Form 2

**Dissertation Abstract**

| Report no. | No. 242 (Dissertation-based) | Name | Ammara Khalid |
|---|---|---|---|
| Dissertation title | Terpenoid production using *Streptomyces reveromyceticus* SN-593<br>*Streptomyces reveromyceticus* SN-593を活用したテルペノイド生産 | | |


Abstract

*※The abstract should be in keeping with the structure of the dissertation (objective, statement of problem, investigation, conclusion) and should convey the substance of the dissertation.*

Terpenoids represent the largest class of natural products, some of which are utilized for pharmaceuticals, fragrances, and fuels. Generally, the mass production of valuable terpenoid compounds was hampered by low abundance in producing organism and the difficulty in chemical synthesis. Therefore, to produce pharmaceutically valuable compounds the development of microbial biosynthetic platform has been a key approach. So far, extended efforts have been made to establish microbial terpenoid production platform using *Escherichia coli* and yeast. On the other hand, a specialized platform for terpenoid production has not been developed for *Streptomyces* species, although they have a large capacity to produce secondary metabolites such as polyketide compounds. Here we describe the development of a host platform in *Streptomyces reveromyceticus* SN-593 by optimizing its precursor supply for terpenoid production. We also demonstrated that a coordination of gene expression between primary and secondary metabolism through metabolically synchronized promoter is essential to achieve higher yield. After introducing farnesyl pyrophosphate from chicken and botryococcene synthase genes, from *Botryococcus braunii,* to the metabolically engineered lines, we achieved 212±20 mg/L botryococcene and 98±12 mg/L squalene respectively. Our findings show that *Streptomyces reveromyceticus* SN-593 has a potential to be developed as an efficient host platform and can produce terpenoid compounds with significant pharmacological applications at a level much higher than previously reported microbial host platforms