become the most common cause of antibiotic-associated diarrhea and gastroenteritis-associated death in developed countries.

Currently, the standard treatment for CDI is antibiotics, with vancomycin or fidaxomicin being the most commonly prescribed compounds. Metronidazole is only used if vancomycin or fidaxomicin are not available. Fecal microbiota transplant (FMT) has only been used as a last resort following multiple recurrences. Probiotics have also been used as a preventive treatment with mixed results while vaccines are not yet available. Within healthcare facilities, preventive measures include judicious use of antibiotics and infection control practices. Use of monoclonal antibodies has also been studied with the aim of improving host resistance to CDI, however this approach has yielded mixed results.

There is a need for novel substances, in particular probiotics, or compositions comprising them, for the treatment and/or prevention of an infection by *C. difficile*.

There is in particular a need for novel substances, in particular probiotics, or compositions comprising them, able to decrease the risk of *C. difficile* infection following a gut microbiota perturbation with antibiotics and/or Proton pump inhibitors (PPI).

There is in particular a need for novel substances, in particular probiotics, or compositions comprising them, able to decrease the risk of *C. difficile* infection recurrence after a given episode.

There is in particular a need for novel substances, in particular probiotics, or compositions comprising them, able to delay intestinal colonisation by *C. difficile*.

There is also a need for novel substances, in particular probiotics, or compositions comprising them, allowing reduced, or even the absence of, symptoms following infection by *C. difficile*.

There is also a need for novel substances, in particular probiotics, or compositions comprising them, allowing limiting intestinal colonization by the bacteria, a faster elimination of *C. difficile* from the intestine and advantageously then a reduced or even the absence of symptoms following infection.

Summary

The objective of the present disclosure is to provide novel substances, in particular probiotics, and compositions for the treatment and/or prevention of a *Clostridioides difficile* infection in an individual.

In the context of the present disclosure, the terms "*prevent*", "*prevention*" and "*preventing*" denote 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 *C. difficile* infection, and in particular the development of symptoms following infection by *C. difficile*. In particular, the terms "*prevent*", "*prevention*" and "*preventing*" denote the reduction to a lesser degree of the risk or of the probability of a first episode of *C. difficile* infection (CDI) and/or the reduction to a lesser degree of the risk or of the probability of recurrence of *C. difficile* infection in an individual. For the prevention of the first episode, the target population may in particular correspond to any patient for whom an antibiotic treatment and/or a treatment comprising administration of Proton pump inhibitors (PPI) is prescribed, and in particular any patient for whom an antibiotic treatment is prescribed.

Recurrence of CDI is defined as recurrence of diarrhea with a positive test for *C. difficile* toxin within 8 weeks of completion of effective anti-*C. difficile* therapy.

As used herein, the terms "*treating*", "*treat*" or "*treatment*" include alleviation of the symptoms associated with a specific disorder or condition and/or elimination of said symptoms as well as the complete disappearance of the considered disorder or condition.

The present disclosure is based on the discovery, by the present inventors, of the ability of the *Faecalibacterium prausnitzii* strain deposited with the CNCM under accession number CNCM I-4573 to prevent and/or treat a *Clostridioides difficile* infection in an individual.

According to the experimental results of the inventors, a specific strain of *Faecalibacterium prausnitzii* (*F. prausnitzii*) deposited with the CNCM on January 21, 2012, under accession number CNCM I-4573 by Institut National de la Recherche Agronomique (INRA) has the unexpected capacity to treat and prevent, *in vivo*, the infection of an individual by *C. difficile*, and in particular the unexpected capacity to delay intestinal colonisation by *C. difficile* of said individual, to rapidly eliminate *C. difficile* from the intestine, and to reduce symptoms following infection by *C. difficile* or even to prevent the appearance of any symptom following infection by *C. difficile*.

In one aspect, the present disclosure provides for a use of a bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or a culture supernatant thereof, in the manufacture of a medicament for treating and/or preventing a *Clostridioides difficile* infection in an individual. According to a first subject, the present disclosure relates to a bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or a culture supernatant thereof, for use in the treatment and/or prevention of a *Clostridioides difficile* infection in an individual.

This strain identified by the inventors is therefore a probiotic strain which may be used for the applications indicated herein.

An individual according to the disclosure may be selected from the group consisting of human beings; *Suidae*, in particular pigs, more particularly piglets; *Bovinae*, in particular cattle, more particularly bulls, and more particularly steers; *Canidae*, in particular dogs; *Equidae*, in particular horses; and *Phasianidae*, in particular poultry, more particularly chickens; preferably a mammal, and more particularly a human being (J. Scott Weese; Journal of Veterinary Diagnostic Investigation 2020, Vol. 32(2) 213–221).

The bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 may be administered to the said individual in a live, inactive and/or dead form, preferably in a live or inactive form, more particularly in a live form.

A live bacterial form means a bacterial strain which is cultivable and/or metabolically active, in particular cultivable and metabolically active.

An inactive form of a bacterial strain according to the disclosure may for example be a lyophilisate, prepared using method of the art well known by the skilled artisan.

According to an example, the *Clostridioides difficile* infection may occur after the use of at least one antibiotic medication and/or at least one Proton pump inhibitors (PPI) medication by the individual. The bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or the culture supernatant thereof, may be administered simultaneously and/or separately, in particular simultaneously, with the at least one antibiotic medication and/or at least one PPI medication. The bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or the culture supernatant thereof, may be administered simultaneously with and/or after the at least one antibiotic medication and/or the at least one PPI medication.

The bacterial strain for use thereof, and/or the culture supernatant thereof, according to the disclosure may be included in a composition comprising a physiologically acceptable medium, preferably in an oral or rectal composition, and more particularly preferably in a pharmaceutical product.

The term "*physiologically 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 or rectal administration, in particular 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 and is, in particular, in the form of a pharmaceutical product.

A composition for use according to the disclosure may be suitable for the administration of a daily dose representing from 10^4 to 10^{15} total cell count (TCC), more preferably from 10^8 to $l0^{13}$ TCC of the *F. prausnitzii* strain of the disclosure as a medicament, for example as a daily dose representing 10^{13} TCC of the bacterial strain according to the disclosure.

Figures' legends

Figure 1 illustrates the evaluation of weight loss in mice treated or not with *F. prausnitzii* I-4573 according to the invention. Mice were weighed to monitor the development of clinical signs after infection with *C. difficile*. Two groups of mice are tested: mice treated with PBS- Glycerol 16% (vehicle); mice treated with *F. prausnitzii* strain I-4573.

Abscissa: Days (from D0 to D20, D0 being the day the mice, previously treated with antibiotics, are fed with *C. difficile* R20291). Ordinate: Weight of the mice (% compared to their weight at D0).

Figure 2 illustrates survival of mice treated with PBS- Glycerol 16% (vehicle) or treated with *F. prausnitzii* strain I-4573 of 7 days

Abscissa: Days (from D0 to D7). Ordinate: Probability of survival (between 0 and 1).

Figure 3 illustrates the colonization of mice (10 mice per group) by *C. difficile* R20291 over time (from D0 to D20 - D0 being the day the mice, previously treated with antibiotics, are fed with *C. difficile* R20291).

CLAIMS

1. Use of a bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or a culture supernatant thereof, in the manufacture of a medicament for treating and/or preventing a *Clostridioides difficile* infection in an individual.

2. The use as claimed in claim 1, characterized in that the individual is selected from the group consisting of human beings; *Suidae*, in particular pigs, more particularly piglets; *Bovinae*, in particular cattle, more particularly bulls, and more particularly steers; *Canidae*, in particular dogs; *Equidae*, in particular horses; and *Phasianidae*, in particular poultry, more particularly chickens.

3. The use as claimed in claim 1 or 2, characterized in that the individual is a mammal and is more particularly a human being.

4. The use as claimed in any one of claims 1 to 3, characterized in that the bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 is to be administered to the said individual in a live, inactive and/or dead form, preferably in a live or inactive form, more particularly in a live form.

5. The use as claimed in any one of claims 1 to 4, characterized in that the *Clostridioides difficile* infection occurs after the use of at least one antibiotic medication and/or at least one Proton pump inhibitors (PPI) medication by the individual.

6. The use as claimed in any one of claims 1 to 5, characterized in that the bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573, and/or the culture supernatant thereof, is to be administered simultaneously with and/or after the at least one antibiotic medication and/or the at least one PPI medication.

7. The use as claimed in any one of claims 1 to 6, wherein the bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number

CNCM I-4573 is included in a composition comprising a physiologically acceptable medium.

8. The use as claimed in claim 7, characterized in that the bacterial strain of the species *Faecalibacterium prausnitzii* deposited with the CNCM under accession number CNCM I-4573 is included in an oral or rectal composition, in particular in an oral composition.

9. The use as claimed in claim 7 or 8, characterized in that the bacterial strain is included in a pharmaceutical product.

10. The use as claimed in any one of claims 7 to 9, characterized in that the composition is suitable for the administration of a daily dose representing from 10^4 to 10^{15} total cell count (TCC) of the bacterial strain as a medicament, preferably in the form of a daily dose representing from 10^8 to $l0^{13}$ TCC, more particular representing 10^{13} TCC.