glycerol helps with weight loss. Intravenous glycerol is helpful in some with acute ischemic cerebral infarct. Oral glycerol has been useful in preventing some of the neurologic and audiologic sequelae of childhood bacterial meningitis.

**RESEARCH SUMMARY**

Pre-exercise administration of glycerol significantly improved cycling endurance time in two double-blind, randomized, cross-over trials. Mean heart rate was also reduced in glycerol-supplemented subjects.

Pre-exercise administration of glycerol in another study, however, failed to affect exercise performance in a group of triathletes. Results of animal work have been similarly mixed. A recent review of the potential ergogenic effects of glycerol hyperhydration concluded that “although some investigators have indicated positive effects of glycerol hyperhydration on fluid retention, thermoregulation, cardiovascular responses and performance, others have shown no advantage to glycerol ingestion.” What is clear, however, these reviewers asserted, is that “glycerol has the capacity to enhance fluid retention. This may provide a performance advantage when compared with fellow athletes who may experience a decrement in performance sooner rather than later.” They have called for better-designed studies. Glycerol did not increase weight loss in a placebo-controlled trial.

Intravenous administration of glycerol in subjects with acute ischemic cerebral infarct has resulted in significantly fewer neurological deficits in one study. Several other trials demonstrating similar benefits have been double-blind, randomized trials, but some of these benefits have been transient.

Glycerol-treated infants and children with bacterial meningitis had less severe hearing impairment and fewer neurologic deficits than did controls. Oral administration of glycerol was utilized.

Anyone using oral glycerol for supplementation must drink plenty of fluid concomitantly. See Dosing and Administration.

Those using glycerol need to be aware that contact of glycerol with strong oxidizing agents, such as potassium permanganate, potassium chlorate or chromium trioxide, may produce an explosion.

**ADVERSE REACTIONS**

There are rare reports of cardiac dysrhythmias occurring with oral glycerol use and one report of hypertension occurring. Other adverse reactions include headache, dizziness, confusion and amnesia (in elderly subjects) and hyperglycemia. Hyperosmolarity, which occurs with oral glycerol, is usually clinically significant only in those with type 2 diabetes. Those with type 2 diabetes may develop nonketotic hyperosmolar hyperglycemia.

The most frequent adverse reactions are gastrointestinal and include nausea and vomiting, bloating and diarrhea.

**DOSAGE AND ADMINISTRATION**

The doses are variable in those who use glycerol for hydration purposes and for possible exercise performance enhancement. Some use 2 to 4 tablespoons of glycerol in water, orange juice or a sports drink. The ratio of fluids to glycerol is about 20 to 1. This is taken approximately 2.5 hours prior to exercise. The volume of a tablespoon is 15 ml, and one ml of glycerol weighs 1.25 grams. The energy value of glycerol is about 4 kcal or 4 Cal per gram. Pharmaceutical grade glycerol is used.

**LITERATURE**


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**Glycine**

**DESCRIPTION**

Glycine is a protein amino acid found in the protein of all life forms. It is the simplest amino acid in the body and the
only protein amino acid that does not have chirality. Although most glycine is found in proteins, free glycine is found in body fluids as well as in plants. The normal diet contributes approximately 2 grams of glycine daily.

Glycine is not considered an essential amino acid, i.e., the cells in the body can synthesize sufficient amounts of glycine to meet physiological requirements. However, glycine is of major importance in the synthesis of proteins, peptides, purines, adenosine triphosphate (ATP), nucleic acids, porphyrins, hemoglobin, glutathione, creatine, bile salts, one-carbon fragments, glucose, glycogen, and L-serine and other amino acids. Glycine is also a neurotransmitter in the central nervous system (CNS). Glycine and gamma-aminobutyric acid (GABA) are the major inhibitory neurotransmitters in the CNS. Recently, a glycine-gated chloride channel has been identified in neurons that can attenuate increases in intracellular calcium ions and diminish oxidant damage mediated by these white blood cells. Thus, glycine may be a novel antioxidant.

Glycine is also known as amino acetic acid, aminoethanolic acid, glycocoll, glycinenium and sucre de gelatine. Its IUPAC abbreviation is Gly and its one-letter abbreviation, used when spelling out protein structures, is G. It is a neutral amino acid. Glycine is a solid water-soluble substance that has a sweetish taste. Its structural formula is:

![Glycine](image)

**ACTIONS AND PHARMACOLOGY**

**ACTIONS**

Supplemental glycine may have antispastic activity. Very early findings suggest it may also have antipsychotic activity as well as antioxidant and anti-inflammatory activities.

**MECHANISM OF ACTION**

In the CNS, there exist strychnine-sensitive glycine binding sites as well as strychnine-insensitive glycine binding sites. The strychnine-insensitive glycine-binding site is located on the NMDA receptor complex. The strychnine-sensitive glycine receptor complex is comprised of a chloride channel and is a member of the ligand-gated ion channel superfamily. The putative antispastic activity of supplemental glycine could be mediated by glycine’s binding to strychnine-sensitive binding sites in the spinal cord. This would result in increased chloride conductance and consequent enhancement of inhibitory neurotransmission.

