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ANTI-INFLAMMATORY EFFECT OF SUZ-NI-SAN

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Szu-Ni-San (四逆散) was used to treat gastoenteritis, mastitis, acute appendicitis, intercostal neuralgia and abdominal pain by Chinese physicians. But there is no any modern pharmacologic study to prove it. So this study researched its anti-inflammatory, analgesic and hypothermic effects. The following results were obtained:

1. The alcohol extracts of Szu-Ni-San (S.N.-Alc) had inhibitory effect on CAG-induced, formalin -iinduced or 5-HT-induced edema.
2. S.N.-Alc had significant inhibitory effect on acetic acid or histamine phosphate induced capillary permeability, while the water extracts of Szu-Ni-San (S.N.-H_2O) had slight inhibitory effect.
3. S.N.-Alc had analgesic effect.
4. S.N.-Alc had hypothermic effect.
5. The inhibitory effect on CAG-induced edema was significantly decreased in adrenalectomized rats.
6. The mechanisms of Szu-Ni-San on anti-inflammatory and hypothermic effect might be similar with aspirin which could inhibit the actions of 5-HT, histamine and the synthesis of PGE.

INTRODUCTION

At present there are many anti-inflammatory agents in western drugs can inhibit the actions of 5-HT[1] and histamine[2] or the synthesis of prostaglandins[3] . By these mechanism anti-inflammatory agents reduced the symptoms of inflammation such as redness, swelling, heat and pain. But they generally produced some adverse reactions. So it is necessary to search for effective Chinese drugs which had little adverse reaction.

Szu-Ni-San was originally described by Chang Chung Ching (張仲景) of Han Dynasty in Treatise on Exogenous Febrile Disease (傷寒論). It composed of Bupleuri Radix, Glycyrrhizae Radix, Paeoniae Radix and Aruantii fructus Immaturus. In ancient Chinese medicine, it mainly applied to treat abdominal pain[4] . But it used to treat gastoenteritis mastitis, acute appendicitis, intercostal neuralgia and abdominal pain by recent Chinese physicians[5]

It implied that Szu-Ni-San had anti-inflammatory and analgesic effects, but there is no any modern pharmacologic study to prove it. So this study performed the test for edema in normal rats or adrenalectomized rats, the test for capillary permeability in mice,

the test for analgesic effects in mice by acetic acid method and hot plate method, and the test for hypothermic effects in normal and adrenalectomized rats, to research the anti-inflammatory, analgesic, hypothermic effects and their mechanisms.

EXPERIMENTAL

Preparations of Szu-Ni-San:

Bupleuri Radix, Glycyrrhizae Radix, Paeoniae Radix and Aŕuantii fructus Immaturus were mixed in the ratio of 1:1:1:1, then grounded into coarse powder. One kg of the coarse powder was extracted with 95% alcohol in water bath at a temperature just below 65°C several times until the solution was clear. All the extracts were mixed then evaporated and concentrated by a rotary vacuum evaporator at a temperature around 55°C. The alcohol extracts obtained by drying the concentrated solution at 50°C was called S.N.-Alc. Its extraction rate was 21.8%.

In the other preparation, we used water as the solvent. With the same method as S.N.-Alc, the water extract was obtained and called S.N.-H_2O. Its extraction rate was 15.4%.

Animals:

Male Sprague-Dawley rats (weighing between 200–250g) and male ICR mice (weighing between 20–25g) were used in the following studies. The animals were controlled at a temperature of 25 ± 2° C and humidity of 55 ± 5%. The solid diet and tap water were provided ad libitum.

Reagents and Equipments:

Carrageenin (CAG), Serotonin (5-HT), Histamine-phosphate, Evan's blue (Sigma), Plethysmometer (UGO, Basile Italy).

Test for edema in normal rats:

According to Winter's method[6], male rats were used in groups of 5 rats. After measuring the volume of the right hind paw(Ec) by plethysmometer, 0.25g/kg and 0.50g/kg of distilled water extracts of Szu-Ni-San (S.N.-H_2O) or ethanol extracts of Szu-Ni-San (S.N.-Alc) were orally administered to these rats as test groups and 0.5% CMC was orally administered as control group.

An hour after the administration, 0.1 ml carrageenin solution (CAG) was injected subcutaneously into the foot pad of the right hind paw. Then, one hour later, the volume of the right hind paw (Et) was measured and the measurement was performed every one hour for next four hours. Aspirin (0.15g/kg) was used as a standard reagent for comparison. The swelling ratio of test groups (St) were compared with that of control group (Sc). And the inhibition of edema was calculated by following equation.

$$S = \frac{Et - Ec}{Ec} \times 100\% \quad , \quad H = \frac{Sc - St}{Sc} \times 100\%$$

In next test, 4% formalin [7] and 0.02% 5-HT[8] were used instead of carrageenin to induce edema. Their swelling ratio and inhibition of edema was measured by the same method as CAG-induced edema. But the folume of right paw was measured every half hour on 5-HT-induced edema rats.

