DESCRIPTION of the invention having the title:

"*Compositions comprising bacterial strains for use in increasing the bioavailability of amino acids derived from proteins*"

Summary

In one aspect, provided herein is use of a composition in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject who takes said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid through oral route,

wherein said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof, and

wherein said composition comprises a mixture M comprising, or alternatively, consisting of at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:

- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,
- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BIIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,

optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient.

In another aspect, provided herein is a food product comprising

- proteins of plant origin, and
- the mixture M comprising or, alternatively, consisting of at least one bacterial strain selected from the group comprising or, alternatively, consisting of:
  - *Lactobacillus paracasei* DG® CNCM I-1572,
  - *Lactobacillus paracasei* LPC-S01 DSM 26760,
  - *Bifidobacterium breve* BbIBS01 DSM 33231,
  - *Bifidobacterium breve* BbIBS02 DSM 33232,
  - *Bifidobacterium animalis subsp. lactis* BIIBS01 DSM 33233,
  - *Lactobacillus plantarum* LpIBS01 DSM 33234, and
  - a mixture thereof.

In another aspect, provided herein is use of the food product as described herein in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from said proteins of plant origin.

In another aspect, provided herein is a non-therapeutic use of a composition for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject taking - through oral route - said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid,
wherein said composition comprises a mixture M comprising, or alternatively, consisting of at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,

- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,
- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BIIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,

optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient, wherein said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof.

In another aspect, provided herein is use of a composition in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject taking - through oral route - said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid, wherein said composition comprises a mixture M comprising or, alternatively, consisting of at least one bacterial strain or a derivative thereof, selected from the group comprising or, alternatively, consisting of:
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,

- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BIIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,

optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient, and wherein,

said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof; and wherein said composition is to be administered to the subject.

In another aspect, provided herein is use of a probiotic bacterial strain (I.i) *Lactobacillus paracasei* DG® CNCM I-1572 (freeze-dried in powder form) in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant or animal origin, preferably from a protein of plant origin, in a subject taking - through oral route - said protein or at least one amino acid or a peptide of plant origin comprising said at least one amino acid.

In another aspect, provided herein is use of a probiotic bacterial strain (I.ii) *Lactobacillus paracasei* LPC-S01 DSM 26760 (freeze-dried in powder form) in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant or animal origin, preferably from a protein of plant origin, in a subject taking - through oral route - said protein or at least one amino acid or a peptide of plant origin comprising said at least one amino acid.

The present invention relates to compositions for use in increasing the blood bioavailability of amino acids derived from proteins, preferably proteins of plant origin, wherein said compositions comprise a mixture M comprising, or alternatively, consisting of at least one bacterial strain, preferably *Lactobacillus paracasei* DG® CNCM I-1572 and/or *Lactobacillus paracasei* LPC-S01™ DSM 26760 (for example, AminoAlta™, trademark registered by Sofar S.p.a., Italy).

Furthermore, the present invention relates to said compositions for use further comprising at least one protein, preferably proteins of plant origin, or a peptide or an amino acid.

Lastly, the present invention relates to a food product comprising proteins, preferably of plant origin, and said mixture M comprising or, alternatively, consisting of at least one bacterial strain, preferably

Lactobacillus paracasei DG® CNCM I-1572 and/or *Lactobacillus paracasei* LPC-S01™ DSM 26760.

Proteins are an essential part of living organisms and they are formed by the union of simpler molecules called amino acids which bind to each other through peptide bonds. Through several reactions, our organism is capable of autonomously synthesising the proteins it needs starting from the individual amino acids contained in food. Many proteins are part of the category of enzymes, whose function is to catalyse the biochemical reactions vital to the metabolism of organisms. Some have structural and mechanical functions, such as actin and myosin in muscles, collagen in bones and tissues, and as components of cell cytoskeleton. Other proteins are important mediators in the transmission of inter- and intra-cellular signals, in immune response, in cell adhesion mechanisms, in the cell-division cycle.

