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(54) Title: PREVENTING SALMONELLA INFECTION INDUCED WEIGHT LOSS

(57) Abstract: A method involving administering pectin degradation product is provided for preventing and/or treating weight reduction in subjects suffering from salmonella infection or susceptible to salmonella in infection.

PREVENTING SALMONELLA INFECTION INDUCED WEIGHT LOSS

FIELD OF THE INVENTION

The invention relates to a nutritional composition and its use in infection-induced weight loss control, particularly in case of (increased risk of) salmonella infections.

BACKGROUND OF THE INVENTION

Both infections and weight loss is a major problem in fragile subjects such as elderly, infants, hospitalized subjects and sick people. More importantly, if both adverse events coincide it may result in life threatening situations.

In case of infection, particularly when salmonella infection or salmonellosis is diagnosed, it may be desirable to attempt to prevent weight loss and/or increase weight gain. Although a suffering subject may ingest sufficient calories, a majority of these subjects lose vital nutrients due to diarrhea, vomiting or malabsorption indicative of such infection.

SUMMARY OF THE INVENTION

The present inventors found that weight loss in subjects suffering from infection, particularly subjects infected with salmonella, or at risk of such infection, can be limited and/or weight gain can be improved by orally ingesting pectin degradation product (PDP) before, during and/or after the infection.

Advantageously, the PDP can be included in foods products which are consumed by the fragile subjects in order to remain well-nourished. For example infants receive infant formula and hospitalized patients can receive liquid enteral nutrition. The PDP can be included in such products. By the inclusion of the PDP in a food product, weight loss can be reduced or prevented, if a subject receiving the food product with PDP becomes infected with salmonella. Alternatively a composition comprising PDP can be administered after the subject has been diagnosed with salmonella infection or salmonellosis.

DETAILED DESCIPTION OF THE INVENTION

The present invention thus concerns a method for prevention and/or treatment of weight reduction in subjects suffering from salmonella infection or susceptible to

salmonella infection, said method comprising adminstering a composition comprising pectin degradation product (PDP).

In other words the invention concerns the use of pectin degradation product (PDP) in the manufacture of a composition for prevention and/or treatment of weight reduction in subjects suffering from salmonella infection or susceptible to salmonella infection.

The invention can also be worded as a composition comprising pectin degradation product (PDP) for use in the prevention and/or treatment of weight reduction in subjects suffering from salmonella infection or susceptible to salmonella infection.

The term 'elderly' as used in the present invention means people aged 55 years and older, more preferably of age 60 years and older. The term 'infants' represents children aged 5 years or younger, more preferably of age 3 years or less, preferably of 0 – 36 months.

Thus in one embodiment of the present invention the treatment and/or prevention is for a subject that has an age of 55 years or more.

In one embodiment of the present invention the treatment and/or prevention is for a subject that has an age of 3 years or less.

PDP

In the context of the invention, the term "pectin degradation *product*" is merely intended to distinguish such pectin-derived preparations as are commercially available from the (nutritional) compositions incorporating such PDP. Here, the term "pectin degradation product" is considered interchangeable by "pectin degradation preparation".

With a "pectin degradation product" it is preferably understood a pectin hydrolysate (prepared by hydrolysis) and/or pectin lyasate (prepared by beta-elimination). The pectin degradation product is preferably prepared from fruit and/or vegetable pectin, more preferably apple pectin, citrus pectin and/or sugar beet pectin. The pectin degradation product is preferably prepared with lyases and/or variations of the temperature and pressure, more preferably by beta-elimination. The pectin degradation product is preferably a pectin lyasate. The pectin degradation product

preferably has a DP between 2 and 250, more preferably between 2 and 100, and this DP is preferably an average DP.

Preferably the present composition comprises uronic acid oligosaccharide. The 'oligosaccharides" preferably have a DP of 2 to 100, even more preferably a DP of 2 to 50, most preferably a DP of 2 to 20. Preferably the pectin degradation product comprises between 25 and 100 wt%, more preferably between 50 and 100 wt% of said uronic acid oligosaccharides, based on total weight of uronic acid in the product. The uronic acid oligosaccharides are preferably obtainable or obtained by enzymatic digestion of pectin with pectin lyases, pectate lyase, endopolygalacturonase and/or pectinase.

