in adults are indicative of vitamin B12 deficiency. Elevated methylmalonic acid levels in blood (values >0.4 micromole/L) may also indicate vitamin B12 deficiency.

Treatments to remedy or alleviate vitamin B12 deficiency-related conditions in a subject include intake of vitamin B12 supplements or vitamin B12 injection and/or changes in diet (i.e. introducing food rich in vitamin B12). One of the limitations of vitamin B12 supplementation is that the efficacy of such treatment may be limited or unsatisfactory in subjects with compromised ability to absorb vitamin B12 across the gastrointestinal tract, such as subject treated with metformin or other drugs causing malabsorption of vitamin B12 or low blood levels of vitamin B12.

Therefore, there is a need for compositions and methods for preventing, treating or alleviating and/or improving vitamin B12 deficiency in a subject.

Summary of the invention

In one aspect, the present invention refers to the use of a composition comprising *Eubacterium hallii* and/or *Intestinimonas butyriciproducens* and a physiologically acceptable carrier in the manufacture of a medicament for treating and/or preventing vitamin B12 deficiency in a subject.

In another aspect, the present invention refers to the use of a composition comprising *I. butyriciproducens* and/or *E. hallii* and a physiologically acceptable carrier for increasing the production of pseudovitamin B12 in the intestine of a subject.

In yet another aspect, the present invention refers to the use of a composition comprising *I. butyriciproducens* and/or *E. hallii* and a physiologically acceptable carrier for increasing the production of propionate in the intestine of a subject.

In yet another aspect, the present invention refers to the use *of I. butyriciproducens* and/or *E. hallii* in the manufacture of a medicament for treating and/or preventing vitamin B12 deficiency in a subject.

In a further aspect, the present invention refers to the use of *I. butyriciproducens* and/or *E. hallii* for increasing the production of pseudovitamin B12 in the intestine of a subject.

In yet another aspect, the present invention refers to the use of *I. butyriciproducens* and/or *E. hallii* for increasing the production of propionate in the intestine of a subject.

The present disclosure relates to a composition comprising *Eubacterium hallii* and/or *Intestinimonas butyriciproducens* and a physiologically acceptable carrier for use in treating and/or preventing vitamin B12 deficiency in a subject.

In an example, the vitamin B12 deficiency in said subject is derived from or caused by metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss (bariatric) surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

The composition for use taught herein may further comprise a propionate-producing bacterium, such as *Akkermansia muciniphila*.

It may be a pharmaceutical or supplement composition, e.g., in a form selected from the group of capsule, tablet, and powder.

aid *E. hallii* and/or *I. butyriciproducens* and, optionally, said propionate-producing bacterium, may be present in lyophilized or microencapsulated form.

Said *E. hallii* and/or *I. butyriciproducens* may be present in an amount ranging from about 10^4 to about 10^{15} cells. Additionally, said propionate-producing bacterium such as *A. muciniphila* may be present in an amount ranging from about 10^4 to about 10^{15} cells.

The composition taught herein may further comprise a mucosal binding agent.

The composition taught herein may further comprise cobalt ions, for example, in the form of a cobalt salt such as cobalt chloride, cobalt sulphate, cobalt acetate, or cobalt nitrate.

The disclosure also pertains to the use of a composition comprising *E. hallii* and/or *I. butyriciproducens* and a physiologically acceptable carrier for increasing the production of pseudovitamin B12 in the intestine of a subject, and/or for increasing the production of propionate in the intestine of a subject.

The subject may suffer from vitamin B12 deficiency. The vitamin B12 deficiency in said subject may be derived from or caused by metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

The disclosure is further directed to *E. hallii* and/or *I. butyriciproducens* for use in treating and/or preventing vitamin B12 deficiency in a subject. The subject may suffer from vitamin B12 deficiency. The vitamin B12 deficiency in said subject may be derived from or caused by metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

The disclosure further provides for *E. hallii* and/or *I. butyriciproducens* for increasing the production of pseudovitamin B12 in the intestine of a subject, and/or for increasing the production of propionate in the intestine of a subject. The subject may suffer from vitamin B12 deficiency. The vitamin B12 deficiency in said subject may be derived from or caused by metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and

CLAIMS

1. Use of a composition comprising *Eubacterium hallii* and/or *Intestinimonas butyriciproducens* and a physiologically acceptable carrier in the manufacture of a medicament for treating and/or preventing vitamin B12 deficiency in a subject.

2. The use according to claim 1, wherein the vitamin B12 deficiency in said subject is derived from metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss (bariatric) surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

3. The use according to any of claims 1 or 2, further comprising a propionate-producing bacterium, such as *Akkermansia muciniphila*.

4. The use according to any of claims 1 or 2, which is a pharmaceutical or supplement composition in a form selected from the group of capsule, tablet, and powder.

5. The use according to any of the preceding claims, wherein said *I. butyriciproducens* and/or *E. hallii* and, optionally, said propionate-producing bacterium, is present in lyophilized or microencapsulated form.

6. The use according to any one of the preceding claims, wherein *I. butyriciproducens* and/or *E. hallii* is present in an amount ranging from about 10^4 to about 10^{15} cells.

7. The use according to any of claims 3-6, wherein said propionate-producing bacterium such as *A. muciniphila* is present in an amount ranging from about 10^4 to about 10^{15} cells.

8. The use according to any one of the preceding claims, further comprising a mucosal binding agent.

9. The use according to any of the preceding claims, further comprising cobalt ions, for example, in the form of a cobalt salt such as cobalt chloride, cobalt sulphate, cobalt acetate, or cobalt nitrate.

10. Use of a composition comprising *I. butyriciproducens* and/or *E. hallii* and a physiologically acceptable carrier for increasing the production of pseudovitamin B12 in the intestine of a subject.

11. Use of a composition comprising *I. butyriciproducens* and/or *E. hallii* and a physiologically acceptable carrier for increasing the production of propionate in the intestine of a subject.

12. The use according to any one of claims 10 or 11, wherein the subject suffers from vitamin B12 deficiency.

13. The use according to any of claims 10-12, wherein the vitamin B12 deficiency in said subject is derived from metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

14. Use *of I. butyriciproducens* and/or *E. hallii* in the manufacture of a medicament for treating and/or preventing vitamin B12 deficiency in a subject.

15. The use of *I. butyriciproducens* and/or *E. hallii* according to claim 14, wherein the vitamin B12 deficiency in said subject is derived from metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.

16. Use of *I. butyriciproducens* and/or *E. hallii* for increasing the production of pseudovitamin B12 in the intestine of a subject.

17. Use of *I. butyriciproducens* and/or *E. hallii* for increasing the production of propionate in the intestine of a subject.

18. The use according to claim 17, wherein the subject suffers from vitamin B12 deficiency.

19. The use according to any one of claims 17 or 18, wherein the vitamin B12 deficiency in said subject is derived from metformin treatment for type-2 diabetes, pernicious anemia, atrophic gastritis, chronic inflammation of the pancreas, surgical procedure where part of the stomach and/or small intestine are removed, weight loss surgery, inflammatory bowel disease, such as Crohn's disease, ulcerative colitis, and the like, celiac disease, bacterial growth, heavy drinking, Graves' disease, lupus, long-term use of acid-reducing drugs, malnutrition, bulimia, and anorexia nervosa, HIV/AIDS, obesity, high body mass index, pre-diabetes state, insulin resistance, or a vegetarian or vegan diet.