locomotor system (muscular and skeletal system), digestive system, urogenital system (urinary system and genital system), respiratory system, integumentary system, immune system and circulatory system. Lastly, the various berries have shown specific antibacterial and prebiotic activities in terms of prevention of bacterial adhesion to the uroepithelial surface, inhibition of biofilm, modification of gene expression and membrane structure, modification of the gut microbiota.

The mixtures and compositions of the invention (compositions (A) of the invention and compositions (B) of the invention, as defined hereinafter) reveal to have anti-inflammatory and immunomodulator effects (IL-10:IL-12 ratio >> 1) and they do not show any significant adverse effects, therefore they can be administered to any type of subject, including pregnant women, paediatric and elderly subjects.
Furthermore, the mixtures and the compositions of the invention are effective, easy to prepare and cost-effective to produce.

These and other objects which will be clearer from the detailed description that follows, are achieved by the bacterial strain, by the compositions and by the mixtures of the present invention thanks to the technical characteristics present in the description and claimed in the attached claims.

SUMMARY

In one aspect, provided herein is a composition comprising a mixture comprising, or alternatively, consisting of:

- a bacterial strain identified as *Bifidobacterium bifidum* MIMBb23sg and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 32708, and

at least one bacterial strain selected from the group comprising or, alternatively, consisting of:

- a bacterial strain identified as *Lactobacillus paracasei* DG® and deposited by SOFAR S.p.A. at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under accession number CNCM I-1572,
- a bacterial strain 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 identified as *Lactobacillus paracasei* CF3 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 32353,
- a bacterial strain identified as *Lactobacillus rhamnosus* GG and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 53103,
- a bacterial strain identified as *Bifidobacterium animalis subsp. lactis* Bb12 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 15954, and mixtures thereof;

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

In another aspect, provided herein is the composition as described herein for use as a medicament.

In another aspect, provided herein is use of the composition as described herein in the manufacture of an immunomodulatory and/or immunostimulatory agent capable of reducing the production of proinflammatory cytokines and/or increasing the production of anti-inflammatory cytokines;
preferably, wherein said immunomodulatory and/or immunostimulatory agent is capable of reducing the production of IL12 and/or TNF-α cytokines and/or of increasing the production of IL10 cytokines.

In another aspect, provided herein is use of the composition as described herein in the manufacture of a medicament for the preventive and/or curative treatment of musculoskeletal inflammatory diseases, rheumatological diseases, inflammatory articular and/or post-surgery inflammatory diseases.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1a, 1b, 1c: response of cytokines IL12, TNF-α and IL10 after stimulation with single bacterial strains of group (I.1), in the presence or absence of LPS (lipopolysaccharide, inflammatory stimulus), [*] = $p < 0.05$, [+] = $p < 0.01$, [$] = $p < 0.001$;

Figure 2a, 2b, 2c: response of cytokines IL12, TNF-α and IL10 after stimulation with mixtures of bacterial strains of group (I.1), [+] = $p < 0.01$; data expressed as pg/mL;

Figure 3: Response of cytokines IL12, TNF-α and IL10 after stimulation with mixtures comprising a bacterial strain of group (I.1) and an extract of berries comprising the polyphenol fraction; C: control (BMDCs stimulated with RPMI medium only).

Figure 4: response of cytokines IL12, TNF-α and IL10 after stimulation with mixtures of at least 1 or 2 bacterial strains of group (I.1) and an extract of berries comprising the polyphenol fraction;

Figure 4a: response of cytokines IL12, TNF-α and IL10 after stimulation with mixtures of at least 2 bacterial strains of group (I.1) and a berry extract comprising the polyphenol fraction; C: control (BMDCs stimulated with RPMI medium only), [*] = $p < 0.05$, [+] = $p < 0.01$, [$] = $p < 0.001$.

In Figures 4 and 4a the polyphenols extracted from the berries are used at a concentration of 50 µg/mL; the combinations of bacteria are used at a final MOI (*multiplicity of infection*) of 5.