Preferably, the uronic acid oligosaccharide has one, preferably two, terminal uronic acid units, which may be free or esterified. Preferably the terminal uronic acid unit is selected from the group consisting of galacturonic acid, glucuronic acid, guluronic acid, iduronic acid, mannuronic acid, riburonic acid and altruronic acid. These units may be free or esterified. In a preferred embodiment at least one of the terminal hexuronic acid units of the uronic acid oligosaccharide has a double bond, which is preferably situated between the C4 and C5 position of the terminal hexuronic acid unit. Preferably one of the terminal hexuronic acid units comprises the double bond. The double bond at terminal hexuronic acid unit can for example be obtained by enzymatic hydrolysis of pectin with lyase. The carboxylic acid groups on these uronic acid units may be free or (partly) esterified, and are preferably at least partly methylated.

The uronic acid oligosaccharides are preferably galacturonic acid oligosaccharides. The present composition contains between 25 and 100 wt%, preferably between 50 and 100 wt% galacturonic acid oligosaccharide with a degree of polymerization (DP) of 2 to 250, more preferably DP 2 – 100, most preferably DP 2 – 50, based on total weight of galacturonic acid in the composition. Most preferably, the degree of polymerisation is an average DP.

Composition; food product

The present composition is preferably administered enterally, more preferably orally. The present composition is preferably a nutritional formula. The present composition preferably comprises lipid, protein, and carbohydrate and is preferably administered in

liquid form. The present invention includes dry compositions, e.g. powders, which are accompanied with instructions as to admix said dry compositions, in particular nutritional formula, with a suitable liquid, e.g. water.

The present (nutritional) composition preferably contains between 0.01 and 5 grams of said PDP, more preferably 0.01- 5 grams galacturonic acid oligosaccharide; more preferably between 0.05 and 2 grams per 100 grams dry weight.

The present method preferably comprises the administration of between 0.05 and 10 grams PDP per day, even more preferably between 0.1 and 5 grams PDP per day. Hence in the use according to the invention, preferably between 0.05 and 10 grams PDP is administered per day.

When formulated as a nutritional composition, the present composition preferably contains 5 to 16 en% protein; 35 to 60 en% fat; and 25 to 75 en% carbohydrates, preferably 5 to 12.0 en% protein; 39 to 50 en% fat; and 40 to 55 en% carbohydrates (en% is short for energy percentage and represents the relative amount each constituent contributes to the total caloric value of the preparation). For calculation of the % of total calories for the protein component, the total of energy provided by the proteins, peptides and amino acids needs to be taken into account. This nutritional composition is particularly suitable for feeding to an infant (i.e. an infant formula) because it provides the infant with the required nutrients.

In one embodiment, the composition is preferably an enteral composition suited for elderly and/or hospitalized patients. These subjects are often troubled by reduced appetite or disturbed eating behaviour. For that purpose, it is strived for a composition that is desirably liquid with a sufficiently low viscosity so it can be easily swallowed. In one embodiment of the present invention, the viscosity of the liquid enteral nutritional composition is lower than 500 mPa.s, measured at 20 °C (i.e. room temperature) at a shear rate of 100 s^{-1}, preferably between 10 and 200 mPa.s, more preferably between 10 and 100 mPa.s. The viscosity may suitably be determined using a rotational viscosity meter using a cone/plate geometry. This viscosity is ideal for orally administering the liquid enteral nutritional composition according to the invention because a person may easily consume a serving having a low viscosity such as that displayed by the present invention. This viscosity is also ideal for unit dosages that are tube fed.

The present composition preferably comprises at least one lipid selected from the group consisting of animal lipid (excluding human lipids) and vegetable lipids. Preferably the present composition comprises a combination of vegetable lipids and at least one oil selected from the group consisting of fish oil, animal oil, algae oil, fungal oil, and bacterial oil.

The protein component used in the nutritional preparation are preferably selected from the group consisting of non-human animal proteins (preferably milk proteins, preferably proteins from cow's milk), vegetable proteins (preferably soy protein and/or rice protein), free amino acids and mixtures thereof. The present composition preferably contains casein, whey, hydrolysed casein and/or hydrolysed whey protein. Preferably the protein comprises intact proteins, more preferably intact bovine whey proteins and/or intact bovine casein proteins. As the present composition is preferably suitably for use by infants suffering from allergy, the protein is preferably selected from the group consisting of hydrolyzed milk protein.

The liquid nutritional composition preferably has a caloric density between 0.1 and 2.5 kcal/ml, even more preferably a caloric density of between 0.5 and 1.5 kcal/ml, most preferably between 0.6 and 0.8 kcal/ml.

Particularly the present invention provides a composition as described herein above accompanied with indications (e.g. written material) comprising statement that the administration of the composition prevents or reduces weight loss, or improves weight gain.

Applications

In one embodiment, the invention pertains to the use of said PDP in the manufacture of a composition for the prevention/treatment of infection-induced weight loss, preferably salmonella infection-induced weight loss.

