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**Datasheet for the decision
of 10 July 2012**

Case Number: T 1013/08 - 3.3.02

Application Number: 02795936.0

Publication Number: 1458373

IPC: A61K 31/232

Language of the proceedings: EN

Title of invention:

Use of lipoxin analogs to promote cell defense against gram-negative infections

Applicant:

The Brigham and Women's Hospital

Headword:

Lipoxin analogs/BRIGHAM

Relevant legal provisions:

EPC Art. 52(2), 84, 53(c)

Keyword:

"Main request: novelty (no)"

"First auxiliary request: medical treatment (yes)"

"Second auxiliary request: clarity (no)"

Decisions cited:

-

Catchword:

-



Case Number: T 1013/08 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 10 July 2012

Appellant: The Brigham and Women's Hospital
(Applicant) 75 Francis Street
Boston, MA 02115 (US)

Representative: Strehl Schübel-Hopf & Partner
Maximilianstraße 54
D-80538 München (DE)

Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 31 October 2007
refusing European patent application
No. 02795936.0.

Composition of the Board:

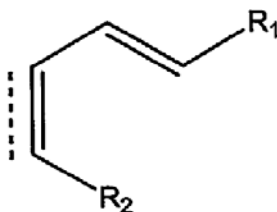
Chairman: U. Oswald
Members: H. Kellner
D. Prietzel-Funk

Summary of Facts and Submissions

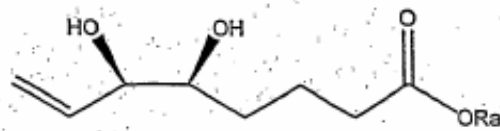
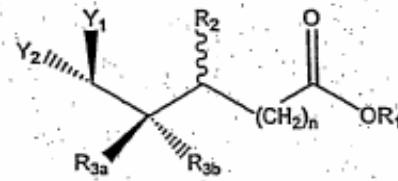
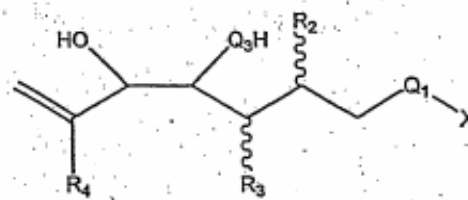
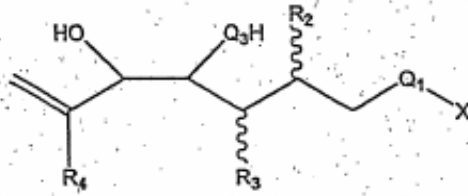
I. European patent application No. 02 795 936.0, filed as international application PCT/US02/40620 and published as WO 03/051350, was refused by a decision of the examining division on the basis of Article 97(1) EPC 1973.

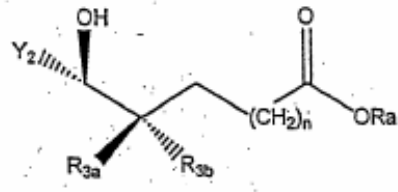
II. The relevant passages of claim 1 of the request before the examining division read as follows (note: starting from the formula, the claim is reproduced as facsimile including its numbering of the pages):

"Use of lipoxin or a lipoxin analog for the preparation of a pharmaceutical agent comprising the lipoxin or lipoxin analog in a therapeutically effective amount for causing a subject's tissue to express increased levels of bactericidal permeability increasing protein (BPI), thereby treating infection caused by gram-negative bacteria, wherein the lipoxin or lipoxin analog has the following formula:

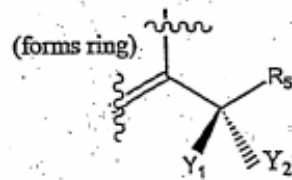
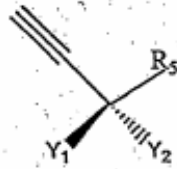
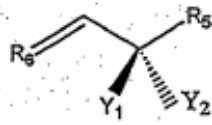