CLAIMS

1. A composition comprising a mixture comprising, or alternatively, consisting of:
- a bacterial strain identified as *Bifidobacterium bifidum* MIMBb23sg and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 32708, and
at least one bacterial strain selected from the group comprising or, alternatively, consisting of:
- a bacterial strain identified as *Lactobacillus paracasei* DG® and deposited by SOFAR S.p.A. at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under accession number CNCM I-1572,
- a bacterial strain 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 identified as *Lactobacillus paracasei* CF3 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 32353,
- a bacterial strain identified as *Lactobacillus rhamnosus* GG and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number DSM 53103,
- a bacterial strain identified as *Bifidobacterium animalis subsp. lactis* Bb12 and deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 15954, and mixtures thereof;
and wherein, optionally, said composition comprises at least one food or pharmacological grade additive and/or excipient.

2. The composition according to claim 1, wherein the mixture comprises or, alternatively, consists of: a bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708 and a bacterial strain *Lactobacillus paracasei* LPC-S01™ DSM 26760.

3. The composition according to claim 2, wherein the mixture comprises or, alternatively, consists of: a bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708, a bacterial strain *Lactobacillus paracasei* LPC-S01™ DSM 26760 and of at least one bacterial strain selected from the group comprising or, alternatively, consisting of: *Lactobacillus paracasei* DG® CNCM I-1572, *Lactobacillus paracasei* CF3 DSM 32353, *Lactobacillus rhamnosus* GG DSM 53103, *Bifidobacterium animalis subsp. lactis* Bb12 DSM 15954 and mixtures thereof.

4. The composition according to claim 1, wherein the mixture comprises or, alternatively, consists of: a bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708 and a bacterial strain *Lactobacillus paracasei* DG® CNCM I-1572.

5. The composition according to claim 4 , wherein the mixture comprises or, alternatively, consists of: a bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708, a bacterial strain *Lactobacillus paracasei* DG® CNCM I-1572 and at least one bacterial strain selected from the group comprising or, alternatively, consisting of: *Lactobacillus paracasei* LPC-S01™ DSM 26760, *Lactobacillus paracasei* CF3 DSM 32353, *Lactobacillus rhamnosus* GG DSM 53103, *Bifidobacterium animalis subsp. lactis* Bb12 DSM 15954 and mixtures thereof.

6. The composition according to any one of the preceding claims, wherein the mixture comprises or, alternatively, consists of a bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708 and a bacterial strain *Lactobacillus paracasei* LPC-S01 DSM 26760 and a bacterial strain *Lactobacillus paracasei* DG® CNCM I-1572.

7. The composition according to any one of claims 1 to 6 for use as a medicament.

8. Use of tThe composition according to any one of claims 1 to 6 ~~for use~~ in the manufacture of ~~as~~ an immunomodulatory and/or immunostimulatory agent capable of reducing the production of proinflammatory cytokines and/or increasing the production of anti-inflammatory cytokines;
preferably, wherein said ~~composition is for use as~~ an immunomodulatory and/or immunostimulatory agent is capable of reducing the production of IL12 and/or TNF-α cytokines and/or of increasing the production of IL10 cytokines.

9. The ~~composition for~~ use according to claim 7 or 8, wherein said immunomodulatory and/or immunostimulatory agent ~~composition~~ is ~~for use as~~ an anti-inflammatory agent.

10. The ~~composition for~~ use according to claim 9, wherein said anti-inflammatory agent ~~composition is for use in a method for the~~ preventsive and/or curatively treatsment ~~of~~ inflammatory gastrointestinal diseases, disorders or symptoms selected from the group comprising or, alternatively, consisting of: Helicobacter pylori, peptic or gastric ulcer, duodenal ulcer, chronic inflammatory bowel diseases (IBD), Crohn's disease, ulcerative colitis, microscopic colitis, diverticular disease and diverticulitis.

11. Use of tThe composition according to any one of claims 1 to 6 ~~for use~~ in the manufacture of a medicamenta ~~method~~ for the preventive and/or curative treatment of musculoskeletal inflammatory diseases, rheumatological diseases, inflammatory articular and/or post-surgery inflammatory diseases.

12. The ~~composition for~~ use according to claim 11, wherein said medicament~~composition is for use in a method for the~~ prevent~~sive~~ and/or curative~~ly~~ treat~~sment of~~ osteoarthritis, rheumatoid arthritis and/or ankylosing spondylitis; preferably osteoarthritis of the joints and/or osteoarthritis of the knee.