

## 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 (*gedC*Δ) with a disrupted (+)-geodin biosynthesis pathway. The *gedC*Δ 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 *gedC*Δ 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