Since proteins cannot be absorbed as such and transported in circulation, some enzymes present in the lumen of the gastrointestinal tract intervene in their digestion breaking them down into individual amino acids. During the digestive process, most proteins are completely reduced into the individual amino acids. Digestion of these macromolecules begins in the stomach, where the combined action of pepsinogen and hydrochloric acid leads to the formation of oligopeptides (short amino acid chains formed by less than ten units). Such digestion is then completed by intestinal proteases of pancreatic origin, which can be divided into endopeptidases and exopeptidases. Specifically, the aforementioned digestion of proteins is completed at the intestinal level thanks to the action of the exopeptidases present in the microvilli of the small intestine, which lead to the formation of the individual amino acids, dipeptides and tripeptides, which can thus be absorbed at the mucosal level by means of an Na+ or H+ transport mechanism.

The intestinal bacterial flora present at the level of the small intestine, especially lactobacilli, also contributes to further digest the peptides, also acting on those not completely hydrolysed by the protease.

CLAIMS

1. Use of ~~A~~a composition ~~for use~~ in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject who takes said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid through oral route,

wherein said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof, and

wherein said composition comprises a mixture M comprising, or alternatively, consisting of at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:

- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,
- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BIIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,

optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient~~, wherein said at least one amino acid is selected from the group A comprising or,~~

~~alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof~~.

2. The ~~composition for~~ use according to claim 1, wherein said at least one amino acid is selected from the group A.1.a comprising or, alternatively, consisting of: asparagine, alanine, methionine, aspartic acid, histidine, valine, tryptophan, leucine, phenylalanine, isoleucine, tyrosine and mixtures thereof.

3. The ~~composition for~~ use according to claim 1 or 2, wherein said mixture M comprises at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:
- *Lactobacillus paracasei* DG® CNCM I-1572,
- *Lactobacillus paracasei* LPC-S01 DSM 26760,
and a mixture thereof, preferably at a 1:1 by weight ratio.

4. The ~~composition for~~ use according to claim 3, wherein said mixture M further comprises at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:
- *Bifidobacterium breve* BbIBS01 DSM 33231,
- *Bifidobacterium breve* BbIBS02 DSM 33232,
- *Bifidobacterium animalis subsp. lactis* BlIBS01 DSM 33233,
- *Lactobacillus plantarum* LpIBS01 DSM 33234, and
- a mixture thereof.

5. The ~~composition for~~ use according to any one of claims 1 to 4, wherein said composition further comprises at least one protein of plant origin, and/or at least one peptide of plant origin, and/or at least one amino acid; preferably wherein said amino acid comprised in the composition is selected from the group A according to claim 2.

6. The ~~composition for~~ use according to any one of claims 1 to 5, wherein said subject suffers from a disease, symptom and/or disorder related with a protein deficiency or with an increased protein requirement.

7. The ~~composition for~~ use according to claim 6, wherein said disease, symptom and/or disorder related with said protein deficiency or with said increased protein requirement is selected from: decrease in metabolic efficiency, decrease in corpusculated elements in the blood, changes in healing processes,

decrease in muscle strength, decrease in muscle mass, muscle depletion, weight loss, decrease in athletic performance, early fatigue, difficulty in concentrating, anxiety, changes in sleep, changes in mood, increased susceptibility to infections, digestive deficiency, changes in blood sugar, increased cholesterol, changes in blood-chemical parameters, malnutrition syndrome, such as for example Kwashiorkor or biafra, osteoporosis, decrease in at least one protein-based component of an organism selected from nails, hair, skin, enzymes, neurotransmitters, hormones and immunoglobulins.

8. A food product comprising

- proteins of plant origin, and
- the mixture M comprising or, alternatively, consisting of at least one bacterial strain selected from the group comprising or, alternatively, consisting of:
    - *Lactobacillus paracasei* DG® CNCM I-1572,
    - *Lactobacillus paracasei* LPC-S01 DSM 26760,
    - *Bifidobacterium breve* BbIBS01 DSM 33231,
    - *Bifidobacterium breve* BbIBS02 DSM 33232,
    - *Bifidobacterium animalis subsp. lactis* BIIBS01 DSM 33233,
    - *Lactobacillus plantarum* LpIBS01 DSM 33234, and
    - a mixture thereof.

