Improved lovastatin production by inhibiting (+)-geodin biosynthesis in aspergillus terreus

ABSTRACT

Lovastatin is widely prescribed to reduce elevated levels of cholesterol and prevent heart-related diseases. Cultivation of Aspergillus terreus (ATCC 20542) with carbohydrates or low-value feedstocks such as glycerol produces lovastatin as a secondary metabolite and (+)-geodin as a by-product. An A. terreus mutant strain was developed (gedCΔ) with a disrupted (+)-geodin biosynthesis pathway. The gedCΔ mutant was created by inserting the antibiotic marker hygromycin B (hyg) within the gedC gene that encodes emodin anthrone polyketide synthase (PKS), a primary gene responsible for initiating (+)-geodin biosynthesis. The effects of emodin anthrone PKS gene disruption on (+)-geodin and lovastatin biosynthesis and the production of the precursors acetyl-CoA and malonyl-CoA were investigated with cultures based on glycerol alone and in combination with lactose. The gedCΔ strain showed improved lovastatin production, particularly when cultivated on the glycerol-lactose mixture, increasing lovastatin production by 80% (113 mg/L) while simultaneously inhibiting (+)-geodin biosynthesis compared to the wild-type strain. This study thus shows that suppression of the (+)-geodin pathway increases lovastatin yield and demonstrates a practical approach of manipulating carbon flux by modulating enzyme activity.

Keyword: (+)-Geodin; Aspergillus terreus; Emodin anthrone polyketide synthase; Gene knockout; Lovastatin