Precursor-directed Biosynthesis of 5-Hydroxytryptophan

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Technology description

Organism :E. coli.
Target product and synonyms : 5-hydroxytryptophan, 5-HTP, Serotonyl, Telesol, 5-Hydroxyl-L-tryptophan
Target identifier(s) : CAS: [4350-09-8]
The invention is comprised of genetically modified organisms, which over-express 5-Hydroxytryptophan (5-HTP). 5-HTP is a natural non-proteinogenic amino acid that serves as a direct biosynthetic precursor to the neurotransmitter serotonin. Deficient serotonin in the central nervous system is thought to be an important physiological factor for depression. 5-HTP has been shown to be effective for the treatment of a variety of conditions, including depression, insomnia, chronic headaches and binge eating associated with obesity. At the same time, it has relatively few side effects. The therapeutic efficacy of 5-HTP is due to its ability to enhance the synthesis of serotonin in the brain. 5-HTP is well absorbed from an oral dose and can easily cross the blood-brain barrier. In most European countries, 5-HTP is a commonly prescribed drug for multiple treatment purposes; while in North America market it is sold as an "over-the-counter" dietary supplement.
Currently, 5-HTP is obtained through extraction from the seeds ofGriffonia simplicifolia, a woody climbing shrub grown in Africa. The season- and region-dependent supply of the raw materials has been largely limiting its cost-effective production and broad clinical applications. In addition,Griffoniaderived 5-HTP has been contaminated with a compound called Peak X, leading to the USDA briefly removing the supplement from shelves in the US. The current bulk wholesale price for 5-HTP ranges from 400 to 1000 USD/kg. Yet despite the current high production cost and limited supply, the global market of 5-HTP is still about 50,000 kg (bulk value 20-50 million dollars).
The invention provides compounds, compositions, non-naturally occurring organisms, and methods useful for production of 5-hydroxytryptophan (5-HTP) in a microbial cell. A microbial system which includes at least one microbial cell, such as a bacterial cell or a yeast cell, is genetically engineered to express all or a portion of non-naturally occurring biosynthetic pathway that catalyzes the conversion of a simple carbon source, such as glucose, to 5-HTP. The invention can result in improved titers of 5-HTP and permits low-cost, large scale production. Methods of making and using the genetically engineered cells are also included in the invention.

Institution

University of Georgia

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com