Abstract:

Agents:

Also provided are combinations that comprise at least one phenolic phytochemical and at least one antimicrobial agent that inhibit the growth of an established biofilm. Further, the present invention provides methods for inhibiting the formation and growth of biofilms.
INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/55119

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01 N 59/02 (201 2.01 )
USPC - 424/714
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)
USPC: 424/714

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)
PubWEST(USPT,PGP8,EPAB,JPAB); Google Web; Google Patents
Search Terms: biofilm, polyphenolic, ellagic, partitioned, water, hexane, ethyl acetate, butanol, methanol, dichloromethane, chromatography, alcohol, sapogenin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>US 6,352,727 B1 (Takahashi) 05 March 2002 (05.03.2002) col 3, in 20-25; col 4, in 15-48; col 6, in 20-49; col 7, in 4-8; col 8, in 63-67; col 9, in 12-17; col 30, in 50 to col 31, in 10</td>
<td>1-10, 20-31</td>
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<td>Y</td>
<td>US 2010/0173860 A1 (Seeram et al.) 08 July 2010 (08.07.2010) para [0005]; [0012]; [0022]-[0023]; [0064]</td>
<td>2-5, 21-24</td>
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</table>

Further documents are listed in the continuation of Box C.

* 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 prior 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

Date of the actual completion of the international search
8 May 2012 (08.05.2012)

Date of mailing of the international search report
18 MAY 2012

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-3201

Authorized officer:
Lee W. Young
PCT Helpdesk: 571-272-4300
PCT OIS: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)
**INTERNATIONAL SEARCH REPORT**

<table>
<thead>
<tr>
<th>Box No. II</th>
<th>Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)</th>
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<tbody>
<tr>
<td></td>
<td>This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:</td>
</tr>
<tr>
<td>1. □</td>
<td>Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:</td>
</tr>
<tr>
<td>2. □</td>
<td>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:</td>
</tr>
<tr>
<td>3. ☑</td>
<td>Claims Nos.: 12, 17, 34, 39 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).</td>
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<table>
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<th>Box No. III</th>
<th>Observations where unity of invention is lacking (Continuation of item 3 of first sheet)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>This International Searching Authority found multiple inventions in this international application, as follows:</td>
</tr>
<tr>
<td></td>
<td>-See Extra Sheet-</td>
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</tbody>
</table>

| 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.: 1-10, 20-31 |

**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.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)
INTERNATIONAL SEARCH REPORT

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 1-10, 20-31 directed to a polyphenolic composition prepared by a process comprising:

a) partitioning an alcohol extract of a plant with a mixture of water and hexane to form a first water partition and a hexane partition;
b) partitioning the first water partition with a mixture of water and ethyl acetate to form a second water partition and an ethyl acetate partition;
c) partitioning the second water partition with a mixture of water and butanol to form a third water partition and a butanol partition; and
d) fractionating the butanol partition by column chromatography with a mobile phase comprising a mixture of methanol and dichloromethane, wherein the polyphenolic composition is eluted by the mobile phase in which the volume ratio of methanol to dichloromethane is about 40:60.

Group II: claims 11, 13-16, 18, 19 directed to a combination comprising at least one phenolic phytochemical and at least one antimicrobial agent.

Group III: claims 32-33, 35-38, 40-43 directed to a method for inhibiting growth of an established biofilm, the method comprising contacting the biofilm with at least one phenolic phytochemical and at least one antimicrobial agent such that the biofilm has a reduced number of microorganisms.

The inventions listed as Groups I-III 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 technical features for the following reasons:

Group I does not include the antimicrobial agent of groups II and III.

Groups I and II do not include the inhibiting growth of an established biofilm of group III.

Groups II and III do not include the polyphenolic composition prepared by the process of group I.

The common features of groups I, II and III of a composition comprising a phenolic compound and the common features of groups II and III of a phenolic phytochemical and antimicrobial agent are taught by US 2006/0018842 A1 (Blumenthal) (para [0014]); 'Efficient delivery of anti-cancer and anti-microbial phytochemicals to subjects can be accomplished with a controlled release composition, or a composition comprising combinations of phytochemicals...composition of the invention thus comprises one or more phytochemicals and a pharmaceutically acceptable controlled release carrier. The composition of the invention can also comprise phytochemicals in a particular combination'; [0024]-[0025]; claim 10; para [0028]; 'The compositions of the invention can comprise combinations of phytochemicals... For example, a composition of the invention can comprise pulverized, powdered or dried green tea, pulverized, powdered or dried white tea, and individual EGCG... - Note that these three components are all phenolic phytochemicals (see para [0025]) and they are also antimicrobial agents (see para [0024] & Table 1), so the composition contains both a phenolic phytochemical and an antimicrobial agent; therefore the common feature is not an improvement over the prior art.

None of these technical features are common to the other groups, nor do they correspond to a special technical feature in the other groups. Therefore, unity of invention is lacking.