



Your ref : P/61493.GB01/PIB/ajh

Application No: GB0815972.5

Applicant : Nicholas John Larkins

Latest date for reply: 30 April 2012

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Date of report : 29 February 2012

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Patents Act 1977 Examination Report under Section 18(3)

Plurality of invention

1. Your claims define a number of separate inventions not forming a single inventive concept. The inventions include at least the following:

- (i) Claims 1-4 and 13-15 (in part).
- (ii) Claims 5-9 and 13-15 (in part).
- (iii) Claims 10-12 and 13-15 (in part).

This situation arises since the first component in claim 1, a catechin, is structurally distinct from the first component in claim 5, a compound within formula (I) and from the first component in claim 10, namely a derivative or metabolite of apocynin.

Although there may be some structural similarity between the compounds of formula (I) and apocynin, it would appear, in light of WO02/032435, that claims 5 and 10 relate to separate inventions. Indeed WO02/032435 discloses compositions comprising ginkgolide B or a ginkgo biloba extract together with apocynin (specified as NADPH oxidase inhibitor) for use in the treatment of asthma in particular. As you will be aware, this document was cited against the WO equivalent of the present application. A copy of this document is enclosed for your convenience.

You will need to amend your claims, so that they relate to only one invention or inventive concept. You will also need to make consequential amendments to the description. You may wish to consider filing a divisional application. Any such application should normally be filed no later than 3 months before the expiry of the period for putting the present application in order, and before grant. **WARNING-** no automatic reminder will be issued regarding the filing of divisional applications.

Scope of search

2. In accordance with Section 17(6), only the first of these inventions has been searched. The other invention can be searched if you wish. In this case you will have to file a further Form 9A.



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What this report covers

3. I have only examined the application in respect to the first invention. I have not been able to consider the novelty or obviousness of the unsearched inventions and have deferred examination of the corresponding claims in respect to clarity and support.

Document cited below in respect to novelty and inventive step

4. Please note that owing to the breadth of claim 1 (for example in respect to unpurified extracts and metabolites of the compounds specified), documents D1-D6 are only examples of documents citable in respect to novelty and/or inventive step.

5. Although D1-D4, D5 and D6 were not cited in the original search, you will be aware of these documents as D1, D2, D4, D5 and D6 were cited against the WO equivalent of the present application, and D3 part of the third party observations received in relation to your application and forwarded to you on 5 November 2010.

Novelty

6. The invention as defined in claims 1-2, 4 is not new because it has already been disclosed in the following documents:

D1: Life Sciences, Vol. 75, 2004, pages 3063-3076. Park, W.-H. et al. "Inhibitory effect of GBH on platelet aggregation through inhibition of intracellular Ca^{2+} mobilization in activated human platelet". See whole document, especially Table 1 and the abstract. Relevant to claims 1 and 2.

D2: Journal of Applied Pharmacology, Vol. 14, 2006, pages 216-219. Choi, Y. H. et al. "Effects of the Constituents of Paeonia lactiflora Root on Arachidonate and NO Metabolism". See whole document, especially Table 1 and Introduction lines 15-17. Relevant to claims 1 and 2.

D3: Qaraabaadeen Axaam wa Akmal (1909) by Mohammad Ahmal Khan. Page 589. Formulation ID: Ah5/2669. Formulation name: Qahwah Bara-e-Zeequ-n-Nafas. This corresponds to Exhibit 1 of the Third party observations, Exhibit 1. Relevant to claims 1 and 4.

7. D1 discloses epicatechin and paeonol as main active ingredients of herbal composition GBH, which is used in herbal medicine for the treatment of atherosclerosis. Therefore D1 anticipates claims 1 and 2.



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8. D2 discloses that *Paeonia lactiflora* root, which is used in Chinese medicine in the treatment of inflammation, contains (+)-catechin and paeonol. Therefore D2 anticipates claims 1 and 2.

9. D3 discloses a composition comprising *Camellia sinensis* and *Glycyrrhiza glabra* along with other ingredients used for the treatment of bronchial asthma. As stated at page 5 lines 19-24, the catechin may be in the form unpurified plant extract from *Camellia sinensis*. As stated at page 6 lines 1-6, the paeonol may be found in *Glycyrrhiza glabra*. Therefore D3 anticipates claims 1 and 4.

Inventive step

10. Notwithstanding the above objections to novelty, the invention as defined in claims 1-4, 13-15 is obvious in view of what has already been disclosed in the following documents:

D1: Life Sciences, Vol. 75, 2004, pages 3063-3076. Relevant to claims 3, 13 and 14.

D2: Journal of Applied Pharmacology, Vol. 14, 2006, pages 216-219. Relevant to claims 13 and 14

D3: Third party observation, Exhibit 1. Relevant to claims 13 and 14.

D4: WO 2004/037015 A1 (NEW SUN NUTRITION COMPANY) - See whole document, especially page 2, lines 18-22; page 3, lines 13-15; page 3, lines 31-36; page 4, lines 27-29. Relevant to claims 1-4 and 13-15.

D5: EP 0303277 A1 (OXO CHEMIE) – See in particular WPI Abstract Accession No. 1989-048086 [07]. Relevant to claims 1-4, 13 and 14.

