SUMMARY ~~OF THE INVENTION~~

The present inventors have found that *Lactobacillus fermentum* ME-3, unlike other *Lactobacillus* sp. (Mikelsaar & Zilmer (2009) Microbial Ecology in Health and Disease, 21: 1-27), is a significant inhibitor of pro-inflammatory markers, such as glycated haemoglobin HbA1c, high sensitivity C-reactive protein (hsCRP) and IL-6, and is also capable of stimulating production of the anti-inflammatory and anti-diabetic peptide adiponectin. Consequently, as a result of identifying the underlying mechanism by which the probiotic strain *Lactobacillus fermentum* ME-3 acts, the present inventors have found that it can be used to prevent, alleviate the symptoms of, treat and/or be used as an adjuvant treatment e.g. as an adjuvant component for inflammatory diseases and in particular metabolic syndrome related conditions (preferably selected from pre-diabetes, diabetes, cardiovascular disease). This is particularly surprising, as *Lactobacillus fermentum* ME-3 has previously been reported as an antimicrobial and antioxidative probiotic (EP1401457 & Mikelsaar & Zilmer (2009) Microbial Ecology in Health and Disease, 21: 1-27).

One aspect of the invention relates to the use of a composition comprising Lactobacillus fermentum ME-3 strain DSM 14241 in the manufacture of a medicament for preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes.

Another aspect relates to the use of a composition comprising Lactobacillum fermentum ME-3 strain DSM 14241 in the manufacture of a medicament for preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes by simultaneously: a.decreasing the level of glycated haemoglobin HbA1c; b. decreasing or preventing low-grade inflammation on a cellular level; and c. increasing the level of adiponectin, in a subject.

The ~~invention~~ disclosure ~~therefore~~ also provides a composition comprising *Lactobacillus fermentum* ME-3, particularly *Lactobacillus fermentum* ME-3 strain DSM 14241 deposited at the Deutsche Sammlung für Mikroorganismen and Zelkulturen GmbH-s on 19/4/2001, for use in preventing, alleviating the symptoms of, treating and/or providing adjuvant treatment, e.g. as an adjuvant component , for an inflammatory disease and in particular metabolic syndrome related conditions. The ~~invention~~ disclosure also provides a method of preventing, alleviating the symptoms of, treating and/or providing adjuvant treatment, e.g. as an adjuvant component, for an inflammatory disease, and in particular metabolic syndrome related conditions in a subject comprising administering an effective amount of a composition comprising *Lactobacillum fermentum* ME-3 strain DSM 14241 to said subject. The ~~invention~~ disclosure further provides the use of *Lactobacillum fermentum* ME-3 strain DSM 14241 in the manufacture of a medicament and/or an adjuvant medicament for the prevention, alleviation of the symptoms, treatment and/or adjuvant treatment, e.g. for an inflammatory disease and in particular metabolic syndrome related conditions.

Because of its mechanism of action, *Lactobacillus fermentum* ME-3 is particularly useful in certain subject sub-populations such as asymptomatic subjects, including those with low-grade inflammation, at risk of developing an inflammatory disease, such as cardiovascular disease (CVD), type 2 diabetes or metabolic syndrome; and patients who have suffered a stroke. The present inventors have also discovered that *Lactobacillus fermentum* ME-3 is also particularly beneficial when used in combination with one or more vitamins and/or monocalin K.

The present ~~invention~~ disclosure therefore also provides a composition comprising *Lactobacillus fermentum* ME-3, for use in preventing, alleviating the symptoms of, treating and/or providing adjuvant treatment (e.g. as an adjuvant

component), for an inflammatory disease and in particular for metabolic syndrome related conditions by one or more of :

a. decreasing the level of glycated haemoglobin HbA1c;
b. decreasing or preventing low-grade inflammation on a cellular level; and
c. increasing the level of adiponectin,

in a subject.

The ~~invention~~ disclosure also provides a method of preventing, alleviating the symptoms of, treating and/or providing adjuvant treatment (e.g. as an adjuvant component), for an inflammatory disease and in particular for metabolic syndrome related conditions in a subject by one or more of :

a. decreasing the level of glycated haemoglobin HbA1c;
b. decreasing or preventing low-grade inflammation on a cellular level; and
c. increasing the level of adiponectin,

comprising administering an effective amount of a composition comprising *Lactobacillum fermentum* ME-3 strain DSM 14241 to said subject.

