BIOTRANS
LA ROCHELLE 2023

N°1504 / PC
TOPIC(s) : Biocatalytic cascade reactions

Multienzymatic biotransformation of flavokawain B by entomopathogenic filamentous fungi.

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PURPOSE OF THE ABSTRACT

Flavokawain B is one of the naturally occurring chalcones in the kava plant (Piper methysticum)[1]. It exhibits anticancer[2]–[4], anti-inflammatory[5], [6] and antimalarial properties[7], [8]. Due to its beneficial therapeutic potential, flavokawain B is likely to be used to treat many diseases. However, its poor bioavailability and low aqueous solubility support the view that the application is still limited. The attachment of a sugar unit impacts the stability and solubility of flavonoids and often also determines their bioavailability and bioactivity[9]–[11]. Biotransformation is an environmentally-friendly way to improve the properties of compounds, for example, to increase their hydrophilicity and thus affect their bioavailability[12].

Recent studies proved that entomopathogenic filamentous fungi from the genus Isaria and Beauveria can perform O-methylglycosylation of hydroxyflavonoids or O-demethylation and hydroxylation of selected chalcones[10] and flavones[11]. In the presented study, we examined the ability of entomopathogenic filamentous fungi from Beauveria bassiana, B. caledonica, Isaria farinosa, I. fumosorosea, and I. tenuipes to transform flavokawain B into its glycosylated derivatives. The main process occurring during the reaction is O-demethylation and/or hydroxylation followed by 4-O-methylglycosylation. The substrate used was characterized by low susceptibility to transformations compared to our previously described transformations of flavones and chalcones in the cultures of the tested strains. However, in the culture of the B. bassiana KCh J1.5 and BBT, Metarhizium anisopilae KCh Ma, and I. farinosa KCh It, the expected methylglycosides were obtained with high yields.

B. bassiana KCh J1.5 performed either 4'-demethylation, 4'-O-methylglycosylation or 4'-O-methylglycosilation with simultaneous hydroxylation in the meta position in the B ring of the substrate. Also formation of products of 3-O-methylglycosylation and 4-hydroxylation with 3-O-methylglycosylation was observed. In the case of M. anisopilae KCh Ma formation of 4'-O¬-methylglicosides and 4'-O-methylglicosides with concurrent meta or para hydroxylation of B ring of the substrate was noticed. The product of 4'-demethylation of flavokawain B was identified as well. Our results prove that multiple enzymes were involved in forming the products in the

entomopathogenic filamentous fungi cultures.

FIGURES

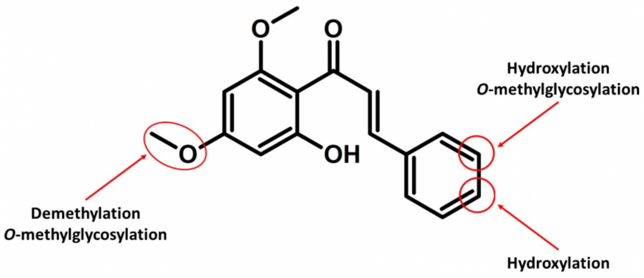

FIGURE 1
Biotransformation sites in flavokawain B.

FIGURE 2

KEYWORDS
biotransformations | entomopathogenic fungi strains | flavokawain B | 4-O-methylglycosylation

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