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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

DOCKET NO. JAB 775

ANTICIPATED CLASSIFICATION OF THIS APPLICATION:

PRIOR APPLICATION: JAB 600

CLASS \_\_\_\_\_ SUBCLASS \_\_\_\_\_

EXAMINER: R. Travers

ART UNIT: 125

The Hon. Commissioner of Patents and Trademarks  
Washington, D. C. 20231

Dear Sir:

This is a request for filing a

Continuation

Divisional

application, under 37 CFR 1.60, of pending prior application Serial No. 325,181, filed on March 16, 1989, of Raymond Mathieu Xhonneux et al.

(Date)

(Inventor)

for METHOD OF LOWERING THE BLOOD PRESSURE  
(Title of Invention)

- Enclosed is a copy of the prior application, including the Oath or Declaration as originally filed.

I hereby verify that the attached papers are a true copy of prior application Serial No. 325,181, as originally filed on March 16, 1989,

and further that this statement was made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

- The filing fee is calculated below:

Claims as filed in the prior application, including any claims added or canceled by amendment below

For--	No. Filed	No. Extra	Rate	Fee
Total Claims .....	8 - 20 =	0.....	x \$20 =	..\$000.00.
Independent Claims .....	2 - 3 =	0.....	x \$72 =	..\$000.00.
Basic fee (minimum amount required) .....				<u>\$690.00</u>
Total Filing Fee .....				<u>\$690.00</u>

- The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Account No. 10-750/JAB 775/CJM. Three copies of this sheet are enclosed.

4.  A check in the amount of \$\_\_\_\_\_ is enclosed.
5.  Cancel in this application original Claims 2-17 of the prior application before calculating the filing fee. (At least one original independent claim must be retained for filing purposes.)
6.  Amend the specification by inserting before the first line the sentence: --- This is a [X] continuation, [ ] division, of application Serial No. 325,181, filed March 16, 1989. ---
- 
7.  Transfer the drawings from the prior application to this application and abandon said prior application as of the filing date accorded this application. A duplicate copy of this sheet is enclosed for filing in the prior application file.
- 7a.  New formal drawings are enclosed.
- 7b.  Priority of application Serial No. \_\_\_\_\_, filed on \_\_\_\_\_ in \_\_\_\_\_ (Country) is claimed under 35 U.S.C. 119.
- 7c.  The certified copy of the priority application has been filed in prior application Serial No. \_\_\_\_\_, filed \_\_\_\_\_.
8.  The prior application is assigned to JANSSEN PHARMACEUTICA NV.
9.  The power of attorney in the prior application is to Robert L. Minier (Reg. #20,083), Audley A. Ciamporcero, Jr. (Reg. #26,051), Steven P. Berman (Reg. #24,772), Wayne R. Eberhardt (Reg. #22,804), Jason Lipow (Reg. #25,509), Donal B. Tobin (Reg. #25,711), and David J. Levy (Reg. #27,655), Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, New Jersey 08933-7003.
- 9a.  The power appears in the original papers in the prior application.
- 9b.  Since the power does not appear in the original papers, a copy of the power in the prior application is enclosed.
- 9c.  Address all future communications to Robert L. Minier (Reg. #20,083), Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ 08933-7003.
10.  A Preliminary Amendment is enclosed.

January 24, 1992  
(Date)

Charles J. Metz  
Charles J. Metz  
Reg. No. 20,359

Address of Signer:  Inventor(s)  
 Johnson & Johnson  Assignee of complete interest  
 One Johnson & Johnson Plaza  Attorney or agent of record  
 New Brunswick, NJ 08933  Filed under Section 1.34(a)

908-524-2814



07/825488

DOCKET NO. JAB-775

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Raymond Mathieu Xhonneux et al.

For : METHOD OF LOWERING THE BLOOD PRESSURE

Express Mail Certificate

"Express Mail" mailing number RB759706376

Date of Deposit January 24, 1992

I hereby certify that this request for filing a Continuation application under 37 CFR 1.60 of prior application Serial No. 325,181 (JAB-600), copy of prior application, Declaration (2) and Preliminary Amendment and Information Disclosure Statement and reference are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patent and Trademarks, Washington, D.C. 20231.

Charles J. Metz

(Typed or printed name of person mailing paper or fee)

Charles J. Metz

(Signature of person mailing paper or fee)



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JAB 600

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METHOD OF LOWERING THE BLOOD PRESSURE

*13110*

Cross-reference to related applications

*Jim*  
*PB*

This is a continuation-in-part of our copending application 172,747 filed March 23, 1988.

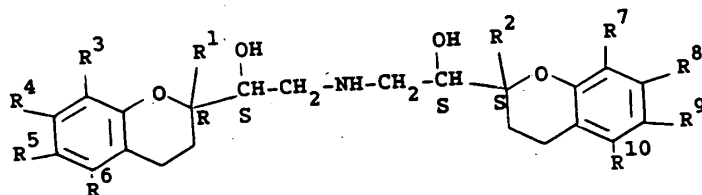
Background of the Invention

In U.S. Pat. No. 4,654,362 there are described 2,2'-iminobisethanol derivatives having  $\beta$  adrenergic blocking properties. It now has been found that a certain class of isomers of said bisethanol derivatives potentiate the activity of blood pressure reducing agents.

Description of the Invention

The present invention is concerned with a group of compounds capable of potentiating the effects of blood pressure reducing agents, said compounds being represented by the formula

*1000030*



(I).

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or the pharmaceutically acceptable acid addition salts thereof, wherein  
R<sup>1</sup> and R<sup>2</sup> each independently are hydrogen or C<sub>1-6</sub> alkyl;  
R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> each independently are hydrogen,  
halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkyloxy, hydroxy, cyano, carboxy or  
5 C<sub>1-6</sub> alkyloxycarbonyl;  
or two vicinal radicals of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> taken  
together may form a -CH=CH-CH=CH- or -(CH<sub>2</sub>)<sub>4</sub>- radical.

As used in the foregoing definitions the term halo is generic to  
10 fluoro, chloro, bromo and iodo; the term "C<sub>1-6</sub> alkyl" defines straight  
and branch chained saturated hydrocarbon radicals having from 1 to 6  
carbon atoms such as, for example, methyl, ethyl, 1-methylethyl,  
1,1-dimethylethyl, propyl, 2-methylpropyl, butyl, pentyl, hexyl and the  
like.

15 The descriptors R and S as used in the above formula (I) indicate  
the absolute configuration at the respective carbon atoms. The carbon  
atom bearing R<sup>1</sup> has the R configuration, whereas the carbon atoms  
bearing the hydroxy functions and the carbon atoms bearing R<sup>2</sup> have the  
S configuration.

20 Preferred compounds of formula (I) are those wherein R<sup>3</sup>, R<sup>4</sup>,  
R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, ~~R<sup>9</sup>~~ and R<sup>10</sup> are hydrogen.

B Particularly preferred are those preferred compounds wherein R<sup>5</sup>  
and R<sup>9</sup> are hydrogen or halo, particularly fluoro.

25 The most preferred compound is [2R,αS,2'S,α'S]-α,α'-[imino-  
bismethylene]bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] or a  
pharmaceutically acceptable acid addition salt thereof.

The compounds of formula (I) can be prepared following the  
30 procedures described in U.S. Pat. No. 4,654,362. Some particular ways of  
obtaining the compounds of formula (I) will be described hereinafter in  
some more detail.

The compounds of formula (I) can be prepared by reacting an oxirane  
35 of formula (II-a) or (II-b) with an amine of formula (III-a) or (III-b).

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