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BETAFIN TH: TOXICOLOGICAL AND ECOLOGICAL INFORMATION

General

BETAFIN TH is betaine monohydrate containing betaine min. 99% on dry matter basis. Betaine is a natural compound having important functions in animal, microbial and plant metabolism. Chemically betaine (glycinebetaine, trimethyl glycine) is a quaternary ammonium compound with three methyl groups attached to the nitrogen atom of a glycine molecule. CAS number of betaine monohydrate is 590-47-6. Betaine monohydrate is hygroscopic product and can absorb moisture from the air.

BETAFIN TH is produced from sugar beet molasses using the chromatographic separation process, developed by Finnsugar Ltd., now DANISCO. The final product is crystallized.

Betaine is present in many organisms, including human body. Especially high levels can be found in several plants, some microbes and marine invertebrate animals. Of the betaine accumulators the best known ones are plants belonging to the Chenopodiaceae family (e.g. sugar beet). Betaine content of sugar beet is in average about 1.9 g/kg(four-year average in October in Germany) (1). In crustaceans, normally used for human consumption,the measured betaine concentrations of fresh muscle have varied from 1 to 9 g/kg and those in molluscs from 6 to 14 g/kg (2).
Betaine concentration in the muscle of young salmon, fed with control diet and betaine containing diet (1.5 %) for 1 - 2 months, was 0.12 - 0.28 and 0.7 - 0.9 g/kg, respectively (3).

Metabolism of betaine is well known. It acts as a natural methyl group donor in several metabolic reactions, such as the synthesis of methionine from homocysteine. Methyl donors generally induce the mobilization of liver lipids. Betaine is thus widely distributed in different organs and cells, the highest concentrations being found in renal medullas, where betaine acts as an osmolyte. In the methylation reaction, betaine is converted to dimethyl glycine and this is further metabolized to sarcosine and glycine. The absorption rate from intestine is unknown, but the apparent digestibility is close to 100 % (5).

Current uses of betaine

Betaine has been widely used for years in commercial feeds for several animal species, including poultry, pigs, calves and fish, at concentrations from 0.2 to 15 kg/tn feed. In the feed betaine is acting as a natural methyl group donor thus enabling the partial replacement of choline and methionine in the feed. Another important function of betaine is acting as an osmoprotectant having stress relieving properties under various kinds of gastrointestinal stress.

Moreover, betaine stabilizes the macromolecular functions, by increasing the temperature and ionic tolerance of enzymes and membranes. Betaine supplementation has been widely adopted in fish feeding to relieve the osmotic stress of fish at seawater transfer. No harmful effects have been observed in several long-term trials.

Betaine is widely used in human foods e.g. in Japan. Betaine has also been used in some pharmaceutical applications, e.g.. in the treatment of human homocystinuria for several months without any harmful effects (15) and in preparations to prevent the development of fatty liver. Betaine has food approval in Japan and Korea and Dietary supplement status by FDA in the US.

Betaine is used globally in cosmetic products, like hair and skin care products.

Betaine has successfully been used in fermentations producing e.g. vitamins, antibiotics and amino acids because of its capability to protect microbes from osmotic stress and its good compatibility with enzymes.

Safety of betaine

Toxicological evaluation of betaine anhydrous/betaine monohydrate shows:

- For betaine anhydrous, acute oral median lethal dosage, LD50 (oral) rats, is 11.179 $\pm$ 0.725 g/kg B.W. Therefore the product is not classified as toxic for acute health hazards (6).

- Bacterial reverse mutation assay (Ames test with Salmonella typhimurium) showed that betaine monohydrate is not mutagenic when assayed up to 5000 mg/plate (7).

- Mouse micronucleus test showed that betaine monohydrate does not induce micronuclei in the bone marrow of mice dosed at levels up to a dose of 2 g/kg by the oral route (8).

- Metaphase analysis of human lymphocytes showed that betaine monohydrate is not a clastogen to human lymphocytes (9).

