

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF: :

YOSHIHIRO FUJIKAWA ET AL : GROUP ART UNIT:

DIVISIONAL APPLICATION DIVIDED FROM

SERIAL NO.: 07/631,092 :

: EXAMINER:

FOR: QUINOLINE TYPE MEVALONOLACTONES :

DECLARATION UNDER 37 CFR 1.132

HONORABLE COMMISSIONER OF PATENTS & TRADEMARKS  
WASHINGTON, D.C. 20231

SIR:

I, Masaki Kitahara, do hereby declare and state that:

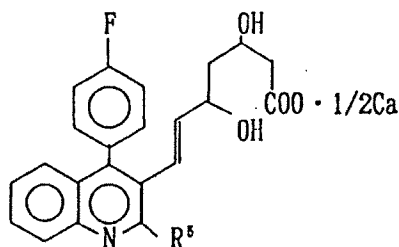
1. I am a named co-inventor in the above-captioned patent application, an employee of Nissan Chemical Industries, Limited, and a citizen and resident of Japan.

2. I am familiar with the above-captioned patent application, and Claims presented by Divisional Application.

3. To demonstrate the unobvious superiority of the subject matter claimed therein, comparative tests were conducted, demonstrating the importance and unobvious superiority conferred on these compounds by the selection

of the cyclopropyl (c-Pr) substituent. These are described as follows:

Data was obtained with regard to the following compound having the formula:



#### TEST METHOD

<u>Compound</u>	<u>R<sup>5</sup></u>	<u>Test A Evaluation</u>	<u>Test B Evaluation</u>
Compound of this Invention	cyclopropyl (c-Pr)	$4.4 \times 10^{-9}$	$35.0 \times 10^{-9}$
Reference Compound	isopropyl (i-Pr)	$23.0 \times 10^{-9}$	$105 \times 10^{-9}$

Test A: Inhibition of cholesterol biosynthesis from acetate in vitro

This test was carried out as described on pages 28-29 of the specification. The above numerical values indicate IC<sub>50</sub> (molar concentration).

Test B:     Inhibition of cholesterol  
              biosynthesis in culture cells

This test was carried out as described on pages 29 to 30 of the specification. The above numerical values indicate IC<sub>50</sub> (molar concentration).

4. Based on the data reported above, it can be determined that the compound of this invention exhibits unobvious superiority, and in particular, sharply enhanced inhibition of cholesterol biosynthesis, in vitro, and culture cell, when compared with the referenced compound of the prior art, and compounds having an identical structure save for the selection of cyclopropyl, as opposed to isopropyl substituent, for R<sup>5</sup>. This enhanced activity could not be predicted on the basis of structure, or information available to those of ordinary skill in the art as of the effective filing date of this application.

All statements made herein of my own knowledge are true, and all statements made on information and belief are believed true. I am aware that willful false statements and the like are punishable by fine, imprisonment or both, 18 U.S.C. §1001, and that such willful false statements may jeopardize the validity of the above-captioned patent application and any patent issuing thereon.

FURTHER, I SAYETH NOT.

May 25, 1992

Date

Masaki Kitahara

Masaki Kitahara