body, thereby improving the health of the host. In general, prebiotics should be largely undigested and fermented by gut flora when they pass through the upper digestive tract. Most importantly, prebiotics can stimulate the growth of beneficial flora, but not stimulate harmful bacteria with potential pathogenicity or spoilage activity. Common prebiotics are oligosaccharides, also known as dietary fibers.

It has been a long-standing topic in this field to regulate gut flora based on probiotics/prebiotics, thereby promoting the health level of the body (e.g., improving immunity).

SUMMARY

In a first aspect, there is provided a use of a probiotic composition comprising *Bifidobacterium bifidum* and *Bifidobacterium longum*, and *Bifidobacterium adolescentis* in the manufacture of a medicament for enhancing therapeutic effect of COVID-19 treatment in a subject. In a first example, there is provided in the application a probiotic composition comprising *Bifidobacterium bifidum* and *Bifidobacterium longum*.

In some examples, the ratio of the amounts of *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is 1: (0.21-2.36).

In some examples, the probiotic composition further comprises *Bifidobacterium adolescentis*.

In some examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36). In some specific examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units is (0.75-1): 1: (0.75-1).

In some examples, the probiotic composition further comprises *Lactobacillus rhamnosus*.

In some examples, the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units is (0.57-3.36): 1: (0.21-2.36): 1.

In some examples, the probiotic composition is in unit dosage form, and the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units are independently in the order of 10^4 to 10^{12} CFU. In some examples, the total amount of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* is in the order of 10^6 to 10^{12} CFU.

In some examples, the probiotic composition is for administration to an adult

and the amount of *Bifidobacterium adolescentis* is 2.59×10^5 - 4.49×10^{11} CFU; and/or the amount of *Bifidobacterium bifidum* is 1.26×10^5 – 7.35×10^{11} CFU; and/or the amount of *Bifidobacterium longum* is 2.23×10^5 – 7.02×10^{11} CFU; and/or the amount of *Lactobacillus rhamnosus* is 1.26×10^5 – 2.59×10^{11} CFU.

In some examples, the probiotic composition is for administration to a child, and the amount of *Bifidobacterium adolescentis* is 2.05×10^5– 4.55×10^{11} CFU; and/or the amount of *Bifidobacterium bifidum* is 1.47×10^5–3.6×10^{11} CFU; and/or the amount of *Bifidobacterium longum* is 7.55×10^4–2.5×10^{11} CFU; and/or the amount of *Lactobacillus rhamnosus* is 1.47×10^5– 3.6×10^{11} CFU.

In some examples, the probiotic composition is free of probiotics other than the probiotics described in various examples of the present application. In some examples, the probiotic composition is free of probiotics other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Lactobacillus rhamnosus*. In some examples, the probiotic composition is free of Bifidobacteria other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum*.

In a second aspect, there is provided in the application a prebiotic composition comprising xylooligosaccharide, galacto-oligosaccharide, and corn dietary fiber.

In some examples, the ratio of the amounts of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is (0.25-5): (0.75-4): (0.5-1). In some specific examples, the ratio of the amounts of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75).

In some examples, the prebiotic composition is in unit dosage form, and the total amount of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is 0.1-12g. In some examples, the prebiotic composition is in unit dosage form, and the total amount of xylooligosaccharide, galactooligosaccharide, and corn dietary fiber by weight is 0.1-5g.

In some examples, the amount of xylooligosaccharide is 0.01g-6g; and/or the amount of galactooligosaccharide is 0.04g-9.6g; and/or the amount of corn dietary fiber is 0.01g-6g.

In some examples, the prebiotic composition is free of prebiotic components other than xylooligosaccharide, galactooligosaccharide, and corn dietary fiber.

In another example, there is provided in the application a dietary composition (in

some cases, also referred to as a synbiotic composition) comprising the probiotic composition according to the first aspect and the prebiotic composition according to the second aspect.

In some specific examples, the dietary composition comprises *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* as the probiotics and xylooligosaccharide, galactooligosaccharide, and corn dietary fiber as the prebiotics, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Bifidobacterium longum* calculated by colony forming units (CFUs) is (0.75-1): 1: (0.75-1), and the total amount of the three bacteria is about 2×10^{11}CFU, and, the ratio of xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75), and the total amount of xylooligosaccharide, galactooligosaccharide and corn dietary fiber is 1.2-1.5g.

In some examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is formulated for peroral administration. In some examples, the peroral administration comprises oral administration, mixing with oral products, and gavage.

In some examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is a food supplement, a food additive, or a food product.

In some examples according to the first to third aspects, the probiotic composition or prebiotic composition or dietary composition is formulated as a powder, a granule, a tablet, or a capsule.

In some examples according to the examples herein, the probiotic composition or prebiotic composition or dietary composition is administered to a subject for assisting in preventing and/or treating a pathogen infection, or for enhancing the therapeutic effect of a pathogen infection, improving the immunity in the subject, or balancing the gut microecology in the subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria). In some examples, the pathogen is a virus, a bacterium, or a fungus. In some examples, the pathogen is a respiratory disease virus, such as COVID-19, an influenza virus, or respiratory syncytial virus.

In another example, there is provided in the application use of the probiotic

composition according to the first aspect, or the prebiotic composition according to the second aspect, or the dietary composition according to the third aspect, in the manufacture of a medicament or a dietary product for preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria). In some examples, the pathogen is a virus, a bacterium, or a fungus. In some examples, the pathogen is a respiratory disease virus, such as a novel coronavirus (COVID-19), an influenza virus, or a respiratory syncytial virus.

