unit dose.

What is claimed is:

1. A composition comprising:
   a. at least about 250 mg of leucine and/or at least about 25 mg of one or more leucine metabolites; and
   b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

   wherein the composition is free of isoleucine and valine.
2. The composition of claim 1, wherein the composition is substantially free of nicotinamide.
3. The composition of claim 1 wherein the composition is substantially free of nicotinic acid metabolites.
4. The composition of claim 1, wherein the component (a) in the composition is leucine and the component (b) in the composition is nicotinic acid.
5. The composition of claim 1, wherein the component (a) in the composition is leucine.
6. The composition of claim 1, wherein the amount of leucine and/or one or more leucine metabolites is less than about 1300 mg.
7. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 1g.
8. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is less than about 250 mg.
9. The composition of claim 1, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is between about 1-100 mg.
10. The composition of claim 1, wherein the composition is effective in reducing triglyceride level, total cholesterol or LDL level in a subject by at least about 5% and the amount of nicotinic acid and/or nicotinamide riboside and/or nicotinic acid metabolites is insufficient to effectuate such reduction in the absence of the leucine and/or one or more leucine metabolites.
11. The composition of claim 1, wherein a portion of the leucine and/or one or more leucine metabolites is in a free form or in a salt form.
12. The composition of claim 1, wherein the composition further comprises resveratrol.
13. The composition of claim 1, wherein the composition is formulated for oral administration.
14. The composition of claim 1, wherein the composition is a tablet, a capsule, or a pill.

15. The composition of claim 1, wherein component (a) and component (b) are separately packaged.
16. The composition of claim 1, wherein component (a) and component (b) are mixed.
17. The composition of claim 1, wherein the composition is substantially free of each amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.
18. The composition of claim 1, wherein the composition contains less than about 0.1% of each free amino acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, valine, isoleucine and tyrosine.
19. The composition of claim 1, wherein the composition contains less than about 10% of non-leucine amino acids.
20. The composition of claim 1, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and HMB.
21. The composition of claim 1, further comprising one or more therapeutic agents that is capable of lowering lipid accumulation.
22. The composition of claim 1, further comprising one or more therapeutic agents selected from the group consisting of HMG-CoA inhibitor, fibrate, bile acid sequestrant, ezetimibe, lomitapide, phytosterols, CETP antagonist, orlistat, and any combination thereof.
23. The composition of claim 1, wherein the molar ratio of component (a) to (b) in said composition is greater than about 20.
24. The composition of claim 1, wherein the composition is formulated in a unit dosage form.
25. A kit comprising a multi-day supply of unit dosages of the composition of claim 24, and instructions directing the administration of said multi-day supply over a period of multiple days.
26. A composition comprising:
    a. leucine and/or one or more leucine metabolites; and
    b. at least about 1 mg of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites,

wherein the molar ratio of component (a) to (b) in said composition is greater than about 5, and wherein the composition is free of isoleucine and valine.

27. The composition of claim 26, where the molar ratio of component (a) to (b) is less than about 100.
28. The composition of claim 26, wherein the composition comprises at least about 250 mg of leucine and/or about 25 mg of one or more leucine metabolites.
29. The composition of claim 26, wherein the composition is substantially free of nicotinamide.
30. The composition of claim 26, wherein the component (a) in the composition is leucine and the component (b) in the composition is nicotinic acid.
31. The composition of claim 26, wherein the amount of leucine and/or one or more leucine metabolites is less than about 1300 mg.
32. The composition of claim 26, wherein the amount of nicotinic acid and/or nicotinamide riboside and/or one or more nicotinic acid metabolites is between about 1-100 mg.
33. The composition of claim 26, wherein a portion of the leucine and/or one or more leucine metabolites is in a free form.
34. The composition of claim 26, wherein the composition is a tablet, a capsule, or a pill
35. The composition of claim 26, wherein the composition is formulated in a unit dosage form.
36. Use of the composition of claim 1, in the manufacture of a medicament for lowering total cholesterol level in a subject in need thereof.
37. Use of the composition of claim 26, in the manufacture of a medicament for lowering total cholesterol level or total lipid content in a subject in need thereof.