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Metabolic pathway engineering for microbial production of aromatic amino acids

María Inés Chávez, Alfredo Martinez, Francisco Bolivar and Guillermo Gosset*
Departamento de Ingenieria Celular y Biocatálisis, Instituto de Biotecnologia, Universidad Nacional Autónoma de México, Apdo Postal 510-3, Cuemavaca, Morelos 62250, México

Abstract

The aromatic amino acids L-tryptophan, L-phenylalanine and L-tyrosine are primary metabolites with multiple applications in the food industry. Fermentative industrial production of these compounds is based on the use of mutant microbial strains selected on the basis of high productivity. The application of metabolic pathway engineering to microbial strain development and improvement. has allowed the rational modification of the metabolic network to reach specific objectives. Metabolic engineering strategies based on the modification of the allosteric and transcriptional regulatory structure of the aromatic pathways. carbohydrate uptake mechanisms and central carbon metabolism. will be presented and discussed in the context of industrial production strain development.

Introduction

Industrial production of amino acids is an economic activity with an estimated annual worldwide sales value of $7.4 billion for 2004. representing a consumption volume of over 2 million tons. World demand for amino acids is expected to grow five percent annually (20). Amino acids have many commercial applications, among them: food-flavoring agents. animal feed supplements and components of pharmaceutical formulations. Of the 20 amino acids found in proteins, three of them. L-tryptophan (L-Trp), L-phenylalanine (L-Phe) and L-tyrosine (L-Tyr) belong to the aromatic group. These amino acids arc essential in the diet of humans and many animals: therefore. they are frequently used as part of animal feed supplements or human enteral and intravenous feeding solutions. About 50 years ago, some of these compounds started to be produced industrially by fermentation processes using microbial strains. In the case of aromatic amino acids. microbial production strains include *Corynebacterium glutamicum*, *Brevibacterium lactofermentum*, *Brevibacterium flavum*, *Bacillus subtilis* and *Escherichia coli*. Generation and improvement of production strains was traditionally carried out by random mutagenesis and selection methods. Although these processes enabled the generation of productive strains. their efficiency and productivity still fell short of the maximum theoretical values estimated for these metabolites. The lack of knowledge about the metabolic pathways involved in the synthesis

*Corresponding author: E-mail: gosset@ibt.unam.mx