

but not alpha-ketoglutarate dehydrogenase mRNA levels in three human cell types. *J Nutr.* 1998; 128:683-687.

Romanski SA, McMahon MM. Metabolic acidosis and thiamine deficiency. *Mayo Clin Proc.* 1999; 74:259-263.

Sato Y, Nakagawa M, Higuchi I, et al. Mitochondrial myopathy and familial thiamine deficiency. *Muscle Nerve.* 2000; 23:1069-1075.

Senapati SK, Dey S, Dwivedi SK, et al. Effect of thiamine hydrochloride on lead induced lipid peroxidation in rat liver and kidney. *Vet Hum Toxicol.* 2000; 42:236-237.

Shimon I, Almog S, Vered Z, et al. Improved left ventricular function after thiamine supplementation in patients with congestive heart failure receiving long-term furosemide therapy. *Am J Med.* 1995; 98:485-490.

Suter PM, Haller J, Hany A. Diuretic use: a risk for subclinical thiamine deficiency in elderly patients. *J Nutr Health Aging.* 2000; 4:69-71.

Suzuki M, Itokawa Y. Effects of thiamine supplementation on exercise-induced fatigue. *Metab Brain Dis.* 1996; 11:95-106.

Tanphaichitr V. Thiamin. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease.* 9th ed. Baltimore, MD: Williams and Wilkins; 1999:381-389.

Todd K, Butterworth RF. Mechanisms of selective neuronal cell death due to thiamine deficiency. *Ann NY Acad Sci.* 1999; 893:404-411.

Webster MJ. Physiological and performance responses to supplementation with thiamin and pantothenic acid derivatives. *Eur J Appl Physiol Occup Physiol.* 1998; 77:486-491.

Webster MJ, Scheett TP, Doyle MR, Branz M. The effect of a thiamin derivative on exercise performance. *Eur J Appl Physiol.* 1997; 75:520-524.

Tin

DESCRIPTION

Tin is a metallic element with atomic number 50 and symbol Sn. It is a heavy metal. Tin is not considered an essential nutrient for humans. A tin-deficiency state has been reported in rats.

Rats fed a diet low in tin showed poor growth, alopecia and lowered response to sound compared with rats fed a tin-rich diet. Abnormalities in mineral status were also noted in the tin-deficient rat group. At least for rats tin, may serve as an essential nutrient.

The typical daily dietary intake of tin ranges from about 1 to 40 milligrams. Tin intake is essentially dependent on food stored in tin cans. Higher intakes of tin are obtained from foods preserved in unlacquered tin cans than from foods preserved in lacquered tin cans.

Regarding potential drug applications of tin, an organotin compound, tin protoporphyrin or Sn-P, a potent inhibitor of heme oxygenase and bilirubin formation, is being studied as a treatment for controlling severe hyperbilirubinemia in full-term breast-fed newborns with high bilirubin levels after birth. It is also being studied as a treatment for neuropathic and incisional pain.

ACTIONS AND PHARMACOLOGY

ACTIONS

The actions and pharmacology of dietary tin are not known.

INDICATIONS AND USAGE

There is no evidence that supplemental tin has immune-enhancing activity in humans; nor is there any evidence that it has anticarcinogenic activity in humans.

RESEARCH SUMMARY

It has been hypothesized that the thymus gland secretes tin-containing substances that possess immune-enhancing properties. There are some animal studies suggesting that tin may have immune-modulating activity and may also have anti-proliferative activity. There is no evidence that tin has these activities in humans. Such studies are needed, especially if the animal studies have any validity.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Tin supplementation is not recommended for anyone.

PRECAUTIONS

Given our present state of knowledge regarding tin, supplemental tin is not recommended for anyone.

DOSAGE AND ADMINISTRATION

No recommended dosage. Tin may be found in colloidal or liquid mineral preparations. It is also found in some multivitamin preparations, typically at a dose of about 10 micrograms.

LITERATURE

Arakawa Y. [Biological activity of tin and immunity.] [Article in Japanese.] *Sangyo Eiseigaku Zasshi.* 1997; 39:1-20

Biego GH, Joyeux M, Hartemann P, Debry G. Determination of tin intake in an adult French citizen. *Arch Environ Contam Toxicol.* 1999; 36:227-232.

Cardarelli N. Tin and the thymus gland: a review. *Thymus.* 1990; 15:223-231.

Martinez JC, Garcia HO, Otheguy LE, et al. Control of severe hyperbilirubinemia in full-term newborns with the inhibitor of bilirubin production Sn-mesoporphyrin. *Pediatrics.* 1999; 103:1-5.