The ability of glycine to potentiate NMDA receptor-mediated neurotransmission raised the possibility of its use in the management of neuroleptic-resistant negative symptoms in schizophrenia.

Animal studies indicate that supplemental glycine protects against endotoxin-induced lethality, hypoxia-reperfusion injury after liver transplantation, and D-galactosamine-mediated liver injury. Neutrophils are thought to participate in these pathologic processes via invasion of tissue and releasing such reactive oxygen species as superoxide. *In vitro* studies have shown that neutrophils contain a glycine-gated chloride channel that can attenuate increases in intracellular calcium and diminish neutrophil oxidant production. This research is early-stage, but suggests that supplementary glycine may turn out to be useful in processes where neutrophil infiltration contributes to toxicity, such as ARDS.

**PHARMACOKINETICS**

Following ingestion of glycine, the amino acid is absorbed from the small intestine via an active transport mechanism. From the small intestine, glycine is transported to the liver by means of the portal circulation where a portion enters into one of several metabolic pathways. Glycine not metabolized in the liver enters the systemic circulation and is distributed to various tissues in the body. Glycine readily crosses the blood-brain barrier.

**INDICATIONS AND USAGE**

Glycine may be indicated to help alleviate the symptoms of spasticity. An indication for potentiating some anti-convulsant drugs and preventing some seizures could emerge, as could an indication for its use in managing schizophrenia. Research in progress also suggests usefulness in some cancers. There is no evidence to support use of glycine as an ergogenic aid, and it is too early to say whether it can play any useful role in lipid metabolism. There are no well-designed clinical trials to support its use in benign prostate hypertrophy.

**RESEARCH SUMMARY**

Glycine first attracted interest in the medical research community for its reputed ability to dampen reflex excitability in the CNS. A pilot study of its effects on severe chronic leg spasticity (most of the subjects were suffering from chronic multiple sclerosis) yielded improvement in spasticity and mobility of the lower limbs, rated at about 25% overall. The dose used was 1 gram daily for six months to a year. All patients noted some benefits, and no adverse events were recorded. Other researchers have since reported that glycine can potentiate some but not all anticonvulsant drugs in some animal models. It has also been shown to prevent some experimentally produced seizures.

The effects of oral glycine (200 mg/kg/day) were tested in two siblings suffering from 3-phosphoglycerate dehydrogenase deficiency, an inborn error of L-serine biosynthesis. A
significant amount of glycine is made from L-serine. Among the features of this disorder are intractable seizures. L-serine in doses up to 500 mg/kg/day failed to control the seizures, but oral glycine completely stopped them, and electroencephalographic abnormalities resolved after six months of treatment.

High-dose glycine may be beneficial in the management of enduring negative symptoms of schizophrenia. Twenty-two treatment-resistant schizophrenic patients participated in a double-blind, placebo-controlled, six-week, crossover treatment trial with 0.8 grams per kilogram daily of glycine added to their ongoing antipsychotic medication. Glycine intake ranged from 40 to 90 grams daily. Only mild gastrointestinal side effects (nausea and vomiting) were reported in one patient taking glycine. Patients taking glycine experienced significantly diminished negative symptoms. Followup studies are planned.

Recent animal studies suggest that glycine may have some anti-cancer properties. In one recent study, 51 weeks of glycine supplementation did not stop early foci formation of cancer but reduced formation of small liver tumors by 23%, medium-sized tumors by 64% and large tumors by nearly 80% in rats given an agent that is a peroxisome proliferator and liver carcinogen.

In another recent study, dietary glycine inhibited B16 melanoma tumors in mice. Glycine-supplemented mice had tumors that were 50 to 70% smaller in size than those in controls. The protective mechanism in this case appeared to be inhibition of angiogenesis effected by suppressed endothelial-cell proliferation. Tumors in mice fed glycine had 70% fewer arteries than were present in the tumors of controls.

Whether very preliminary data suggesting some positive effects of glycine on lipid metabolism will be mirrored in human research remains to be seen.

Partly because glycine is a precursor of creatine, some have assumed that it might have some of the same ergogenic potential that has been claimed for creatine. This, so far, has not been demonstrated. Glycine is claimed to be beneficial for benign prostatic hypertrophy based on a dated clinical study that has never been confirmed.

**CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**

**CONTRAINDICATIONS**

Glycine supplementation is contraindicated in those hypersensitive to any component of the preparation. It is also contraindicated in those who are anuric (some glycine gets converted to ammonia).

**PRECAUTIONS**

Glycine supplementation should be avoided by pregnant women and nursing mothers. Because of some conversion of glycine to ammonia, those with hepatic impairment should avoid glycine supplementation unless prescribed.