In another embodiment, the invention pertains to the above-described nutritional composition comprising PDP for use in the prevention and/or treatment of infection-induced weight loss, preferably salmonella infection-induced weight loss.

In another embodiment, the invention pertains to a method for preventing and/or treatment infection-induced weight loss, preferably salmonella infection-induced weight loss, in a subject suffering from said infection, or a subject being at risk of said infection, wherein said method involves administering to said subject a nutritional

composition comprising PDP as described above. A subject suffering from salmonella infection includes subjects diagnosed with gastroenteritis, typhoid fever, paratyphoid fever.

The present invention aims to prevent body weight reduction, and perferably aims to increase body weight, preferably in subjects infected with salmonella, and subjects susceptible to salmonella infection, particularly infants and elderly. The subjects susceptible to (i.e. at risk of) salmonella infection include infants, elderly, hospitalized patients, subjects with an impaired health status, particularly malnourished subjects.

In one embodiment, the invention is for prevention of weight loss. In one embodiment the invention is for reducing the risk of weight loss. In one embodiment the invention is for treatment of weight loss.

In one embodiment according to the present invention, the salmonella infection is infection by *Salmonella enteritidis*.

The PDP may be co-administered with antibiotics aiming to treat the infection.

EXAMPLE

Example 1:

In this study it was examined whether dietary intervention with different concentrations of pectin derived acidic oligosaccharides (pAOS) can prevent or reduce weight reduction in an *in vivo Salmonella enteritidis* infection model.

Method: Two concentrations of pectin-derived acidic oligosaccharides (1% and 5% w/w) were tested in a *Salmonella enteritidis* infection model in young male BALB/c mice. Mice (26 per group) were supplemented via the chow with these acidic oligosaccharides during the entire experiment (34 days). After 28 days the mice (20 per group) were challenged with 10^5 cfu of a virulent *Salmonella enteritidis* strain by oral gavage and subsequently sacrificed six days after infection. An infection control group was also included in this study as positive control, receiving standard rodent show (AIN-93G). Weight development was monitored during the entire experiment. After sacrificing the animals, gross weight was measured.

Results and Discussion: *Salmonella enteritidis* infected mice fed with acidic oligosaccharides showed improved health related behavior in a dose dependent manner.

Infection related weight loss was significantly ameliorated in the pAOS supplemented mice.

CLAIMS

1. Use of pectin degradation product (PDP) in the manufacture of a composition for prevention and/or treatment of weight reduction in subjects suffering from salmonella infection or susceptible to salmonella infection.

2. The use according to claim 1, wherein said PDP has a degree of polymerisation (DP) between 2 and 250, preferably between 2 and 100.

3. The use according to claim 1 or 2, wherein said subject infected with salmonella infection or said subjects susceptible to salmonella infection are infants, elderly, hospitalized patients, subjects with an impaired health status, particularly malnourished subjects.

4. The use according to any one of the preceding claims, wherein said PDP comprises uronic acid oligosaccharides, preferably galacturonic acid oligosaccharides.

5. The use according to any one of the preceding claims, wherein said composition contains between 0.01 and 5 grams of said PDP per 100 g dry weight of the composition.

6. The use according to any one of the preceding claims, wherein said composition comprises 5 to 16 en% protein; 35 to 60 en% fat; and 25 to 75 en% carbohydrates.

7. The use according to any one of the preceding claims, wherein between 0.05 and 10 grams PDP with a DP of 2 to 100 is administered per day.

8. The use according to any one of the preceding claims, wherein the subject has an age of 55 years or more.

9. The use according to any one of claims 1-7, wherein the subject has an age of 3 years or less.

10. The use according to any one of the preceding claims , wherein the salmonella infection is infection by *Salmonella enteritidis*.

11. A composition comprising pectin degradation product (PDP) for use in prevention and/or treatment of weight reduction in subjects suffering from salmonella infection or susceptible to salmonella infection.

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2010/050226

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/702 A61K31/715 A61P1/00 A23L1/29
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A23L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/075564 A1 (NUTRICIA NV [NL]; GOEDHART ANNA CHRISTINA [NL]; ALLES MARTINE SANDRA [) 18 June 2009 (2009-06-18) page 22; example 3 claims 1, 2, 6, 11	1-11
X	WO 2009/067000 A1 (NUTRICIA NV [NL]; KNOL JAN [NL]; STAHL BERND [DE]) 28 May 2009 (2009-05-28) page 7, lines 27-31 page 8, lines 25-30 page 12, lines 18-19 claims 1, 2, 6, 9-11	1-11
X	EP 2 130 440 A1 (NUTRICIA NV [NL]) 9 December 2009 (2009-12-09) claims 1-6	1-7,9-11

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2010/050226

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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