The ~~invention~~ disclosure also provides *Lactobacillus fermentum* ME-3 strain DSM 14241 for use in the manufacture of a medicament and/or an adjuvant medicament for the prevention, alleviation of the symptoms, treatment and/or adjuvant treatment (e.g. as an adjuvant component), for an inflammatory disease and in particular for metabolic syndrome related conditions by one or more of :

a. decreasing the level of glycated haemoglobin HbA1c;
b. decreasing or preventing low-grade inflammation on a cellular level; and
c. increasing the level of adiponectin

in a subject.

In all cases, as a result of the treatment with *Lactobacillus fermentum* ME-3 strain DSM 14241, preferably at least two and preferably all of :

a. decreasing the level of glycated haemoglobin HbA1c;
b. decreasing or preventing low-grade inflammation on a cellular level; and
c. increasing the level of adiponectin

occurs. Preferably these occur simultaneously.

For example treatment with *Lactobacillus fermentum* ME-3 strain DSM 14241 may result in decreasing the level of glycated haemoglobin HbA1c and decreasing or preventing low-grade inflammation on a cellular level; decreasing the level of glycated haemoglobin HbA1c and increasing the level of adiponectin; or decreasing or preventing low-grade inflammation on a cellular level and increasing the level of adiponectin. Preferably these occur simultaneously.

CLAIMS:

1. Use of ~~A~~a composition comprising *Lactobacillus fermentum* ME-3 strain DSM 14241 in the manufacture of a medicament for ~~use in~~ preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes.

2. Use of ~~A~~a composition comprising *Lactobacillum fermentum* ME-3 strain DSM 14241 in the manufacture of a medicament for ~~use in~~ preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes by simultaneously:
    a. decreasing the level of glycated haemoglobin HbA1c;
    b. decreasing or preventing low-grade inflammation on a cellular level; and
    c. increasing the level of adiponectin,

    in a subject.

~~3. A method of preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes in a subject comprising administering an effective amount of a composition comprising *Lactobacillum fermentum* ME-3 strain DSM 14241 to said subject.~~

~~4. A method of preventing, alleviating the symptoms of or treating, alone or as an adjuvant component, a metabolic syndrome related disorder selected from prediabetes, cardiovascular disease and type 2 diabetes in a subject by simultaneously:~~
    ~~a. decreasing the level of glycated haemoglobin HbA1c;~~
    ~~b. decreasing or preventing low-grade inflammation on a cellular level; and~~
    ~~c. increasing the level of adiponectin,~~

~~comprising administering an effective amount of a composition comprising *Lactobacillum fermentum* ME-3 strain DSM 14241 to said subject.~~

5.3. The ~~composition~~ use of claim 1 or claim 2 ~~or the method of claim 3 or claim 4~~, wherein the decreased or absent inflammation on a cellular level is measured using the pro-inflammatory markers hsCRP and IL-6.

6.4. The ~~composition~~ use ~~or the method~~of any preceding claim, wherein the subject is asymptomatic for said metabolic syndrome related disorder.

7.5. The use~~composition or the method~~ of claim 44, wherein the asymptomatic subject has a CRP level of ≤ 10 mg/l.

8.6. The use~~composition or the method~~ of claim 75, wherein the asymptomatic subject has a CRP level of 3-10 mg/l.

9.7. The ~~composition or method~~use of any preceding claim, wherein said composition is a food product, a food supplement or a pharmaceutical composition.

10.8. The ~~composition or method~~use of claim 97, wherein the food product is a medical food product or a functional food product.

11.9. The ~~composition or method~~ use of claim 9-7 or 108, wherein the food product is a dairy product such as milk, yogurt, cheese, kefir, or a milk- or whey-based fermented dairy product, or a chocolate product.

12.10. The ~~composition or method~~use of any preceding claim, wherein said composition is administered prior to, simultaneously with, or subsequently to another active compound, such as an anti-inflammatory composition, one or more vitamins, and/or monacolin K.

13.11. The ~~composition or method~~use of any preceding claim, wherein said composition further comprises one or more vitamins and/or monacolin K.

14.12. The ~~composition or method~~use of any preceding claim, wherein said composition comprises *Lactobacillum fermentum* ME-3 strain DSM 14241 in an encapsulated form, in a freeze-dried form, in a coated form, in a capsule, in a tablet or in a powder.

15.13. The ~~composition or method~~use of any preceding claim, wherein said composition comprises 10^6-10^{11} CFU of *Lactobacillum fermentum* ME-3 strain DSM 14241.