Revised: October 2014 (7th version)

Standard Commodity Classification No. of Japan
875200

■48■

- Kampo-preparation-

TSUMURA Juzentaihoto 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)1124
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 Juzentaihoto extract granules (hereafter TJ-48) contains 5.0 g of a dried extract of the following mixed crude drugs. JP Astragalus Root ..... 3.0 g JP Cinnamon Bark ..... 3.0 g JP Rehmannia Root ..... 3.0 g JP Peony Root ..... 3.0 g JP Cnidium Rhizome ..... 3.0 g JP Atractylodes Lancea Rhizome ..... 3.0 g JP Japanese Angelica Root ..... 3.0 g JP Ginseng ..... 3.0 g JP Poria Sclerotium ..... 3.0 g JP Glycyrrhiza ..... 1.5 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate
Description	Dosage form	Granules
	Color	Grayish-brown
	Smell	Characteristic smell
	Taste	Slightly sweet
	ID code	TSUMURA/48

INDICATIONS

TJ-48 is indicated for the relief of declined constitution after recovery from disease, fatigue and malaise, anorexia, perspiration during sleep, cold limbs, anemia.

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-48 should be administered with care in the following patients.)

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

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

2. Important Precautions

(1) When TJ-48 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-48 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-48 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-48 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.

4. Adverse Reactions

TJ-48 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, Urticaria, etc.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Vomiting, Diarrhea, 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-48 in pregnant women has not been established. Therefore, the product 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-48 in children has not been established. [Insufficient clinical data.]

8. Other Precautions

Eczema, dermatitis, etc. may be aggravated.

PHARMACOLOGY

1. Actions on a reduction of physical fitness after disease

(1) Relief of an immunosuppressive state

Oral pre-administration of Juzentaihoto to elderly mice inhibited a CDDP-induced reduction of antibody production [1].

(2) Actions on a reduction of physical fitness in the presence of infection

- Oral pretreatment with Juzentaihoto in *C.albicans*-infected mice immunosuppressed with cyclophosphamide prolonged survival[2].
- Oral administration of Juzentaihoto to mice inhibited *Plasmodium* infection[3].

(3) Actions on a reduction of physical fitness in the presence of cancer

- Oral pretreatment with Juzentaihoto in mice inhibited the liver metastasis of colon cancer cells (Colon 26-L5), which frequently metastasize to the liver[4].
- A diet containing Juzentaihoto was given to mice, and a malignant glioma was implanted. The diet inhibited the proliferation of the malignant glioma, and prolonged survival[5].
- Oral administration of Juzentaihoto to a mouse recurrent tumor model, in which Meth-A fibrosarcoma cells were implanted after post-growth removal of Meth-A fibrosarcoma initially implanted, inhibited the growth of secondarily implanted Meth-A fibrosarcoma cells[6].

(4) Inhibitory effect of anorexia and hematotoxicity of anticancer agents

- Oral administration of Juzentaihoto to mice and rats inhibited MMC- or CDDP-induced weight loss, and prolonged survival when an anticancer agent at the lethal dose was administered. Furthermore, oral administration of Juzentaihoto to mice inhibited MMC-induced decreases in the leukocyte count, erythrocyte count, and hematocrit value as well as decreases in spleen, testis, and thymus weights. In addition, Juzentaihoto inhibited CDDP-induced increases in BUN and creatinine as well as degeneration of the kidney, and increased the LD_{50} value of CDDP[7]
- A diet containing Juzentaihoto was given to mice. It inhibited CDDP-induced degeneration of the uriniferous tubule, necrosis, and cast formation[8]. Oral pretreatment in mice inhibited a CDDP-induced increase in BUN, and prolonged survival1[9].

2. Actions on anemia

(1) Oral administration of Juzentaihoto to mice immunosuppressed with MMC inhibited a decrease in the CFU-S count[10].

(2) In the culture supernatant of peyer's patch cells after oral administration of Juzentaihoto to mice, the proliferative activity of bone marrow cells were observed (*in vitro*) [11].

3. Action mechanism

Juzentaihoto shows pharmacological effects via the following actions:

Regulation of immunity

(1) Actions on humoral immunity

Oral pretreatment with Juzentaihoto in elderly mice increased the production of IgG against SRBC. Furthermore, oral pretreatment with Juzentaihoto in mice inhibited CDDP-induced decrease in the production of IgM against SRBC [12].

(2) Actions on cell-mediated immunity

Oral pretreatment with Juzentaihoto in mice enhanced the delayed-type hypersensitivity (DTH) reaction, and increased cytotoxic T cell (CTL) activity in splenocytes[13].

(3) Actions on natural killer (NK) activity

Oral pretreatment with a diet containing Juzentaihoto in mice bearing malignant glioma cells enhanced NK cell activity in splenocytes[5].

(4) Actions on macrophage activity

- Oral administration of Juzentaihoto to mice enhanced the phagocytic activity of peritoneal exudates cells and bone marrow cells[14].
- Antibody production-enhancing actions of Juzentaihoto were not observed in mice pretreated with carrageenan which had an affect to inactivate macrophage[12].
- Oral administration of Juzentaihoto to mice before implanted with colon cancer cells inhibited liver metastasis. This inhibitory effect was not observed in mice pretreated with 2-chloroadenosine which had an affect to inactivate macrophage[4].

(5) Actions on the production of cytokines

- In human peripheral blood mononuclear cells (PBMC), Juzentaihoto increased the production of interleukin (IL)-1β and GM-CSF (*in vitro*) [15].
- In PBMC, Juzentaihoto enhanced the production of IL-2 and IFN-γ by PHA stimulation (*in vitro*) [16].
- Pretreatment of a diet containing Juzentaihoto in mice implanted with human malignant glioma cells increased the production of TNF α in peripheral blood[5].
- In the culture supernatant of peyer's patch cells after oral administration of Juzentaihoto to mice, the production of GM-CSF and IL-6 was increased (*in vitro*) [11].

PACKAGING

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

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