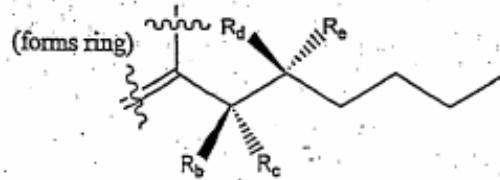
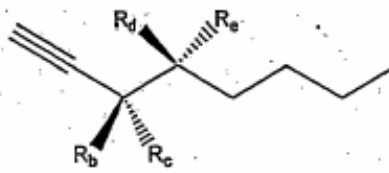
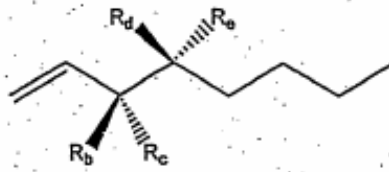
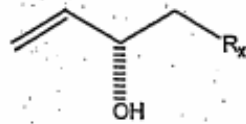
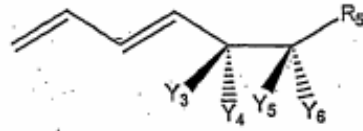
wherein R_1 if present can be





and R₂ if present can be





wherein X is R₁, OR₁, or SR₁;

wherein R₁ is

(i) a hydrogen atom;

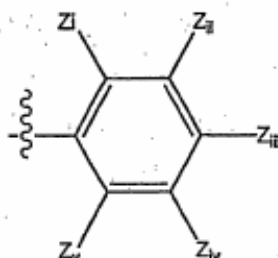
(ii) an alkyl of 1 to 8 carbon atoms, inclusive, which can be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms, inclusive;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from -NO₂, -CN, -C(=O)-R₁, -SO₃H, a hydrogen atom, halogen, methyl, -OR_x, wherein R_x is 1 to 8 carbon atoms, inclusive, which can be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms,

inclusive;

wherein Q₁ is (C=O), SO₂ or (CN);

wherein Q₃ is O, S or NH;

wherein one of R₂ and R₃ is a hydrogen atom and the other is

(a) a hydrogen atom;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which can be straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which can be straight chain or branched; or

(e) $R_3Q_2R_6$

wherein Q_2 is -O- or -S-;

wherein R_3 is alkylene of 0 to 6 carbon atoms, inclusive, which can be straight chain or branched; and wherein R_6 is alkyl of 0 to 8 carbon atoms, inclusive, which can be straight chain or branched;

wherein R_4 is

(a) a hydrogen atom;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which can be straight chain or branched;

wherein Y_1 or Y_2 is -OH, methyl, or -SH and wherein the other is

(a) a hydrogen atom

(b) CH_2Z_b

where $a+b=3$, $a=0$ to 3, $b=0$ to 3; and

each Z , independently, is a cyano, a nitro, or a halogen atom;

(c) an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched;

or

(d) an alkoxy of 1 to 4 carbon atoms, inclusive;

or Y_1 and Y_2 taken together are

(a) =NH; or

(b) =O;

wherein R_5 is

(a) an alkyl of 1 to 9 carbon atoms which can be straight chain or branched;

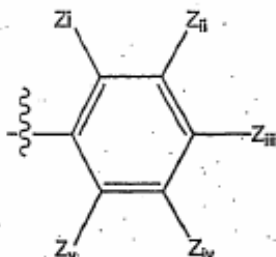
(b) $-(CH_2)_n-R_1$

wherein $n=0$ to 4 and R_1 is

(i) a cycloalkyl of 3 to 10 carbon atoms, inclusive;

(ii) a phenyl; or

(iii) substituted phenyl



wherein Z_i , Z_{ii} , Z_{iii} , Z_{iv} and Z_v are each independently selected from $-\text{NO}_2$, $-\text{CN}$, $-\text{C}(=\text{O})-\text{R}_1$, $-\text{SO}_3\text{H}$, a hydrogen atom, halogen, methyl, $-\text{OR}_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which can be a straight chain or branched, and hydroxyl;

