Revised: August 2007 (7th version)

Standard Commodity Classification No. of Japan
875200

■ 1 ■

- Kampo-preparation-

TSUMURA Kakkonto 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)3292
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 Kakkonto extract granules (hereafter TJ-1) contains 3.75 g of a dried extract of the following mixed crude drugs. JP Pueraria Root ..... 4.0 g JP Jujube ..... 3.0 g JP Ephedra Herb ..... 3.0 g JP Glycyrrhiza ..... 2.0 g JP Cinnamon Bark ..... 2.0 g JP Peony Root ..... 2.0 g JP Ginger ..... 2.0 g (JP: The Japanese Pharma copoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate Sucrose Esters of Fatty Acids
Description	Dosage form	Granules
	Color	Light brown
	Smell	Characteristic smell
	Taste	Pungent
	ID code	TSUMURA/1

INDICATIONS

TJ-1 is indicated for the relief of the following symptoms of those patients with comparatively strong constitution having headache, fever, rigor, and shoulder stiffness without spontaneous sweating:

Common cold, coryza, the initial stage of febrile diseases, inflammatory diseases (conjunctivitis, keratitis, otitis media, tonsillitis, mastitis, and lymphadenitis), shoulder stiffness, neuralgia in the upper body, and urticaria.

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-1 should be administered with care in the following patients.)

(1) Patients in a period of weakness after disease or with greatly declined constitution [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

(2) Patients with an extremely weak gastrointestinal tract [Anorexia, epigastric distress, nausea, vomiting, etc. may occur.]

(3) Patients with anorexia, nausea or vomiting [These symptoms may be aggravated.]

(4) Patients showing a remarkable tendency of sweating [Excess sweating and/or generalized weakness may occur.]

(5) Patients with cardiovascular disorders including angina pectoris and myocardial infarction, etc. or those with a history of such disorders.

(6) Patients with severe hypertension

(7) Patients with severe renal dysfunction

(8) Patients with dysuria

(9) Patients with hyperthyroidism

[(5)-(9): These disease and symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-1 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) Since TJ-1 contains Glycyrrhiza, careful attention should be paid to the serum potassium level, blood pressure, etc., and if any abnormality is observed, administration should be discontinued.

(3) When TJ-1 is coadministered with other Kampo-preparations (Japanese traditional herbal medicines), etc., attention should be paid to the duplication of the contained crude drugs.

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. Drug Interactions

Precautions for coadministration (TJ-1 should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
(1) Preparations containing Ephedra Herb (2) Preparations containing ephedrine-related compounds (3) Monoamine oxidase (MAO) inhibitors (4) Thyroid preparations Thyroxine Liothyronine (5) Catecholamine preparations Epinephrine Isoprenaline (6) Xanthine preparations Theophylline Diprophylline	Insomnia, excessive sweating, tachycardia, palpitation, general weakness, mental excitation, etc. are likely to occur. In such cases, TJ-1 should be administered with care by measures such as reducing the dosage.	An enhancement of the sympathetic nerve-stimulating action has been suggested.
(1) Preparations containing Glycyrrhiza (2) Preparations containing glycyrrhizinic acid or glycyrrhizinates	Pseudoaldosteronism is likely to occur. Besides, myopathy is likely to occur as a result of hypokalemia. (Refer to the section "Clinically significant adverse reactions".)	Since glycyrrhizinic acid has an accelerating action on the potassium excretion at the renal tubules, an acceleration of decrease in the serum potassium level has been suggested.

4. Adverse Reactions

TJ-1 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) Pseudoaldosteronism: Pseudoaldosteronism such as hypokalemia, increased blood pressure, retention of sodium/body fluid, edema, increased body weight, etc. may occur. The patient should be carefully monitored (measurement of serum potassium level, etc.), and if any abnormality is observed, administration should be discontinued and appropriate measures such as administration of potassium preparations should be taken.

2) Myopathy: Myopathy may occur as a result of hypokalemia. The patient should be carefully monitored, and if any abnormality such as weakness, convulsion/paralysis of limbs, etc. are observed, administration should be discontinued and appropriate measures such as administration of potassium preparations should be taken.

3) 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
Hypersensitivity Note 1)	Rash, Redness, Pruritus, etc.
Autonomic	Insomnia, Excess sweating, Tachycardia, Palpitation, Generalized weakness, Mental excitation, etc.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Vomiting, etc.
Urinary	Urination disorder, etc.

Note 1) If such symptoms are observed, administration should be discontinued.

5. Use in the Elderly

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

6. Use during Pregnancy, Delivery or Lactation

The safety of TJ-1 in pregnant women has not been established. Therefore, TJ-1 should be used in pregnant women, women who may possibly be pregnant only if the expected therapeutic benefits outweigh the possible risks associated with treatment.

7. Pediatric Use

The safety of TJ-1 in children has not been established. [Insufficient clinical data.]

8. Other Precautions

Eczema, dermatitis, etc. may be aggravated.

PHARMACOLOGY

1. Anti-allergic actions

Oral pretreatment with Kakkonto inhibited food pad swelling response of sheep red blood cell-induced delayed-type hypersensitivity (SRBC-DTH) in mice[1].

2. Actions on influenza virus infection

Oral pretreatment of mice with Kakkonto reduced fever by influenza virus infection to lead lower mortality[2].

3. Action mechanisms

Kakkonto exhibits pharmacological effects via the following actions:

(1) Actions on prostaglandin E_2 (PGE_2)

- Short term treatment (10 min) with Kakkonto inhibited the synthesis of prostaglandin E_2 by bradykinin, but long term treatment (18 hr) increased it in cultured rabbit astrocytes. After 18 hr-incubation Kakkonto reduced endogenous PGE_2 release (*in vitro*) [3].
- Kakkonto inhibited the release of prostaglandin E_2 by a calcium ionophore A23187 in rat C6 glioma cells (*in vitro*) [4].

(2) Actions on cytokines
Oral pretreatment of mice with Kakkonto inhibited the elevation of Interleukin (IL)-1a in bronchoalveolar lavage fluid and serum induced by influenza virus infection[2]. The concentration of IL-12 in bronchoalveolar lavage fluid was elevated [5].

PACKAGING

Bottles of 500 g and boxes of 5 kg (500 g × 10 bottles)
2.5 g × 42 packets
2.5 g × 189 packets

REFERENCES

1) Matsuda, H. et al. J. Med. Pharm. Soc. WAKAN-YAKU. 1990, 7(1), p.35.
2) Kurokawa, K. et al. J. Traditional Med. 1996, 13(3), p.201.
3) Kutsuwa, M. et al. Phytomedicine. 1998, 5(4), p.275.
4) Nakahata, N. et al. J. Traditional Med. 1998, 15(2), p.116.
5) Kurokawa, M. et al. Antivaral Res. 2002, 56(2), p.183.

REQUEST FOR LITERATURE SHOULD BE MADE TO:

Consumer Information Services Center
Tsumura & Co.
2-17-11 Akasaka, Minato-ku, Tokyo 107-8521, Japan
TEL:0120-329970 FAX:03-5574-6610

Manufactured and Distributed by:

Tsumura & Co.
2-17-11 Akasaka, Minato-ku, Tokyo 107-8521, Japan