WHAT IS CLAIMED IS:

1. A composition formulated for oral consumption, comprising:

(a) at least about 500 mg of leucine and/or at least about 200 mg of one or more leucine metabolites, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymethylbutyrate (HMB); and

(b) at least about 10 mg of a sirtuin pathway activator;

wherein the composition is substantially free of the individual amino acids alanine, glutamic acid, glycine, and proline.

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

3. The composition of claim 1, wherein the sirtuin pathway activator is in an amount of at least 35 mg.

4. The composition of claims 1, wherein the sirtuin pathway activator activates one or more of SIRT1, SIRT3, AMPK, and PGC1α.

5. The composition of claim 1, wherein the composition comprises less than about 1% of the individual amino acids alanine, glutamic acid, glycine, and proline.

6. The composition of claim 1, wherein the sirtuin pathway activator is a phosphodiesterase inhibitor.

7. The composition of claim 1, wherein the sirtuin pathway activator is a polyphenol or polyphenol precursor.

8. The composition of claim 7, wherein the polyphenol or polyphenol precursor is selected from the group consisting of chlorogenic acid, resveratrol, caffeic acid, cinnamic acid, ferulic acid, piceatannol, ellagic acid, epigallocatechin gallate, grape seed extract, and any analog thereof.

9. The composition of claim 7, wherein the polyphenol is a hydroxycinnamic acid or a stilbene.

10. The composition of claim 1, wherein the composition further comprises an anti-diabetic agent.

11. The composition of claim 1, wherein the composition is formulated as a food composition, tablet, capsule, gel capsule, beverage, or snack bar.

12. Use of a composition of claims 1-11 to effect an increase in fat oxidation in a subject, in the manufacture of a medicament for enhancing fat oxidation in a subject in need thereof.

13. Use of a composition of claims 1-11, 15 and 19 to effect an increase in insulin sensitivity in a subject, in the manufacture of a medicament for treating diabetes.

14. Use of a composition of claims 1-11, 15 and 19 to effect an increase in irisin production, in the manufacture of a medicament for increasing production of irisin in a cell.

15. The composition of claim 1,

wherein the components of (a) and (b) are present in an amount that is effective in increasing sirtuin pathway output by at least about 1 fold as compared to that of component (a) or (b) when being used alone, wherein the increased sirtuin-pathway output is evidenced by an increase in a physiological effect selected from the group consisting of fatty acid oxidation, mitochondrial biogenesis, glucose uptake, palmitate uptake, oxygen consumption, weight loss, visceral adipose tissue loss, insulin sensitivity, an inflammation marker level, vasodilatation, and body temperature, when (i) media from myotubes or adipocytes treated with the composition is administered to the other of the myotubes or adipocytes, (ii) the composition is administered to myotubes or adipocytes, or (iii) the composition is administered to a subject, and

wherein the sirtuin pathway output is about 20% greater than the additive effect of component (a) and component (b) as if each of component (a) and component (b) exerted its effect independently.

16. The composition of claim 1, wherein the composition comprises less than about 1% of the individual amino acids alanine, glutamic acid, glycine, and proline, and wherein the composition is additionally substantially free of an individual non-branched amino acid selected from the group consisting of arginine, asparagine, aspartic acid, cysteine, glutamine, histidine, lysine, methionine, phenylalanine, serine, threonine, tryptophan, and tyrosine.

17. A composition comprising:

(a) leucine and/or one or more leucine metabolites, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymethylbutyrate (HMB); and

(b) a sub-therapeutic amount of an anti-diabetic agent selected from the group consisting of biguanide and thiazolidinedione.

18. The composition of claim 17, wherein the anti-diabetic agent is metformin, rosiglitazone or any analog thereof.

19. The composition of claim 17, wherein the composition comprises at least about 500 mg of leucine and/or at least about 200 mg of one or more leucine metabolites.

20. The composition of claim 17, wherein the composition comprises at least about 25 mg of the anti-diabetic agent.

21. The composition of claim 17, wherein the composition comprises at least about 250 mg of the anti-diabetic agent.

22. The composition of claim 17, wherein the composition is formulated as a unit dose comprising one or more tablets or capsules, each unit dose comprising at least 500 mg of leucine and at least 50 mg of metformin.

23. The composition of claim 17, wherein each unit dose comprises at least about 1000 mg of leucine and at least about 100 mg of metformin.

