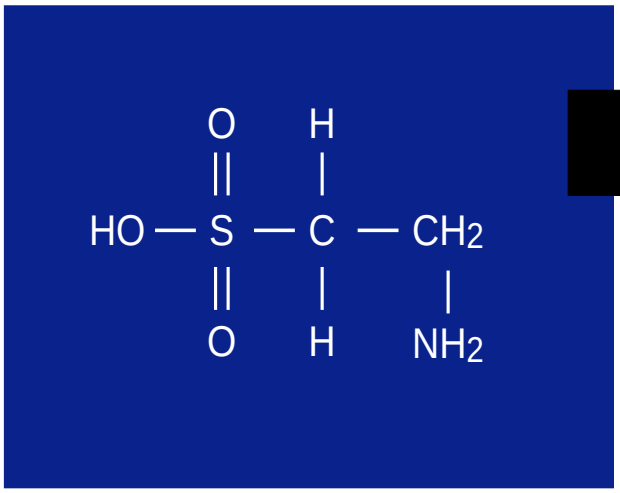

Monograph

Taurine

Introduction

Taurine is a conditionally essential amino acid that is found in the tissues of most animal species. It is not incorporated into proteins, but is found free in many tissues. Taurine is involved in a number of physiological processes including bile acid conjugation, osmoregulation, detoxification of xenobiotics, cell membrane stabilization, modulation of cellular calcium flux, and modulation of neuronal excitability. Low levels of taurine have been associated with retinal degeneration, growth retardation, and cardiomyopathy. Taurine has been used clinically in the treatment of cardiovascular diseases, hypercholesterolemia, seizure disorders, ocular disorders, diabetes, Alzheimer's disease, hepatic disorders, cystic fibrosis, and alcoholism.

Biochemistry and Biosynthesis

Taurine (2-aminoethanesulfonic acid) is different from other amino acids in that it contains a sulfonic acid group in place of the carboxylic acid group, and it is not incorporated into proteins. Therefore, it is not an amino acid in the true sense of the word.[1] It is synthesized in human liver tissue from cysteine and methionine via three known pathways, all of which require pyridoxal-5'-phosphate, the active coenzyme form of vitamin B6.[2] The highest concentrations of taurine are found in the neutrophil and the retina, and the largest pools of taurine are found in skeletal and cardiac muscles.[3] Taurine excretion is via the urine or in the bile as bile salts.[4]

Physiological Functions

Bile Acid Conjugation

Bile acids, primarily cholic acid and chenodeoxycholic acid, result from cholesterol metabolism in the liver and are involved in emulsification and absorption of lipids and fat-soluble vitamins. In order for this to occur, bile acids must be bound to either glycine or taurine, forming bile salt conjugates. The conjugation of bile acids by taurine results in increased cholesterol solubility and excretion.[5,6]

Detoxification

Research has demonstrated that taurine reacts with and neutralizes hypochlorous acid, which is generated during oxidative neutrophil burst. The result is a stable taurochloramine compound, as opposed to unstable aldehyde compounds formed in states of taurine deficiency. Individuals who are taurine deficient may become more susceptible to tissue damage by xenobiotic agents such as aldehydes, chlorine, and certain amines.[3] Animal studies have also demonstrated taurine's ability to complex with and neutralize the xenobiotic effects of carbon tetrachloride and retinol.[7,8] Research also suggests that translocation of bacterial endotoxins may be a factor in determining a person's response

to xenobiotic insult. Even small amounts of endotoxin markedly enhance liver injury from hepatotoxic substances such as carbon tetrachloride, ethanol, and cadmium. Taurine was found to significantly inhibit intestinal endotoxin translocation and subsequently decrease hepatic injury from these substances.[9,10]

Membrane Stabilization

Taurine's ability to stabilize cell membranes may be attributed to several events. Taurine has been shown to regulate osmotic pressure in the cell, maintain homeostasis of intracellular ions, inhibit phosphorylation of membrane proteins, and prevent lipid peroxidation. As an osmotic regulator, it has been suggested that taurine, along with glutamic acid, is instrumental in the transport of metabolically-generated water from the brain.[11]

Calcium Flux

Taurine is both an intra- and extracellular calcium regulator. Excessive accumulation of intracellular calcium ultimately leads to cell death. Excessive influx of calcium into cells has been demonstrated in various types of myocardial injury, as well as migraines and prolonged epileptic episodes. Taurine supplementation has been shown to be cardioprotective, and of benefit in patients predisposed to epilepsy or migraine.[4,12]

Clinical Indications

Cardiovascular Disease

Several studies indicate taurine is a safe, effective therapeutic tool in the management of various types of cardiovascular disease. Research indicates supplementation with taurine at three to six grams daily for two to three weeks results in reduced serum cholesterol levels in human subjects when compared to placebo.[5,6] In addition, taurine aids in the regulation of intracellular calcium levels, thereby protecting heart muscle from intracellular calcium imbalances, which can lead to cell death, and subsequent myocardial damage.[11] Taurine's use in preventing cardiac arrhythmia is well documented and it is thought it may act by modulating potassium flux in and out of cardiac muscle cells.[13] Research has also shown taurine to be capable of lowering blood pressure, due to its positive inotropic effects.[14,15]

