MICROBIAL PLATFORM TO SYNTHESIZE CHORISMATE DERIVATIVES VIA METABOLIC ENGINEERING APPROACH

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A synthetic metabolic pathway suitable for the production of chorismate derivatives was designed in *Escherichia coli*. An L-phenylalanine-overproducing E. coli strain was engineered to enhance the availability of phosphoenolpyruvate (PEP), which is a key precursor in the biosynthesis of aromatic compounds in microbes. Two major reactions converting PEP to pyruvate were inactivated. Using this modified *E.coli* as a base strain, we tested our system by carrying out the production of salicylate, a high-demand aromatic chemical. The titer of salicylate reached 11.5 g/L in batch culture after 48 h cultivation in a 1-liter jar fermentor, and the yield from glucose as the sole carbon source exceeded 40% (mol/mol). In this test case, we found that pyruvate was synthesized primarily via salicylate formation and the reaction converting oxaloacetate to pyruvate. In order to demonstrate the generality of our designed strain, we employed this platform for the production of each of 7 different chorismate derivatives. Each of these industrially important chemicals was successfully produced to levels of 1-3 g/L in test tube-scale culture. In addition, by extending chorismate pathway, we successfully achieved maleate production, which is one of significant dicarboxylic acid as well as succinate and malate. A novel synthetic pathway of maleate was constructed in our base strain, and the productivity reached 7.1 g/L. This is the first report about maleate production using genetically engineered micro-organisms.