24. The composition of claim 17, wherein the molar ratio of component (a) to (b) in said composition is greater than about 2 or optionally greater than about 5.

25. The composition of claim 17, further comprising resveratrol.

26. The composition of claim 17, wherein the anti-diabetic agent is a sirtuin pathway activator.

27. The composition of claim 17, wherein the component of (a) and (b) are present in an amount that, when administered to a subject synergistically increases insulin sensitivity in said subject as compared to administering to a subject component (a) or component (b) alone.

28. The composition of claim 27, wherein said increase in insulin sensitivity is at least about a 1-fold increase.

29. The composition of claim 17, wherein the composition comprises less than about 1% of the individual amino acids alanine, glutamic acid, glycine, and proline, and wherein the composition is additionally substantially free of an individual non-branched amino acid selected from the group consisting of arginine, asparagine, aspartic acid, cysteine, glutamine, histidine, lysine, methionine, phenylalanine, serine, threonine, tryptophan, and tyrosine.

30. The composition of claim 17, wherein the composition is formulated as a food composition, tablet, capsule, gel capsule, beverage, or snack bar.

31. The composition of claims 17-30, wherein the composition is substantially free of the individual amino acids alanine, glutamic acid, glycine, and proline.

32. The composition of claims 17-31, wherein the composition is formulated as a unit dose that is administered 1, 2 or 3 times daily.

33. Use of a composition of claims 17-32 to effect an increase in insulin sensitivity in a subject, in the manufacture of a medicament for enhancing insulin sensitivity in a subject in need thereof.

34. Use of the unit dose of claims 22-23 in the manufacture of a medicament for enhancing insulin sensitivity in a subject in need thereof, wherein the medicament is to be administered to the subject twice daily.

35. A composition comprising:

(a) leucine and/or one or more leucine metabolites selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymethylbutyrate (HMB); and

(b) a sirtuin-pathway activator;

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

wherein the composition is substantially free of non-branched amino acids; and

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.

36. The composition of claim 35, wherein the sirtuin pathway activator activates one or more of SIRT1, SIRT3, AMPK, and PGC1 α.

37. The composition of claim 35, wherein the sirtuin pathway activator is a polyphenol or polyphenol precursor is selected from the group consisting of chlorogenic acid, resveratrol, caffeic acid, cinnamic

acid, ferulic acid, piceatannol, ellagic acid, epigallocatechin gallate, grape seed extract, and any analog thereof.

38. The composition of claim 35, wherein the sirtuin pathway activator is a hydroxycinnamic acid or a stilbene.

39. The composition of claim 35, wherein the composition further comprises an anti-diabetic agent.

40. The composition of claim 35, wherein the composition is formulated as a unit dosage in liquid or solid form for oral consumption.

41. The composition of claim 35, wherein the composition when administered to a subject in need thereof synergistically enhances mitochondrial biogenesis as measured by a decrease in weight gain of a subject, a decrease in visceral adipose volume of a subject, an increase in fat oxidation of a subject, an increase in irisin production of a subject, an increase in insulin sensitivity of a subject, an increase of glucose uptake in muscle of a subject, a decrease in inflammation markers, an increase in vasodilatation, and/or an increase in body temperature

wherein the mitochondrial biogenesis is about 20% greater than the additive effect of component (a) and component (b) as if each of component (a) and component (b) exerted its effect independently.

42. A food composition comprising:

(a) leucine and/or one or more leucine metabolites selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymethylbutyrate (HMB);

(b) a sirtuin pathway activator, wherein (a) and (b) are present in an amount that synergistically effect an increase in sirtuin pathway output as measured by a decrease in weight gain of a subject, a decrease in visceral adipose volume of a subject, an increase in fat oxidation of a subject, an increase in insulin sensitivity of a subject, an increase of glucose uptake in muscle of a subject, an increase in vasodilatation, and/or an increase in body temperature; and

(c) a food carrier;

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

wherein the composition is substantially free of non-branched amino acids; and

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.

43. The composition of claim 42, wherein the sirtuin pathway activator is a polyphenol or polyphenol precursor.

44. The composition of claim 42, wherein the sirtuin pathway activator is a phosphodiesterase inhibitor.

45. The composition of claim 42, wherein the increase in sirtuin pathway output is at least about 1fold.

46. The composition of claim 42, wherein the composition further comprises an anti-diabetic agent.

47. The composition of claim 42, wherein the sirtuin pathway output is about 20% greater than the additive effect of component (a) and component (b) as if each of component (a) and component (b) exerted its effect independently.