(c) $\text{R}_a\text{Q}_a\text{R}_b$

wherein Q_a is O or S;

wherein R_a is alkylene of 0 to 6 carbon atoms, inclusive, which can be straight chain or branched;

wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which can be straight chain or branched;

(d) $-\text{C}(\text{R}_{iii})(\text{R}_{iv})-\text{R}_4$

wherein R_{iii} and R_{iv} are each, independently:

(i) a hydrogen atom;

(ii) CH_2Z_5 where $a+b=3$, $a=0$ to 3, $b=0$ to 3, and wherein each Z_5 independently, is a cyano, a nitro, or a halogen atom;

(e) a haloalkyl of 1 to 8 carbon atoms, inclusive, and 1 to 6 halogen atoms, inclusive, straight chain or branched; and

wherein R_6 is

(a) a hydrogen atom;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

(c) a halogen;

wherein R_{3a} , and R_{3b} are each independently:

- (a) a hydrogen atom;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which can be straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which can be straight chain or branched; or

(e) $R_1Q_2R_3$

wherein Q_2 is -O- or -S-;

wherein R_1 is alkylene of 0 to 6 carbon atoms, inclusive, which can be straight chain or branched; and wherein R_3 is alkyl of 0 to 8 carbon atoms, inclusive, which can be straight chain or branched;

wherein Y_3 or Y_4 is -OH, methyl, hydrogen, or -SH and

wherein the other is

(a) a hydrogen atom;

(b) CH_2Z_b

wherein $a+b=3$, $a=0$ to 3, $b=0$ to 3,

and wherein each Z, independently, is a cyano, a nitro, or a halogen atom;

(c) an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched;

(d) an alkoxy of 1 to 4 carbon atoms, inclusive, straight chain or branched;

or Y_3 and Y_4 taken together are

(a) =NH; or

(b) =O;

wherein Y_5 or Y_6 is -OH, methyl, hydrogen, or -SH and

wherein the other is

(a) a hydrogen atom;

(b) CH_2Z_b

where $a+b=3$, $a=0$ to 3, $b=0$ to 3

wherein each Z, independently, is a cyano, a nitro, or a halogen atom;

(c) an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched;

(d) an alkoxy of 1 to 4 carbon atoms, inclusive, straight chain or branched;

or Y_5 and Y_6 taken together are

(a) =NH; or

(b) =O;

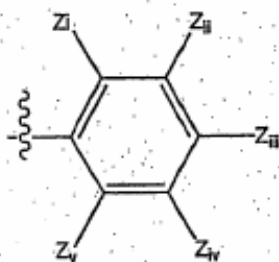
wherein R_a is

(a) a hydrogen atom; or

(b) alkyl of 1 to 8 carbon atoms;

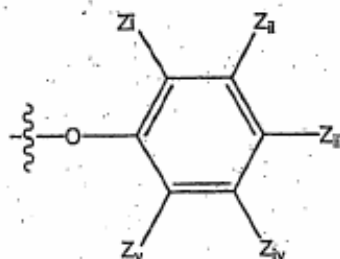
wherein R_x is

(a) substituted phenyl

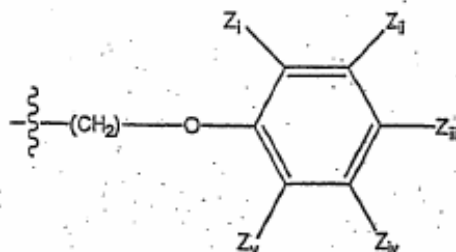


wherein Z_i , Z_{ii} , Z_{iii} , Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which can be a straight chain or branched, and hydroxyl;

(b) a substituted phenoxy



wherein Z_i through Z_v are as defined above; or



wherein Z_i through Z_l are as defined above.