Nielsen FH. Ultratrace minerals. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease.* 9th ed. Baltimore, MD: Williams and Wilkins; 1999; 283-303.

Pekelharing HL, Lemmens AG, Beynan AC. Iron, copper and zinc status in rats fed on diets containing various concentrations of tin. *Br J Nutr.* 1994; 71:103-109.

Yokoi K, Kimura M, Itokawa Y. Effect of dietary tin deficiency on growth and mineral status in rats. *Biol Trace Elem Res.* 1990; 223-231.

Tiratricol (TRIAC)

FDA warns against consuming dietary supplements containing Tiratricol.

DESCRIPTION

Tiratricol is an orphan drug for use in combination with levothyroxine to suppress thyroid stimulating hormone (TSH) in patients with well-differentiated thyroid cancer who are intolerant to adequate doses of levothyroxine alone. Tiratricol is a metabolite of the thyroid hormone triiodothyronine (T_3) and has thyroid hormone activity.

Tiratricol is also marketed as a dietary supplement for weight-loss purposes. In November 2000, the Food and Drug Administration (FDA) warned against consuming dietary supplements containing tiratricol. This was based on reports of individuals using tiratricol developing side effects, such as fatigue, lethargy, profound weight loss and severe diarrhea. They were also found to have abnormal thyroid function tests. Further action by the FDA is being considered.

Tiratricol is also known as triiodothyroacetic acid, TRIAC, 3,5,3'-triiodothyroacetic acid and [4-(4-hydroxy-3-iodophenoxy)-3,5-di-iodophenyl]acetic acid. Its molecular formula is $C_{14}H_9I_3O_4$, and its molecular weight is 621.9 daltons.

ACTIONS AND PHARMACOLOGY

ACTIONS

Tiratricol has thyroid hormone activity, including various metabolic effects. It also inhibits the secretion of thyroid-stimulating hormone (TSH) by the pituitary gland. Tiratricol is a product of triiodothyronine or T_3 metabolism, derived by deamination and oxidative decarboxylation of the alanine chain. In humans, tiratricol production by the liver and other tissues accounts for about 14% of T_3 metabolism and is increased under certain physiological conditions, such as fasting. Tiratricol may play a role in regulating energy balance.

MECHANISM OF ACTION

The mechanism by which thyroid hormones exert their various actions has not been completely elucidated. Tiratricol is known to act as a feedback inhibitor of TSH secretion by the pituitary gland.

PHARMACOKINETICS

Much is unknown about the pharmacokinetics of tiratricol in humans. The pharmacokinetics of tiratricol appears to be similar to those of thyroxine and triiodothyronine. Tiratricol is absorbed from the small intestine following ingestion. Distribution of tiratricol in the body has not been fully elucidated. Most of this substance appears to be bound to serum proteins, including thyroxine-binding protein and albumin. It appears to be less firmly bound to serum proteins than are T_4 and T_3 . The liver appears to be the major site of degradation of tiratricol. Tiratricol appears to be conjugated with glucuronic acid and sulfuric acid and excreted in the bile. Mainly because it is less tightly bound to serum proteins, tiratricol has a shorter half-life than T_4 or T_3 .

INDICATIONS AND USAGE

The FDA has warned consumers not to purchase tiratricol-containing dietary supplements due to risk of serious health consequences, including heart attacks and strokes. Tiratricol should be used only under a physician's supervision. Tiratricol is currently used by some as a supplement to burn fat. The doses required to achieve this effect pose significant health risks.

RESEARCH SUMMARY

Tiratricol is an orphan drug. The FDA has determined that it should not be used as a dietary supplement due to serious potential health risks including heart attack and stroke.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Tiratricol is contraindicated in those with untreated thyrotoxicosis of any etiology and in those with uncorrected adrenal insufficiency. Thyroid hormones increase tissue demands for adrenocortical hormones and may thereby precipitate acute adrenal crisis. Tiratricol is also contraindicated in those who are hypersensitive to any component of a tiratricol-containing product. FDA warns against consuming dietary supplements containing tiratricol.

PRECAUTIONS

Tiratricol should only be used for specific approved indications and only under strict medical supervision. Tiratricol should not be used as a treatment for obesity. Tiratricol should be used with extreme caution in those with cardiovascular disorders (including angina, coronary artery disease and hypertension) and in the elderly who have a greater likelihood of occult cardiac disease. Concomitant use of tiratricol and sympathomimetic agents in those with coronary artery disease may increase the risk of coronary insufficiency. Use of tiratricol in those with concomitant diabetes mellitus, diabetes insipidus or adrenal cortical insufficiency may aggravate the intensity of their symptoms.