48. Use of a composition of claims 42-47 to effect an increase in fat oxidation in a subject, in the manufacture of a medicament for enhancing fat oxidation in a subject in need thereof.

49. A composition comprising a unit dosage suitable for oral ingestion, said unit dosage comprising:

(a) leucine and/or one or more leucine metabolites selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymetylbutyrate (HMB); and

(b) a substantially homogeneous population of polyphenol or polyphenol precursor molecules;

wherein the unit dosage is effective in inducing an increase in sirtuin pathway output as measured by a decrease in weight gain of a subject, a decrease in visceral adipose volume of a subject, an increase in fat oxidation of a subject, an increase in insulin sensitivity of a subject, an increase of glucose uptake in muscle of a subject, an increase in vasodilatation, and/or an increase in body temperature;

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

wherein the composition is substantially free of non-branched amino acids; and

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.

50. The composition of claim 49, wherein the polyphenol or polyphenol precursor molecules are selected from the group consisting of chlorogenic acid, resveratrol, caffeic acid, cinnamic acid, ferulic acid, piceatannol, ellagic acid, epigallocatechin gallate, grape seed extract, and any analog thereof.

51. The composition of claim 49, wherein the increase in sirtuin pathway output is at least about 1 fold.

52. The composition of claim 49, wherein the composition further comprises an anti-diabetic agent.

53. Use of a composition of claims 49-52 to effect an increase in fat oxidation in a subject, in the manufacture of a medicament for enhancing fat oxidation in a subject in need thereof.

54. Use of a composition of claim 49-52 to effect an increase in insulin sensitivity in a subject, in the manufacture of a medicament for treating diabetes.

WHAT IS CLAIMED IS:

1. A composition formulated for oral consumption, comprising:
   (a) at least 500 mg of leucine and/or at least 200 mg of one or more leucine metabolites, wherein the one or more leucine metabolites are selected from the group consisting of keto-isocaproic acid (KIC), alpha-hydroxy-isocaproic acid, and hydroxymethylbutyrate (HMB); and
   (b) at least 10 mg of a polyphenol; and
   (c) an anti-diabetic agent,
   wherein the composition is substantially free of the individual amino acids alanine, glutamic acid, glycine, and proline.
2. The composition of claim 1, wherein the molar ratio of component (a) to (b) in said composition is greater than 20.
3. The composition of claim 1, wherein the polyphenol is in an amount of at least 35 mg.
4. The composition of claim 1, wherein the anti-diabetic agent is metformin or rosiglitazone.
5. The composition of claim 1, wherein the composition comprises less than 1% of the individual amino acids alanine, glutamic acid, glycine, and proline.
6. The composition of claim 1, wherein the composition comprises at least 1000 mg of leucine and at least 100 mg of metformin.
7. The composition of claim 1, wherein the polyphenol is resveratrol.
8. The composition of claim 1, wherein the polyphenol is selected from the group consisting of chlorogenic acid, resveratrol, caffeic acid, cinnamic acid, hydroxycinnamic acid, ferulic acid, piceatannol, ellagic acid, and epigallocatechin gallate.
9. The composition of claim 1, wherein the polyphenol is a hydroxycinnamic acid or a stilbene.
10. The composition of claim 1, wherein the molar ratio of component (a) to (c) in said composition is greater than 2, wherein component (a) is leucine and component (c) is metformin.

11. The composition of claim 1, wherein the composition is formulated as a tablet, capsule, or gel capsule.
12. The composition of claim 1, wherein the composition comprises at least 250 mg of metformin.
13. The composition of claim 1, wherein the composition comprises less than 1% of the individual amino acids alanine, glutamic acid, glycine, and proline, and wherein the composition is additionally substantially free of an individual non-branched amino acid selected from the group consisting of arginine, asparagine, aspartic acid, cysteine, glutamine, histidine, lysine, methionine, phenylalanine, serine, threonine, tryptophan, and tyrosine.
14. Use of a composition of claims 1-13 in the manufacture of a medicament for reducing obesity in a subject.
15. Use of a composition of claims 1-13 in the manufacture of a medicament for treating diabetes in a subject.