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(51) International Patent Classification:
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(54) Title: COMPOSITIONS AND METHODS FOR IMPROVING MITOCHONDRIAL FUNCTION AND TREATING NEURODEGENERATIVE DISEASES AND COGNITIVE DISORDERS

(57) Abstract: Provided are compositions comprising compounds or precursors to compounds which may be used for a variety of therapeutic applications including, for example, treating and/or preventing a disease or disorder related to reduced mitochondrial activity, including aging or stress, diabetes, obesity, and neurodegenerative diseases. The compounds relate generally to urolithins and precursors thereof, including but not limited to ellagitannins and urolithin A. In certain embodiments the compositions are presented in or as food products or nutritional supplements. These same compounds and compositions can also be used advantageously in generally healthy individuals to increase or maintain metabolic rate, decrease percent body fat, increase or maintain muscle mass, manage body weight, improve or maintain mental performance (including memory), improve or maintain muscle performance, improve or maintain mood, and manage stress.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. A23L1/30 A61K31/352 A61K36/00 A61K36/185

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 practicable, search terms used)

EPO-Internal, WPI Data, FSTA, EMBASE, BIOSIS

**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>
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* 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 (e.g. an official report, an academic treatise) containing general background art which is not technically comparable to the inventive concept of the document cited but which is considered useful for a further understanding of the principle or theory underlying the invention.

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

**Date of the actual completion of the international search**

16 April 2012

**Date of mailing of the international search report**

25/07/2012

**Name and mailing address of the ISA/Authorized officer**

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk

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Korb, Margit

Form PCT/ISA210 (second sheet) (April 2003)
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### 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:

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see additional sheet
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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.:

   6, 7, 9-11, 25-29, 31, 32 (completely); 1-5, 8, 20, 30, 58-80 (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.
This International Search Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 6, 7, 9-11, 25-29, 31, 32 (completely); 1-5, 8, 20, 30, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagitannin or punicalagin or ellagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting of obesity, diabetes mellitus, cardi ovascular disease, hyperlipidemia, and its method.

2. Claims: 12, 33-36 (completely); 1-5, 20, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagitannin or punicalagin or ellagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting neurodegenerative disease, and its method.

3. Claims: 13, 41-45 (completely); 1-5, 20, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagitannin or punicalagin or ellagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting of cognitive disorder, and its method.

4. Claims: 14, 46-48 (completely); 1-5, 20, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagitannin or punicalagin or ellagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting of mood disorder, and its method.

5. Claims: 15 (completely); 1-5, 20 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagitannin or punicalagin or ellagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting of stress, and its method.
6. claims: 16, 49-52 (completely); 1-5, 20, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagic tannin or punicalagic acid or urolithin for the treatment or prevention of a condition selected from the group consisting of anxiety disorder, and its method.

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7. claims: 17 (completely); 1-5, 20 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagic tannin or punicalagic acid or urolithin to increase muscle performance, and its method.

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8. claims: 18, 54, 55 (completely); 1-5, 20, 58-80 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagic tannin or punicalagic acid or urolithin to increase mental performance, and its method.

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9. claims: 19 (completely); 1-5, 20 (partially)

A food product or nutritional supplement comprising an effective amount of pomegranate extract or the specific compound ellagic tannin or punicalagic acid or urolithin to increase mental performance, and its method.

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10. claims: 21, 22 (completely); 58-80 (partially)

A method of increasing or maintaining mitochondrial function, comprising: contacting cells with an effective amount of urolithin or a precursor thereof, to increase function of the mitochondria; and a method of treating, preventing, or managing a mitochondrial-related disease or condition associated with altered mitochondrial function or a reduced mitochondrial density, comprising: administering to a subject in need thereof a therapeutically effective amount of urolithin or a precursor thereof, to treat the disease or condition associated with altered mitochondrial function or reduced mitochondrial density.

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11. claims: 37-40 (completely); 58-80 (partially)

A method of improving cognitive function, comprising: administering to a subject in need thereof an effective amount of urolithin or a precursor thereof, to improve cognitive function.
FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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12. claims: 53 (completely) ; 58-80 (partially)

A method of treating a musculoskeletal disorder, comprising: administering to a subject in need thereof a therapeutically effective amount of a urolithin or a precursor thereof, to improve muscle function.

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13. claims: 56, 57 (completely) ; 58-80 (partially)

A method of promoting nerve outgrowth, comprising: contacting a nerve cell with an effective amount of a urolithin or a precursor thereof, to promote nerve outgrowth.

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