contained in berries account for considerable metabolic effects. The considerable presence of anthocyanidins (polyphenols) also contributes to a specific anti-inflammatory action at the level of the 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 immunomodulatory 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: at least one bacterial strain selected from the group comprising or, alternatively, consisting of a bacterial strain identified as Lactobacillus *paracasei* DG® deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under access number CNCM I-1572 by SOFAR S.p.A., a bacterial strain identified as *Lactobacillus paracasei* LPC-S01™ deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 26760, a bacterial strain identified as *Lactobacillus paracasei* CF3 deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 32353; and at least one extract of at least one species of berries comprising or, alternatively, consisting of a polyphenol fraction of said berries; and wherein, optionally, said composition B 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 a 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 a use of the composition as described herein in the manufacture of an anti-inflammatory agent for the preventive and/or curative treatment of inflammatory gastrointestinal diseases, disorders and/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.

In another aspect, provided herein is a 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:

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

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

- a bacterial strain identified as Lactobacillus *paracasei* DG® deposited at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under access number CNCM I-1572 by SOFAR S.p.A.,

- a bacterial strain identified as *Lactobacillus paracasei* LPC-S01™ deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 26760,

- a bacterial strain identified as *Lactobacillus paracasei* CF3 deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 32353,

~~- a bacterial strain identified as *Lactobacillus rhamnosus* GG deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 53103,~~

~~- a bacterial strain identified as *Bifidobacterium animalis subsp. lactis* Bb12 deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 15954, and mixtures thereof~~; and

- at least one extract of at least one species of berries comprising or, alternatively, consisting of a polyphenol fraction of said berries;

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

2. The composition according to claim 1, wherein said at least one bacterial strain comprises at least one further bacterial strain selected from the group comprising or, alternatively, consisting of:

- a~~the~~ bacterial strain *Bifidobacterium bifidum* MIMBb23sg deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 32708 ~~and furthermore at least one further bacterial strain selected from the group comprising or, alternatively, consisting of:~~

~~- *Lactobacillus paracasei* DG® deposited by SOFAR S.p.A. at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under access number CNCM I-1572,~~

~~- *Lactobacillus paracasei* LPC-S01™ deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 26760,~~

~~- *Lactobacillus paracasei* CF3 deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 32353~~,

- a bacterial strain identified as *Lactobacillus rhamnosus* GG deposited at Deutsche Sammlung von

Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 53103,
- a bacterial strain identified as *Bifidobacterium animalis subsp. lactis* Bb12 deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under deposit number DSM 15954,
and mixtures thereof.

3. The composition according to claim 1 or 2, wherein said at least one bacterial strain comprises a ~~the bacterial~~ *Lactobacillus paracasei* strain ~~*Bifidobacterium bifidum* MIMBb23sg DSM 32708 and furthermore at least one further bacterial strain~~ selected from the group comprising or, alternatively, consisting of:
- *Lactobacillus paracasei* DG® deposited by SOFAR S.p.A. at the National Collection of Cultures of Microorganisms of the Pasteur Institute in Paris under access number CNCM I-1572,
- *Lactobacillus paracasei* LPC-S01™ deposited at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under access number DSM 26760, and a mixture thereof; and
- furthermore the bacterial strain *Bifidobacterium bifidum* MIMBb23sg DSM 32708.

4. The composition according to any one of the preceding claims, wherein said at least one species of berries is selected from the group comprising or, alternatively, consisting of: blueberry or European blueberry (*Vaccinium cyanococcus* or *Vaccinium myrtillus or Vaccinium angustifolium*), oxycoccus or cranberry (*Vaccinium oxycoccos or Vaccinium macrocarpon*), wild strawberry or strawberry (*Fragaria vesca or Fragaria spp. or Fragaria ananassa*), elderberry (*Sambucus nigra*), cowberry (*Vaccinium vitis-idaea*), blackberry (*Rubus ulmifolius*), red raspberry (*Rubus idaeus*), black raspberry (*Rubus leucodermis or Rubus occidentalis*), black currant (*Ribes nigrum*), red currant (*Ribes rubrum*), black mulberry (*Morus nigra*), red mulberry (*Morus rubra*), white mulberry (*Morus alba*), cornelian cherry (cornus mas), gooseberry (Ribes uva-crispa), barberry (*berberis vulgaris*), *Amelanchier ovalis*, *Amelanchier canadensis*, marasca cherry(*Prunus mahaleb*), sour cherries and black cherries (Prunus cerasus), strawberry tree (*Arbutus unedo*);
blueberry or European blueberry (*Vaccinium cyanococcus* or *Vaccinium myrtillus or Vaccinium angustifolium*), oxycoccus or cranberry (*Vaccinium oxycoccos or Vaccinium macrocarpon*), wild strawberry or *strawberry* (*Fragaria vesca or Fragaria spp. or Fragaria ananassa*), elderberry (*Sambucus nigra*), and mixtures thereof.