D6: American Journal of Clinical Nutrition, Vol. 71 (suppl.), 2000, pages 1698S-1702S. Mukhtar, H. et al. "Tea polyphenols: preventin of cancer and optimizing health". See whole document, especially Figure 1; page 1700S ("Antiinflammatory effects of tea"). Relevant to claims 1-4, 13 and 14.

11. As should be self apparent from the above discussion of D1-D3, these documents teach therapeutic uses relevant to claims 13 and 14.

12. Furthermore the (-)-epicatechin feature of claim 3 lacks an inventive step over the disclosure of D1 which relates to epicatechin.

13. D4 discloses formulations 1-3 which comprise various catechins (e.g. epicatechin, epigallocatechin and gallates thereof) from green tea. A *Ginkgo biloba* extract may be added. It is reasonable to consider that this extract would be a source of a ginkgolide. Therefore D4



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questions the inventive step of claims 1-4. D4 further teaches that the compositions may be useful in the treatment of diseases including arthritis, cancer, inflammatory bowel syndrome, which renders obvious claims 13-15.

14. (a) D5 discloses that Ginkgo biloba extracts containing ginkgolides may be in the treatment of inflammation, especially associated with sunburns and radiation injuries.

(b) D6 discloses that the polyphenolic fraction of green tea (ie Camellia sinensis), which contains mainly epicatechins and gallates thereof, is useful in the treatment of inflammation, including inflammation caused by ultraviolet radiation.

(c) Therefore it would be obvious to the skilled person investigating treatments for inflammation to combine D5 and D6. Such combination renders obvious claims 1-4, 13 and 14.

Further consideration in respect to unity of invention

15. Claim 1 in effect defines at least three types of compositions as follows.

- (a) A composition comprising a catechin and a ginkgolide or metabolite thereof;
- (b) A composition comprising a catechin and a paeonol or metabolite thereof; and
- (c) A composition comprising a catechin and a 2-hydroxy-4-methoxybenzaldehyde or metabolite thereof.

16. In your application as filed, there would not appear to be any suitable support in respect to specific therapeutic applications that would clearly underlie all three types of compositions encompassed by claim 1 and thereby provide unity to claim 1.

It is noted that claims 13-15 do specify a number of diseases. However, these diseases correspond to such a breadth of therapeutic applications that it is difficult to identify how they would unify the three compositions of claim 1.

In addition, in your application as filed, there is no evidence to suggest that each of the three compositions of claim 1 has any beneficial use in the diseases as specified in claims 13-15.

17. Furthermore, in light of the documents cited above in respect to novelty and inventive step, it would appear that compositions a), b) and c) may form part of three separate inventions.

18. Further consideration to plurality of invention within claim 1 is deferred at this stage. Nevertheless you should give this matter particular thought upon amending as it will be given further consideration at amendment stage.



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Patentability

19. Claim 14 relates to a method of treatment by therapy and is therefore unpatentable under Section 4A(1) of the Patents Act 1977. This claim should be deleted. Consequential amendment to the description is also required.

Clarity and support

20. The claims lack clarity and support in respect to the term "metabolite" as used within the wording "a ginkgolide or metabolite thereof", "a paeonol or metabolite thereof" and "2-hydroxy-4-methoxybenzaldehyde or metabolite thereof".

(a) The scope of the term "metabolite" is unclear in that it is unclear which compounds would be suitable metabolites of a ginkgolide, a paeonol and/or 2-hydroxy-4-methoxybenzaldehyde. This places an undue burden on the skilled worker attempting to determine the exact scope of your claims.

(b) In addition your specification does not provide appropriate support for the large number of compounds that may be encompassed by the above wordings. It is unclear whether any of the claimed metabolites of ginkgolide, paeonol and/or 2-hydroxy-4-methoxybenzaldehyde would actually form a stable composition with a catechin.

(c) It is noted that passages of the description (e.g. page 6 lines 24-26) do refer to a few specific compounds that are considered as metabolites of paeonol. However, it remains unclear whether any of the claimed metabolites of paeonol would actually form a stable composition with a catechin.

21. Similar support and clarity issues are additionally found in the unsearched claims in respect to the terms "metabolite" and "derivative" as found for example within the wording "a derivative or metabolite of apocynin" (e.g. claim 10) or "a compound according to formula (I) or metabolite thereof" (claim 5). However as mentioned in above item 3, clarity and support of the unsearched claims has not been given full consideration at this stage.

22. It is noted that none of the exemplified compositions comprise 2-hydroxy-4-methoxybenzaldehyde and a catechin. In addition there would not appear to be any apparent inventive concept linking 2-hydroxy-4-methoxybenzaldehyde to any of the compounds which are exemplified in compositions also comprising a catechin. Therefore it is questioned whether the claims are supported in respect to compositions comprising 2-hydroxy-4-methoxybenzaldehyde.

23. The "and the gallates" obscures the scope of claim 2. This is because it is unclear whether this is meant to refer to gallate salts and/or to gallate derivatives (e.g. esters) of the catechins defined in claim 2.

24. The description should be brought into full agreement with the claims as amended.



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Deferred matters

25. Please note that I have given consideration to the documents cited against the WO equivalent of your application and to the third party observations received regarding your application. However, at this stage I have deferred the top-up of the original search.

26. In addition, further examination in respect to clarity and support, beyond the above objections, has also been deferred at this stage.