

EP 2456772

The examination is being carried out on the **following application documents**

**Description, Pages**

1-80 as published

**Claims, Numbers**

1-9 received on 31-07-2014 with letter of 31-07-2014

**Drawings, Sheets**

1/31-31/31 as published

Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure.

- D1 WO 2006/022502 A1 (HERBIO INC [KR]; LIM JONG SOON [KR]; LEE SANG IK [KR]) 2 March 2006 (2006-03-02)
- D2 WASSEEM ROCK ET AL: "Consumption of Wonderful Variety Pomegranate Juice and Extract by Diabetic Patients Increases Paraoxonase 1 Association with High-Density Lipoprotein and Stimulates Its Catalytic Activities", JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, vol. 56, no. 18, 24 September 2008 (2008-09-24), pages 8704-8713, XP55049536, ISSN: 0021-8561, DOI: 10.1021/jf801756x
- D3 WO 2005/089066 A2 (RIMONEST LTD [IL]; LANSKY EPHRAIM [IL]) 29 September 2005 (2005-09-29)
- D4 JP 2009 102288 A (HARUNIRE BIO KENKYUSHO KK; JAPAN SCIENCE & TECH AGENCY; UNIV TOKYO AGR) 14 May 2009 (2009-05-14)
- D5 MICHAEL AVIRAM ET AL: "Pomegranate Phenolics from the Peels, Arils, and Flowers Are Antiatherogenic: Studies in Vivo in Atherosclerotic Apolipoprotein E-Deficient (E 0 ) Mice and in Vitro in Cultured Macrophages and Lipoproteins", JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY,

- vol. 56, no. 3, 1 February 2008 (2008-02-01), pages 1148-1157,  
XP55049801,  
ISSN: 0021-8561, DOI: 10.1021/jf071811q
- D6 WO 2008/080162 A2 (UNIV JOHNS HOPKINS [US]; MERLION  
PHARMACEUTICAL PTC LTD [SG]; CHATTERJ) 3 July 2008 (2008-07-03)
- D7 WO 2009/031023 A2 (PROBELTE PHARMA S A [ES]; LOPEZ MAS JOSE A  
[ES]; STREITENBERGER SERGIO) 12 March 2009 (2009-03-12)
- D8 IKURO ABE ET AL: "Ellagitannins and Hexahydroxydiphenoyl Esters as  
Inhibitors of Vertebrate Squalene Epoxidase",  
JOURNAL OF NATURAL PRODUCTS,  
vol. 64, no. 8, 1 August 2001 (2001-08-01), pages 1010-1014, XP55049800,  
ISSN: 0163-3864, DOI: 10.1021/np010100y
- D9 WO 2006/127832 A2 (POM WONDERFUL LLC [US]; BATES BYRON [US];  
FRITZ ERICH A [US]; HENIG YA) 30 November 2006 (2006-11-30)
- D10 DAVID J LOREN ET AL: "Maternal Dietary Supplementation with  
Pomegranate Juice Is Neuroprotective in an Animal Model of Neonatal  
Hypoxic-Ischemic Brain Injury",  
PEDIATRIC RESEARCH,  
vol. 57, no. 6, 1 June 2005 (2005-06-01), pages 858-864, XP055049958,  
ISSN: 0031-3998, DOI: 10.1203/01.PDR.0000157722.07810.15
- D11 HYE-MIN KWAK ET AL: "[beta]-Secretase(BACE1) inhibitors from  
pomegranate (Punica granatum) husk",  
ARCHIVES OF PHARMACAL RESEARCH,  
vol. 28, no. 12, 1 December 2005 (2005-12-01), pages 1328-1332,  
XP055049960,  
ISSN: 0253-6269, DOI: 10.1007/BF02977896
- D12 HARTMAN R E ET AL: "Pomegranate juice decreases amyloid load and  
improves behavior in a mouse model of Alzheimer's disease",  
NEUROBIOLOGY OF DISEASE, BLACKWELL SCIENTIFIC  
PUBLICATIONS, OXFORD, GB,  
vol. 24, no. 3, 1 December 2006 (2006-12-01), pages 506-515,  
XP024901473,  
ISSN: 0969-9961, DOI: 10.1016/J.NBD.2006.08.006  
[retrieved on 2006-12-01]

