Beneficial effects of Glycine in the Organism

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Glycine is an amino acid that our bodies can produce naturally, so we don't necessarily need to get it from our diet. Nevertheless, it plays a vital role in various functions throughout our entire body. Glycine interacts with specific receptors and transporters found in many different types of cells, which allows it to have important effects on our health. One of the most fascinating things about glycine is its potential to reduce inflammation in our body. Researchers have conducted many studies focusing on this aspect. Glycine has been shown to decrease pro-inflammatory molecules called cytokines, which are responsible for promoting inflammation. Additionally, it can lower the levels of free fatty acids, which are sometimes linked to inflammation in certain situations. Moreover, glycine seems to positively influence how our body responds to insulin, which is crucial for maintaining stable blood sugar levels. It also appears to bring about other beneficial changes in our body, although scientists are still investigating the specific details of these effects. Glycine is a remarkable amino acid that offers many health benefits, especially in terms of reducing inflammation and possibly enhancing how our bodies respond to insulin. It's fascinating because it is present throughout our entire body, and we can obtain it through our diet or nutraceuticals, affecting our health in various ways. Scientists continue to study glycine to unlock its full potential and better understand its role in supporting our well-being.

glycine immunomodulator

1. Introduction

Glycine, also called amino acetic acid, is a vital building block for many proteins and plays a key role in creating important biomolecules like creatine and purine nucleotides . It was discovered in 1820 when gelatine was broken down with acid. Its name comes from the Greek word for "sweet," and it's the smallest amino acid with a molecular weight of 75.067 g/mol [1]. In our bloodstream, glycine makes up about 11.5% of all amino acids and contributes to 20% of the nitrogen in our body's proteins, accounting for 80% of our overall protein content [2][3]. For a typical daily intake, we need about 1.5–3 grams of glycine from our diet [4]. In young men, the rate at which glycine moves through the body is about 34–35 milligrams per kilogram per hour when we're fed, and about half that amount (around 18 mg/kg/h) when we're in the post-absorptive state [5][6]. Around 35% of the glycine in our body is produced internally (endogenous synthesis), while the rest comes from the food we eat [7]. On average, our body generates about 12–15 milligrams of new glycine per kilogram per hour, contributing to about 81% of the total glycine flow in our system [5][8]. The normal glycine concentration in our bloodstream typically ranges from 200 to

300 micromoles per liter. In summary, glycine plays a significant role in our body, and its levels are carefully regulated to support various essential functions [9].

In our bodies, glycine is made from serine, choline, threonine, and glyoxylate [10][11]. This means that our bodies can produce glycine on their own, so it's considered a non-essential amino acid for mammals [2]. Despite not being essential, glycine still has many important roles in various systems within our body (**Figure 1**). Its primary function is connected to the suppression of various parts of the brain. For instance, in the central nervous system (CNS), glycine attaches to specific ion channels that are sensitive to chloride. This action helps in blocking the activity of certain neurons after they receive signals from other neurons [12]. Moreover, glycine plays a critical role in how pain signals are transmitted in our body. If we interfere with the signals related to glycine, either through drugs or genetic changes, it can cause heightened sensitivity to pain in living organisms [13].

Glycine has also been linked to controlling our body's motor functions because it can help improve any motor issues that might occur after surgery [14]. Moreover, glycine is essential for regulating how our genes are expressed, influencing how proteins are shaped and function, and has a hand in various other vital biological processes . Glycine is also involved in several other helpful activities. It can act as an antacid, helping to relieve acidity in the stomach. Moreover, glycine plays a role in regulating the growth hormone (GH) synthesis, which affects our body's growth process. It has positive effects on muscle tone, collagen production, and helps with tissue repair, including scar formation. Additionally, glycine has been reported to protect the intestines from the damaging effects of radiotherapy during cancer treatment .

