VERSITA

Chemical Papers 67 (6) 667–671 (2013)
DOI: 10.2478/s11696-013-0323-y

SHORT COMMUNICATION

In situ bioconversion of compactin to pravastatin by *Actinomadura* species in fermentation broth of *Penicillium citrinum*

[a]Ajaz Ahmad, [b]Mohd Mujeeb, [b]Rohit Kapoor, [b]Bibhu Prasad Panda*

[a]*Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh-11451; Saudi Arabia*

[b]*Microbial & Pharmaceutical Biotechnology Laboratory, Centre for Advanced Research in Pharmaceutical Science, Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, New Delhi-110062, India*

Received 20 August 2012; Revised 28 October 2012; Accepted 9 November 2012

The biocatalytic production of pravastatin from compactin by hydroxylation has found many applications in health care and pharmaceuticals. *Actinomadura macra*, *Actinomadura madurae*, and *Actinomadura livida* can efficiently bioconvert compactin to pravastatin. The fermentation broth (*Penicillium citrinum* fermented media) harvested on the eighth day contained 388.90 mg L^{-1} of compactin and an undetectable level of mycotoxin (citrinin). Bioconversion by *A. macra* was highest (87 %) in the yeast extract-amended medium. The anti-actinomadura effects of citrinin reduce the bioconversion capacity of *Actinomadura*. The in situ hydroxylation of compactin produced by *P. citrinum* represents a preferable alternative for the use of purified compactin, as a way to reduce cost and time processing.

Keywords: *Actinomadura* sp., *P. citrinum*, compactin, pravasatin, in situ bioconversion

Pravastatin suppresses cholesterol biosynthesis by inhibiting a 3-hydroxy-3-methyl glutaryl CoA reductase. Initially, pravastatin was isolated as a metabolite product of compactin from canine urine. Subsequently, pravastatin was developed as a new therapeutic agent for the treatment of hypercholesterolemia (Yamashita et al., 1985; Shepherd et al., 1995; Barrios-González & Miranda, 2010). Pravastatin is produced by chemical synthesis from compactin. However, due to the high cost and the occurrence of stereoisomers, pravastatin production by microbial hydroxylation is preferred. Pravastatin can be produced by a two-step process, in which the first step is the production of compactin by an appropriate microbial strain such as *Penicillium citrinum*; subsequently, hydroxylation of compactin at the C-6 position can be performed either by a chemical method or by a fermentation process (Chen et al., 2006).

An extensive survey of the literature shows the use of purified compactin for the production of pravastatin by actinomycetes such as *Streptomyces carbophillus* SANK 62585, Streptomyces sp. Y-110, catalysed by the cytochrome P450 monooxygenase system, or by *Actinomadura* sp. ATCC 55678, catalysed by the hydroxylase enzyme (Hosobuchi et al., 1993; Peng & Demain, 2000; Park et al., 2003). To reduce the cost and time of processing, the present research proposes use of the entire fermented broth containing compactin rather than the purified compactin. To this end, a fermented broth containing spent medium, compactin, mycotoxin (citrinin), and *Penicillium citrinum* cell fragments were used for testing the bioconversion of compactin to pravastatin by three *Actinomadura* species, namely *Actinomadura livida*, *Actinomadura macra*, and *Actinomadura madurae*.

Cultures of *Penicillium citrinum* MTCC 1256, *Actinomadura madurae* MTCC 1120, *Actinomadura macra* MTCC 2559, and *Actinomadura livida* MTCC 1382 were obtained from MTCC, IMTECH, India. *P. citrinum* was maintained on PDA slants. *A. madurae* and *A. livida* were maintained in a growth medium, *A. macra* was maintained in a growth

*Corresponding author, e-mail: bibhu_panda31@rediffmail.com