

Claims

1. A method for treating, preventing or ameliorating at least one symptom of depression, anxiety or a depressive or anxiety-related disorder, comprising administering to a subject in need thereof an effective dose of orotic acid or a salt thereof.
2. A method according to claim 1, wherein the orotic acid salt comprises one or more of magnesium orotate, carnitine orotate, creatinine orotate, sodium orotate, calcium orotate, zinc orotate, chromium orotate, potassium orotate, copper orotate, iron orotate, manganese orotate, or choline orotate.
3. A method according to claim 1 or claim 2, wherein the orotic acid salt comprises magnesium orotate or creatinine orotate.
4. A method according to any one of claims 1 to 3, wherein the orotic acid salt is not lithium orotate.
5. A method according to any one of claims 1 to 3, wherein the orotic acid salt comprises magnesium orotate and the effective dose of magnesium orotate is about 800 mg per day or more.
6. A method according to any one of claims 1 to 3, wherein the orotic acid salt comprises magnesium orotate and the effective dose of magnesium orotate is about 1600 mg per day.
7. A method according to any one of claims 1 to 6, wherein the orotic acid or salt thereof is administered orally.
8. A method according to claim 7, wherein the orotic acid or salt thereof is in the form of a beverage, food, or beverage or food supplement.
9. A method according to claim 7, wherein the orotic acid or salt thereof is in unit dosage form.
10. A method according to claim 9, wherein the unit dosage form is a capsule.

11. A method according to any one of claims 1 to 10, wherein the orotic acid or salt thereof is administered in combination with at least one additional agent selected from:
- (i) one or more probiotic microorganisms;
 - (ii) coenzyme Q10 (optionally as a reduced or oxidized form); and/or
 - (iii) SAmE or a salt thereof.
12. A method according to claim 11, wherein the orotic acid or salt thereof and the at least one additional agent are administered as a single composition or formulation.
13. A method according to claim 11, wherein the one or more probiotic microorganisms comprises at least one *Lactobacillus* species, at least one *Lactococcus* species, at least one *Bifidobacterium* species, at least one *Streptococcus* species and/or at least one yeast.
14. A method according to claim 11, wherein the one or more probiotic microorganisms are selected from *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus bulgaricus*, *Lactobacillus gasseri*, *Lactobacillus reuteri*, *Lactobacillus paracasei*, *Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus fermentum*, *Lactobacillus salvarius*, *Lactococcus lactis*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *Bifidobacterium bifidum*, *Bifidobacterium animalis* subsp. *lactis*, *Bifidobacterium animalis* subsp. *animalis*, *Bifidobacterium infantis*, *Bifidobacterium longum*, *Bifidobacterium pseudocatenulatum*, *Saccharomyces boulardii* or *Saccharomyces cerevisiae*.
15. A method according to claim 13, wherein the *Lactobacillus* species is selected from *L. bulgaricus*, *L. paracasei*, *L. gasseri* and *L. rhamnosus*; the *Lactococcus* species is *L. lactis*; the *Bifidobacterium* species is selected from *B. animalis* subsp. *lactis*, *B. bifidum* and *B. infantis*; and the *Streptococcus* species is *S. thermophilus*.
16. A method according to any one of claims 11 to 15, comprising the administration of a multi-strain probiotic combination.
17. A method according to claim 16, wherein the multi-strain combination comprises *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium animalis* subsp. *lactis* and *Bifidobacterium bifidum*.