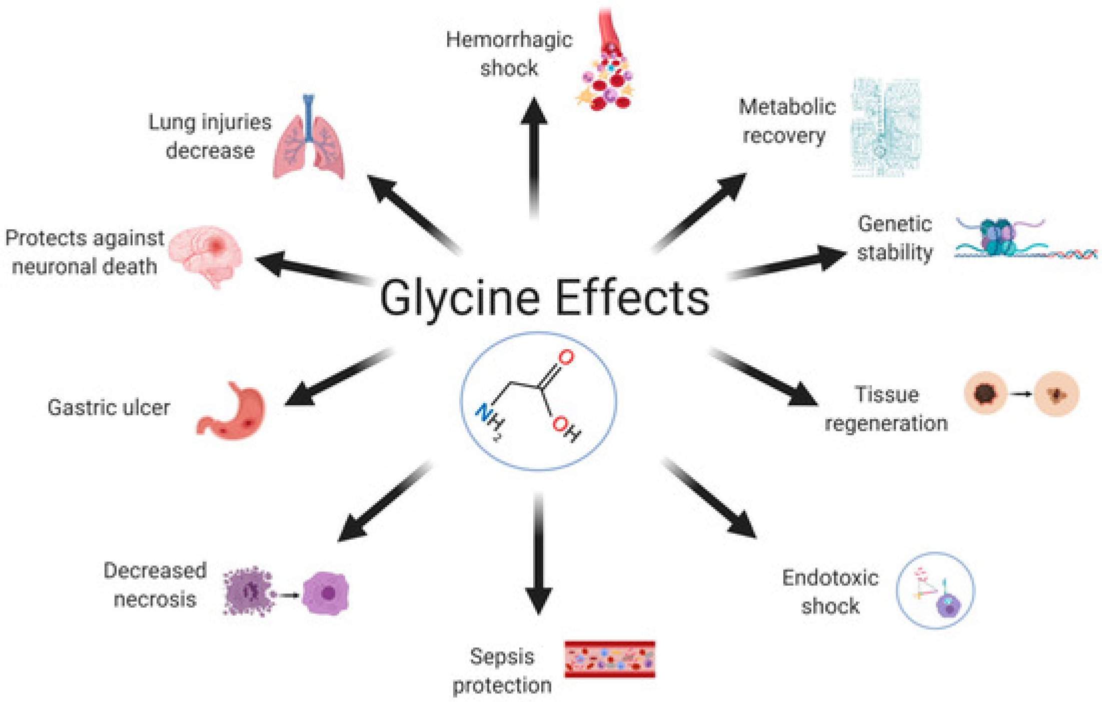

Figure 1. Glycine effects. Glycine is an aminoacid synthetized endogenous and there has been describe many activities in which it participates that include a variety of systems. Glycine has a protective effect in lung, brain, stomach, and intestine; participates in metabolic process; modulate process of the immune system such as tissue

regeneration, decrease necrosis, sepsis protection; and finally, glycine is considerate as a genic expression modulator.

In diabetes, glycine plays a role in stimulating the release of certain hormones that help control blood sugar levels. It acts as a trigger for glucagon-like peptide-1 (GLP-1), insulin, and glucagon . Studies have shown that when glycine is consumed along with other amino acids, it can enhance the secretion of insulin, which helps in managing glucose levels after meals [18]. In people with type 2 diabetes mellitus (T2DM), there is a decrease in the expression of glycine receptors (GlyR) in their cells, which affects how glycine can trigger insulin release [15]. Interestingly, research has found that having higher levels of glycine in the bloodstream is linked to a reduced risk of developing T2DM [16].

2. Effects of Glycine in the Organism

2.1. Neurotransmission

Glycine plays a role in the fast communication between nerve cells, which is controlled by NMDA receptors. These receptors need both glutamate and glycine to work properly and transmit signals effectively 27 [17][18]. Playing a part in neuroplasticity processes, such as learning, memory, and cognition [19][20]. These receptors are important targets for developing therapies to address conditions like Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, schizophrenia, and other psychiatric disorders [21]. Additionally, glycine influences the communication between nerve cells through GlyT1 and GlyT2 [22][23][24]. Mice model without GlyT1 expression experience significant breathing and movement problems because of overly active glycinergic signaling [25][26]. In other scenario when glycine stimulates GPR6, it can reduce cAMP levels in certain brain tissues and increase dopamine (which helps improve movement) [27], This finding suggests a potential target for treating Parkinson's disease [28].

Glycine has shown to be beneficial in safeguarding neurons from damage in both lab experiments (in vitro) and live animal studies (in vivo) [29]. It also exhibits protective effects on neurons and microglia after an injury caused by ischemic stroke, which is a condition where blood supply to the brain is reduced. Glycine achieves this by inhibiting certain factors, such as NF-κB p65 and HIF-1α, while activating AKT and downregulating PTEN. This process helps prevent excessive inflammation and harmful microglia activation caused by the ischemic injury [30]. Clinical studies have revealed that glycine can enhance the outcome for patients recovering from an ischemic stroke [31].

