

Title	7-oxo-24, 25-dihydrolanosterol : a novel lanosterol 14 α -demethylase P-450 ₁₄ DM inhibitor which blocks electron transfer to the oxyferro intermediate
Sub Title	
Author	青山, 由利(Aoyama, Yuri) 吉田, 雄三(Yoshida, Yuzo) 園田, よし子(Sonoda, Yoshiko) 佐藤, 良博(Sato, Yoshihiro)
Publisher	共立薬科大学
Publication year	1988
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.33 (1988.) ,p.158- 158
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000033-0158

慶應義塾大学学術情報リポジトリ(KOARA)に掲載されているコンテンツの著作権は、それぞれの著作者、学会または出版社/発行者に帰属し、その権利は著作権法によって保護されています。引用にあたっては、著作権法を遵守してご利用ください。

The copyrights of content available on the KeiO Associated Repository of Academic resources (KOARA) belong to the respective authors, academic societies, or publishers/issuers, and these rights are protected by the Japanese Copyright Act. When quoting the content, please follow the Japanese copyright act.

**7-Oxo-24,25-dihydrolanosterol: a novel lanosterol 14 α -demethylase
P-450_{14DM} inhibitor which blocks electron transfer
to the oxyferro intermediate***

Yuri AOYAMA,** Yuza YOSHIDA,** Yoshiko SONODA,
and Yoshihiro SATO

青山由利, 吉田雄三, 園田よし子, 佐藤良博

7-Oxo-24,25-dihydrolanosterol (3 β -hydroxy-8-lanosten-7-one, 7-oxo-DHL) was a potent competitive inhibitor for lanosterol 14 α -demethylase (cytochrome P-450_{14DM}) of *Saccharomyces cerevisiae*. Affinity of 7-oxo-DHL for the enzyme was more than 50-times higher than those of the inherent substrates, lanosterol and 24,25-dihydrolanosterol. 7-Oxo-DHL accelated NADPH-dependent reduction of cytochrome P-450_{14DM} in the reconstituted system consisting of the cytochrome and NADPH-cytochrome P-450 reductase. These observations indicated that 7-oxo-DHL interacted with the substrate site of cytochrome P-450_{14DM}. However, 7-oxo-DHL was not metabolized by the reconstituted system. Incubation of 7-oxo-DHL with the reconstituted system caused accumulation of oxyferro intermediate of cytochrome P-450_{14DM}. It can thus be concluded that 7-oxo-DHL interfered with electron transfer to the oxyferro intermediate of the cytochrome, though it stimulated reduction of the heme iron. So far as we know, 7-oxo-DHL is the first example of a cytochrome P-450 inhibitor which selectively interferes with the electron transfer to oxyferro intermediate. 7 α -Hydroxy-24,25-dihydrolanosterol was also a competitive inhibitor of cytochrome P-450_{14DM}. However, this compound was metabolized by the reconstituted system and could not block the electron transfer to oxyferro intermediate. 11-Oxo-24,25-dihydrolanosterol, an isomer of 7-oxo-DHL, did not have such inhibitory effects. These lines of evidence suggest a possibility that the keto group at C-7 of lanost-8-ene skeleton may interact with a certain site of cytochrome P-450_{14DM} which has an important role in the electron transfer to oxyferro intermediate.

* 本報告は *Biochim. Biophys. Acta* 922: 270-277 (1987) に発表.

** 武庫川女子大学, 薬学部.