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Standard Commodity Classification No. of Japan
875200

■114■

- Kampo-preparation-

TSUMURA Saireito 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)3275
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986

DESCRIPTION

Composition	9.0 g of TSUMURA Saireito extract granules (hereafter TJ-114) contains 6.0 g of a dried extract of the following mixed crude drugs. JP Bupleurum Root..... 7.0 g JP Alisma Rhizome..... 5.0 g JP Pinellia Tuber..... 5.0 g JP Scutellaria Root..... 3.0 g JP Astractylodes Lancea Rhizome ..... 3.0 g JP Jujube..... 3.0 g JP Polyporus Sclerotium..... 3.0 g JP Ginseng..... 3.0 g JP Poria Sclerotium..... 3.0 g JP Glycyrrhiza..... 2.0 g JP Cinnamon Bark..... 2.0 g JP Ginger..... 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	Yellow-brown
	Smell	Characteristic smell
	Taste	Slightly astringent
	ID code	TSUMURA/114

INDICATIONS

TJ-114 is indicated for the relief of the following symptoms of those patients with nausea, anorexia, thirst, and oliguria:
Watery diarrhea, acute gastroenteritis, sunstroke, and edema

DOSAGE AND ADMINISTRATION

The usual adult dose is 9.0 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-114 should be administered with care in the following patients.)

Patients with severe apophylaxis [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-114 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-114 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-114 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

(1) Precautions for coadministration (TJ-114 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-114 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-114 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-114 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) **Fulminant hepatitis, hepatic dysfunction and jaundice**: Fulminant hepatitis, hepatic dysfunction and/or jaundice with remarkable elevation of AST (GOT), ALT (GPT), Al-P and γ-GTP etc. 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	Dry mouth, Anorexia, Epigastric distress, Nausea, Vomiting, Feeling of enlarged abdomen, Abdominal pain, Diarrhea, Constipation, etc.
Urinary	Pollakiuria, Micturition pain, Hematuria, Feeling of residual urine, Cystitis, etc.
Others	General malaise

Note1) If such symptoms are observed, administration should be discontinued.

Note2) The patient should be carefully monitored, and if abnormalities are observed, administration of the drug should be discontinued and appropriate therapeutic measures taken.

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-114 in pregnant women has not been established. Therefore, TJ-114 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-114 in children has not been established. [Insufficient clinical data]

8. Other Precautions

Adverse reactions of interstitial pneumonia, liver dysfunction and cystitis have been reported with a similar prescription "shosaikoto". In particular, interstitial pneumonia has been reported frequently in the case of combined use with interferon-α.

PHARMACOLOGY

1. Amelioration of edema

Oral administration of Saireito reduced the amounts of extracellular fluid and intercellular fluid in mice with anti-glomerular basement membrane (GBM) nephritis[1].

2. Diuretic effect

Oral administration of Saireito increased urine volume in a water-loading mouse model produced by desmopressin acetate and saline preloading. On the other hand, urine volume did not change in a water-deprivation mouse model deprived of food and water[2].

3. Anti-inflammatory effect

(1) Oral administration of Saireito increased the concentration of adrenocorticotropic hormone (ACTH) and corticosterone in the blood in rats.[3]

(2) Administration of Saireito in the diet suppressed infiltration of Ia-positive cells and T cells in glomeruli in Masugi nephritis model rats[4].

(3) Oral administration of Saireito suppressed increased expression of adhesion molecules such as ICAM-1 and LFA-1 and crescent formation in the initial stage of inflammation in rats with anti-glomerular basement membrane (GBM) nephritis[5]. In addition, increased production of endothelin-1 in glomeruli in the chronic phase of nephritis was suppressed and urinary protein excretions were improved[6].

(4) Administration of Saireito to mice with diet at the onset of type II collagen arthritis decreased the incidence of arthritis and histologically suppressed the stratification of synovial cells and the edema at the synovial soft tissue (*in vivo*). In addition, lymphocyte blastogenesis stimulated by type II collagen and killed tubercle bacilli was suppressed in the spleen removed from the same animal (*ex vivo)*[7].

(5) Administration of Saireito in the diet reduced antinuclear antibody and rheumatoid factor (RF) in MRL/lpr mice that model lupus dermatitis[8].

4. Mechanism of action

Saireito shows pharmacological effects via the following actions:

(1) Sodium channel blocking effect
Sodium channels were inhibited in distal tubular cells derived from dog kidney (MDCK cells) *in vitro*[9].

(2) Anti-inflammatory effect
Oral administration of Saireito increased plasma ACTH levels and expression of proopiomelanocortin (POMC) mRNA, a precursor of ACTH in the anterior pituitary in rats[10]. In addition, these effects were inhibited by ACTH-releasing factor (CRF) antiserum[11].

(3) Inhibition on DNA synthesis
DNA synthesis by serum, platelet-derived growth factor (PDGF), and epidermal growth factor (EGF) in rat mesangial cells was inhibited (*in vitro)* [12].

PACKAGING

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

REFERENCES

1)Tada, K. et al. J. Trad. Med. 2004, 21(3), p.125.
2)Ohnishi, N. et al. J. Traditional Med. 2000, 17(3), p.131.
3)Iwai, I. et al. Clin. Endocrinol. 1992, 40(7), p.745.
4)Nagata, M. et al. Jpn. J. Nephrol. 1989, 31(7), p.713.
5)Hattori, T. et al. Jpn. J. Nephrol. 1995, 37(7), p.373.
6)Hattori, T. et al. Jpn. J. Nephrol. 1997, 39(2), p.121.
7)Kikukawa, T. et al. Jpn. J. Inflammation. 1995, 15(2), p.129.
8)Kanauchi, H. et al. J. Dermatol. 1994, 21(12), p.935.
9)Kuwahara, M. et al. Kidney and Dialysis. 1996, 41(2), p.251.
10)Iwai, I. et al. Neurosci.Lett. 1993, 157, p.37.
11)Nakano, Y. et al. Nuerosci. Lett. 1993, 160, p.93.
12)Awazu, M. et al. Nephron. 2002, 92, p.652.

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