9. The food product according to claim 8, wherein said mixture M comprises at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:

- *Lactobacillus paracasei* DG® CNCM I-1572,
- *Lactobacillus paracasei* LPC-S01 DSM 26760, and
- a mixture thereof;

and, optionally, wherein said mixture M further comprises at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:

- *Bifidobacterium breve* BbIBS01 DSM 33231,
- *Bifidobacterium breve* BbIBS02 DSM 33232,
- *Bifidobacterium animalis subsp. lactis* BIIBS01 DSM 33233,
- *Lactobacillus plantarum* LpIBS01 DSM 33234, and
- a mixture thereof.

10. The food product according to claim 8 or 9, wherein said at least one bacterial strain is in a form of coated viable bacterial strain or coated probiotic, paraprobriotic or postbiotic; preferably at least one bacterial strain is in a form selected from the group comprising or, alternatively, consisting of: coated

viable bacterial strain, tyndallized bacterial strain, sonicated bacterial strain, inactivated bacterial strain, lysate of the bacterial strain, extract of the bacterial strain, a component of the bacterial strain selected from exopolysaccharide, parietal fraction, metabolite and metabolic bioproduct.

11. Use of t~~T~~he food product according to any one of claims 8 to 10 ~~for use~~ in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from said proteins of plant origin.

12. A non-therapeutic use of a composition for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject taking - through oral route - said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid, wherein said composition comprises a mixture M comprising, or alternatively, consisting of at least one bacterial strain, or a derivative thereof, selected from the group comprising, or alternatively, consisting of:
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,
- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BlIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,
optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient, wherein said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine,

ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof.

13. Use of ~~A~~a composition~~method~~ in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant origin in a subject taking - through oral route - said protein of plant origin or said at least one amino acid or a peptide of plant origin comprising said at least one amino acid, wherein said ~~method comprises administering a~~ composition compris~~es~~~~ing~~ a mixture M comprising or, alternatively, consisting of at least one bacterial strain or a derivative thereof, selected from the group comprising or, alternatively, consisting of:

- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* DG® and deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under the accession number CNCM I-1572,
- a bacterial strain belonging to the species *Lactobacillus paracasei* identified as *Lactobacillus paracasei* LPC-S01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 26760,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33231,
- a bacterial strain belonging to the species *Bifidobacterium breve* identified as *Bifidobacterium breve* BbIBS02 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33232,
- a bacterial strain belonging to the species *Bifidobacterium animalis* identified as *Bifidobacterium animalis subsp. lactis* BIIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33233,
- a bacterial strain belonging to the species *Lactobacillus plantarum* identified as *Lactobacillus plantarum* LpIBS01 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 33234, and
- a mixture thereof; and,

optionally, said composition comprises at least one acceptable pharmaceutical or food grade additive and/or excipient, and wherein,

said at least one amino acid is selected from the group A comprising or, alternatively, consisting of: arginine, glutamine, citrulline, serine, asparagine, glycine, threonine, alanine, ornithine, methionine, proline, lysine, aspartic acid, histidine, valine, glutamic acid, tryptophan, leucine, phenylalanine, isoleucine, cysteine, tyrosine and mixtures thereof; and wherein said composition is to be administered to the subject.

14. Use of ~~A~~a probiotic bacterial strain (I.i) *Lactobacillus paracasei* DG® CNCM I-1572 (freeze-dried in powder form)~~, for use~~ in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant or animal origin, preferably from a protein of plant origin, in a subject taking - through oral route - said protein or at least one amino acid or a peptide of plant origin comprising said at least one amino acid.

15. Use of ~~A~~a probiotic bacterial strain (I.ii) *Lactobacillus paracasei* LPC-S01 DSM 26760 (freeze-dried in powder form)~~, for use~~ in the manufacture of a medicament for increasing the blood bioavailability of at least one amino acid derived from a protein of plant or animal origin, preferably from a protein of plant origin, in a subject taking - through oral route - said protein or at least one amino acid or a peptide of plant origin comprising said at least one amino acid.