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Designing in vitro enzymatic cascades for the synthesis of Amaryllidaceae alkaloids

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PURPOSE OF THE ABSTRACT
Designing in vitro enzymatic cascades for the synthesis of Amaryllidaceae alkaloids

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"Amaryllidaceae alkaloids are plant medicinal compounds that have been used as natural remedies for centuries in various cultures. The structural complexity of these compounds makes them challenging to produce through chemical synthesis at scale. Therefore, new more environmentally friendly alternatives are being explored to produce these alkaloids. Some examples include the metabolic engineering of plants or in vivo heterologous expression of the biosynthetic pathway in model organisms like yeast [1], while others focus on in vitro biosynthetic pathway assembly by designing modular enzymatic cascades that lead to rapid and selective product formation [2]. This research focuses on the later approach since it allows better control of the individual components of the reaction and provides flexibility with regards to the product analogues that can be chosen as targets, rather than being limited to the natural product. This approach has been particularly successful with the benzylisoquinoline alkaloids (BIAs) family [3], however, the Amaryllidaceae alkaloids remain relatively unexplored.
In this work, the first-committed enzyme of the Amaryllidaceae biosynthetic pathway, norbelladine synthase [4], has been coupled to other enzymes in a cascade with the aim to generate an in vitro platform for the production of novel alkaloids. Furthermore, in-silico analysis of the central enzyme from the BIAs pathway, norcoclaurine synthase revealed significant sequence homology with norbelladine synthase and rational mutagenesis has been performed to explore their specificities."

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FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

Biosynthetic Pathway | Amaryllidaceae Alkaloid | Enzyme engineering | In-silico modelling

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