2.2. Antioxidant

Glycine provides protection against the harmful effects of alcohol on the liver by reducing the levels of alcohol and its by-products in the bloodstream. This, in turn, helps to minimize liver damage and slows down the rate at which alcohol is emptied from the stomach [32]. In cell cultures, glycine has been shown to prevent excessive increases in calcium levels inside Kupffer cells at concentrations similar to the levels found in the blood of animals that are fed with glycine [33]. Additionally, glycine plays a protective role against the harmful effects of oxidized oil, leading to notable improvements in the structure and function of the liver [34].

2.3. Immunomodulation

Glycine exerts anti-inflammatory and immunomodulatory effects in several cell types [35][36]. However, the underlying mechanisms responsible for these beneficial effects remain unknown. There are some hypotheses about the actions of glycine in living organisms, and accumulating evidence suggests that glycine protects cells from oxidative stress-induced inflammation [37][38]. In a mouse model of cancer cachexia, glycine attenuated oxidative and inflammatory environments [39]. In a model of acute pancreatitis, glycine reduced the severity of pancreatic damage [40]. Moreover, glycine suppressed zymosan-induced joint inflammation [41]. Some studies have shown that supplementation with glycine can reduce acute and systemic allergic responses. Although the exact mechanism of action is still unknown, glycine may exert an effect on key effector cells, such as basophils and mast cells [38].

Glycine has the ability to control inflammatory responses and regulate the production of molecules called cytokines in various types of cells that are part of our body's natural defense system, such as monocytes, intestinal, and alveolar macrophages [42][43][44]. The primary pathway through which glycine achieves these effects involves specific receptors known as GlyRs. However, glycine can also use alternative pathways, independent of GlyR, to carry out its protective functions against inflammation [45].

When the central nervous system (CNS) experiences insults like ischemia, it can trigger a process called neuroinflammation, involving certain immune cells called microglia. These microglia can adopt different states, one being pro-inflammatory (M1) and the other anti-inflammatory (M2). However, when glycine is used as treatment, it helps reduce neuroinflammation by suppressing the pro-inflammatory M1 state and promoting the anti-inflammatory M2 state [46][47][48][49][50]. In an animal model of ischemic stroke, glycine was also found to counteract the pro-inflammatory M1 state induced by the ischemic injury and encourage the anti-inflammatory M2 state [30].

On a molecular level, glycine helps to reduce the harmful effects of certain substances like LPS (lipopolysaccharides), peptidoglycans, and peroxisome proliferators. This amino acid can regulate the secretion of cytokines (molecules involved in inflammation) and the activation of proteases (enzymes that break down proteins) and lower the occurrence of increased cell death (apoptosis) in different animal models [51][52][53].

2.4. Low Glycine Plasma Levels Are Associated with Low-Grade Inflammation

High blood sugar levels (hyperglycemia) or excessive insulin in the bloodstream (hyperinsulinemia) can decrease the rate at which our body produces glycine [5]. Studies have shown that having low levels of glycine in the blood is linked to conditions like insulin resistance in the liver, obesity, and type 2 diabetes (T2DM) [54]. This decrease in glycine is caused by three different factors: (a) reduced absorption of glycine from the gut, (b) decreased production of glycine within the body, and (c) increased breakdown of glycine or excretion of it through urine [1].

Obesity and metabolic disorders show elevated plasma glucagon concentrations that reduce circulating glycine and increase its degradation [55][56]. On the other hand, an impaired hepatic branched-chain amino acid metabolism in obesity decreases circulating glycine concentrations [57]. Glycine supplementation (5 g/day or 0.1 g of glycine/kg/day for 14 days in association with N-acetylcysteine) improves the insulin response and glucose tolerance in patients with obesity [58].

3. Effects of Glycine supplementation

In animal models, dietary supplementation with glycine reduces inflammation, morbidity, and mortality from pathogenic infections [59]. Betaine supplementation is associated with circulating levels of dimethylglycine. Betaine metabolism may be hampered by the activity of dimethylglycine dehydrogenase (DMGDH), which connects betaine to glycine synthesis via the demethylation of dimethylglycine into sarcosine [60]. Glycine supplementation has shown beneficial cardiac effects in a burn model [61] and in a skeletal muscle ischemia model, with decreased reperfusion-mediated necrosis and increased metabolic and functional recovery [62]. The protective effects of glycine have been reported for several sepsis models [63][64] and for hemorrhagic shock [65]. Normal levels of glycine in the body prevent lipopolysaccharide (LPS)-induced endotoxemia by binding to GlyRs on Kupffer cells [66]. Dietary supplementation with glycine decreases adipocyte size, adiposity, and the concentrations of free fatty acids and triglycerides in animal models [67][68]. It also inhibits the nonenzymatic glycation of proteins and hemoglobin in diabetic rats [69] and patients with T2DM [69][70].

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