D13 DATABASE MEDLINE [Online]

US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 2008,  
KUMAR SOKINDRA ET AL: "Protective effects of Punica granatum seeds  
extract against aging and scopolamine induced cognitive impairments in  
mice.",

Database accession no. NLM20162041 ; & KUMAR SOKINDRA ET AL:  
"Protective effects of Punica granatum seeds extract against aging and  
scopolamine induced cognitive impairments in mice.",

AFRICAN JOURNAL OF TRADITIONAL, COMPLEMENTARY, AND  
ALTERNATIVE MEDICINES : AJTCAM / AFRICAN NETWORKS ON  
ETHNOMEDICINES 2008,

vol. 6, no. 1, 2008, pages 49-56,

ISSN: 0189-6016

1 The third-party observations have been taken into account.

1.1 It is not contested that punicalin is a pomegranate phenolic, i.e. a phenolic  
constituent of pomegranate (*Punica granatum* Linn., Cf. e.g. D5). It is to be  
noted that none of the third party submissions specifically mention the  
compound Punicalin. The different therapeutic uses of pomegranate disclosed  
in the third party observations are acknowledged.

2 The present application does not meet the requirements of Article 52(1) EPC,  
because the subject-matter of claims 1-3,5-7,9 is not new in the sense of  
Article 54(1), (2) and (3) EPC:

2.1 D9 discloses the subject-matter of claims 1,2,4-8, i.e. pharmaceutical and  
nutraceutical compositions comprising Punicalin as active ingredient that are  
useful to treat diabetes, Alzheimer's disease and dementia. See paragraph  
[0012], [0022], [0024], [0033], [0043], example 2, table 1. The compound is  
disclosed to have antioxidant properties. Even if the concentration of Punicalin  
in D9 table 1 is lower than of punicalagin, the antioxidant and therapeutic  
activity is recognized for Punicalin. Accordingly no novelty of said claims  
exists because the activity of punicalin is disclosed. Accordingly, it appears  
credible that this compound is useful for treating diabetes, Alzheimer's  
disease and dementia, in particular in view of the fact that antioxidants, in  
particular *Punica granatum* extracts are known to reverse age induced or  
scopolamine induced retention deficits and cognitive impairment in mice. See  
for example D12 (Hartman et al.), which discloses that Mice treated with  
Pomegranate juice had significantly less (approximately 50%) accumulation of  
soluble Abeta42 and amyloid deposition in the hippocampus as compared to  
control mice.

Furthermore, D13 discloses that Punica granatum preparations could be protective in the treatment of cognitive disorders such as dementia and Alzheimer's disease. The applicant objection that D13 refers to Punica granatum seeds is acknowledged, However, D5 does not allow to conclude that the seeds do not contain Punicalin. D5 concludes that the fraction POMa which contains the seeds and arils also contains punicalin (see table 1 and comment referring thereto).

- 2.2 D10 discloses the neuroprotective properties of Pomegranate juice.
- 3 Should the applicant overcome the above raised objections of lack of novelty, an inventive step has to be demonstrated over D9, D12, D13 as the present claimed subject matter, as far as novel, appears to be obvious over said documents (Art. 56 EPC). For example D12, page 513, left column, Discussion states that pomegranate and/or their constituent substances should be further explored as potentially useful therapeutic agents (in the therapy of AD-like pathology). Accordingly, the identification of Punicalin as one of the active agents of Punica granatum for treating AD and associated AD-like pathology appears obvious over D9 and D12, D13.
- 4 It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 43(1) EPC. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.
- 5 When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).
- 6 To meet the requirements of Rule 42(1)(b) EPC, the document D1-D12 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.
- 7 The statement in the description referring to "documents incorporated by reference" implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in a lack of clarity of the claims (Article 84 EPC) when used to interpret them (see the Guidelines Part F - Chapter III-8). This statement should therefore be amended to remove this inconsistency.