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(71) Applicants (for all designated States except US): **MUTUAL PHARMACEUTICAL COMPANY, INC.** [US/US]; 1100 Orthodox Street, Philadelphia, Pennsylvania 19124 (US). **SUN, Tong** [CN/US]; 3903 Buxmont Road, Marlton, New Jersey 08053 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **NIELSEN, Kurt, R.** [US/US]; 9 Feldspar Drive, Chadds Ford, Pennsylvania 19317 (US). **MANCHANDA, Rajesh** [US/US]; 522 Yale Avenue, Morton, Pennsylvania 19070 (US). **WATSON, Shawn, G.** [US/US]; 131 Ashford Road, Cherry Hill, New Jersey 08003 (US).

(74) Agent: **PELLETIER, Roberta, L.**; Cantor Colburn LLP, 20 Church Street, 22nd Floor, Hartford, Connecticut 06103 (US).

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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:
10 November 2011



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(54) Title: THIOCOLCHICINE AND COLCHICINE ANALOGS, METHODS OF MAKING AND METHODS OF USE THEREOF

(57) Abstract: Disclosed herein are thiocholchicine and colchicine analogs and derivatives suitable for use as a muscle relaxant, an anti-inflammatory agent, an anti-gout agent, an anti-proliferative agent, or an anti-cancer agent; methods of making the compounds, and compositions comprising the compounds.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2011/021826

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07C391/00
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)

C07C

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)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PASSARELLA D ET AL: "Inhibitors of tubulin polymerization: Synthesis and biological evaluation of hybrids of vindoline, anhydrovinblastine and vinorelbine with thiocolchicine, podophyllotoxin and baccatin III", BIOORGANIC & MEDICINAL CHEMISTRY, PERGAMON, GB, vol. 16, no. 11, 1 June 2008 (2008-06-01), pages 6269-6285, XP022700357, ISSN: 0968-0896, DOI: DOI:10.1016/J.BMC.2008.04.025 [retrieved on 2008-05-28] figure 1 ----- -/--	1-4, 11-15

 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 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

24 May 2011

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Pérez Carlón, Raquel

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2011/021826

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>TRELLU, FILALI-ANSARY, FRANÇON, ADAM, LLUEL, DUBRUCK, THÉNOT: "New metabolic and pharmacokinetic characteristics of thiocolchicoside and its active metabolite in healthy humans", FUNDAMENTAL AND CLINICAL PHARMACOLOGY, vol. 18, 2004, pages 493-501, XP002638435, figure 3; compound TCC</p> <p style="text-align: center;">-----</p>	1-4, 11-15
A	<p>LEYNADIER D ET AL: "Selenium: Inhibition of microtubule formation and interaction with tubulin", CHEMICO-BIOLOGICAL INTERACTIONS, ELSEVIER SCIENCE IRLAND, IR, vol. 79, no. 1, 1 January 1991 (1991-01-01), pages 91-102, XP023831395, ISSN: 0009-2797, DOI: DOI:10.1016/0009-2797(91)90055-C [retrieved on 1991-01-01] abstract</p> <p style="text-align: center;">-----</p>	1-4, 11-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/021826

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.:

1-4, 11-15(all 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is SeR1 (option A) in claim 1, in part)

2. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is TeR1 (option A) in claim 1, in part)

3. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is PoR1 (option A) in claim 1, in part)

4. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is P(R2) (option A) in claim 1, in part)

5. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is N(R3)2 (option A) in claim 1, in part)

6. claims: 1-4, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G1 is Si(R4)3 (option A) in claim 1, in part)

7. claims: 5, 6(completely); 1, 2, 11-15(partially)

Colchicine and thiocolchicine analogues which bear a polyethylenglycol side chain -L-PEG (option B) in claim 1)

8. claims: 7, 8(completely); 1, 2, 11-15(partially)

Colchicine and thiocolchicine analogues in which the central seven member ring in the center of the structure bears two substituents (option C) in claim 1)

9. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is OH

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(option D) in claim 1, in part)

10. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is ORa
(option D) in claim 1, in part)

11. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is SRa
(option D) in claim 1, in part)

12. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is
heterocycloalkyl, aryl, heteroaryl (option D) in claim 1, in
part)

13. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is a
carbohydrate group linked via an O- N- or S- glycosidic bond
(option D) in claim 1, in part)

14. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is
N(Rb)₂, and one Rb is alkyl (option D) in claim 1, in part)

15. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is
N(Rb)₂, and one Rb is alkenyl (option D) in claim 1, in
part)

16. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is
N(Rb)₂, and one Rb is cycloalkyl, aryl, heteroaryl or
heterocycloalkyl (option D) in claim 1, in part)

17. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is
N(Rb)₂, and one Rb is haloalkyl (option D) in claim 1, in
part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

18. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is N(Rb)₂, and one Rb is alkoxy carbonyl (option D) in claim 1, in part)

19. claims: 1, 2, 9, 11-15(all partially)

Colchicine and thiocolchicine analogues in which G2 is N(Rb)₂, and Rb is alkanoyl different from acetyl (option D) in claim 1, in part)

20. claims: 10(completely); 11-15(partially)

Colchicine and thiocolchicine analogues bearing an additional condensed ring.
