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Research Progress of Gamma-Aminobutyric Acid（GABA）

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Abstract. Authores reviewed GABA's physiological functions, preparation methods and the development prospects. Earlier researchers produced GABA by chemical synthesis method. However, it pollutes the enviroment,the reaction is intense, and can't add to the food. Researchers now use microbial fermentation method, in which the lactic acid bacteria fermentation method has good development prospects.

Introduction

Gamma-Aminobutyric Acid(GABA), also known as 4-aminobutyric acid or aminobutyric acid, is a non-protein amino acid. Researchers discovered it in 1883 and found it in animal brain tissue in 1950[1,2]. GABA is widely in nature such as animals, plants and microorganisms[3,4]. In 2009, the Chinese Ministry of Health established γ-aminobutyric acid as a new source of food. It has many physiological functions and has a wide range of applications in the fields of food, medicine, health care and feed processing, and its market demand is growing.

Physiological function and application prospect

Treatment of neurological diseases. GABA is a neurotransmitter with inhibitory effect in brain[5] . Allen [6]prove that virtually every neuron within the suprachiasmatic nucleus (SCN) communicates via GABAergic signaling. The extracellular levels of GABA within the SCN are determined by a complex interaction of synthesis and transport, as well as synaptic and non-synaptic release. Zhou[7] prove that the GABA combined with sertraline is more significant than that of sertraline to improve depression's cognitive function. There are excitatory and inhibitory amino acids in the nervous system. When the excitatory amino acid content is too high, the neurological inhibitory effect will be reduced, which may lead to epilepsy. Lack of GABA or gamma-aminobutyric acid-mediated inhibitory transmission problems, it will lead to excessive neurons[8,9]. Epilepsy is associated with GABA-A receptor plasticity in the brain[10]. GABA can enhance the human anti-convulsive threshold, can effectively treat refractory epilepsy[11]. Okada [12] found that the content of γ-aminobutyric acid in cerebrospinal fluid was negatively correlated with the degree of epilepsy in patients with epilepsy, and the content of GABA was lower than that of normal subjects. Therefore, in the treatment of epilepsy patients, people can improve the cerebrospinal fluid GABA content to improve the treatment of patients with epilepsy. When cerebral ischemia, GABA can effectively reduce glutamate-induced neurogenic excitement, and the damage to nerve cells[13]. GABA can treat Parkinson and stiff-person syndrome[14].

Improve cardiovascular and cerebrovascular diseases. Diabetes and hypertension significantly increased the number of patients. So far, there are about 114 million and 266 million patients with diabetes and hypertension in China, respectively[15]. GABA has a certain pharmacological function in the blood pressure and soothing blood vessels[16]. GABA modulates cardiovascular system by

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acting on central nervous system and peripheral tissues[17]. Huang[18] demonstrated that GABA can reduce blood sugar, he fed the rats with water GABA tea extracts of containing GABA either 3.01 or 30.1 μg/rat per day for 6 weeks. Treatment with GABA tea dose-dependently lowered blood glucose level in the diabetic rats compared with vehicle. GABA tea reduced the diabetic-induced Fas-dependent and mitochondrial-dependent apoptotic pathway in the diabetic cerebral cortex compared with vehicle, the evidence for which is based on decreases in Fas, activated caspase-8, pro-apoptotic t-Bid, Bax, cytosolic cytochrome c, activated caspase-9 and activated caspase-3.

Other functions. GABA can help people improve sleep, memory,liver function,fertilization rate and so on. In addition, it has a similar glutamic acid sweet, can enhance food flavor. GABA can treat uremia, carbon monoxide poisoning, reduce chronic diseases in clinical medicine [19,20].

GABA preparation and production methods

Chemical synthesis method. Chemical synthesis method is the first industrial production of GABA method, there are two main methods. One is Gamma-valeronitrile and phthalimide potassium reaction at 180℃,then the reaction product reacts with concentrated sulfuric acid, and finally the GABA is obtained by crystallization purification. The other is in turn used calcium hydroxide, ammonium bicarbonate pyrrolidone water loose the ring[21]. However, these two methods pollute the enviroment, the reaction is intense, and can't add to the food.So that he chemical synthesis method's application range is greatly affected.

Plant enrichment method. In plants, GABA can be accumulated by glutamic acid via glutamate decarboxylase decarboxylation[22]. Many Chinese researchers have also carried out plant enrichment of GABA research in recent years[23]. Pretreatment of tea can increase GABA's content. It can change cell membrane function for most plants. It can change cell membrane function for most plants, it also can inhibit microbes in a certain concentration range[24]. Lin S D[25]found that various ethanolic concentrations (0–95%, v/v) and temperatures (25–95 °C) were used to extract GABA tea leaves. It is proved by experiment that water at 50–75 °C gave higher GABA and theanine contents of extracts.

Microbial fermentation method. Lactic acid bacteria(LAB) is widely used, domestic and foreign biologists confirmed that intestinal lactic acid bacteria and health has a very close direct relationship[26]. LAB can improve the body's intestinal function, restore the body's intestinal flora balance, enhance the body's immune capacity, inhibit the growth of spoilage bacteria, lower cholesterol, anti-oxidation, antihypertensive, anti-tumor and so on[27-29]. LAB can also improve food quality and safety. It can inhibit pathogenic bacteria and degrade nitrite in fermented meat[30]. It can effectively remove aflatoxins in dairy products[31]. LAB application technology to become the focus, such as genetic engineering lactic acid bacteria, lactic acid bacteria production enzyme, lactic acid bacteria preparation, starch embedding preparation of microcapsule lactic acid bacteria, selenium-enriched lactic acid bacteria and so on[32-36].Tamura[37] screened a lactic acid bacteria(Enterococcus avium G-15) has a high GABA conversion capability, the conversion rate reached (86.0 ± 5.0)%. Liang[1] isolated the strain from pickled cabbage juice using lactic acid bacteria isolation medium, he obtained strain (Lp-Lw-131) after re-screening and it had better ability to produce GABA. This strain was irradiated with ultraviolet light andthen mutagenized with diethyl sulfate (DES) to improve its ability for GABA production, GABA's average yield was 1.815 g/L. Barla F [38] isolated 10 strains of lactic acid bacteria from traditional Japanese fermented foods that had a high GABA-producing ability of >500 mg/100 ml after 72 h of incubation at 35 ℃. Qiu[39] isolated 23 strains from five kinds of yoghurt and pickles, then selected six strains with high GABA cotent , optimized fermentation medium and the final GABA conversion was 3.9 g/L.

Conclusions and future outlook

There are many reports on GABA's health function, but there is lacking authoritative and conclusive experimental data. A number of domestic and foreign companies have developed GABA related products, of which the most perfect in the Japanese market, the types of food, tea, dairy products, beverages, chocolate and supplements. The use of microbial fermentation to prepare GABA has a good prospect, because of short cycle, mild reaction conditions and environmental pollution. Early studies on the preparation of GABA by microbiological methods have focused on E. coli. The research in recent years has focused on microorganisms that can be safely used for food such as LAB and yeast . LAB has many physiological functions, widely used in the food industry, but we difficult to obtain efficient strains. Future studies will be based on microbial fermentation mechanism and screening with glutamic acid decarboxylase lactic acid bacteria, LAB specific mutagenic treatment, so that the bacteria in specific conditions for abnormal metabolism to get the required high yield and quality of bacteria. We explore Its fermentation conditions, the GABA production is higher, to adapt to industrial production. We further explore its fermentation conditions, so that GABA production is higher to adapt to industrial production.

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