Revised: October 2014 (9th version)

Standard Commodity Classification No. of Japan
875200

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- Kampo-preparation-

TSUMURA Daisaikoto Extract Granules for Ethical Use

Storage
Store in light-resistant, air-tight containers.

Expiration date
Use before the expiration date indicated on the container and the outer package.

Approval No.	(61AM)3261
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986

DESCRIPTION

Composition	7.5 g of TSUMURA Daisaikoto extract granules (hereafter TJ-8) contains 4.5 g of a dried extract of the following mixed crude drugs. JP Bupleurum Root ……..... 6.0 g JP Pinellia Tuber ..... 4.0 g JP Scutellaria Root …..... 3.0 g JP Peony Root ..... 3.0 g JP Jujube ..... 3.0 g JP Immature Orange ..... 2.0 g JP Ginger ..... 1.0 g JP Rhubarb ..... 1.0 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate Sucrose Esters of Fatty Acids
Description	Dosage form	Granules
	Color	Light yellow-brown
	Smell	Characteristic smell
	Taste	Bitter
	ID code	TSUMURA/8

INDICATIONS

TJ-8 is indicated for the relief of the following symptoms of those patients with comparatively strong constitution having a tendency to constipation, right upper abdominal tenderness accompanied by fullness and discomfort, tinnitus, shoulder stiffness, etc:

Cholelithiasis, cholecystitis, jaundice, hepatic dysfunction, hypertension, cerebral hemorrhage, urticaria, hyperchylia, acute gastrointestinal catarrh, nausea, vomiting, anorexia, hemorrhoid, diabetes mellitus, neurosis, and insomnia

DOSAGE AND ADMINISTRATION

The usual adult dose is 7.5 g/day orally in 2 or 3 divided doses before or between meals. The dosage may be adjusted according to the patient's age and body weight, and symptoms.

PRECAUTIONS

1. Careful Administration (TJ-8 should be administered with care in the following patients.)

(1) Patients with diarrhea, soft feces [These symptoms may be aggravated.]

(2) Patients with an extremely weak gastrointestinal tract [Anorexia, abdominal pain, diarrhea, etc. may occur.]

(3) Patients with greatly declined constitution [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-8 is used, the patient's "SHO" (constitution/symptoms) should be taken into account. The patient's progress should be carefully monitored, and if no improvement in symptoms/findings is observed, continuous treatment should be avoided.

(2) When TJ-8 is coadministered with other Kampo- preparations (Japanese traditional herbal medicines), etc., attention should be paid to the duplication of the contained crude drugs. Special caution should be exercised when TJ-8 is coadministered with preparations containing Rhubarb.

(3) Since there is an individual difference in the cathartic action of Rhubarb, caution should be exercised concerning the dosage and administration.

SHO: The term "SHO" refers to a particular pathological status of a patient evaluated by the Kampo diagnosis, and is patterned according to the patient's constitution, symptoms, etc. Kampo-preparations (Japanese traditional herbal medicines) should be used after confirmation that it is suitable for the identified "SHO" of the patient.

3. Adverse Reactions

TJ-8 has not been investigated (drug use investigations, etc.) to determine the incidence of adverse reactions. Therefore, the incidence of adverse reactions is not known.

(1) Clinically significant adverse reactions

1) **Interstitial pneumonia**: If fever, cough, dyspnea, abnormal pulmonary sound (fine crackle), etc. are observed, administration of this product should be discontinued, and examinations such as X-ray should be performed immediately and appropriate measures such as administration of adrenocortical hormones taken. Besides, the patient should be advised to discontinue TJ-8 immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) **Hepatic dysfunction and jaundice**: Hepatic dysfunction and/or jaundice with elevation of AST (GOT), ALT (GPT), Al-P and γ-GTP or other symptoms may occur. The patient should be carefully monitored for abnormal findings. Administration should be discontinued and appropriate therapeutic measures should be taken, if abnormalities are observed.