Taurine's antioxidant properties are seen in its ability to inhibit neutrophil burst and subsequent oxidative stress, which can result in reperfusion injury to heart tissue.[16] It is also capable of improving the clinical manifestations of congestive heart failure. A Japanese study revealed taurine was significantly more effective than placebo at decreasing the severity of dyspnea, palpitation, crackles, and edema in congestive heart failure patients, while increasing their capacity for exercise.[17]

Seizure Disorders

A number of studies have been conducted on taurine's role in alleviating seizure conditions. Unfortunately, many had design flaws, dosages varied greatly, and no firm conclusions can be drawn. Some patients with epilepsy have an aberration in taurine and glutamic acid metabolism. It is believed that taurine's anti-epileptic activity is due to its ability to maintain a normal glutamic acid concentration in the central nervous system.[2] As mentioned above, benefits may also be due to taurine's effect on intracellular calcium.[12] It appears however, that taurine's anti-epileptic action is transient and disappears rapidly over a period of a few weeks.[18]

Retinal Degeneration

Taurine is very abundant in the vertebrate retina, and taurine deficiency in cats has been shown to cause damage to the cone photoreceptor cells, resulting in permanent retinal degeneration. It is also thought that abnormalities in taurine metabolism might be associated with retinitis pigmentosa in humans.[1] Retinal taurine appears to regulate osmotic pressure, stabilize cell membranes as well as calcium ion concentrations, inhibit lipid peroxidation after oxidant exposure, and act as an antioxidant by scavenging damaging free radicals.[1,4]

Growth and Development

The research on retinal degeneration in taurine-deficient kittens[1] prompted further studies of taurine deficiency in formula-fed pre-term and full-term infants. Taurine is present in high concentrations in human milk, but significantly decreases over the first few months of the infant's life. Because humans have limited ability to synthesize taurine and infants have decreased capacity to store it, a dietary source of taurine is essential for normal development during the neonatal period.[19] Research on taurine's effects on growth and development in humans shows it may act as a "growth modulator" and that taurine deficiency is responsible for neurological defects involving motor dysfunction and cerebral activity, growth retardation, and retinal degeneration.[4] Animal and *in vitro* studies also support the theory that taurine is essential for proper growth and development. [20,21] As a result, taurine has been added to most commercially-available infant formulas.

Diabetes

Animal and human studies indicate that taurine supplementation is effective in alleviating some of the complications of insulin-dependant diabetes. Taurine has been found to influence blood glucose and insulin levels, as well as increasing glycogen synthesis, and it may also be involved in the functioning and integrity of pancreatic beta cells.[3] In insulin-dependent diabetic patients, both plasma and platelet taurine levels were decreased but were corrected by oral taurine supplementation.[22]

Cystic Fibrosis

Cystic fibrosis is usually characterized by nutrient malabsorption in the ileum, impaired bile acid conjugation, and steatorrhea.[23] Human studies using 30 mg/kg taurine daily for four months resulted in a significant decrease in fecal fatty acids.[23]

Alzheimer's Disease

Low levels of the neurotransmitter acetylcholine and altered taurine metabolism have been found in patients with Alzheimer's disease, and it is thought these abnormalities might contribute to the characteristic memory loss.[4] Also, taurine levels in cerebrospinal fluid were decreased in patients with advanced Alzheimer's disease.[24] To date, no clinical trials of taurine supplementation in patients with Alzheimer's disease have been conducted, but in animal models supplementation increased acetylcholine levels in brain tissue.[25]

Hepatic Disorders

In a double-blind, randomized study, acute hepatitis patients with significantly elevated bilirubin levels were given oral taurine — four grams three times daily after meals. Taurine-supplemented patients exhibited notable decreases in bilirubin, total bile acids, and biliary glycine:taurine ratios within one week when compared to control subjects. The icteric period was also decreased.[26]

In patients undergoing ursodeoxycholic acid (UDC) treatment for cholesterol gallstones, taurine therapy may also be beneficial. The taurine conjugate of UDC is better able to solubilize cholesterol than the glycine conjugate, thereby effecting a greater decrease in the bile acid pool size.[27]

Alcoholism

Both taurine and acamprosate (a synthetic taurine analog) have been shown to be clinically useful in treating patients with alcohol dependence. In patients undergoing alcohol withdrawal, taurine given at one gram three times daily for seven days resulted in significantly fewer psychotic episodes when compared to control subjects.[28] A pooled analysis of 11 studies involving over 3,000 patients given oral acamprosate at similar doses revealed it was more effective than placebo at preventing alcohol relapse. The efficacy appeared to be dose dependent and was enhanced by the addition of disulfiram.[29]

Safety

With few exceptions, animal and human studies have shown taurine administration to be safe, even at higher doses. Intense, temporary itching has been noted to occur in psoriasis patients at dosages of 2 g taurine daily[1] and some epileptic patients reported dosages of 1.5 g daily resulted in nausea, headache, dizziness, and gait disturbances.[30] One study found that taurine administration to patients with uncompensated adrenocortical insufficiency can induce hypothermia and hyperkalemia.[2]

Dosage and Administration

Taurine is usually administered orally, with the adult dosage being 500 mg to 3 g daily in divided doses. Pediatric dosages vary according to the size and age of the child, but range from 250 mg to 1 g daily in divided doses. Patients should be monitored for possible side effects, and taurine administration should be discontinued if serious side effects develop.

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