

Preparation of Crucial Chiral Intermediate for The Synthesis of Ezetimibe by Asymmetric Bioreduction

Abstract

Ezetimibe (Zetia®) is a novel selective cholesterol absorption inhibitor cholesterol-lowering drug. (5*S*)-(4-fluorophenyl)-5-hydroxypentanoic acid is a crucial chiral intermediate for the synthesis of cholesterol-lowering drug Ezetimibe (Zetia®), which can be prepared by chemical synthesis or biocatalytic asymmetric reduction. Biocatalytic asymmetric reduction has the characteristics of high stereoselectivity and environment friendly compared with chemical method. The synthesis of a crucial chiral intermediate (5*S*)-(4-Fluorophenyl)-5-hydroxypentanoic acid for Ezetimibe by biocatalytic asymmetric reduction is a research hotspot in recent years.

In this study, we optimized the fermentation conditions and the parameters for microbial transformation of 5-(4-fluorophenyl)-5-oxopentanoic acid(FPOPA) to (5*S*)-(4-Fluorophenyl)-5-hydroxypentanoic acid ((5*S*)-FPHPA) using a novel bacterial strain ZJPH1305, which was isolated from soil samples. Under the optimum medium conditions, the biomass is 1.2-fold over the initial level, and the enzyme activity is 7.1-fold increase over the original medium components.