**ADVERSE REACTIONS**

Doses of 1 gram daily are very well tolerated. Mild gastrointestinal symptoms are infrequently noted. In one study doses of 90 grams daily were also well tolerated.

**INTERACTIONS**

Antispastic drugs. Theoretically, supplemental glycine might have additive effects when used in conjunction with baclofen, diazepam, dantrolene sodium and tizanidine.

No other drug, nutritional supplement, food or herb interactions are known.

**OVERDOSAGE**

There are no reports of overdose in humans. The majority of mice receiving 3 to 4.5 grams per kilogram by intravenous infusion experienced bradycardia, prolongation of the PQ interval, QRS duration and death.

**DOSE AND ADMINISTRATION**

Glycine is available in 500 milligram tablets and capsules. Those who supplement use up to 1 gram daily in divided doses. Doses used for management of schizophrenia have ranged from 40 to 90 grams daily.

**LITERATURE**


Glycitein

DESCRIPTION
Glycitein belongs to the isoflavone class of flavonoids. It is also classified as a phytoestrogen since it is a plant-derived nonsteroidal compound that possesses estrogen-like biological activity. Glycitein has been found to have weak estrogenic activity.

Glycitein is the aglycone of glycinin. The isoflavone is found naturally as the glycoside (glucoside) glycitin and as the glycosides 6'-0-malonylglycinin and 6'-0-acetylglcyitin. Glycitein and its glycosides are mainly found in legumes, such as soybeans and chickpeas. Soybeans and soy foods are the major dietary sources of these substances. Glycitein glycosides are the least abundant of the isoflavones in soybeans and soy foods, where they comprise about 5 to 10% of the total isoflavones. However, in soy germ, glycitein glycosides comprise about 40% of the isoflavones.

Glycitein is a solid substance that is virtually insoluble in water. Glycitein is also known as 7-hydroxy-6-methoxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one and 4', 7-dihydroxy-6-methoxyisoflavone.

Glycitein, when marketed as a nutritional supplement, is mainly present in the form of its beta-glucoside, glycitin.

See also Soy Isoflavones.

ACTIONS AND PHARMACOLOGY

ACTIONS
Glycitein may have estrogenic and antiestrogenic activities. It may also have antioxidant, anticarcinogenic, anti-atherogenic and neuroprotective activities.

MECHANISM OF ACTION
Of all the soy isoflavones, glycitein has been the least studied. Glycitein has weak estrogenic activity as measured in in vivo and in vitro assays. In vivo, its estrogenic activity is the highest of the soy isoflavones: three times greater than that of genistein and 12 times greater than that of daidzein.

Glycitein’s antioxidant activity has been demonstrated by its ability to scavenge hydroxyl radicals generated via the Fenton reaction, superoxide anion radicals generated via the xanthine/xanthine oxidase reaction and peroxynitrite radicals generated via the reaction of superoxide anions with nitric oxide.

Observational studies have shown an inverse relation between soy consumption and risk of prostate cancer. However, the specific cellular mechanisms responsible for this putative anticancer activity are not clear. Signaling cascades are involved in cellular growth, proliferation and differentiation. The extracellular signal-regulated kinase (ERK1/2) signaling cascade is necessary for the survival, growth and development of normal prostate epithelium. The role of ERK1/2 signaling in prostate carcinogenesis is unclear.

Glycitein was demonstrated to activate ERK1/2 via vascular endothelial growth factor receptor (VEGFR) signaling in nontumorigenic (RWPE-1) prostate epithelial cells. Of the three soy isoflavones (genistein, daidzein and glycitein) and equol, glycitein was the most potent activator of ERK1/2 and glycitein decreased RWPE-1 cell proliferation by approximately 40%. The ability of isoflavones, and in particular glycitein, to modulate the ERK1/2 signaling cascade via VEGFR signaling in the prostate may be responsible, in part, for the possible anticancer activity of soy.

Glycitein was found to protect against beta amyloid-induced toxicity and oxidative stress in transgenic Caenorhabditis elegans (C. elegans). Alzheimer’s disease is characterized by the presence of amyloid beta peptide aggregation and increased oxidative stress, both causing neuronal injury and neuronal death. In order to better understand the possible neuroprotective mechanisms of soy isoflavones, several experiments were performed using a transgenic C. elegans model expressing the human amyloid-beta peptide. Among the three soy isoflavones tested—genistein, daidzein and glycitein—only glycitein alleviated beta amyloid (Abeta) expression-induced paralysis in the transgenic C. elegans model. The activity of glycitein correlated with a reduced level of the reactive oxygen species hydrogen peroxide in the transgenic C. elegans. Further, the transgenic C. elegans treated with glycitein exhibited reduced formation of beta-amyloid. One can conclude from this study that glycitein may suppress Abeta toxicity via combined antioxidant activity and inhibition of Abeta deposition. Further research