(2) Other adverse reactions

	Incidence unknown
Gastrointestinal	Anorexia, Abdominal pain, Diarrhea, etc.

4. Use in the Elderly

Because elderly patients often have reduced physiological function, careful supervision and measures such as reducing the dose are recommended.

5. Use during Pregnancy, Delivery or Lactation

(1) Use of TJ-8 in pregnant women, women who may possibly be pregnant is not recommended. [The uterotonic action and congestive action on the intrapelvic organs of Rhubarb contained in TJ-8 may cause premature birth or abortion.]

(2) TJ-8 should be administered with care in nursing mothers. [Anthraquinone derivatives in Rhubarb contained in this product may be excreted in breast milk and induce diarrhea in nursing infants.]

6. Pediatric Use

The safety of TJ-8 in children has not been established. [Insufficient clinical data]

PHARMACOLOGY

1. Improvement in lipid metabolism in the liver

Oral administration of Daisaikoto inhibited the increases in serum AST(GOT), serum ALT(GPT) and hepatic LPO, and decrease in G-6-Pase in carbon tetrachloride-induced hepatic disorder rat models[1].

2. Improvement on lipid metabolism

Administration of Daisaikoto to rats with high-fat diet inhibited the increases in serum total cholesterol and phospholipids[2].

3. Inhibition on gallstone formation

Administration of Daisaikoto to hamsters with glucose-diet which induce the formation of cholesterol gallstones inhibited the formation of gallstones[3].

4. Anti-allergic actions

In mouse peritoneal mast cells, Daisaikoto inhibited compound 48/80-induced histamine release and degranulation (*in vitro*)[4].

5. Effects on the circulatory system

(1) A diet containing Daisaikoto given to spontaneously hyperlipidemic (SHC) rats inhibited the elevation of the serum total cholesterol[5].

(2) A high-cholesterol diet containing Daisaikoto given to rabbits improved vascular elasticity, and inhibited the elevation of the thoracic aorta levels of lipids and hydroxyproline. Furthermore, it improved the arteriosclerosis index in the thoracic aorta[6].

(3) A high-cholesterol diet was given to rabbits to elevate serum lipid levels. Then, a standard diet containing Daisaikoto was given for 3 or 6 months. It decreased the serum triglyceride level. After 6 months, the level of free cholesterol in aortic wall intima/media cell components decreased. It improved the arteriosclerosis index in the aorta, and the deterioration of histopathological findings[7].

(4) A diet containing Daisaikoto was given to spontaneously hyperlipidemic (KHC) rabbits. It inhibited LDL oxidation, and prevented the deterioration of atherosclerotic lesions in the thoracic aortic arch[8].

6. Action mechanism

Daisaikoto shows pharmacological effects via the following actions:

(1) Inhibition of lipid hyperoxidation in the liver

Oral administration of Daisaikoto to rats with carbon tetrachloride-induced hepatopathy inhibited the reduction of the liver tissue levels of glutathione and ascorbic acid[8], and, in addition, of the superoxide dismutase, catalase, and glutathione reductase activities[9].

(2) Improvement in lipid metabolism in the liver

- In a human hepatocellular model (HepG2 cells), Daisaikoto inhibited the intracellular synthesis of cholesterol ester and triglyceride[10][11], and reduced apoB secretion (*in vitro*)[10].
- A high-cholesterol diet containing Daisaikoto was given to rabbits. It decreased the liver tissue level of apoB mRNA, and increased the levels of apoE and LDL receptor mRNA[12].

PACKAGING

Bottles of 500 g
2.5 g × 42 packets
2.5 g × 189 packets

REFERENCES

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10) Furukawa, S. et al. J. Traditional Med. 1994, 11(3), p.236.
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12) Iizuka, A. et al. Res. Commun. Pharmacol. Toxicol. 2001, 6(3·4), p.205.

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