Test for edema in adrenalectomized rats:

5 male rats in one group were adrenalectomized under ether-induced anaesthesia, by dorsal approach and the control group were treated with a sham operation. The operated rats were employed 96 hr. later to perform the test for CAG-induced edema by the same method as normal rats[9]

Test for capillary permeability in mice:

According to B.A. Whittle's method[10], 10 male mice in one group were orally administered with S.N.-H_2O (0.25g/kg, 0.50g/kg) or S.N.-Alc (0.25g/kg, 0.50g/kg). One hour later, a 4% (W/V) solution of Evan's blue dissolved in physiological saline was intravenously given through the tail vein (0.05ml/10g body weight). 40 minutes after the administration, 0.3 ml of a 0.5% (V/V) acetic acid or 0.2 ml of 0.2mg/ml histamine-phosphate was injected intraperitoneally. Then 20 minutes later, beheading and blooding were performed. Their viscera were irrigated with saline, and each washing was added to 10 ml with saline. After adding 0.1 ml of 0.1 N NaOH, the amount of the leaked dye was determined by the absorbance measurement at 610 nm by U.V. spectophotometer. Aspirin (0.15g/kg) was used as a standard reagent for comparison.

Test for analgesic effects in mice:

(a) Acetic method[11]:

10 mice in one group were orally administered with S.N.-H_2O (0.25g/kg, 0.50g/kg) or S.N.-Alc (0.25, 0.50g/kg). 1 hr. later, 0.7% acetic acid (0.1 ml/10g body weight) was administered intraperitoneally to produce pain. The frequency of writhing response was used as the index of pain response.

(b) Hot plate method[12]:

1 hr. after administration of S.N.-H_2O (0.25g/kg, 0.50g/kg) or S.N.-Alc, (0.25g/kg, 0.50g/kg), 10 mice in one group were placed on a hot plate (55.0 + 0.2℃). The latency to produce jumping, licking or withdraw legs was used as the index of pain response. In this experiment, 0.5% CMC was administered orally as control group and aspirin (0.20g/kg) was used as a standard reagent for comparison.

Test for hypothermic effect in normal rats:

6 rats with a rectal temperature between 37.5–38.3°C were used in one group. 1 hr. after administration with S.N.-H_2O (0.5g/kg, 1.0g/kg), S.N.-Alc (0.50g/kg, 1.0g/kg) or 0.5% CMC (control group), rectal temperatures of rats were measured at intervals of one hour for 4 hrs.

Test for hypothermic effect in carrageenin-induced hyperthermic rats:

6 rats with a rectal temperature between 37.5–38.3°C in one group were injected with 1.0% CAG (2ml/body) subcutaneously into the thigh. 1 hr. later, rectal temperature of rats were measured at interval of one hour. At the 8th hour, administered orally with S.N.-H_2O (0.50g/kg, 1.0g/kg), S.N.-Alc (0.50g/kg, 1.0g/kg) or 0.5% CMC (control group). Then measured their rectal temperature at interval of one hour to the 12th hour.

Statistical Analysis:

The statistical analysis of results was performed by means of the student's t test for unpaired data. Results were considered significant if $p < 0.05$.

RESULT

Acute toxicity:

As shown Table 1. by the route of P.0. the LD_{50} of S.N.-Alc and S.N.-H_2O in rats or in mice are also more than 12g/kg. By the route of I.P., thd LD_{50} of S.N.-Alc is 1.92g/kg in mice, 1.77g/kg in rats, and the LD_{50} of S.N.-H_2O is 4.10g/kg in mice but 3.56g/kg in rats. These data implied the toxicity of Szu-Ni-San is little by P.0., but the toxicity of S.N.-Alc is stronger than that of S.N.-H_2O by I.P.

Effects on edema in rats:

As shown in Table 2, S.N.-Alc 0.5g/kg had inhibitory effect on CAG-induced edema ($P < 0.05$) (inhibition: 33.7%) and the effect had maintained for 4 hrs. But S.N.-H_2O had no effect.

As shown in Table 3, S.N.-Alc 0.50g/kg had significant inhibitory effect on formalin-induced edema ($P < 0.01 - P < 0.001$) (inhibition: 42.5 – 46.5%). S.N.-Alc 0.25 g/kg had slight inhibitory effect like that of S.N.-H_2O 0.50g/kg ($P < 0.05$).

As shown in Table 4, S.N.-Alc 0.5g/kg had significant inhibitory effect on 5-HT-induced edema ($P < 0.01 - P < 0.001$) (inhibition: 35.0–43.7%). S.N.-Alc 0.25g/kg had slight inhibitory effect ($P < 0.05 - P < 0.01$). And S.N.-H_2O had no effect.

Effects on carrageenin-induced edema in adrenalectomized rats:

As shown in Table 5, the inhibitory effect of S.N.-Alc 0.50g/kg on carrageenin-induced edema in normal rats was significantly decreased if these rats were adrenalectomized ($P < 0.05$).

