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60/126,489 26 March 1999 (26.03.1999) US
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- (72) Inventors; and
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



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(54) Title: COMPOSITIONS OF CHROMIUM OR VANADIUM WITH ANTIDIABETICS FOR GLUCOSE METABOLISM DISORDERS

(57) Abstract: Compositions and methods of using the same for the treatment of diabetes and other disorders of glucose metabolism are provided. Compositions may include an anti-diabetic agent and one or more of a bioavailable source of chromium and vanadium.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/555 A61K33/24 A61K31/64 A61K31/155 A61K31/425

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)

IPC 7 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 practical, search terms used)

EMBASE, CHEM ABS Data, MEDLINE, BIOSIS, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>MCCARTY M F: "Complementary measures for promoting insulin sensitivity in skeletal muscle." MEDICAL HYPOTHESES, (1998) 51 (6) 451-64. REF: 193, XP000908774 abstract page 455, column 2 -page 456 page 458, column 2, paragraph 4 -page 459 ---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
X	<p>PERFETTI R. ET AL: "Novel therapeutic strategies for the treatment of Type 2 diabetes." DIABETES/METABOLISM REVIEWS, (1998) 14/3 (207-225)., XP000908775 page 217 -page 218 ---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
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Further documents are listed in the continuation of box C.



Patent family members are listed in 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 document 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

10 July 2000

Date of mailing of the international search report

22. 12. 00

Name and mailing address of the ISA

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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.
X	<p>AMOIKON, 3. K. ET AL: "Effect of chromium tripicolinate on growth, glucose tolerance, insulin sensitivity, plasma metabolites, and growth hormone in pigs" J. ANIM. SCI. (1995), 73(4), 1123-30, XP000901969 abstract</p> <p style="text-align: center;">---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
Y	<p>GREGORY BOYD, S. ET AL: "Combined dietary chromium picolinate supplementation and an exercise program leads to a reduction of serum cholesterol and insulin in college-aged subjects" J. NUTR. BIOCHEM. (1998), 9(8), 471-475, XP000901822 abstract</p> <p style="text-align: center;">---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
Y	<p>SPEARS, J. W. (1): "Reevaluation of the metabolic essentiality of the minerals: Review." ASIAN-AUSTRALASIAN JOURNAL OF ANIMAL SCIENCES, (SEPT., 1999) VOL. 12, NO. 6, PP. 1002-1008., XP000901962 abstract page 1004 -page 1006</p> <p style="text-align: center;">---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
E	<p>US 5 980 905 A (DE LA HARPE JON ET AL) 9 November 1999 (1999-11-09) abstract</p> <p style="text-align: center;">---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
E	<p>US 5 962 030 A (FINE STUART A) 5 October 1999 (1999-10-05) column 10; claims 1,15,26,28,44</p> <p style="text-align: center;">---</p>	<p>1-7, 16-25, 34-49, 58-96</p>
X,P	<p>WO 98 42211 A (PROGRESSIVE RESEARCH LABS) 1 October 1998 (1998-10-01) abstract claims 1-4,16,24-26; example 1</p> <p style="text-align: center;">-----</p>	<p>1-7, 16-25, 34-49, 58-96</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/21377

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 II Observations where unity of invention is lacking (Continuation of item 2 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 fee, this Authority did not invite payment of any additional fee.

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.:

See annex

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 6,7,24,25,41,49,57,62,73,78 complete, 1-5,16-23, 34-48,52-56,58-61,63-72,74-77,79-96 partially

Pharmaceutical composition comprising insulin or metformin and a bioavailable source of chromium or vanadium and optionally Mg, aspirin and/or vitamin E. Formulations, methods and kits using said combination.

2. Claims: 10,11,28,29,50,51 complete, 1-5,16-23,34-48,52-56, 58-61,63-72,74-77,79-96 partially

Pharmaceutical composition comprising a thiazolidinedione and a bioavailable source of chromium or vanadium and optionally Mg, aspirin and/or vitamin E. Formulations, methods and kits using said combination.

3. Claims: 8, 9,26,27 complete, 1-5,16-23,34-48,52-56,58-61, 63-72,74-77,79-96 partially

Pharmaceutical composition comprising a sulfonyleurea and a bioavailable source of chromium or vanadium and optionally Mg, aspirin and/or vitamin E. Formulations, methods and kits using said combination.

4. Claims: 14,15,32,33 complete, 1-5,16-23,34-48,52-56,58-61, 63-72,74-77,79-96 partially

Pharmaceutical composition comprising a benzoic acid derivative and a bioavailable source of chromium or vanadium and optionally Mg, aspirin and/or vitamin E. Formulations, methods and kits using said combination.

5. Claims: 12,13,30,31 complete, 1-5,16-23,34-48,52-56,58-61, 63-72,74-77,79-96 partially

Pharmaceutical composition comprising an alpha-glucosidase inhibitor and a bioavailable source of chromium or vanadium and optionally Mg, aspirin and/or vitamin E. Formulations, methods and kits using said combination.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ ~~306~~ 210

Continuation of Box 3.

Claims Nos.: 1-96

Present claims relate to compositions/compounds defined by reference to desirable characteristics or properties, namely "antidiabetic agent", "bioavailable source of chromium", "bioavailable source of vanadium". The claims cover all compositions/compounds having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compositions/compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound/composition by reference to a result to be achieved (antidiabetic agent; reduction of initial Hb1Ac levels). Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search for the first invention has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compositions/compounds used in the examples and those specifically mentioned in the claims with due regard to the general idea underlying the present application. Example 3 refers to certain tables not present in the application as filed and therefore has not been considered for the purpose of the search.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/21377

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5980905 A	09-11-1999	US 6100250 A	08-08-2000
		US 5905075 A	18-05-1999
		AU 4724999 A	21-03-2000
		WO 0012095 A	09-03-2000
		US 6100251 A	08-08-2000
		FR 2782640 A	03-03-2000
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		AU 6768998 A	20-10-1998
		GB 2338187 A	15-12-1999
