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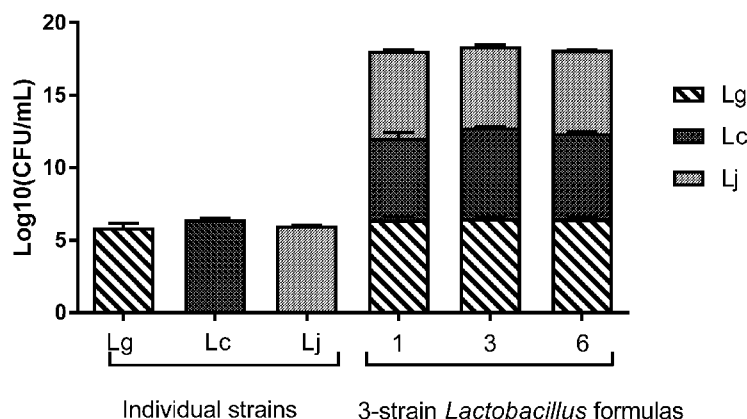
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(54) Title: MEDICINAL VAGINAL *LACTOBACILLUS* COCKTAIL

FIG. 20

Reproducible colonization of cervicovaginal bioengineered tissue (VEC100)



(57) Abstract: Described herein are methods and compositions for the use of treating and/or preventing vaginal bacterial infection and promoting healthy vaginal flora. Aspects of the invention relate to administering to a subject in need thereof a composition comprising a bacterial mixture of *L. crispatus*, *L. gasseri*, and *L. jensenii*.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/41558

## A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61P 13/02, 31/04, 15/02, 31/10, 13/10; A61K 35/744, 35/74, 35/747, 9/20, 33/22, 9/02 (2017.01)

CPC - A61K 35/74, 35/744, 35/747, 9/02, 9/20, 33/22; A23L 33/135; C12R 1/225

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)

See Search History document

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

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	WO 2015/173693 A1 (PIZETA GROUP SRL) 19 November 2015; page 8, 3rd paragraph; page 9, 2nd paragraph; page 9, 3rd paragraph; page 9, 4th paragraph; page 9, 5th paragraph; page 10, 4th paragraph; page 11, 7th paragraph; page 12, 1st paragraph	1, 6, 12-14, 16, 18, 21-22, 26-29, 33-35, 37, 39, 43/1-4, 43/6, 43/12-14, 43/16, 43/18, 43/21-22, 43/26-29, 43/33-35, 43/37, 43/39  2-5, 7-11, 15, 17, 19-20, 23-25, 30-32, 36, 38, 40-42, 43/1-42, 44/1-42, 45/1-42
Y	WO 2016/100086 A1 (THE JOHNS HOPKINS UNIVERSITY) 23 June 2016; page 7, 1st paragraph; page 15, line 30	5, 8-11, 25, 30-32, 41-42, 43/1-6, 43/8-14, 43/16, 43/18, 43/21-22, 43/26-35, 43/37, 43/39, 43/41-42, 44/1-42, 45/5, 45/8-11, 45/25, 45/30-32
Y	US 2013/0171253 A1 (KISS, H et al.) 04 July 2013; paragraphs [0020], [0045]; Tables 1-2, 5	7-11, 25, 30-32, 41-42, 43/7-11, 43/30-32, 43/41-42, 44/7-11, 44/25, 44/30-32, 45/7-11, 45/25,

 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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"E" earlier application or patent but published on or after the international filing date

