Claims

1. Use of orotic acid or a salt thereof in the manufacture of a composition for treating, preventing or ameliorating at least one symptom of depression, anxiety or a depressive or anxiety-related disorder.

2. Use 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. Use according to claim 1 or claim 2, wherein the orotic acid salt comprises magnesium orotate or creatinine orotate.

4. Use according to any one of claims 1 to 3, wherein the orotic acid salt is not lithium orotate.

5. Use 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. Use 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. Use according to any one of claims 1 to 6, wherein the composition is administered orally.

8. Use according to claim 7, wherein the composition in the form of a beverage, food, or beverage or food supplement.

9. Use according to claim 7, wherein the composition is in unit dosage form.

10. Use according to claim 9, wherein the unit dosage form is a capsule.

11. Use according to any one of claims 1 to 10, wherein the orotic acid or salt thereof is to be 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. Use according to claim 11, wherein the at least one additional agent is present in the same composition as the orotic acid or salt thereof.

13. Use according to claim 11, wherein the one or more probiotic microorganisms comprise 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. Use 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. Use 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. Use according to claim 15, wherein the one or more probiotic microorganisms comprise *Lactobacillus rhamnosus, Streptococcus thermophilus, Bifidobacterium animalis* subsp. *lactis* and *Bifidobacterium bifidum*.

17. Use according to claim 15, wherein the one or more probiotic microorganisms comprise *Lactobacillus bulgaricus, Lactobacillus paracasei, Lactobcillus gasseri, Lactobacillus*

rhamnosus, Lactococcus lactis, Bifidobacterium animalis subsp. *lactis, Bifidobacterium infantis* and *Streptococcus thermophilus.*

18. Use according to any one of claims 11 to 17, wherein the SAMe is present as a salt.

19. Use according to claim 18, wherein the SAMe salt is selected from SAMe tosylate, SAMe disulfate tosylate, SAMe disulfate monotosylate and SAMe butane disulfonate.

20. Use according to any one of claims 1 to 19, wherein the composition is to be administered with one or more prebiotic components.

21. Use according to any one of claims 1 to 20, wherein the depressive disorder is major depressive disorder, dysthymic disorder, seasonal affective disorder, mood disorder, mixed anxiety-depressive disorder or bipolar disorder.

22. Use according to any one of claims 1 to 20, wherein the depression is mild depression, moderate depression, severe depression or postpartum depression.

23. Use according to any one of claims 1 to 20, wherein the anxiety-related disorder is generalised anxiety disorder, mixed anxiety-depressive disorder or post traumatic stress disorder.

24. Use according to any one of claims 1 to 23, wherein the composition is employed as an adjunct to one or more other treatments or therapies for depression, anxiety or depressive or anxiety-related disorders.

25. Use according to any one of claims 1 to 24, wherein the subject suffers from treatment-resistant depression, anxiety or a depressive or anxiety-related disorder.

26. Use according to any one of claims 1 to 25, 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.

27. Use of orotic acid or a salt thereof in the manufacture of a medicament for treating or ameliorating at least one symptom of treatment-resistant depression.

28. Use according to claim 27, wherein the treatment-resistant depression is depression that is resistant or non-responsive to one or more SSRIs and/or SAMe.

29. 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.

30. A composition according to claim 29, wherein the composition is in a form suitable for oral delivery.

31. A composition according to claim 29 or 30, wherein the composition is in the form of a beverage, food, or beverage or food supplement.

32. A composition according to claim 29 or 30, wherein the composition is in unit dosage form.

33. A composition according to claim 32, wherein the unit dosage form is a capsule.

34. 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.

35. A composition according to claim 34, wherein the treatment-resistant depression is depression that is resistant or non-responsive to one or more SSRIs and/or SAMe.

36. 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.

37. 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.