Van Slambrouck S, Parmar VS, Sharma SK, et al. Tangeretin inhibits extracellular-signal-regulated kinase (ERK) phosphorylation. *FEBS Lett.* 2005;579(7):1665-1669.

Walle T. Methoxylated flavones, a superior cancer chemopreventive flavonoid subclass? *Semin Cancer Biol.* 2007;17(5):354-362.

Taurine

DESCRIPTION

Taurine is a nonprotein amino acid. It is an end product of L-cysteine metabolism and the principal free intracellular amino acid in many tissues of humans and other animal species. Taurine is present in high amounts in the brain, retina, myocardium, skeletal and smooth muscle, platelets and neutrophils. It is classified as a conditionally essential amino acid because it is necessary to be supplied in the diet of infants for normal retinal and brain development.

Research of taurine was greatly stimulated by the finding that it is an essential nutrient for cats. Taurine deficiency in cats can result in a variety of clinical abnormalities, including central retinal degeneration, dilated cardiomyopathy and platelet function abnormalities. Shortly after the discovery that dietary taurine deficiency leads to retinal degeneration in cats, it was observed that infants who were fed formulas lacking taurine had lower plasma levels of this amino acid than did infants fed human milk. Further, it was discovered that children receiving total parenteral nutrition not containing taurine had abnormal electroretinograms, as well as low plasma taurine levels. Taurine has been added to most human infant formulas since the mid-1980s.

Taurine is produced in the body from L-cysteine. The first reaction in the pathway is the formation of cysteine sulfinic acid. Cysteine sulfinic acid (CSA) is converted to hypotaurine via the enzyme CSA-decarboxylase, and taurine is formed from hypotaurine. Cats have low activity of CSA-decarboxylase. Dietary taurine mainly comes from animal food. Taurine is present in very low levels in plant foods. Taurine is found in seaweeds.

The most understood role of taurine in humans is its involvement in the formation of taurine bile acid conjugates in the liver, which are essential for micelle formation and fat absorption. Taurine is involved in the pre-and post-natal development of the central nervous system and visual system, although the details of its involvement in these processes are unclear. Taurine also has antioxidant and membrane-stabilizing activities. Much remains to be learned about the role of taurine in human physiology.

Taurine is different from most biological amino acids in a few particulars. It is a sulfonic acid rather than a carboxylic acid; it is a beta-amino acid rather than an alpha-amino acid and it does not have a chiral center. Taurine is also known as 2-aminoethane sulfonic acid. Its molecular formula is $C_2H_7NO_3S$, and its molecular weight is 215.15 daltons.

ACTIONS AND PHARMACOLOGY

ACTIONS

Taurine has antioxidant activity. It has putative hypocholesterolemic, hypotensive, antiatherogenic and detoxifying activities. It may also have steatorrhea-reducing activity in those with cystic fibrosis and has putative antidiabetic, inotropic and antiseizure activities.

The major antioxidant activity of taurine derives from its ability to scavenge the reactive oxygen species hypochlorite, which is generated in neutrophils during respiratory-burst activity of these cells. Taurine reacts with excess hypochlorite produced in the process of phagocytosis to form the relatively harmless N-chlorotaurine. N-chlorotaurine is then reduced to taurine and chloride. This activity may protect against collateral tissue damage that can occur from the respiratory burst of neutrophils. Taurine may also suppress peroxidation of membrane lipoproteins by other reactive oxygen species. It is thought that this effect is not due to taurine's scavenging of these reactive oxygen species, but rather to taurine's membrane-stabilizing activity, which confers greater resistance to the membrane lipoproteins against lipid peroxidation.

Taurine has been demonstrated to reduce cholesterol levels in animals, but results in humans have been contradictory. The hypocholesterolemic effect of taurine in animals is thought to be due, in large part, to the stimulation of bile acid synthesis and enhancement of cholesterol 7 alpha-hydroxylase activity. Taurine has been found to have antiatherogenic activity in animals, but there is less evidence that it does in humans. The antiatherogenic activity of taurine in animals is thought to be due, in large part, to its hypocholesterolemic activity.

Taurine has been found to normalize blood pressure in spontaneous hypertensive rats, and there is some evidence from human studies that it also has hypotensive activity in hypertensive, but not normotensive, individuals. It is speculated that the hypotensive effect of taurine may result from the normalization of increased sympathetic activity in hypertensive individuals.

