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D E C I S I O N
of 10 October 2000

Case Number: W 0020/99 - 3.3.2

Application Number: PCT/NL 98/00343

Publication Number: WO 99/65501

IPC: A61K 31/70

Language of the proceedings: EN

Title of invention:
A process for the treatment of organophosphate poisoning

Applicant:
Nederlandse Organisatie voor toegepastnatuurwetenschappelijk onderzoek TNO

Opponent:
-

Headword:
Receptor agonists/NEDERLANDSE T.N.O.

Relevant legal provisions:
PCT Art. 17(3)(a)
PCT R. 13, 40

Keyword:
"Lack of unity a priori - no"
"Method of treating human or animal body by therapy"

Decisions cited:
-

Catchword:
-

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Case Number: W 0020/99 - 3.3.2
International Application No. PCT/NL 98/00343

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 10 October 2000

Applicant: Nederlandse Organisatie voor toegepastnatuurwetenschappelijk onderzoek TNO
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Subject of the Decision: **Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicant against the invitation (payment of additional fee) of the European Patent Office (branch at The Hague) dated 29 March 1999.**

Composition of the Board:

Chairman: P. Lançon
Members: C. Germinario
R. Teschemacher

Summary of Facts and Submissions

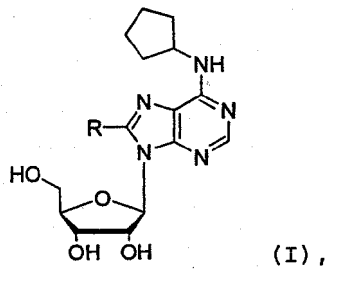
I. The applicant filed international patent application PCT/NL98/00343 with a set of 16 claims. Claims 1 to 7 read:

"1. A process for treating organophosphate poisoning in a mammal comprising the administration of an A_1 receptor adenosine agonist.

2. A process according to claim 1, wherein a partial A_1 receptor adenosine agonist is administered.

3. A process according to claim 2, wherein the partial A_1 receptor adenosine agonist is chosen from the group of 8-alkylamino-substituted analogues of N6-cyclopentyladenosine, 8-substituted adenosine, 8-substituted theophylline-7-ribose analogues, and deoxyribose analogues of N6-cyclopentyladenosine (CPA), N6-cyclohexyladenosine (CHA), N6-R-phenylisopropyladenosine (R-PIA) and N6-S-phenylisopropyladenosine.

4. A process according to claim 3, wherein the partial A_l adenosine agonist is a 8-alkylamino-substituted analogue of N6-cyclopentyladenosine having the formula (I)



(I),

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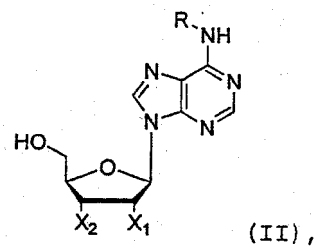
wherein R is $-NHCH_3$, $-NHCH_2CH_3$, $-NH(CH_2)_2CH_3$, $-NH(CH_3)_3CH_3$, or -NH-cyclopentyl.

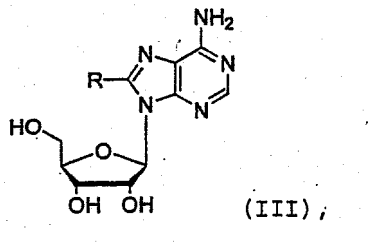
5. A process according to claim 3, wherein the partial A_1 adenosine agonist is a deoxyribose analogue of N6-cyclopentyladenosine (CPA), N6-cyclohexyladenosine (CHA), N6-R-phenylisopropyladenosine (R-PIA) or N6-S-phenylisopropyladenosine having the formula (II)



(II),

wherein R is cyclopentyl, cyclohexyl, R-phenylisopropyl, or S-phenylisopropyl, and wherein X_1 and X_2 are different from each other and chosen from hydrogen and hydroxyl.

6. A process according to claim 3, wherein the partial A_1 adenosine agonist is an 8-substituted adenosine having the formula (III)

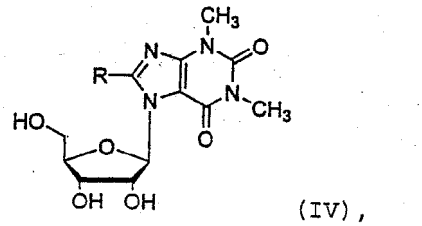


(III),

wherein R is methyl, ethyl, vinyl, thiophenyl, hydroxyl, methyoxy, amino, aminoalkyl with from 1 to 5 carbon atoms, aminoalkylamine with from 1 to 5 carbon

atoms, aminocyclopentyl, cyclohexyl, or halogen.

7. A process according to claim 3, wherein the partial A_1 adenosine agonist is an 8-substituted theophylline-7-ribose having the formula (IV)



(IV),

wherein R is hydrogen, amino, aminoalkyl with from 1 to 7 carbon atoms, or aminophenyl."

II. The EPO acting as an International Searching Authority (ISA) found multiple inventions covered by the international application namely by

claims 4 to 6, and partially 1 to 3 and 8 to 16 directed to the

use of **adenosine** analogues of formulae I to III for preparing a medicament for treating organophosphate poisoning,

and by claim 7 and partially 1 to 3 and 8 to 16 directed to the

use of **theophylline** derivatives of formula IV for the preparation of a medicament for treating organophosphate poisoning.

