renal impairment in patients with IBD treated with 5-ASA is estimated to be one in 100 patients, and interstitial nephritis occurs in one in 500 patients

Moreover, 5-ASA is known for being efficient in mild to moderate diseases forms, but also for being significantly less effective in more severe forms of the diseases. Accordingly, when 5-ASA is identified as being inefficient, the only available alternative consists in the use of immunosuppressive therapies. However, such therapies are quite expensive and are associated with potentially severe side effects such as infection and neoplasia.

Accordingly, there remains a need for an alternative solution to immunosuppressive therapies when 5-ASA is not sufficient enough in the treatment and/or prevention of inflammatory gastrointestinal diseases. There in particular remains a need for a novel solution allowing to improve the properties of mesalamine and its derivatives thereof in the treatment and/or prevention of inflammatory gastrointestinal diseases. There is more generally a constant need for novel substances, or combination of substances, for the treatment and/or prevention of inflammatory gastrointestinal diseases, in particular inflammatory bowel diseases, in an individual.

The present invention provides a solution to these problems.

Summary

The objective of the present disclosure is to describe a new association of substances, and compositions comprising it, for the treatment and/or prevention of inflammatory gastrointestinal diseases in an individual, in particular inflammatory bowel diseases in an individual.

In the context of the present disclosure, the term “prevent” denotes the reduction to a lesser degree of the risk or of the probability of occurrence of a given phenomenon, that is to say, in the present disclosure, a gastrointestinal inflammation, in particular an inflammatory bowel disease. The term “prevent” must also be understood as encompassing the reduction to a lesser degree of the risk or of the probability of relapse of a disease according to the present disclosure, in particular of an inflammatory bowel disease.

In the context of the present disclosure, the term “treat”, in particular when used in relation with a disease, denotes slowing down or stopping the development or progression of the disease, causing regression of the associated clinical symptoms or relieving the

disease partially or completely. The term "treat" must also be understood as encompassing the reduction of number of relapses and/or the reduction of intensity of the relapses and/or the increase of the time separating two relapses of a disease according to the present disclosure, in particular of an inflammatory bowel disease.

The present disclosure is based on the discovery, by the present inventors, that when mesalamine, or a derivative thereof, is used in association with the *Faecalibacterium prausnitzii* strain CNCM I-4573, this leads to an improvement of its anti-inflammatory properties.

In particular, the present inventors discovered that when mesalamine, or a derivative thereof, is used in a low ineffective quantity when alone, its administration to an individual in association with the *Faecalibacterium prausnitzii* strain CNCM I-4573, also in an inefficient quantity when used alone, is unexpectedly able to provide anti-inflammatory properties.

According to the experimental results of the inventors, the association of mesalamine, or a derivative thereof, with a specific strain of *Faecalibacterium prausnitzii* (*F. prausnitzii*), deposited with the CNCM under accession number CNCM I-4573 on January 31, 2012, has the unexpected capacity to synergistically reduce a gastrointestinal inflammation, in particular a bowel inflammation, in an individual.

According to a first subject, the present disclosure accordingly relates to an association of a bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 with mesalamine or a derivative thereof.

Derivatives of mesalamine can for example be selected from the group consisting of Mesalazine, Olsalazine, 4-ASA (4-Aminosalicylic acid) and Sulfasalazine.

Another object of the present disclosure is a pharmaceutical composition comprising, in a pharmaceutically acceptable medium, an association of the disclosure.

The disclosure further relates to an association according to the disclosure for use in the treatment and/or prevention of an inflammatory gastrointestinal disease in an individual. In one aspect, the present disclosure refers to a use of an association as disclosed herein in the manufacture of a medicament for treating and/or preventing an inflammatory gastrointestinal disease in an individual.

An individual according to the disclosure is preferably a mammal, including a non-human mammal, and is, in particular, a human being.

The inflammatory gastrointestinal disease is, in particular, an inflammatory bowel disease (IBD), more particularly a colonic inflammatory bowel disease.

Said colonic inflammatory bowel disease may, in particular, be chosen from the group consisting of Crohn's disease, ulcerative colitis and pouchitis, in particular Crohn's disease and ulcerative colitis.

