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Datasheet for the decision of 1 June 2017

Case Number: T 2130/14 - 3.3.10

Application Number: 07841534.6

Publication Number: 2057112

IPC: C07C63/00

Language of the proceedings: EN

Title of invention:
COMPOUNDS AND COMPOSITIONS FOR DELIVERING ACTIVE AGENTS

Applicant:
Emisphere Technologies, Inc.
Liao, Jun
Tang, Pingwah
Gschneidner, David
Maeyer, Jonathan

Headword:

Relevant legal provisions:
EPC Art. 123(2), 84, 54, 56

Keyword:

Amendments - allowable (yes)
Claims - clarity (yes)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

Catchword:

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Office européen des brevets

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Chambres de recours

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Case Number: T 2130/14 - 3.3.10

D E C I S I O N
of Technical Board of Appeal 3.3.10
of 1 June 2017

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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted on 10 April 2014 refusing European patent application No. 07841534.6 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairwoman	J. Mercey
Members:	R. Pérez Carlón
	T. Bokor

Summary of Facts and Submissions

I. The appellants (applicants) lodged an appeal against the decision of the examining division to refuse European patent application No. 07 841 534.6.

II. The documents forming part of the examination proceedings included the following:

D7: WO 01/32596

During the appeal proceedings, the following documents were cited:

D8: Bădilescu et al. Revista de Chimie, vol. 20, 1969, pp. 11-12
D9: Dann et al. Justus Liebigs Annalen der Chemie, vol. 587, 1954, pp. 38-47
D10: Freedman et al. J. Heterocyclic Chem. vol. 26, 1989, pp. 1547-1554
D11: Nioche et al. Eur. J. Med. Chem. vol. 30, 1995, pp. 377-385

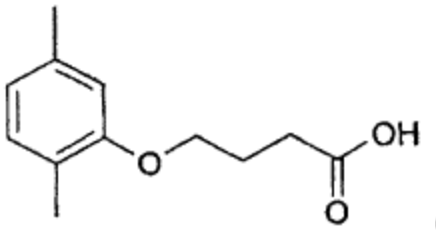
III. The examining division concluded that the delivery agents of claim 1 of the then pending main request were not inventive over those of document D7, which was the closest prior art. The problem underlying the claimed invention was to provide alternative delivery agents, and the solution was obvious as the claimed compounds were embodiments of the general formula of D7.

IV. Claim 1 of the main request, filed as second auxiliary request with a letter dated 30 August 2016, reads as follows:

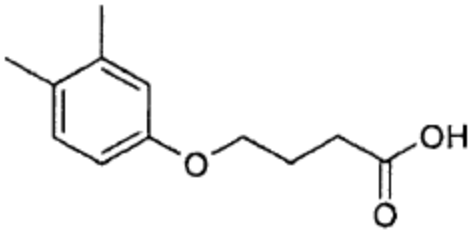
"A pharmaceutical composition comprising:

(A) a biologically active agent selected from insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone, argatroban and any combination thereof; and

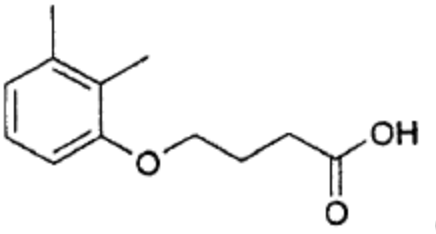
(B) at least one delivery agent compound selected from the group consisting of:



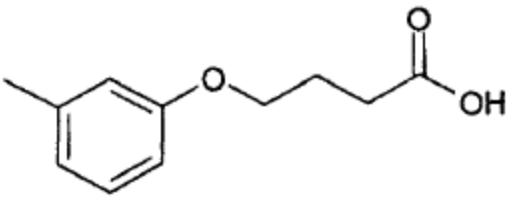
Compound 1;



Compound 4;



Compound 5;



Compound 6;

and pharmaceutically acceptable salts thereof."

