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TOPIC(s) : Biocatalytic cascade reactions

Microbial transformation of bromo and chloro flavonoids in the culture of entomopathogenic filamentous fungi

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PURPOSE OF THE ABSTRACT

Bacterial resistance to antibiotics is a significant global problem nowadays. The pharmaceutical industry is constantly looking for new compounds that prevent antibiotic resistance. Flavonoid compounds with bromine and chlorine atoms may be the solution, as some of them show bacteriostatic/bactericidal properties [1] [2].

Many naturally bioactive chemical compounds, including flavonoids, occur in nature in the form of glycosides, which improves their solubility [3]. Obtaining flavonoid glycosides using a chemical method is extremely difficult and requires toxic reagents. Contrary, biotransformation is a simple method that allows obtaining flavonoid derivatives, including glycosides, under mild reaction conditions [4] [5].

The presented research aimed to combine chemical synthesis with microbial transformation to obtain flavonoid glycosides with bromine and chlorine atoms. As a result of the Claisen-Schmidt condensation reaction and its further transformations, chalcone, flavanone, and flavone containing -Br and -Cl in the A ring were obtained. Then, the biotransformations of these compounds were carried out in cultures of entomopathogenic strains of the filamentous fungi Beauveria bassiana KCH J1.5, Isaria fumosorosea KCH J2, and Isaria farinosa KCH J2.6. For the compound 3'-bromo-5'-chloro-2'-hydroxychalcone, the biotransformation was the most effective in the culture of the B. bassiana KCH J1.5 strain. As a result of the reaction, 8-bromo-6-chloroflavanone 3'-O-β-D-(4"-O-methyl)-glucopyranoside was obtained. Another compound, 8-bromo-6-chloroflavanone, was transformed by I. fumosorosea KCH J2 to give 8-bromo-6-chloroflavan-4-ol 4'-O-β-D-(4”-O-methyl)-glucopyranoside. 8-bromo-6-chloroflavone was most efficiently transformed by I. farinosa KCH J2.6 into 8-bromo-6-chloroflavone 4'-O-β-D-(4”-O-methyl)-glucopyranoside. Because the properties of the obtained glycosides have never been described in the literature, activity prediction of the above products was carried out. Pass online and Swiss ADME platforms have shown that all obtained glycoside products are potential CDP-glycerol glycerophosphotransferase inhibitors with a probability of over 90%. CDP-glycerol glycerophosphotransferase polymerizes the main chain of wall teichoic acid (WTA) associated with the cell wall of gram-positive bacteria, which in turn is responsible, among others, for antibiotic resistance. In the absence of WTA, bacteria are sensitive to external factors (temperature, salt content), which can contribute to the fight against pathogenic gram-positive bacteria in the human body [6]. Moreover, activity predictions of the products of the biotransformation process showed many other properties, such as anti-carcinogenic, anti-inflammatory, or hepatoprotective. However, further in vitro studies are needed to confirm them.

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FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

microbial transformation | entomopathogenic filamentous fungi | halogenated flavonoids | antibiotic resistance

BIBLIOGRAPHY