18. A method according to claim 16, wherein the multi-strain combination comprises *Lactobacillus bulgaricus*, *Lactobacillus paracasei*, *Lactobacillus gasseri*, *Lactobacillus rhamnosus*, *Lactococcus lactis*, *Bifidobacterium animalis* subsp. *lactis*, *Bifidobacterium infantis* and *Streptococcus thermophilus*.
19. A method according to any one of claims 11 to 18, wherein the SAME is present as a salt.
20. A method according to claim 19, wherein the SAME salt is selected from SAME tosylate, SAME disulfate tosylate, SAME disulfate monotosylate and SAME butane disulfonate.
21. A method according to any one of claims 1 to 20, further comprising the administration of one or more prebiotic components.
22. A method according to any one of claims 1 to 21, wherein the depressive disorder is major depressive disorder, dysthymic disorder, seasonal affective disorder, mood disorder, mixed anxiety-depressive disorder or bipolar disorder.
23. A method according to any one of claims 1 to 21, wherein the depression is mild depression, moderate depression, severe depression or postpartum depression.
24. A method according to any one of claims 1 to 21, wherein the anxiety-related disorder is generalised anxiety disorder, mixed anxiety-depressive disorder or post traumatic stress disorder.
25. A method according to any one of claims 1 to 24, wherein the method is employed as an adjunct to one or more other treatments or therapies for depression, anxiety or depressive or anxiety-related disorders.
26. A method according to any one of claims 1 to 25, wherein the subject suffers from treatment-resistant depression, anxiety or a depressive or anxiety-related disorder.

27. A method according to any one of claims 1 to 26, wherein the subject is a non-responder or suboptimal responder for SAME treatment of the depression, anxiety or a depressive or anxiety-related disorder, SSRI treatment of the depression, anxiety or a depressive or anxiety-related disorder, or SAME + SSRI treatment of the depression, anxiety or a depressive or anxiety-related disorder.

28. A method for treating or ameliorating at least one symptom of treatment-resistant depression, comprising administering to a subject in need thereof an effective dose of orotic acid or a salt thereof.

29. A method according to claim 28, wherein the treatment-resistant depression is depression that is resistant or non-responsive to one or more SSRIs and/or SAME.

30. A composition for the treatment, prevention or amelioration of at least one symptom of depression, anxiety or a depressive or anxiety-related disorder, wherein the composition comprises orotic acid or a salt thereof in combination with one or more of the following:

- (i) one or more probiotic microorganisms;
- (ii) coenzyme Q10 (optionally as a reduced or oxidized form); and/or
- (iii) SAME or a salt thereof.

31. A composition according to claim 30, wherein the composition is in a form suitable for oral delivery.

32. A composition according to claim 30 or 31, wherein the composition is in the form of a beverage, food, or beverage or food supplement.

33. A composition according to claim 30 or 31, wherein the composition is in unit dosage form.

34. A composition according to claim 33, wherein the unit dosage form is a capsule.

35. A composition for the treatment, prevention or amelioration of at least one symptom of treatment-resistant depression, wherein the composition comprises orotic acid or a salt thereof in combination with one or more of the following:

- (i) one or more probiotic microorganisms;
- (ii) coenzyme Q10 (optionally as a reduced or oxidized form); and/or
- (iii) SAME or a salt thereof.

36. A composition according to claim 35, wherein the treatment-resistant depression is depression that is resistant or non-responsive to one or more SSRIs and/or SAME.

37. Use of orotic acid or orotate as an active agent for the treatment, prevention or amelioration of at least one symptom of depression, anxiety or a depressive or anxiety-related disorder.

38. Use of orotic acid or a salt thereof in the manufacture of a medicament, food, beverage or supplement for the treatment, prevention or amelioration of at least one symptom of depression, anxiety or a depressive or anxiety-related disorder.

39. A method for treating, preventing or ameliorating at least one symptom of depression, anxiety or a depressive or anxiety-related disorder, comprising administering to a subject in need thereof an effective amount of one or more probiotic microorganisms selected from at least one *Lactobacillus* species, at least one *Lactococcus* species, at least one *Bifidobacterium* species, at least one *Streptococcus* species and/or at least one yeast.

40. A composition for the treatment, prevention or amelioration of at least one symptom of depression, anxiety or a depressive or anxiety-related disorder, wherein the composition comprises one or more probiotic microorganisms selected from at least one *Lactobacillus* species, at least one *Lactococcus* species, at least one *Bifidobacterium* species, at least one *Streptococcus* species and/or at least one yeast.

41. Use of one or more probiotic microorganisms selected from at least one *Lactobacillus* species, at least one *Lactococcus* species, at least one *Bifidobacterium* species, at least one *Streptococcus* species and/or at least one yeast in the manufacture of a medicament, food, beverage or supplement for the treatment, prevention or amelioration of at least one symptom of depression, anxiety or a depressive or anxiety-related disorder.