

## Biosynthesis of Natural and Halogenated Plant Alkaloids in Yeast

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**Abstract :** Monoterpenoid indole alkaloids (MIAs) represent a large class of natural plant products with marketed pharmaceutical activities against a wide range of applications, including cancer and mental disorders. Halogenated MIAs have shown improved pharmaceutical properties; however, characterisation and synthesis of new-to-nature halogenated MIAs remain a challenge in slow-growing plants with limited genetic tractability. Here, we demonstrate a platform for de novo biosynthesis of two bioactive MIAs, serpentine and alstonine, in baker's yeast *Saccharomyces cerevisiae*, reaching titers of 8.85 mg/L and 4.48 mg/L, respectively, when cultivated in fed-batch micro bioreactors. Using this MIA biosynthesis platform, we undertake a systematic exploration of the derivative space surrounding these compounds and produce halogenated MIAs. The aim of the current study is to develop a fermentation process for halogenated MIAs.

**Keywords :** monoterpenoid indole alkaloids, *Saccharomyces cerevisiae*, halogenated derivatives, fermentation

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