US009408879B2

(12) **United States Patent**
Guglielmetti et al.

(10) **Patent No.: US 9,408,879 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **BIFIDOBACTERIUM BIFIDUM STRAINS FOR APPLICATION IN GASTROINTESTINAL DISEASES**

(75) Inventors: **Simone Guglielmetti**, Milan (IT); **Diego Mora**, Milan (IT)

(73) Assignee: **Naturewohl Pharma GmbH**, Graefelfing (DE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 145 days.

(21) Appl. No.: **13/982,932**

(22) PCT Filed: **Jan. 27, 2012**

(86) PCT No.: **PCT/EP2012/051369**

§ 371 (c)(1),
(2), (4) Date: **Nov. 13, 2013**

(87) PCT Pub. No.: **WO2012/104226**

PCT Pub. Date: **Aug. 9, 2012**

(65) **Prior Publication Data**

US 2014/0056852 A1 Feb. 27, 2014

(30) **Foreign Application Priority Data**

Jan. 31, 2011 (EP) 11000744

(51) **Int. Cl.**
A61K 35/74 (2015.01)
A23L 1/30 (2006.01)
A61K 35/745 (2015.01)

(52) **U.S. Cl.**
CPC ***A61K 35/745*** (2013.01); ***A23L 1/3014*** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2009/0274662 A1* 11/2009 Magowan et al. 424/93.4

FOREIGN PATENT DOCUMENTS

EP	1141235	B1	5/2006
EP	1930407	A1	6/2008
EP	2270133	A1	1/2011
RU	2152993	C1	7/2000
RU	2184146	C1	6/2002
WO	WO-2009151329	A1	12/2009

OTHER PUBLICATIONS

Brenner et al. "Bifidobacterium Infantis 35624: A Novel Probiotic for the Treatment of Irritable Bowel Sndrome." Reviews in Gastroenterolgical Disorder vol. 9, No. 1 (2009) pp. 7-15.

Kassinen et al. "The Fecal Microbiota or Irritable Bowel Syndrome Patients Differs Significantly from that of Health Subjects." Gastroenterology 2007; 133:24-33.

Marshall et al. "Intestinal Permeability in Patients with Irritable Bowel Syndrome after a Waterborne Outbreak of Gastroenteritis in Walkerton, Ontario." Aliment Pharmacol Ther 2004; 1317-1322.

Whorwell et al. "Efficacy of an Encapsultated Probiotic Bifidobacterium infantis 35624 in Women with Irritable Bowel Syndrome." Am J Gastroenterol 2006; 101: 1581-1590.

O'Mahony et al. "Lactobacillus and Bifidobacterium in Irritable Bowel Syndrome: Symptom Responses and Relationship to Cytokine Profiles." Gastroenterology 2005;128: 541-551.

Kajander et al. "A Probiotic Mixture Alleviates Symptoms in Irritable Bowel Syndrome Patients: a Controlled 6-Month Intervention." Aliment Pharmacol Ther 2005; 22: 387-394.

Williams et al. "Clinical Trial: a Multi-strain Probiotic Preparation Significantly Reduces Symptoms of Irritable Bowel Syndrome in a Double-Blind Placebo-Controlled Study." Aliment Pharmacol Ther 29, 97-103.

Guyonnet et al. "Effect of a Fermented Milk Containing Bifidobacterium Animalis DN-173 010 on the Health-Related Quality of Life and Sympoms in Irritable Bowel Syndrome in Adults in Primary Care: a Multicentre, Randomized, Double-Blind, Controlled Trial." Aliment Pharmacol Ther 26, 475-486.

Guglielmetti et al. "Implication of an Outer Surface Lipoprotein in Adhesion of Bifidobacterium bifidum to Caco-2 Cells." Applied and Environmental Microbiology, Aug. 2008, p. 4695-4702.

Guglielmetti et al. "Study of the Adhesion of Bifidobacterium bifidum MIMBb75 to Human Intestinal Cell Lines." Curr Microbiol (2009) 59: 167-172.

Preising et al. "Selection of Bifidobacteria Based on Adhesion and Anti-Inflammatory Capacity In Vitro for Amelioration of Murine Colitis." Applied and Environmental Microbiology, May 2010, p. 3048-3051.

Wang et al. "Influence of Cell Surface Properties on Adhesion Ability of Bifidobacteria." World J Microbiol Biotechnol (2010) 26: 1999-2007.

Riedel et al. "Interaction of Bifidobacteria with Caco-2 Cells-Adhesion and Impact on Expression Profiles." International Journal of Food Microbiology 110 (2006) 62-68.

(Continued)

Primary Examiner — Robert Yamasaki

Assistant Examiner — Charles Zoltan Constantine

(74) *Attorney, Agent, or Firm* — Venable LLP; Keith G. Haddaway; Miguel A. Lopez

(57) **ABSTRACT**

The present invention provides a strain of *Bifidobacterium bifidum* or mutant or variant thereof showing at least an adhesion of about 10 bacterial cells per mm2 of epithelial cell monolayer or having at least an adhesion index of 1.5 and a strain of *Bifidobacterium bifidum* or mutant or variant thereof being *Bifidobacterium bifidum* MIMBb75, deposited under deposit No. DSM 24514, or a mutant or variant thereof for use as probiotic, in foodstuff and/or as a medicament. Further provided is a probiotic for mulation, comprising any of the strains, mutants or variants mentioned above, uses of said probiotic formulation, strains, mutants and variants thereof and a method for producing said probiotic formulation.

20 Claims, 8 Drawing Sheets