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(54) Title: COMPOSITIONS COMPRISING HYDROXYCINNAMIC ACID AND RELATED CONJUGATES, ANALOGUES AND DERIVATIVES, AND METHODS OF USE THEREOF

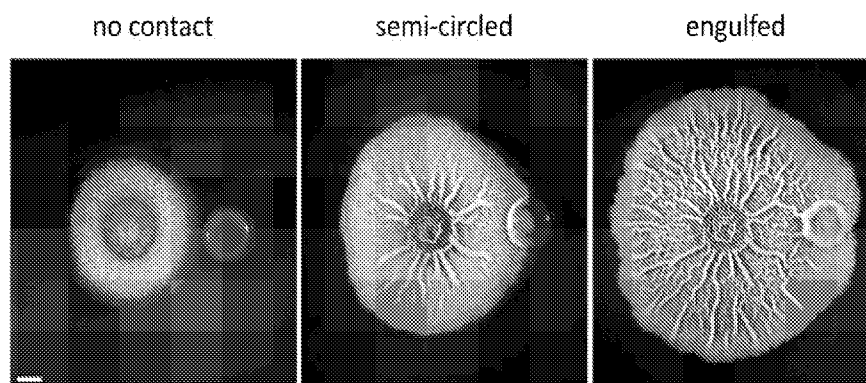


FIGURE 4

(57) Abstract: The present invention provides anti-microbial compositions comprising a hydroxycinnamic acid and related conjugates, analogues and derivatives, and methods of use thereof for enhancing production of anti-microbial agents in bacteria as well as for protecting plants from microbial infection.



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2018/050744

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N1/38 C12P13/00 A01N37/10 C07C51/42
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)
C12N A01N C07C C12P

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 practicable, 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	NADIA PONTS ET AL: "Cinnamic-Derived Acids Significantly Affect Fusarium graminearum Growth and In Vitro Synthesis of Type B Trichothecenes", PHYTOPATHOLOGY, vol. 101, no. 8, 1 August 2011 (2011-08-01), pages 929-934, XP055520639, US ISSN: 0031-949X, DOI: 10.1094/PHYTO-09-10-0230 the whole document ----- -/-	1-5, 7-12, 34-38



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

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

"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)

"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

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search

19 November 2018

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2018/050744

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.:
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:

see additional sheet

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 an 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.:

1-5(completely); 7-12, 34-38(partially)

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.

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2018/050744

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZHOU TAN-CHE ET AL: "Production of validamycin A from hemicellulose hydrolysate by <i>Streptomyces hygroscopicus</i> 5008", BIORESOURCE TECHNOLOGY, vol. 175, 20 October 2014 (2014-10-20), pages 160-166, XP029098254, ISSN: 0960-8524, DOI: 10.1016/J.BIORTECH.2014.10.051 the whole document	1
A	----- GU YIAN ET AL: "Pathogen invasion indirectly changes the composition of soil microbiome via shifts in root exudation profile", BIOLOGY AND FERTILITY OF SOILS, SPRINGER BERLIN HEIDELBERG, BERLIN/HEIDELBERG, vol. 52, no. 7, 27 July 2016 (2016-07-27), pages 997-1005, XP036057098, ISSN: 0178-2762, DOI: 10.1007/S00374-016-1136-2 [retrieved on 2016-07-27] the whole document	1-5, 7-12, 34-38
A	----- D. BURTIN ET AL: "Polyamines, Hydroxycinnamoylputrescines, and Root Formation in Leaf Explants of Tobacco Cultivated in Vitro: Effects of the Suicide Inhibitors of Putrescine Synthesis", PLANT PHYSIOLOGY, vol. 93, no. 4, 1 August 1990 (1990-08-01), pages 1398-1404, XP055520620, Rockville, Md, USA ISSN: 0032-0889, DOI: 10.1104/pp.93.4.1398 the whole document	1-5, 7-12, 34-38
A	----- J MARTIN TANGUY: "The occurrence and possible function of hydroxycinnamoyl acid amides in plants", PLANT GROWTH REGULATION, SPRINGER, DORDRECHT, NL, [Online] vol. 3, no. 3, 1 January 1985 (1985-01-01), pages 381-399, XP009509079, ISSN: 0167-6903, DOI: 10.1007%2FBBF00117595 Retrieved from the Internet: URL:https://link.springer.com/article/10.1007%2FBBF00117595> the whole document ----- -/--	1-5, 7-12, 34-38

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2018/050744

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BEN FAN ET AL: "Transcriptomic profiling of <i>Bacillus amyloliquefaciens</i> FZB42 in response to maize root exudates", BMC MICROBIOLOGY, BIOMED CENTRAL LTD, GB, vol. 12, no. 1, 21 June 2012 (2012-06-21), page 116, XP021115231, ISSN: 1471-2180, DOI: 10.1186/1471-2180-12-116 page 6; table 3 -----	1-5, 7-12, 34-38
A	CAIRN S. ELY ET AL: "Bacteria from wheat and cucurbit plant roots metabolize PAHs and aromatic root exudates: Implications for rhizodegradation", INTERNATIONAL JOURNAL OF PHYTOREMEDIATION, vol. 19, no. 10, 20 March 2017 (2017-03-20), pages 877-883, XP055520228, US ISSN: 1522-6514, DOI: 10.1080/15226514.2017.1303805 the whole document -----	1-5, 7-12, 34-38
A	ARGUELLES-ARIAS ANTHONY ET AL: " <i>Bacillus amyloliquefaciens</i> GA1 as a source of potent antibiotics and other secondary metabolites for biocontrol of plant pathogens", MICROBIAL CELL FACTORIES,, vol. 8, no. 1, 26 November 2009 (2009-11-26), page 63, XP021063197, ISSN: 1475-2859, DOI: 10.1186/1475-2859-8-63 the whole document -----	1-5, 7-12, 34-38

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5(completely); 7-12, 34-38(partially)

A method of synthesizing an antimicrobial agent in a bacterium or activating a pks gene operon in a bacterium by administration of a hydroxycinnamic acid.

2. claims: 6, 13, 14(completely); 7-12, 28-38(partially)

A method for enhancing extracellular matrix production in a bacterium or for inducing, enhancing or maintaining biofilm formation by a beneficial rhizobacterium on a plant, by administration of a hydroxycinnamic acid.

3. claims: 15-27(completely); 28-38(partially)

A method for increasing resistance to disease in a plant, treating a disease in a plant or suppressing the growth or survival of a biological agent on or near a plant, by administration of a hydroxycinnamic acid

4. claims: 39-43

A method for isolating caffeoyl putrescine from the root or root exudate of a plant.

5. claims: 44-50

A composition comprising a mixture of a hydroxycinnamic acid and a polyamine.
