Revised: October 2014 (11th version)

Standard Commodity Classification No. of Japan
875200

■41■

- Kampo-preparation-

TSUMURA Hochuekkito 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)1164
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 Hochuekkito extract granules (hereafter TJ-41) contains 5.0 g of a dried extract of the following mixed crude drugs. JP Astragalus Root ..... 4.0 g JP Atractylodes Lancea Rhizome ..... 4.0 g JP Ginseng ..... 4.0 g JP Japanese Angelica Root ..... 3.0 g JP Bupleurum Root ..... 2.0 g JP Jujube ..... 2.0 g JP Citrus Unshiu Peel ..... 2.0 g JP Glycyrrhiza ..... 1.5 g JP Cimicifuga Rhizome ..... 1.0 g JP Ginger ..... 0.5 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate
Description	Dosage form	Granules
	Color	Light brown
	Smell	Characteristic smell
	Taste	Slightly sweet
	ID code	TSUMURA/41

INDICATIONS

TJ-41 is indicated for the following symptoms/conditions of patients having delicate constitution, reduced digestive functions, and severe fatigability of limbs:

Summer emaciation, reinforcement of physical strength after illness, tuberculosis, anorexia, gastroptosis, cold, hemorrhoid, anal prolapse, uterine prolapse, impotence, hemiplegia, and hyperhidrosis

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. Important Precautions

(1) When TJ-41 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-41 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-41 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.

2. Drug Interactions

Precautions for coadministration (TJ-41 should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
(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.

3. Adverse Reactions

TJ-41 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 TJ-41 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 this product immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) 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.

3) 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.

4) 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, Urticaria, etc.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Diarrhea, etc.

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

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

The safety of TJ-41 in pregnant women has not been established. Therefore, TJ-41 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.

6. Pediatric Use

The safety of TJ-41 in children has not been established. [Insufficient clinical data]

7. Other Precautions

Eczema, dermatitis, etc. may be aggravated.

PHARMACOLOGY

1. Action against weakness in convalescence

(1) Improvement of immune dysfunction

Administration of Hochuekkito elevated the activity of blood natural killer (NK) cells in the patients with decreased strength due to chronic diseases or persistent infections (n=35)[1].

(2)Effects on weakness during infection

- Oral administration of Hochuekkito prolonged survival in prednisolone-induced immunosuppressed mice infected with *C. albicans*[2].
- Oral administration of Hochuekkito increased survival rate and prolonged survival in MMC-induced immunosuppressed mice infected with herpes simplex virus type I (HSV-1)[3].

(3) Restoration of biological defense mechanism in tumor-bearing state

- Oral administration of Hochuekkito promoted antitumor immunity against secondary Meth A and suppressed tumor growth in mice[4].

(4) Actions on compromised immune function caused by anticancer agents

Oral administration of Hochuekkito suppressed testis weight reduction by adriamycin in mice[5].

2. Effect on weakness in elderly

Oral administration of Hochuekkito restored reduced T cell counts, NK cell counts, CD4/CD8 ratio, and production of antibodies against sheep red blood cell (SRBC) antigen in aged mice[6].

3. Effect on anorexia

Administration of Hochuekkito in the diet to Colon26-L20 adenocarcinoma-induced cachexia model mice inhibited decreased body weight, food intake, water intake, gastrocnemius muscle volume, and the weight of peripheral testicular fat, as well as triglycerides[7].

4. Action against the common cold

Oral pre-administration of Hochuekkito prolonged the survival period in mice infected with influenza[8].

5. Actions on testis

(1) Administration of Hochuekkito to mice inhibited the testicular weight-lowering effect of doxorubicin where Hochuekkito was administered with diet for 14 weeks (0-14 w) and doxorubicin was administered intraperitoneally for 6 weeks (1-6 w)[10].

(2) Oral administration of Hochuekkito to mice inhibited the testicular weight-lowering effect of adriamucin[11].

6. Mechanism of action

Hochuekkito shows pharmacological effects via the following actions:

(1) Immune modulating effects

1) Effect on humoral immunity

Oral administration of Hochuekkito increased production of antibodies against SRBC antigen in mice[6].

2) Effects on NK activity
   - Oral administration of Hochuekkito enhanced NK activity of spleen cells in mice[4].
   - Oral pre-administration of Hochuekkito to a mouse model of cancer metastasis transplanted with mouse colon cancer Colon26-L5 cells suppressed reduction of cancer metastasis by removing NK cells[9].

3) Effects on macrophages
   - Oral administration of Hochuekkito increased phagocytic activity of intraperitoneal cells, spleen cells and bone marrow cells in mice[10].
   - Oral administration of Hochuekkito increased tumor growth inhibitory activity of intraperitoneally infiltrating cells in mice[4].

4) Effects on cytokine production
   - Oral pre-administration of Hochuekkito induced early production of IFN in mice infected with influenza[8].
   - Administration of Hochuekkito in drinking water restored serum interleukin (IL)-12 concentration reduced by restraint stress in tumor-bearing mice[11].

(2) Effects on the testes
   - Protein synthesis was promoted in hamster epididymal duct cells (*in vitro)*[12].
   - Hochuekkito inhibited the decline in human sperm motility rate caused by anti-sperm antibodies (*in vitro)*[13].
   - Sperm velocity and linear velocity were improved in the human sperm (*in vitro)*[14].

PACKAGING

Bottles of 500 g , Boxes of 5 kg (500 g bottle× 10),
2.5 g × 42 packets, 2.5 g × 189 packets

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