wherein R_b and R_c are each independently:

- (a) a hydrogen atom;
- (b) a hydroxyl, or a thiol;
- (c) a methyl or a halomethyl;
- (d) a halogen;
- (e) an alkoxy of 1 to 3 carbon atoms;

wherein R_d and R_e are each independently:

- (a) a hydrogen atom;
- (b) a hydroxyl, or thiol;
- (c) a methyl or halomethyl;
- (d) a halogen;
- (e) an alkoxy of 1 to 3 carbon atoms; or
- (f) an alkyl or haloalkyl of 2 to 4 carbon atoms, inclusive, which can be straight chain or branched.

or

6. The method of any one of claims 1 to 4, wherein the lipoxin analog has the formula:

III. The documents cited during the proceedings before the examining division and the board of appeal include the following:

(1) WO-A-01/70664

(2) WO-A-95/01179

IV. The examining division held the subject-matter of the request not to be new with respect to documents (1) and (2).

V. The appellant lodged an appeal against said decision of the examining division and filed grounds of appeal relating to the set of claims filed with letter of 28 April 2005 and on the basis of which the examining division had taken its decision. In addition, this submission of 10 March 2008 contained two further sets of claims as first and second auxiliary request.

The wording of claim 1 of the first auxiliary request is as follows:

"A method for lessening an inflammatory response resulting from a bacterial infection comprising: administering to a subject a therapeutically effective amount of a purified lipoxin, such that the subject's tissues express increased levels of bactericidal permeability increasing protein (BPI); and wherein the bacteria are sensitive to BPI and the infection is decreased."

Claim 1 of the second auxiliary request reads as follows:

"A method of investigating the ability of a lipoxin compound to treat an infection caused by gram-negative bacteria, which method comprises testing the effect of said lipoxin on the expression regulation of bactericidal permeability increasing protein (BPI)."

- VI. Oral proceedings took place on 10 July 2012 in the presence of the representative of the appellant.
- VII. The arguments of the appellant in both the written and oral proceedings may be summarised as follows:

With respect to Article 52(2) EPC and relating to claim 1 of the main request it was emphasised that documents (1) and (2) did not refer to the use of any lipoxin, as defined by the formulae, in a medicament for treating infection caused by gram-negative bacteria by way of causing a subject's tissue to express increased levels of bactericidal permeability increasing protein (BPI). This subject-matter was new in particular because of the disclosure of the mechanism for causing expression of increased levels of BPI.

In the applicant's opinion, the wording of claim 1 of the first auxiliary request involved no problem with respect to Article 53(c) EPC.

Claim 1 of the second auxiliary request was to be derived from the overall content of the application as filed, exhibited no problems with respect to

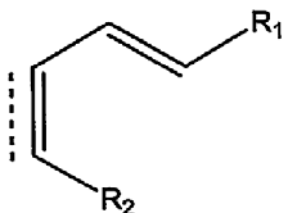
Article 83 EPC because of the examples that were disclosed in the application and, finally, there were no problems with respect to Article 84 EPC, even with regard to the considerations set out by the examining division in the communications cited in its decision.

VIII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request filed with the letter dated 28 April 2005 or, alternatively, on the basis of one of the two auxiliary requests filed with the letter dated 10 March 2008.

Reasons for the Decision

1. The appeal is admissible.
2. The amended claims filed by the appellant with letter of 10 March 2008 represent an attempt to overcome the objections raised by the examining division in its decision. Consequently, they are admitted into the proceedings.
3. *Claim 1 of the main request; Article 52 EPC*
 - 3.1 The subject-matter of this claim relates to the use of lipoxin or a lipoxin analog selected from the pool defined by a generic formula for the preparation of a medicament for treating infection caused by gram-negative bacteria by causing a subject's tissue to express increased levels of bactericidal permeability increasing protein (BPI).