V. The arguments of the appellants relevant for the present decision were the following:

The compositions of D7 comprising compounds 94 and 97, structurally close to component (B) of claim 1, were the closest prior art. Having regard to the experimental data provided with a letter dated 30 August 2016 and to those in example 16 of the application, the problem of providing pharmaceutical compositions which improved enhanced delivery of insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone and argatroban was credibly solved by the claimed compositions. There was no hint in the prior art which would have led the skilled person towards compositions comprising delivery agents having a shorter aliphatic chain in order to solve this problem, and thus the claimed compositions were inventive.

At the oral proceedings before the board, which took place on 1 June 2017, the appellants did not object to the case being remitted to the examining division for adapting the description.

VI. The final request of the appellants was that the decision under appeal be set aside and a patent be granted on the basis of the main request, filed as second auxiliary request with a letter dated 30 August 2016.

VII. At the end of the oral proceedings, the decision was announced.

Reasons for the Decision

1. The appeal is admissible.

Amendments

2. Claim 1 finds a basis in the combination of claims 2, 5, 6, 7, 15 and 19 (in part) as originally filed.

Claims 2 to 5 relate to compositions comprising each of the compounds required by claim 1, and find the same basis as the latter in the application as originally filed.

Claims 6 to 8 find a basis in claims 20 to 22, respectively, of the application as originally filed, in combination with the claims cited with respect to claim 1.

The requirements of Article 123(2) EPC are thus fulfilled.

Clarity

3. In a communication dated 30 June 2016, the board objected to the feature "biologically active agent" in the context of the requests then pending for not clearly defining the boundaries of the subject-matter claimed.

In claim 1 of the main request, said feature is further defined as "insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone, argatroban and any combination thereof", so that this objection no longer applies to claim 1 of the main request.

The board is satisfied that the claim as a whole is now clear under Article 84 EPC.

Novelty

4. Claim 1 of the main request relates to pharmaceutical compositions comprising delivery agents and insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone, argatroban and any combination thereof.

5. In the communication dated 30 June 2016, the board introduced documents D8 to D11 into the proceedings, and raised an objection of lack of novelty of the delivery agents which were the subject-matter of claim 1 then pending.

Inter alia, compound 1 is disclosed in document D9 as (IId) on page 44. Compound 4 is compound (IIe) on page 43 of D9, and compound (IV) of D8. Compound 6 corresponds to compound (II) of D8. Documents D10 and D11 do not disclose any of compounds 1, 4, 5 or 6.

Neither D8 nor D9 discloses a composition comprising insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone or argatroban. Thus, the claimed pharmaceutical compositions are novel, as required by Article 54 EPC.

Inventive step

6. Closest prior art

6.1 Claim 1 is directed to compositions comprising

- a biologically active agent selected from insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone, argatroban and any combination thereof, and

- at least one delivery agent selected from compounds 1, 4, 5 and 6. These compounds are mono- or dimethyl- substituted-4-phenoxybutyric acids, having a $-(CH_2)_3-$ chain linking the phenoxy and the carboxylic acid moiety,

and pharmaceutically acceptable salts thereof.

6.2 Document D7 is the closest prior art, and discloses compositions comprising delivery agents and biologically active compounds such as insulin, heparin and recombinant human growth hormone. It is further not disputed that the delivery agents required by claim 1 are embodiments of the general formula of D7 (claim 1, page 3, line 19 to page 5, line 3).

It has however to be examined which embodiment of document D7 comes closest to the claimed invention.

Document D7 discloses compositions comprising 2'-ethylcarbonyl-4-phenoxybutyric (26), 2',5'-dimethyl-6-phenoxyhexanoic acid (94) or 2,2-dimethyl-5-[2',5'-dimethylphenoxy]pentanoic acid (97).