- Sensitization test in the guinea pig showed that there is no evidence to suggest that betaine monohydrate acts as a sensitizer in the guinea pig. Betaine would be classified as a non-allergenic or as a Weak, Grade 1 sensitizer on the Magnusson and Kligman scale, having produced a sensitization rate of 0 % (10).

- Acute eye irritation study with 10 % (w/v betaine monohydrate in distilled water) did not result in any ocular irritation, and it can be considered non-irritant at this concentration (11).

- The primary skin irritation potential test showed that betaine monohydrate at levels over 3.5 % produced a highly significant reduction in the irritant potential of solutions containing 5.15 % to 10.3 % Sodium Lauryl Ether Sulphate (SLES). The extent of this effect was shown to be concentration dependent. In addition, 50 % (w/v) solution of betaine monohydrate appeared to give rise to even less irritation than the de-ionized water control sample (12).

- The effect of exaggerated treatment with a cosmetic lotion containing betaine monohydrate on the rate of transepidermal water loss (TEWL) of intact skin identical treatment with the placebo lotion was tested.
  There were clear indications that the addition of betaine to a skin care lotion resulted in improved moisture retention when the product was applied to the skin(13).

- The Minimum Inhibitory Concentration (MIC) of betaine monohydrate against nine selected microorganisms was shown to be greater that 10 % w/v.
  Betaine monohydrate did not appear to affect the growth rate of any of the microorganisms at concentrations up to 10% w/v (14).

- 90-Day sub-chronic toxicity study in the rat with Betaine

- 28-Day sub acute toxicity and reversibility study in the rat with Betaine

- Betaine 28-day Rat Study

Biodegradability of betaine

Betaine is naturally occurring in many animals, plants and microbes. When betaine is released into the environment either by death of the organism or excretion, it becomes available as a substrate for microbial growth. The ability to decompose betaine is widespread among microorganisms and both anaerobic and aerobic are known to degrade betaine.

Our own laboratory tests have shown that betaine degrades fully within two weeks in the sandy clay soil due to the action of soil microbes.

Biological oxygen demand of technical grade betaine anhydrous crystals (purity over 97 % on dry matter basis) has been analyzed to be 1000 mg O2/ 1 g betaine.

Chemical oxygen demand (COD) values analyzed have been somewhat higher, up to 1300 mg O/ 1 g betaine.

Chemical oxygen demand (CODCr) values analyzed have been around 70 - 100 mg O/ 1 g betaine.

Betaine is highly water soluble (about 160 g/ 100 g water) and it can be considered readily biodegradable.

Partition coefficient

Partition coefficient of betaine in water/n-octanol system:

Pow = 8.1 x 10-4
log = -3.1

Betaine in water environment

Betaine is rich in several marine invertebrate animals and, being as prey animals of fish, they form an important source of betaine for the fish. In artificial feeds for salmonids, betaine (+ some amino acids) is commonly added at 2 - 15 g/kg concentrations with beneficial effects on feed palatability, growth and feed conversion rate. Thus, assuming a feeding rate of 1 - 8 %/ body weight/ day and a betaine content of 2 - 15 g/ kg feed, the betaine uptake by fish via food varies from 20 to 1200 mg/ kg/ day, and no harmful effects have been observed in several long-term (up to one year) trials.

Betaine concentration in the muscle of young salmon, fed with control diet and betaine containing diet (15 g/kg feed) for 1 - 2 months, was 0.12 - 0.28 and 0.7 - 0.9 g/ kg, respectively(3). For comparison, in crustaceans, normally used for human consumption, the measured betaine concentrations of fresh muscle have varied from 1 to 9 g/kg and those in molluscs from 6 to 14 g/kg (2).

According to our understanding betaine is not harmful to human beings, animals or to the environment. We do not consider the determination of the aquatic toxicity of betaine necessary to evaluate the environmental effects of betaine.

Conclusions

BETAFIN TH is a natural product, extracted and separated from plant material, sugar beet molasses. According to our understanding betaine is not harmful to human beings, animals or environment.

Literature

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