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NOVEL ARYLSULFOTRANSFERASES FOR SULFATION OF (POLY)PHENOLS

AUTHORS
Kateřina VALENTOVÁ / INSTITUTE OF MICROBIOLOGY OF THE CZECH ACADEMY OF SCIENCES, VÍDEŇSKÁ 1083, PRAGUE
Katerina BRODSKY / INSTITUTE OF MICROBIOLOGY OF THE CZECH ACADEMY OF SCIENCES, VÍDEŇSKÁ 1083, PRAGUE
Barbora PETRÁNKOVÁ / INSTITUTE OF MICROBIOLOGY OF THE CZECH ACADEMY OF SCIENCES, VÍDEŇSKÁ 1083, PRAGUE
Lucie PETRÁSKOVÁ / INSTITUTE OF MICROBIOLOGY OF THE CZECH ACADEMY OF SCIENCES, VÍDEŇSKÁ 1083, PRAGUE
Pavla BOJAROVÁ / INSTITUTE OF MICROBIOLOGY OF THE CZECH ACADEMY OF SCIENCES, VÍDEŇSKÁ 1083, PRAGUE

PURPOSE OF THE ABSTRACT
Sulfation is an important reaction in nature, and sulfated (poly)phenolic compounds are of interest as standards of mammalian phase II metabolites or pro-drugs. Due to their complex structure, a large number of structurally different metabolites, such as mono-, di- or trisulfates, can be formed. Their isolation from biological material is impractical; however, they can be synthesized in vitro.
Nature has developed efficient sulfation tools using 3′-phosphoadenosine 5′-phosphosulfate (PAPS) as a sulfate donor for a variety sulfotransferases (SULTs, EC 2.8.2). In general, sulfotransferases catalyze the transfer of a sulfuryl group from a donor to an acceptor substrate. Most sulfation reactions in vivo are catalyzed by various SULTs. However, these typically intracellular enzymes are inherently unstable under in vitro conditions. The major bottleneck in SULT-catalyzed reactions is the need to use PAPS, which is extremely expensive and unstable (1). A more promising group of enzymes for potential use in the laboratory are PAPS-independent arylsulfotransferases (ASTs, EC 2.8.2.1) that use simple aromatic sulfate donors such as p-nitrophenyl sulfate (p-NPS). These enzymes of bacterial origin appear as an elegant synthetic tool for the "green" and sustainable sulfation of polyphenols. Moreover, they are easily expressed heterologously in E. coli.
There are only a few arylsulfotrasferases that have been characterized and used for the sulfation of (poly)phenols. The best studied is the recombinant AST from Desulfitobacterium hafniense (2-8).
In the present study, five potential recombinant arylsulfotrasferases were produced in E. coli, purified to homogeneity, and characterized. These enzymes were then tested in sulfation reactions with p-NPS as the donor and various phenolic compounds as acceptors: Flavonoids, flavones, phenolic acids, and even phenolic glycosides. The reactions were performed both on an analytical and preparative scale. The tested enzymes showed different substrate preferences, which helped us to find the optimal conditions for the preparation of sulfate derivatives of phenolic compounds. The products were detected by HPLC and some of them were isolated for NMR analysis. Obtaining sufficient amounts of sulfated compounds should allow us to characterize the human metabolites in terms of their stereochemistry and sulfation sites.
In conclusion, enzymatic sulfation of polyphenols with bacterial ASTs is an effective method for producing metabolites identical to metabolic intermediates found in the human body.

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FIGURES

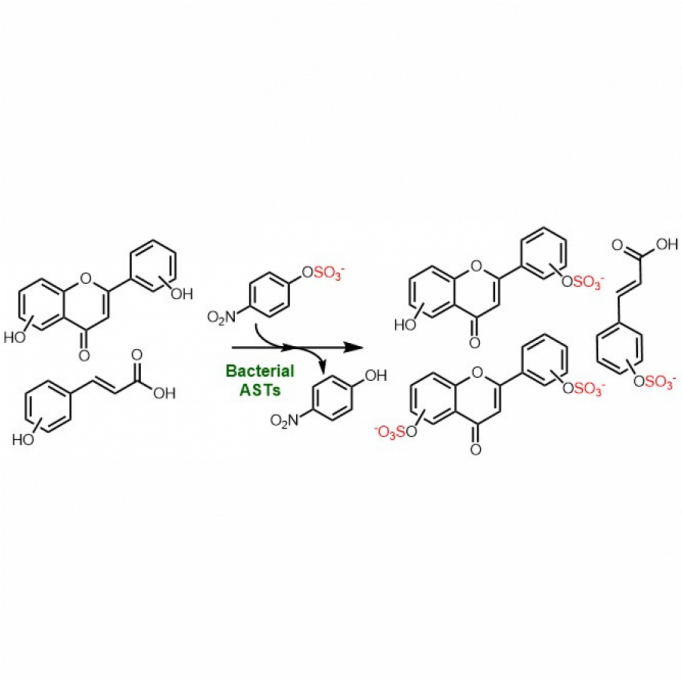

FIGURE 1

Sulfation of phenols by bacterial arylsulfotransferases

AST - arylsulfotransfererase

FIGURE 2

KEYWORDS

arylsulfotransferase | polyphenols | sulfation | enzyme catalysis

BIBLIOGRAPHY