Terpenoids play a major role as natural products in pharma, food and cosmetics. Among these terpene-based natural products play a major role, especially for drugs like paclitaxel, artesiminin and steriods, terpenoids are a structural source in the drug discovery process. Most natural products are produced in low quantities only why alternative production systems like microorganisms are of high interest. Xanthophyllomyces dendrorhous is well known as high producer for astaxanthin as orange dye in salmon. Due to high biosynthetic rates for corresponding precursor X. dendrorhous was studied for its capability to accept heterologous genes for biosynthesis of non carotenoids like sequiterpenoids.

By metabolic engineering, approaches knock out mutants have been constructed to accumulate farnesyl diphasphate as central precursor towards α-cuprenene as model compound (Figure 1).

The heterologous gene (Cop6) derived from the fungus Coprinus cinereus was cloned into X. dendrorhous. Cop6 produces, starting from FPP, the sesquiterpene α-cuprenene, which is the basic structure for the formation of lagopodin A, an antimicrobial sesquiterpene quinon. We compared the production of α-cuprenene in E. coli, S. cerevisiae and with main focus on three different mutants obtained for X. dendrorhous to identify the organism that could accumulate the highest concentration of sesquiterpene (Figure 2).

α-cuprenene was successfully identified by GC-MS and structure elucidated (Figure 3). For the first time a heterologous gene was cloned and expressed successful in X. dendrorhous, which may give a start for genetic and biochemical exploration of this important technical strain as terpenoid platform organism in the future.

Figure 2. Production of α-cuprenene in minimal medium in X. dendrorhous

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Figure 3. Chromatograms of the diluted dodecane from X. dendrorhous and ΔE-Cop6. The peak at 13.5 minutes is the -hexadecane used as internal standard. The α-cuprenene has a retention time of approximately 12.8 minutes

**Publications:**


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*Dr. E. Mellilo carried out the practical work at the RUG.*