[0037] The SAMe may be present as a salt. The SAMe salt may be selected from, for example, SAMe tosylate, SAMe disulfate tosylate, SAMe disulfate monotosylate and SAMe butane disulfonate.

[0038] The composition may further comprise one or more prebiotic components.

[0039] The composition may be administered as an adjunct to one or more other treatments or therapies for depression, anxiety or depressive or anxiety-related disorders.

[0040] In one embodiment the present disclosure provides 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 a reduced or oxidized form thereof); and/or
(iii) SAMe or a salt thereof.

[0041] By way of example only, the treatment-resistant depression may be depression that is resistant or non-responsive to one or more SSRIs and/or SAMe.

[0042] In one embodiment the present disclosure provides the 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.

[0043] In one embodiment the present disclosure provides the 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.

[0043a] Disclosed herein is the use of magnesium orotate in the manufacture of a medicament for treating, preventing or ameliorating at least one symptom of depression or a depressive disorder, wherein the depression or depressive disorder is resistant or non-responsive to S-adenosyl methionine (SAMe) treatment or to serotonin reuptake inhibitor (SSRI) and SAMe treatment, and wherein the effective dose of magnesium orotate is about 1600 mg or more per day.

[0044] In one embodiment the present disclosure provides 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*

Claims

1. Use of magnesium orotate in the manufacture of a medicament for treating, preventing or ameliorating at least one symptom of depression or a depressive disorder, wherein the depression or depressive disorder is resistant or non-responsive to S-adenosyl methionine (SAMe) treatment or to serotonin reuptake inhibitor (SSRI) and SAMe treatment, and wherein the effective dose of magnesium orotate is about 1600 mg or more per day.

2. Use according to claim 1, wherein the medicament is to be administered orally.

3. Use according to claim 2, wherein the medicament in the form of a beverage, food, or beverage or food supplement.

4. Use according to claim 2, wherein the medicament is in unit dosage form.

5. Use according to claim 4, wherein the unit dosage form is a capsule.

6. Use according to claim 1, wherein the medicament 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.

7. Use according to claim 1, wherein the medicament further comprises 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.

8. Use according to claim 6 or 7, 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.

9. Use according to claim 8, 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*.

10. Use according to claim 9, 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*.

11. Use according to claim 10, wherein the one or more probiotic microorganisms comprise *Lactobacillus rhamnosus*, *Streptococcus thermophilus, Bifidobacterium animalis* subsp. *lactis* and *Bifidobacterium bifidum*.

12. Use according to claim 10, 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*.

13. Use according to any one of claims 6 to 12, wherein the SAMe is present as a salt.

14. Use according to claim 13, wherein the SAMe salt is selected from SAMe tosylate, SAMe disulfate tosylate, SAMe disulfate monotosylate and SAMe butane disulfonate.

15. Use according to any one of claims 1 to 14, wherein the medicament is to be administered with one or more prebiotic components.

16. Use according to any one of claims 1 to 15, wherein the depressive disorder is major depressive disorder, dysthymic disorder, seasonal affective disorder, mood disorder, mixed anxiety-depressive disorder or bipolar disorder.

17. Use according to any one of claims 1 to 15, wherein the depression is mild depression, moderate depression, severe depression or postpartum depression.