For this reason the ISA sent on 29 March 1999 to the applicant an invitation to pay one additional search

fee pursuant to Article 17(3)(a) and Rule 40.1 PCT.

In the invitation, the ISA stated that the problem underlying the invention was to provide a medicament for treating organophosphate poisoning, especially nerve gas poisoning. This problem was solved by the use of A_1 receptor adenosine agonists.

However, the receptor agonists mentioned in the claims related to several series of adenosine analogues of formulas (I), (II) and (III) and to the theophylline derivatives of formula (IV).

Although such compounds shared a common activity, namely the A_1 receptor adenosine agonism, they neither shared a significant structural element nor belonged to a recognised class of chemical compounds in the specific field of the invention as required by Annex B, paragraph (f) of the PCT Administrative Instructions (1998).

III. The applicant paid the additional search fee under protest pursuant to Rule 40.2(c) PCT. It argued that the objection raised by ISA was that of lack of unity *a priori* as the novelty and the inventive step of the claimed subject-matter had not been considered or contested in view of any prior art document. Under these circumstances, the requirement of unity of invention had to be considered only in relation to claim 1, not to any dependent claim. Since claim 1 did not relate to any alternative, but only to the unique group of the A_1 receptor agonists, no objection of unity was justified.

IV. On 24 August 1999, the Review Panel of the ISA

confirmed the finding of lack of unity and invited the applicant to pay a protest fee, which was duly paid.

Reasons for the Decision

1. The protest is admissible

2. As laid down in Annex B, Part 1 paragraph (c) of the PCT Administrative Instruction (1998), unity of invention has to be considered in the first place only in relation to the independent claims. If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of claims that depend on the independent claims. Only if the independent claim does not avoid the prior art then the question whether there is still an inventive link between the claims dependent on that claim needs to be considered and, if it is the case an objection of lack of unity *a posteriori* may be raised (paragraph (c)(i) and (ii)).

3. In the present case, the ISA raised the objection of lack of unity of invention before considering the claims in relation to any prior art, thus it envisaged an *a priori* objection of lack of unity. Accordingly, until no proof of the contrary is produced, the subject-matter of claim 1 must be considered as novel and as involving an inventive step. In this case, the issue of unity of invention may only be assessed in relation to claim 1 and after proper consideration of the invention as defined therein.

4. According to claim 1, the invention consists in a

process for treating organophosphate (OP) poisoning in a mammal by administering an A_1 receptor adenosine agonist.

The problem to be solved by the present invention, as appears from the description and claims of the application is that of finding a new chemotherapeutic treatment for OP poisoning in mammals, and the solution proposed by the invention is administering an A_1 receptor adenosine agonist to patients in need.

5. As evident from the wording of claim 1, the active agent to be administered is not defined structurally but in functional terms. Functional definitions of the claimed subject-matter or elements thereof are normally allowable, when certain conditions are met. In the present case, the essential and characterising feature of the invention is the capability of the active agent selectively to bind the A_1 adenosine receptor thereby eliciting an adenosine-agonistic effect. Provided that effect is achieved by an active substance, that substance falls within the scope of the claim regardless of its chemical structure. In other words, the invention, as claimed in the independent claims, implies the use of a class of substances comprising a multiplicity of alternative members which, regardless of their chemical difference, are for the purpose of the invention all functionally equivalent and therefore unitarian. In fact the different A_1 receptor agonists are only defined by way of their chemical structure in dependent claims (see claims 3 to 7). Yet, the function of the dependent claims is that of simply specifying practical preferred, but not essential embodiments of the main invention (Rule 13.4 PCT).

The Board therefore considers that independent claim 1 satisfies the requirement of unity of invention as laid down by Rule 13.1 PCT.

The objection raised by the ISA was directed to an alleged lack of technical link between the subject-matter of dependent claims, in particular, between the chemical structures defined in claims 4 to 6, on the one hand, and claim 7 on the other.

However, insofar as no evidence exists that the subject matter of claim 1 lacks novelty or inventive step, and since this subject-matter satisfies the requirement of unity, no problem of lack of unity may be raised in respect of the dependent claims. In fact claim 1 defines a valid general inventive concept which is the technical link between all the dependent claims, as provided by the Annex B, part 1, paragraph (c)(i) of the PCT Administrative Instructions (1998).

6. Under these circumstances, it is no longer necessary for the board to consider the validity of the arguments produced by the ISA that the expression "A_1 receptor adenosine agonist" did not refer to a single chemical entity, but to a variety of chemical entities defined by more than one Markush formulas.

Nor exists the need to consider the validity of the arguments of the Review Panel, since they are essentially intended to corroborate the opinion of the ISA concerning the structural difference between adenosine and theophylline analogues, which difference, as seen above, is immaterial to any issue of lack of unity *a priori.*

In view of the foregoing, the Board considers that there is no reason for an *a priori* objection of lack of unity of the invention and that the applicant's protest against the invitation to pay additional fees is entirely justified.

Order

For these reasons it is decided that:

Refund of the additional search fee and of the protest fee is ordered.

The Registrar: The Chairman:

P. Martorana P. A. M. Lançon