5. The composition according to any one of the preceding claims, wherein said at least one species of berries is selected from the group comprising or, alternatively, consisting of:
blueberry or European blueberry (*Vaccinium cyanococcus* or *Vaccinium myrtillus or Vaccinium angustifolium)*, oxycoccus or cranberry (*Vaccinium oxycoccos or Vaccinium macrocarpon*), wild strawberry or strawberry (*Fragaria vesca or Fragaria spp. or Fragaria ananassa*), elderberry (*Sambucus nigra*), and

mixtures thereof; preferably wherein said at least one species of berries is selected from the group comprising or, alternatively, consisting of blueberry, cranberry, and a mixture thereof.

6. The composition according to any one of the preceding claims, wherein said polyphenol fraction of said extract of at least one species of berries comprises proanthocyanidins and/or anthocyanins and/or anthocyanidins.

7. The composition according to any one of the preceding claims, wherein said at least one bacterial strain comprises or, alternatively, consists of *Bifidobacterium bifidum* MIMBb23sg DSM 32708 and *Lactobacillus paracasei* LPC-S01™ DSM 26760.

8. The composition according to any one of the preceding claims, wherein said at least one bacterial strain comprises or, alternatively, consists of *Bifidobacterium bifidum* MIMBb23sg DSM 32708 and *Lactobacillus paracasei* DG® CNCM I-1572.

9. The composition according to any one of the preceding claims,
wherein said at least one bacterial strain comprises or, alternatively, consists of ~~*Bifidobacterium bifidum* MIMBb23sg DSM 32708 and furthermore~~ *Lactobacillus paracasei* LPC-S01™ DSM 26760 or *Lactobacillus paracasei* DG® CNCM I-1572, and furthermore *Bifidobacterium bifidum* MIMBb23sg DSM 32708, ~~and~~
wherein said at least one extract of at least one species of berries comprising or, alternatively, consisting of the polyphenol fraction of said berries is an extract of blueberry or European blueberry (*Vaccinium cyanococcus* or *Vaccinium myrtillus* or*Vaccinium angustifolium*) or, alternatively, of oxycoccus or cranberry (*Vaccinium oxycoccos* or *Vaccinium* macrocarpon) comprising or, alternatively, consisting of the polyphenol fraction of said berries.

10. The composition according to any one of claims 1 to 9 for use as a medicament.

11. Use of ~~T~~the composition according to any one of claims 1 to 9 in the manufacture of ~~for use 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.

12. The ~~composition for~~ use according to claim 10 or 11, wherein said immunomodulatory and/or

immunostimulatory agent~~composition~~ is ~~for use as~~ an anti-inflammatory agent.

13. Use of ~~T~~the composition ~~for use~~ according to any one of claims 1-9~~12~~, in the manufacture of an anti-inflammatory agent for ~~wherein said composition is for use in a method for~~ the preventive and/or curative treatment of inflammatory gastrointestinal diseases, disorders and/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.

14. Use of ~~The~~the composition according to any one of claims 1 to 9 in the manufacture of a medicament for ~~use in a method for~~ the preventive and/or curative treatment of musculoskeletal inflammatory diseases, rheumatological diseases, inflammatory articular and/or post-surgery inflammatory diseases.

15. The ~~composition for~~ use according to claim 14, wherein said musculoskeletal inflammatory diseases, rheumatological diseases, inflammatory articular and/or post-surgery inflammatory diseases are~~composition is for use in a method for the preventive and/or curative treatment of~~ osteoarthritis, rheumatoid arthritis and/or ankylosing spondylitis; preferably osteoarthritis of the joints and/or osteoarthritis of the knee.