Therapeutic agent for improving hepatic and cardiovascular function

TAURINE Powder 98% (Taisho)  
(Taurine)

Storage: Store in a well-closed container at room temperature

Expiration date: Indicated on the package

FORMULATION

<table>
<thead>
<tr>
<th>Brand name</th>
<th>TAURINE Powder 98% (Taisho)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active ingredient</td>
<td>Taurine (1 g per 1.02 g powder)</td>
</tr>
<tr>
<td>Inactive ingredients</td>
<td>Light anhydrous silicic acid, Talc</td>
</tr>
<tr>
<td>Dosage form</td>
<td>White, tasteless, odorless powder (1.02 g sachet powder, 1 kg bulk powder)</td>
</tr>
<tr>
<td>ID code</td>
<td>T317 (printed on each sachet)</td>
</tr>
</tbody>
</table>

INDICATIONS

TAURINE Powder is indicated:

- For the improvement of liver function in patients with hyperbilirubinemia (except that due to obstructive jaundice).
- For the treatment of congestive heart failure.

DOSEAGE AND ADMINISTRATION

The usual adult oral dose is 1.02 g of TAURINE Powder (containing 1 g of taurine) three times a day, after meals.

For the treatment of congestive heart failure, use this product concomitantly with cardiac diuretics only if an adequate effect cannot be obtained with cardiac diuretics alone.

PRECAUTIONS

1. Adverse Reactions

A total of 38 adverse reactions were encountered in 30 (2.82%) of 1,064 patients treated with taurine. The most common adverse reactions included nausea in 5 cases and diarrhea in 4 cases. [Data submitted for the latest reevaluation]

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Gastrointestinal</th>
<th>Hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, diarrhea, abdominal discomfort, constipation, anorexia</td>
<td>&lt; 0.5%</td>
<td>Rash</td>
</tr>
</tbody>
</table>

2. Geriatric Use

Because elderly patients are more likely to have decreased physiological functions, caution should be exercised in the administration of this product (e.g., reduction of dosage).

PHARMACOKINETICS

1. Absorption

When a single dose of 2.04 g* of TAURINE Powder was administered orally to healthy adults under fasting conditions, the blood concentrations of taurine peaked at 84 µg/ml after approx. one hour and dropped to baseline levels (i.e., normal blood levels of endogenous taurine) within 7 hours of dosing. The elimination half-life was approx. two hours.

[* Note: The approved dosing is 1.02 g of TAURINE Powder (i.e., 1 g of taurine) as a single dose.]

2. Distribution

Animal studies:

Rats were given [35S]taurine per os, and the radioactivity levels in various organs and tissues were measured. Approx. 20% of the administered radioactivity was found in the liver 3 hours after dosing. Approx. 7% was found in the kidney 30 min after dosing, and then the levels in the kidney declined rapidly. The radioactivity levels in the heart and skeletal muscle gradually increased each day, while radioactivity in the brain and spinal cord was negligible.

3. Metabolism and excretion

Pharmacokinetic studies in non-Japanese subjects have shown that a minor part of the orally administered taurine is metabolized by conversion to isethionic acid, but the majority of the drug is not metabolized, being excreted unchanged in the urine. Less than 2% of the oral dose is excreted in the feces. It is presumed that oral taurine is partly excreted as taurine-conjugated bile acids in the bile.

CLINICAL STUDIES

1. Liver function in patients with hyperbilirubinemia

A double-blind, controlled clinical trial of taurine was conducted in acute hepatitis patients with serum bilirubin levels of 5 mg/dl or higher (patients with obstructive jaundice were excluded). Liver function was improved with taurine treatment as follows: markedly/moderately improved, 75.4% (49/65); and markedly/moderately/mildly improved, 100% (65/65). Patients treated with taurine showed an improvement in serum AST(GOT) and ALT(GPT) levels.
2. Congestive heart failure

A double-blind, controlled clinical trial of taurine was conducted in patients with congestive heart failure. Based on the efficacy and safety profile, the therapeutic usefulness of taurine was confirmed. The rate of overall improvement in subjective symptoms and objective clinical findings was as follows: markedly/moderately improved, 26.7% (12/45); and markedly/moderately/mildly improved, 73.3% (33/45).

PHARMACOLOGY

1. Stimulation of bile secretion

When taurine was administered orally to rabbits, a two-fold increase in the volume of bile secreted from the liver was observed 3–6 hours after dosing, with increases in the concentration of bile acids in the bile and in the secretion rate of bile acids.

2. Effect on experimentally induced liver injury

In rabbits with carbon tetrachloride- or yellow phosphorus-induced liver injury, oral taurine improved liver function parameters (ALP, γ-globulin, bromosulphthalein [BSP] excretion, serum free cholesterol/cholesterol ester ratio). Histopathologic observations also revealed that taurine caused rapid recovery from toxic liver injury and promoted hepatocyte regeneration, and, in addition, that it inhibited hepatic fibrosis in chronic liver injury.

3. Effect on hepatic energy metabolism and function

In isolated, perfused rat liver, taurine partially prevented hypoxia-induced and anoxia-induced decreases in hepatic ATP levels and a hypoxia-induced decrease in bile secretion. These findings indicate that taurine can exert hepatoprotective effects by improving energy metabolism under hypoxic and anoxic conditions.

4. Effect on cardiac contractility

(1) In rabbits (in vivo), taurine did not affect the heart rate, but it increased the cardiac output (measured as ascending aorta flow), demonstrating that taurine can enhance cardiac contractility.

(2) In guinea-pig ventricular strips (in vitro), taurine increased the internal calcium levels in the isolated strips at lower external calcium concentrations, but a decrease in the internal calcium levels was observed in a high-calcium medium. A similar biphasic change occurred in contractile force: taurine was positively inotropic at lower external calcium concentrations and negatively inotropic at higher external calcium concentrations. These results suggest that taurine may act as a calcium modulator and affect cardiac contractility.

5. Effect on myocardial energy metabolism

In isolated working rat hearts (paced at 300 beats/min), taurine increased ATP synthesis.

6. Effect on hypoxia-induced myocardial cell damage

In the isolated, perfused guinea-pig heart, taurine reduced hypoxia-induced lactate dehydrogenase (LDH) release (a marker of cell death).

7. Effect on experimentally induced heart failure

In rabbits with congestive heart failure induced by chronic aortic regurgitation, taurine reduced mortality.

DESCRIPTION

Generic name: Taurine
Chemical name: 2-Aminoethanesulfonic acid
Structural formula:

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H2N
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|       |
|       |
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       SO3H
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Molecular formula: C2H7NO3S
Molecular weight: 125.15

Physicochemical properties:
- Taurine occurs as colorless-white crystals or a white, crystalline powder. It is odorless. It is soluble in water and practically insoluble in 99.5% ethanol.
- The pH of an aqueous solution of taurine (2 → 40) is 4.1–5.6.
- Melting point: 311–312 °C

PACKAGING

<table>
<thead>
<tr>
<th>Taurine Powder 98% (Taisho)</th>
<th>Package with 1.02 g × 90 or 1200 sachet packs</th>
</tr>
</thead>
</table>

REFERENCES

1) Data on file, Taisho (in Japanese)
2) Iwata H et al.: Oyayou-yakuri, 16, 179 (1978)
6) Yamamura Y et al.: Igaku no Ayumi, 147, 141 (1988)
8) Matsuoka T: Nagasaki Igaku-aminosan, 35, 352 (1960)

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Revised in June 2007: No changes to the PRECAUTIONS section