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"&amp;" document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2006/065873 A2 (POLY-MED, INC.) 22 June 2006; page 7, line 16; page 9, line 8	15, 23, 36, 43/15, 43/23, 43/36, 44/15, 44/23, 44/36, 45/15, 45/23, 45/36
Y	(SAULNIER, DM et al.) Identification of Prebiotic Fructooligosaccharide Metabolism in <i>Lactobacillus plantarum</i> WCFS1 through Microarrays. <i>Applied and Environmental Microbiology</i> . March 2007; Vol. 73, No. 6, pages 1753-1765; page 1755, 2nd column, 2nd paragraph; DOI: 10.1128/AEM.01151-06	17, 38, 43/17, 43/38, 44/17, 44/38, 45/17, 45/38
Y	(FICHOROVA, RN et al.) Novel Vaginal Microflora Colonization Model Providing New Insight into Microbicide Mechanism of Action. <i>mBio</i> . 25 October 2011; Vol. 2, No. 6, pages 1-10; page 1, 1st column, 1st paragraph; page 3, 1st column, 2nd paragraph; page 4, 2nd column, 2nd paragraph; DOI: 10.1128/mBio.00168-11.	19, 24, 40, 42, 43/19, 43/24, 43/40, 43/42, 44/19, 44/24, 44/40, 44/42, 44/42, 45/19, 45/24, 45/40, 45/42
Y	(SANDRINI, MPB et al.) Deoxyribonucleoside Kinases Activate Nucleoside Antibiotics in Severely Pathogenic Bacteria. <i>Antimicrobial Agents and Chemotherapy</i> . August 2007; Vol. 51, No. 8, pages 2726-2732; page 2728, 1st column, 2nd paragraph; Table 1 DOI: 10.1128/AAC.00081-07	20, 41, 43/20, 43/41, 44/20, 44/41, 45/20, 45/41
Y	US 2008/0274162 A1 (NESSA, JB et al.) 06 November 2008; paragraph [0013]	45/1-42
Y	WO 2015/067141 A1 (SUZHOU OSEL BIO PHARM CO LTD) 14 May 2015; abstract; page 8, 3rd paragraph	2, 43/2, 44/2, 45/2
Y	(PAVLOVA, SI et al.) Genetic diversity of vaginal lactobacilli from women in different countries based on 16S rRNA gene sequences. <i>Journal of Applied Microbiology</i> . 2002; Vol. 92, pages 451-459; page 451, 2nd column, 2nd paragraph; page 453, 1st column, 4th paragraph; supplemental data	3-4, 43/3-4, 44/3-4, 45/3-4
A	(ATCC) <i>Salmonella enterica</i> subsp. <i>enterica</i> (ex Kauffmann and Edwards) Le Minor and Popoff serovar Typhimurium (ATCC(R) 6994(TM)). Website [online]. 2005 [Retrieved on 1 December 2017]. Retrieved from the Internet: <URL: <a href="https://www.atcc.org/Products/All/6994.aspx">https://www.atcc.org/Products/All/6994.aspx</a> >	2, 26
P, X	WO 2017/035412 A1 (KALEIDO BIOSCIENCES, INC.) 02 March 2017; entire document	1-42, 43/1-42, 44/1-42, 45/1-42

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US17/41558

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.: 46-65  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

\*\*\*-Please See Supplemental Page-\*\*\*

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-45

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

\*\*\*-Continued from Box No. III: Observations where unity of invention is lacking-\*\*\*

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, Claims 1-45 are directed toward a composition for promoting a healthy human vaginal microbiota balance.  
Group II, Claims 66-69 are directed toward a method of isolating a bacterial strain.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include a composition for promoting a healthy human vaginal microbiota balance, not present in Group II; the special technical features of Group II include a method of isolating a bacterial strain, not present in Group I.

Groups I and II share the technical features including: Lactobacillus species present in a healthy human vaginal microbiota.

However, these shared technical features are previously disclosed by the publication entitled 'Novel Vaginal Microflora Colonization Model Providing New Insight into Microbicide Mechanism of Action' by 'Fichorova', et al. (hereinafter 'Fichorova').

Fichorova discloses Lactobacillus species present in a healthy human vaginal microbiota (a healthy human vaginal microbiota; page 7, second column, second paragraph).

Since none of the special technical features of the Groups I and II inventions are found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Fichorova reference, unity of invention is lacking.