According to another example, the association for use according to the disclosure is in a pharmaceutically acceptable medium of a pharmaceutical composition, preferably in an oral composition, and more particularly preferably in a pharmaceutical product.

The term "*pharmaceutically acceptable medium*" is intended to denote a medium which is compatible with the body of the individual to whom said composition must be administered. It is, for example, a non-toxic solvent such as water. In particular, said medium is compatible with oral administration.

A composition of the disclosure is preferably for oral administration.

A composition of the disclosure for oral administration may be chosen from the group consisting of a food product, a beverage, a pharmaceutical product, a nutraceutical, a food additive, a food supplement and a milk product.

Figures' legends

Figure 1 illustrates the Disease Activity Index (DAI) score obtained with, from the left to the right on the abscissa axis, (i) control mice (without colitis) receiving only water and PBS with glycerol; (ii) control mice having a DSS-induced colitis and treated with PBS with glycerol; (iii) mice having a DSS-induced colitis and treated with the *F. prausnitzii* strain CNCM I-4573; (iv) mice having a DSS-induced colitis and treated with the association of *F. prausnitzii* strain CNCM I-4573 and Pentasa®; and (v) mice having a DSS-induced colitis and treated with Pentasa® and PBS with glycerol. The DAI score is evaluated on a scale of 0 (no inflammation) to 4 (ordinate) (n=10/group except for Water+PBS/glycerol n=5).

Figure 2 illustrates the presence of blood in the faeces of, from the left to the right on the abscissa axis, (i) control mice (without colitis) receiving only water and PBS with glycerol; (ii) control mice having a DSS-induced colitis and treated with PBS with glycerol; (iii) mice having a DSS-induced colitis and treated with the *F. prausnitzii* strain CNCM I-4573; (iv) mice having a DSS-induced colitis and treated with the association of *F. prausnitzii* strain CNCM I-4573 and Pentasa®; and (v) mice having a DSS-induced colitis

CLAIMS

1. Association of a bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 with mesalamine or a derivative thereof.

2. Association according to claim 1, wherein the mesalamine derivative is selected from the group consisting of Mesalazine, Olsalazine, 4-ASA (4-Aminosalicylic acid) and Sulfasalazine.

3. Pharmaceutical composition comprising, in a pharmaceutically acceptable medium, an association as defined in claim 1 or 2.

4. Use of an association as defined in claim 1 or 2, in the manufacture of a medicament for treating and/or preventing an inflammatory gastrointestinal disease in an individual.

5. The use according to claim 4, wherein the individual is a mammal.

6. The use according to claim 4 or 5, wherein the individual is a human being.

7. The use according to any one of claims 4 to 6, wherein the inflammatory gastrointestinal disease is an inflammatory bowel disease.

8. The use according to any one of claims 4 to 7, wherein the inflammatory gastrointestinal disease is a colonic inflammatory bowel disease.

9. The use according to claim 8, wherein the colonic inflammatory bowel disease is chosen from the group consisting of Crohn’s disease, ulcerative colitis and pouchitis.

10. The use according to claim 8 or 9, wherein the colonic inflammatory bowel disease is chosen from the group consisting of Crohn's disease and ulcerative colitis.

11. The use according to any one of claims 4 to 10, wherein the association is in a pharmaceutically acceptable medium of a pharmaceutical composition.

12. The use according to claim 11, wherein the composition is to be administered in a daily dose of the bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 representing from 10^3 bacteria to 10^{12} bacteria, in particular a daily dose representing from 10^4 bacteria to 10^{12} bacteria, more particularly a daily dose representing from 10^6 to 10^{12} bacteria, preferably in the form of a daily dose equivalent to 10^{10} bacteria.

13. The use according to claim 11 or 12, wherein the composition is for oral administration, and is in particular chosen from the group consisting of a food product, a beverage, a pharmaceutical product, a nutraceutical, a food additive, a food supplement and a milk product.

14. The use according to claim 13, characterized in that the composition is a pharmaceutical product.