High Yield, Scalable Microbial Production of the Serotonin Precursor 5-hydroxytryptophan

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Technology description

Introduction

Depression is a common mental disorder that threatens millions of people over the world. Deficit of the neurotransmitter serotonin in the central nervous system (CNS) is thought to be an important physiological factor for depression. 5-Hydroxytryptophan (5-HTP) is the direct biosynthetic precursor to serotonin in humans and animals. It has been proven(1,2) to be clinically effective in treating depression, as well as insomnia, fibromyalgia, obesity, cerebellar ataxia, chronic headaches, etc. At the same time, it has relatively few side effects. In most European countries and in Australia 5-HTP is a commonly prescribed drug for multiple treatment purposes; while in the North America market it is sold as an "over-the-counter" dietary supplement. The compound is also prescribed as a appetite suppressant and sleep aid.

Currently, 5-HTP is produced mainly through the extraction from the seeds ofGriffonia simplicifolia, a woody climbing shrub grown in Africa. The season- and region-dependent supply of the raw materials has limited its cost-effective production and broad clinical applications. In addition,Griffoniaderived 5-HTP has been contaminated with a com-pound called "Peak X", leading the USDA to briefly remove the supplement from shelves in the US.

The current bulk wholesale price for 5-HTP ranges from 400 to 1000+ USD/kg. Despite the current high production cost and limited supply, the global market of 5-HTP is still about 25,000 kg—35,000 kg (bulk value US$ 20-40 M). Derivatives of 5-HTP are even more expensive, representing an additional high-value market opportunity.

Consequently, the development of a industrial, inexpensive, reliable and scalable process for the production of 5-HTP and its derivatives that circumvents the cumbersome and expensive plant extract process is highly desirable, and may facilitate the expansion of this high-value market.

1. Birdsall TC (1998) 5-Hydroxytryptophan: a clinically-effective serotonin precursor.Altern. Med. Rev. 3(4):271-280.

2. Turner EH, Blackwell AD (2005). "5-Hydroxytryptophan plus SSRIs for interferon-induced depression: synergistic mechanisms for normalizing synaptic serotonin".Medical Hypotheses65 (1): 138–44.

Summary

UGA bioengineers have developed a novel, highly efficient microbial method for the production of 5-HTP in high titers (over 1.5 g/L after 24h). The method is based on especially constructed

microorganisms that are capable of metabolizing tryptophan into 5-HTP. The method can be implemented using any ofE. coli,S. cerevisiae, PichiaandB. subtilisas the host cell, using inexpensive glucose as the carbon source. This technology is relatively insensitive to temperature, with high titers being observed in the 30oC—37oC range. Addition of small amounts of simple polycarboxylic acids further increases the process yield.

Institution

University of Georgia

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com