Taurine has been found to ameliorate bleomycin-induced lung fibrosis in hamsters and also to ameliorate the side effects of some nitrogen mustards. It is thought that the possible antioxidant and membrane-stabilizing activities of taurine may account for these detoxifying actions.

Some studies have shown decreased steatorrhea in cystic fibrosis patients receiving taurine. It is though that the mechanism of this effect is taurine's stimulation of bile acid formation resulting in increased fat absorption in these individuals.

Again in animals, but not in humans, taurine has been found to have antidiabetic activity. The mechanism of this effect is unclear. It is thought that taurine may decrease insulin resistance.

Cats who are deficient in taurine develop dilated cardiomyopathy and congestive heart failure. Taurine has an inotropic effect when given to these animals. Some studies suggest that taurine has an inotropic effect in humans with congestive heart failure. The mechanism of this possible effect is unclear. It is thought that taurine may modulate the calcium current.

The mechanism of taurine's putative antiseizure activity is unknown.

PHARMACOKINETICS

Following ingestion, taurine is absorbed from the small intestine via the beta-amino acid or taurine transport system, a sodium- and chloride-dependent carrier system that serves gamma-aminobutyric acid and beta-alanine, as well as taurine. This carrier system is located in the apical membrane of intestinal mucosa cells. Taurine is transported to the liver via the portal circulation, where much of it forms conjugates with bile acids. Taurocholate, the bile salt conjugate of taurine and cholic acid, is the principal conjugate formed via the action of the enzyme choloyl-CoA N-acyltransferase. The taurine conjugates are excreted via the biliary route. Taurine that is not conjugated in the liver is distributed via the systemic circulation to various tissues in the body. Taurine is not usually completely reabsorbed from the kidneys, and some fraction of an ingested dose of taurine is excreted in the urine.

INDICATIONS AND USAGE

Taurine may be helpful in some with congestive heart failure and hypertension. It has demonstrated some antiatherogenic effects in both animal and human studies. There is the suggestion, mostly from animal data, that taurine might improve glucose tolerance and protect against some toxins. Some older studies suggest if might have some antiseizure activity. There is preliminary evidence that it might be helpful in some with cystic fibrosis.

RESEARCH SUMMARY

In a study of 24 subjects with congestive heart failure, administration of 2 grams of taurine, twice a day, resulted in clinical improvement in 19 patients. Roentgenographic data helped confirm the improvement. These positive results were subsequently confirmed in a double-blind, randomized, crossover, placebo-controlled study in which taurine was added to conventional treatment for a four-week period. Compared with placebo, taurine produced significant improvement as evaluated by a number of measures, including chest films. In still another study, supplemental taurine, but not coenzyme Q10, was said to have significant benefit in patients with congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. This was a double-blind study using 3 grams of taurine daily.

Taurine has demonstrated hypotensive effects in some animal studies. In humans, it has lowered blood pressure in borderline hypertensive patients using 6 grams of taurine daily for seven days. Lipid-lowering effects have been seen in animals, but human data are few and contradictory. There is some preliminary evidence from one small study that 0.4 to 1.6 grams of taurine daily for eight days inhibited platelet aggregation in a dose-dependent manner. Supplementation with 1.5 grams of taurine daily decreased platelet aggregation in subjects with type 1 diabetes. Insulin sensitivity was significantly improved by taurine supplementation in a rat model of spontaneous type 2 diabetes. Serum cholesterol and triacylglycerol were decreased in the supplemented animals. Taurine was also effective in another animal model of insulin resistance.

Taurine has exerted some detoxifying effects in animal experiments. It helped prevent bleomycin-induced lung injury and fibrosis in mice. It also appeared to have protective effects, as measured by changes in memory and lipid peroxidation levels in the brain, in rats exposed to ozone. Additionally, it has inhibited ethanol-induced elevation of plasma acetaldehyde in other animal studies. In one of these, it prevented the development of ethanol-induced hypertension in rats.

In some older studies, taurine demonstrated some preliminary ability to suppress some epileptic seizures. Follow-up is needed.

Finally, taurine was shown to be of benefit in a study of 22 Canadian children with cystic fibrosis and documented steatorrhea. They were given taurine (30 mg/kg/day) and placebo during separate six-month periods. Severity of fat malabsorption was significantly reduced in most of the subjects, especially in those with the most severe steatorrhea. A more recent study, however, failed to note these benefits, but significant differences in the two study groups may account for this discrepancy. A second study by the Canadian group showed positive effects of taurine on fat absorption in cystic fibrosis patients. Again, those with the greatest malabsorption at baseline seemed to benefit the most.