Compound 26 contains a 2'-ethylcarbonyl substituent, whereas the compounds required by claim 1 bear one or two methyl substituents on the phenoxy group. Thus, compound 26 differs from compounds 1, 4, 5 and 6 by the nature of the substituents and by the substitution pattern of the phenoxy ring.

Compounds 94 and 97 contain a 2',5'-dimethylphenoxy residue, i.e. also contain methyl substituents on the phenoxy group, and differ from compounds 1, 2, 5 and 6 by virtue of the length of the chain linking the phenoxy and the carboxylic acid moiety, namely $-(CH_2)_5-$ and $-(CH_2)_3-(CMe_2)_2-$ instead of $-(CH_2)_3-$.

6.3 The board agrees with the appellants that compositions comprising compounds 94 and 97, which bear, as the compounds required by claim 1, methyl groups attached to the phenoxy residue, come closer than compound 26 to the claimed invention.

7. Technical problem underlying the invention

The technical problem underlying the claimed invention comprises providing pharmaceutical compositions which improve the enhanced delivery of insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone and argatroban.

8. Solution

The solution to this technical problem is the pharmaceutical composition of claim 1, characterised in that it contains at least one delivery agent selected from the group consisting of compounds 1, 4, 5 and 6, which all have a $-(CH_2)_3-$ group linking the phenoxy and carboxylic acid moieties.

9. Success

With a letter dated 30 August 2016, the appellants have provided comparative tests which show that the delivery agents required by claim 1 increase insulin-induced glucose reduction in blood with respect to compositions

containing compounds 97 and 94 of D7.

Document D7 discloses that compounds which have a good activity for insulin delivery have also a good activity for delivering many other biologically active agents (see for examples claims 5-7). For this reason, the board accepts that the comparative data provided for insulin can be extrapolated to leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone and argatroban.

In addition, figures 1 and 5 of the application as originally filed show that compounds 1 and 6 according to claim 1 enhance plasma concentration of argatroban after oral administration compared to the intake of argatroban alone.

For these reasons, the problem as formulated above is considered as credibly solved by all of the claimed compositions.

10. It thus remains to be decided whether or not the proposed solution to the objective problem defined above is obvious in view of the state of the art.

The skilled person finds in D7 the information that the compounds falling within its general formula are suitable delivery agents for various biologically active compounds.

However, the skilled person, starting from the closest prior art compositions comprising a delivery agent 94 or 97, and seeking to provide compositions which improve the enhanced delivery of the biologically active agents insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth

hormone and argatroban, does not find in D7, or elsewhere in the available prior art, an indication that shortening the chain linking the substituted phenoxy and carboxy moieties in the delivery agents from 4 or 5 to 3 carbon atoms would lead to better delivery of the biological agent. On the contrary, comparison of delivery agents in D7 which differ only by virtue of the length of the alkylene chain linking the substituted phenoxy unit and the carboxy group (see examples 26-29 with respect to delivery of recombinant growth hormone on page 68 of D7) would seem to show that, with increasing chain length, the delivery agents become in fact more effective.

For this reason, it is considered that the skilled person does not find any indication that the delivery agents required by claim 1 could improve the enhanced delivery of insulin, leutenizing-hormone releasing hormone, GLP-1, heparin, recombinant human growth hormone and argatroban, with the consequence that the subject-matter of claim 1, and thus also of dependent claims 2 to 8, is considered to involve an inventive step, as required by Article 56 EPC.

Remittal

11. Due to the amendments carried out during these appeal proceedings, the description includes a large number of embodiments no longer covered by the claimed invention, both with respect to the delivery agents and of the active compounds required by claim 1. The appellants did not object to the board remitting the case to the examining division for adaptation of the description (Article 111(1) EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent on the basis of claims 1 to 8 of the main request, previous second auxiliary request, as filed with letter of 30 August 2016, and a description yet to be adapted.

The Registrar: The Chairwoman:

C. Rodríguez Rodríguez J. Mercey

Decision electronically authenticated