In another example, there is provided in the application a method for assisting in preventing and/or treating the pathogen infection in a subject, enhancing the therapeutic effect of a pathogen infection in a subject, or improving the immunity in a subject, or balancing the gut microecology in a subject (including increasing microbial abundance, increasing desirable bacterial species, and/or reducing undesirable bacteria), comprising administering to the subject the probiotic composition according to the first aspect, or the prebiotic composition of the second aspect, or the dietary composition according to the third aspect. In some embodiments, the pathogen is a virus, a bacterium, or a fungus. In some embodiments, the pathogen is a respiratory disease virus, such as COVID-19, an influenza virus, or respiratory syncytial virus.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the relationship between the desirable bacterial species and various probiotics identified in previous studies. desirable bacterial species have the potential to enhance immunity and their abundances are negatively correlated with COVID-19 disease severity or SARS-CoV-2 viral load. The circle represents a positive correlation between the abundance of the desirable bacterial species and the probiotics, the size indicates the strength of the positive correlation, and the box circles the target probiotics identified in the present application.

Figure 2 shows partial results of the cohort studies in Example 2, wherein panel A shows the positive rates and the overall positive rates of *Bifidobacterium adolescentis*,

WHAT IS CLAIMED IS:

1. Use of a probiotic composition comprising *Bifidobacterium bifidum* and *Bifidobacterium longum*, and *Bifidobacterium adolescentis* in the manufacture of a medicament for enhancing therapeutic effect of COVID-19 treatment in a subject.

2. The use of claim 1, wherein the ratio of the amounts of *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is 1: (0.21-2.36).

3. The use of claim 1, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36).

4. The use of claim 3, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units is (0.75-1): 1: (0.75-1).

5. The use of claim 1, wherein the composition further comprises *Lactobacillus rhamnosus*.

6. The use of claim 5, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Lactobacillus rhamnosus* calculated by colony forming units is (0.57-3.56): 1: (0.21-2.36): 1.

7. The use of claim 5, wherein the probiotic composition is in unit dosage form, and the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* calculated by colony forming units are independently in the order of 10^4 to 10^{12} CFU.

8. The use of claim 7, wherein the total amount of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Lactobacillus rhamnosus* is in the order of 10^6 to 10^{12} CFU.

9. The use of claim 7, wherein the probiotic composition is for administration to an adult, and

the amount of *Bifidobacterium adolescentis* is 2.59×10^5-4.49×10^{11} CFU; and/or

the amount of *Bifidobacterium bifidum* is 1.26×10^5-7.35×10^{11} CFU; and/or

the amount of *Bifidobacterium longum* is 2.23×10^5-7.02×10^{11} CFU; and/or

the amount of *Lactobacillus rhamnosus* is 1.26×10^5-2.59×10^{11} CFU.

10. The use of claim 7, wherein the probiotic composition is for administration to a child, and

the amount of *Bifidobacterium adolescentis* is 2.05×10^5-4.55×10^{11} CFU; and/or

the amount of *Bifidobacterium bifidum* is 1.47×10^5-3.6×10^{11} CFU; and/or

the amount of *Bifidobacterium longum* is 7.55×10^4- 2.5×10^{11} CFU; and/or

the amount of *Lactobacillus rhamnosus* is 1.47×10^5-3.6×10^{11} CFU.

11. The use of claim 1, wherein the probiotic composition is free of Bifidobacteria other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum*.

12. The use of claim 11, wherein the probiotic composition is free of probiotics other than *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, *Bifidobacterium longum* and *Lactobacillus rhamnosus*.

13. The use of claim 1, wherein the probiotic composition further comprises xylooligosaccharide, galactooligosaccharide and corn dietary fiber.

14. The use of claim 13, wherein the ratio of the amounts of xylooligosaccharide, galactooligosaccharides and corn dietary fiber by weight is (0.25-5): (0.75-4): (0.5-1).

15. The use of claim 14, wherein the ratio of the amounts of xylooligosaccharide, galactooligosaccharides and corn dietary fiber by weight is (0.25-0.5): (2- 4): (0.5-0.75).

16. The use of claim 13, wherein the probiotic composition is in unit dosage form, and the total amount of the xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is 0.1-12g.

17. The use of claim 16, wherein the total amount of the xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is 0.1-5g.

18. The use of claim 16, wherein

the amount of xylooligosaccharide is 0.01g-6g; and/or

the amount of galactooligosaccharide is 0.04g-9.6g; and/or

the amount of corn dietary fiber is 0.01g-6g.

19. The use of claim 13, wherein the probiotic composition is free of prebiotic components other than xylooligosaccharide, galactooligosaccharide and corn dietary

fiber.

20. The use of claim 1, wherein the probiotic composition is a dietary composition, and wherein the dietary composition comprises *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* as the probiotics, and xylooligosaccharide, galactooligosaccharide and corn dietary fiber as the prebiotics, wherein the ratio of the amounts of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum* and *Bifidobacterium longum* calculated by colony forming units (CFUs) is (0.75-1): 1: (0.75-1), and the total amount of the three bacteria is about 2×10^{11}CFU, and the ratio of xylooligosaccharide, galactooligosaccharide and corn dietary fiber by weight is (0.25-0.5): (2-4): (0.5-0.75), and the total amount of xylooligosaccharide, galactooligosaccharide and corn dietary fiber is 1.2-1.5g.

21. The use of claim 20, wherein the dietary composition is formulated for oral administration.

22. The use of claim 20, wherein the dietary composition is a food supplement, a food additive or a food.

23. The use of claim 20, wherein the dietary composition is formulated into a powder, a granule, a tablet or a capsule.