DEcision
of 2 February 2004

Case Number: W 0025/03 - 3.3.1
Application Number: PCT/US 02/21292
Publication Number: -
IPC: C07D 401/14
Language of the proceedings: EN
Title of invention: Chemical Compounds
Patentee: Eli Lilly and Company
Opponent: -
Headword: Chemical Compounds/ELI LILLY
Relevant legal provisions:
EPC Art. 155(3)
PCT Art. 34(3)(a) and (c)
PCT R. 13.1 and 2; 68.2; 68.3(c)
Keyword: "Lack of unity 'a posteriori' (no)"
Decisions cited: -
Catchword: -
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DECISION
of the Technical Board of Appeal 3.3.1
of 2 February 2004

Applicant: Eli Lilly and Company
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IN-46285 (US)

Representative: Hay, Martin Alexander
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Decision under appeal: Protest according to Rule 68.3(c) of the Patent Cooperation Treaty made by the applicants against the invitation of the European Patent Office (International Preliminary Examining Authority) to restrict the claims or pay additional fees dated 12 May 2003.

Composition of the Board:
Chairman: A. J. Nuss
Members: P. P. Bracke
M. B. Günzel
Summary of Facts and Submissions

I. International patent application PCT/US 02/21292 was filed on 24 July 2002 with twenty four claims of which the independent claims read:

"1. A compound of formula (I)

\[ \text{in which} \]

- \( R^1 \) represents (1-4C)alkyl, (2-4C)alkenyl or (2-4C)alkynyl;

and

- \( R^2 \) is selected from

\[ \text{in which} \]

- \( X^1 \) represents a hydrogen atom or a halogen atom;
- \( X^2 \) represents a hydrogen atom, a methyl group, a chlorine atom or a bromine atom;
- \( X^3 \) represents a hydrogen atom, a methyl group or a halogen atom;
- \( X^5 \) represents chloro, methoxy or methyl;
- \( X^6 \) represents a hydrogen atom, a halogen atom or a methyl group; and
X\textsuperscript{4} represents CH or N; or a pharmaceutically acceptable salt thereof.

"18. A pharmaceutical composition, which comprises a compound as claimed in any one of Claims 1 to 17, together with a pharmaceutically acceptable diluent or carrier."

"19. A process for preparing a compound as claimed in any one of Claims 1 to 17, which comprises

(a) reacting a compound of formula (II)

\[
\text{II}
\]

or a salt thereof, with a compound of formula (III)

\[
\text{III}
\]

or a derivative thereof; or

(b) reacting a compound of formula (IV)

\[
\text{IV}
\]

or a salt thereof, with a compound of formula (V)

\[
\text{V}
\]

or a reactive derivative thereof;

followed, if a pharmaceutically acceptable salt is desired, by forming a pharmaceutically acceptable salt."
20. A compound of formula (III) or a salt thereof, in which \( R^1 \) and \( R^2 \) are as defined in Claim 19.

21. A compound of formula (IV) or a salt thereof, in which \( R^1 \) and \( X^4 \) are as defined in Claim 19.

22. A compound as claimed in any one of Claims 1 to 17, for use in therapy.

23. Use of a compound as claimed in any one of Claims 1 to 17, for the manufacture of a medicament for the treatment of a thrombotic disorder.


Claims 2 to 17 were dependent on Claim 1.

II. On 12 May 2003 the European Patent Office (EPO), acting as an International Preliminary Examining Authority (IPEA), informed the applicant that the application did
not comply with the requirement of unity of invention and invited him to restrict the claims or to pay one additional examination fee pursuant to Article 34(3)(a) and Rule 68.2 PCT within a period of one month.

In an annex to this invitation the IPEA submitted that the application related to structurally distinct groups of compounds, namely:

(i) compounds of formula (I) and (III) wherein $R_2$ is an optionally substituted methoxy- or aminophenyl group and compounds of formula (IV);

(ii) compounds of formula (I) and (III) wherein $R_2$ is an optionally substituted indole group; and

(iii) compounds of formula (I) and (III) wherein $R_2$ is an optionally substituted benzothiophen group.

In particular, the IPEA found that 1-glycine-4-piperidylpiperazines and -piperidines were known from documents

(1) WO-A-00/76971;

(2) WO-A-99/11657; and

(3) Bioorg. Med. Chem. Lett. 11, 2001, pages 733 to 736, as inhibitors of Factor Xa, that structural variation of the lipophilic substituent $R_1$ was known from page 3, lines 18 to 23, of document (2) and Table 1 of document (3) and that the broad variability of substituent $R_2$ was known from page 33, line 15 to page 37, line 10 of document (1), wherein substituted phenyl, indole and benzothiazole moieties had been explicitly disclosed. Since all the different structural features of the claimed compounds were known from the state of the art,
the IPEA was of the opinion that the claimed compounds were not linked by a single inventive concept.

III. By letter of 4 June 2003, the applicant paid one additional fee under protest pursuant to Rule 68.3(c) PCT and in his reasoned statement he submitted that the claimed compounds shared a novel common structural feature, namely the group attached to R², and at least one common property, namely the inhibition of Factor Xa.