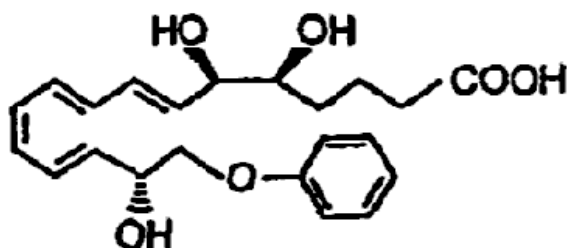
One example of a lipoxin or lipoxin analog comprised in the generic formula



is where R_1 is the fourth member out of the list following the formula on page 94 of claim 1 and R_a is hydrogen (lines 6 and 7 on page 101 of the claim),

and where R_2 is the sixth member out of the second list following the formula on page 95 of claim 1 and R_x is substituted phenoxy containing Z_i , Z_{ii} , Z_{iii} , Z_{iv} and Z_v as hydrogen according to lines 9 and 15 to 17 together with line 12 on page 101 of the claim,

which results in the following chemical formula:



3.2 Document (1) relates to the treatment of illnesses caused by gram-negative bacteria (see claim 12 together with page 2, lines 25 to 28) by use of lipoxin analogs (see claim 11 together with claim 10 and claim 2); the suggested lipoxin analogs comprise exactly the lipoxin

analog of the application in suit as defined above (see document (1), figure 4 and page 30, lines 4 to 10).

Thus, one of the lipoxin analogs, disclosed as an individualised, particular substance administered in an experiment showing its usefulness for the treatment of illnesses caused by gram-negative bacteria according to document (1) matches the generic formula claimed in the application in suit.

- 3.3 Accordingly, the technical teaching set out in claim 1 of the main request in the form of a second medical use which refers to the substance to be used, to the medicament to be prepared and to the illness to be cured is the same in this claim 1 as in the technical teaching disclosed in document (1). The same substance must inevitably act in the same manner and follow the same mechanism or mechanisms in both cases.

Therefore, the subject-matter of claim 1 of the main request is not new with respect to the teaching of document (1).

4. *Claim 1 of auxiliary request 1; Article 53(c) EPC*

- 4.1 Article 53(c) EPC stipulates:

"European patents shall not be granted in respect of:

(c) methods for treatment of the human or animal body by surgery or therapy ...; this provision shall not apply to products, in particular substances or compositions, for use in any of these methods."

4.2 Claim 1 of the first auxiliary request relates to

a method for lessening an inflammatory response
resulting from a bacterial infection comprising:
administering to a subject

with the definition of "subject" being "intended to
include living organisms susceptible to conditions or
diseases caused or contributed bacteria and pathogens
as generally disclosed, but not limited to, throughout
this specification. Examples of subjects include humans,
dogs, cats, cows, goats, and mice. The term subject is
further intended to include transgenic species." (see
page 64 of the description as originally filed, lines 6
to 10).

4.3 "Lessening an inflammatory response resulting from a
bacterial infection" is a therapeutical treatment.
Consequently, the subject-matter of claim 1 of the
first auxiliary request is a method for treatment of
the human or animal body by therapy and therefore is
not patentable.

5. *Claim 1 of the second auxiliary request; Article 84 EPC*

5.1 This claim relates to

a method of investigating the ability of a lipoxin
compound

The feature that "a lipoxin compound" is defined to be
the subject of the investigation means that the pool of
substances to be tested is intended to be limited in

order not to comprise all organic compounds in their entirety.

Therefore, also this feature in claim 1 of the second auxiliary request - just like the other features contained in the claim - must comply with Article 84 EPC requiring the claims to define the matter for which protection is sought and to be clear and concise.

The term "a lipoxin compound" *per se* cannot provide a sufficient definition of the limited pool of related compounds, because it is not clear what kinds of compounds similar to lipoxines are being included by opening the term "lipoxin" to the broader term "lipoxin compounds".

5.2 Accordingly, the teaching of claim 1 of the second auxiliary request is in breach of Article 84 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

U. Oswald