IV. On 26 September 2003, the IPEA issued a communication informing the applicant that after a prior review of the justification for the invitation to pay an additional fee, the requirement to pay the same was upheld. The applicant was thus invited under Rule 68.3(e) PCT to pay the protest fee.

V. The protest fee was paid by letter dated 22 October 2003.

**Reasons for the Decision**

1. The protest meets the requirements of Rule 68.3(c) and (e) and is, thus, admissible. The Board, which, according to Article 155(3) EPC, is responsible for deciding on a protest made by an applicant against an additional fee charged by the EPO under the provisions of Article 34(3)(a) PCT, is competent to examine the present protest.

2. According to Rules 13.1 and 13.2 PCT the requirement of unity of invention may only be fulfilled if a group of inventions is so linked as to form a single *general inventive concept*, i.e. if there is a technical
relationship among the inventions involving one or more of the same or corresponding technical features, wherein by the expression "special technical features" those technical features are meant that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

3. Claim 1 of the application in suit is directed to compounds, which have inhibitory activity on Factor Xa and which contain particular aromatic groups as R₂, a \(-\text{CO-NH-CHR}^1\text{-CO-}\) radical, wherein \(R^1\) is (1-4C)alkyl, (2-4C)alkenyl or (2-4C)alkynyl, and a 4-(1-methylpiperidin-4-yl)piperidin-1-yl or 4-(1-methylpiperidin-4-yl)piperazin-1-yl group.

4. The Applicant agreed that inhibitors of Factor Xa having similar chemical structures were known from documents (1), (2) and (3). However, the applicant was of the opinion that the single general inventive concept of the presently claimed compounds was based on the chemical structure of the group attached to R₂. Therefore, in deciding whether the invitation by the IPEA to restrict the claims or to pay one additional fee (see point II above) was correct, the question arises whether compounds containing a \(-\text{CO-NH-CHR}^1\text{-CO-A}\) radical, wherein \(R^1\) is (1-4C)alkyl, (2-4C)alkenyl or (2-4C)alkynyl and A represents a 4-(1-methylpiperidin-4-yl)piperidin-1-yl or 4-(1-methylpiperidin-4-yl)piperazin-1-yl group were known from any of the documents cited by the IPEA.

4.1 Document (1), which discloses compounds containing a \(-\text{CO-NH-CHR}^1\text{-CO-A}\) radical, wherein \(R^1\) is a saturated or unsaturated, mono- or polycyclic homo- or heterocyclic
4.2 Moreover, document (2) describes compounds of formula

\[
\begin{align*}
\text{R} & \quad \text{X-X-Y(R7)-L-Lp(D)n.}
\end{align*}
\]

According to the general description, X-X may represent -CONH-, Y may represent -CH-, R7 may represent alkyl or alkenyl, L may represent a -CO- group, Lp may represent a 4-(1-methylpiperidin-4-yl)piperidin-1-yl radical and n may be 0.

However, according to the jurisprudence of the Boards of Appeal of the EPO, if multiple selections from a prior art document are necessary in order to arrive at a specific group of compounds, such prior art document is considered not to disclose those compounds.

Since, in the present case, a selection had to be made for each of X-X, Y, R7, L, Lp and n in order to arrive at a group attached to \( R^2 \) as defined in present Claim 1, compounds bearing a -CO-NH-CHR1-CO-A radical, as defined in present Claim 1, are not disclosed in the general description of document (2).

Moreover, the only specifically described compound containing a 4-(1-methylpiperidin-4-yl)piperidin-1-yl group is the one described in example 75. Since, however, this compound contains a phenyl group as \( R^7 \),
the experimental part does not disclose compounds containing a group attached to \( R^2 \) as defined in present Claim 1 either.

4.3 Finally, since compounds containing a 4-(1-methylpiperidin-4-yl)piperidin-1-yl or 4-(1-methylpiperidin-4-yl)piperazin-1-yl group are not described in document (3), this document cannot be considered to disclose compounds containing the group attached to \( R^2 \) as defined in present Claim 1 either.

4.4 As, thus, compounds containing a group attached to \( R^2 \) as defined in present Claim 1 were not disclosed in any of documents (1) to (3), it is the chemical structure of the group attached to \( R^2 \) as defined in present Claim 1 that defines the contribution over the prior art. It is this "special technical feature" that links the compounds of Claim 1 together in such a way that they form a single general inventive concept.

4.5 Furthermore, since the compounds of formula (III) and (IV) are intermediates for the preparation of compounds of formula (I), they also are linked by the same single general inventive concept.

5. Therefore, the Board cannot follow the IPEA's reasoning according to which the claimed subject-matter is not considered to comply with the requirement of unity of invention. Hence, the invitation provided for in Article 34(3)(a) and Rule 68.2 PCT to pay an additional fee was not justified.
Order

For these reasons it is decided that:

1. Refund of the additional examination fee paid by the Applicant is ordered.

2. The protest fee is to be refunded.

The Registrar: The Chairman:

N. Maslin A. Nuss