Effects on capillary permeability:

As shown in Table 6, S.N.-Alc 0.5g/kg significantly decreased capillary permeability in histamine-phosphate-induced mice ($P < 0.001$) while S.N.-H_2O 0.5g/kg decreased it slightly ($P < 0.05$).

As shown in Table 7, S.N.-Alc 0.5g/kg significantly decreased permeability in acetic acid-induced mice ($P < 0.001$). While S.N.-Alc 0.25g/kg and S.N.-H_2O 0.5g/kg decreased just slightly ($P < 0.05$).

Analgesic effects:

As shown in Table 7, S.N.-Alc 0.5g/kg had significant analgesic effect ($P < 0.001$) by acetic acid method, while S.N.-H_2O 0.5g/kg had slight analgesic effect ($P < 0.01$).

As shown in table 8, S.N.-Alc 0.5g/kg had slight analgesic effect by hot plate method, while S.N.-H_2O had no effect.

Hypothermic effects:

As shown in Table 10, S.N.-Alc 1.0g/kg had hypothermic effect ($P < 0.05$) in normal rats, while S.N.-H_2O had no effect.

As shown in fig. 1, S.N.-Alc 1.0g/kg had hypothermic effect ($P < 0.05$) in carrageenin -induced hyperhtermic rats, while S.N.-H_2O had no effect.

DISCUSSION

The present experiment showed S.N-Alc had inhibitory effect on CAG-induced edema, while S.N.-H_2O had no effect. Dirose M, et, al. had reported that in the first phase of edema induced by CAG, it was mediated by 5-HT and histamine[13] , B.J. Northover et, al. had reported that formalin-induced edema related to 5-HT[14] . In this experiment, S.N.-Alc had inhibitory effect on formalin-induced edema and 5-HT-induced edema while S.N.-H_2O had no effect. That implied the inhibitory effect of S.N.-Alc in edema related to 5-HT. E. Keleman had reported Aspirin had inhibitory effect on 5-HT-induced edema in rats[15] . So the inhibitory effect of S.N.-Alc on edema may be the same as that of Aspirin.

Because 5-HT and histamine all potentiated capillary permeability[16] . And S.N.-Alc decreased permeability induced by acetic acid or histamine phosphate significantly while S.N.-H_2O just decreased slightly. According to B.J. Northover's report, Aspirin could inhibite dye leakage induced by histamine [15] . These results implied that the anti-inflammatory effect of S.N.-Alc may be dependent on the inhibition of the action of histamine and 5-HT.

In this study, the inhibitory effect of S.N.-Alc on CAG-induced edema in normal rats were significantly decreased if these rats were adrenalectomized. E. Keleman[1] and B.J. Northover[2] had reported that the inhibitory effects of aspirin on edema and permeability in adrenalectomized were weaker than those in normal rats. Because corticosterone had an effective anti-inflammatory action in the rats[17] , being like aspirin, stimulation of the hypothalamopituitary-adrenal system may be responsible for the anti-inflammatory effect of Szu-Ni-San.

S.N.-Alc had analgesic effect by both acetic acid method and hot plate method. But aspirin had analgesic effect only by acetic acid method. Shohei Higuchi[3] had reported that the analgesic effect of aspirin was due to the inhibition of PGE biosynthesis. Those implied that the analgesic effect of Szu-Ni-San was not completely like that of

aspirin.

S.N.-Alc had hypothermic effect in normal or CAG-induced hyperthermic rats. Dirose M.[13] had reported that rats induced with CAG produced PGE in the late stage. A.L. Willis[19] and A.S. Milton[18] had reported PGE could induced hyperthermic response in rats. And the hyperthermic response after inducing with CAG was parallel to the production of PGE[20]. So the CAG-induced hyperthermic response related to PGE synthesis. These results implied that the inhibition of PGE may be responsible for the hypothermic effect of Szu-Ni-San.

In the preparations of Chinese medical prescription, decoction or tincture were absorbed and responsed faster than powder. In this study, the ethanol extracts of Szu-Ni-San had stronger anti-inflammatory, analgesic and hypothermic effects than water extracts. It implied that efficient components of Szu-Ni-San might exist in the fraction of alcohol extracts. So tincture might be the best preparation in clinical application. But Chinese ancient prescription used powder instead of tincture, because tincture didn't suit for these patients with "live disease", "cardiac disease" or "hypotension". Then we considered the preparation of Chinese ancient prescription was reasonable.

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Table 1. LD_{50} and 95% confidence limits of Szu-Ni-San

Drugs	Route	Animal	LD_{50}	95% Confidence Limits
S.N.-Alc.	P.O.	mice	> 12 g/kg	(1.78 -- 2.08 g/kg)
	I.P.	mice	1.92 g/kg	
S.N.-H_2O	P.O.	mice	> 12 g/kg	(3.71 – 4.53 g/kg)
	I.P.	mice	4.10 g/kg	
S.N.-Alc.	P.O.	rats	> 12 g/kg	(1.52 – 2.06 g/kg)
	I.P.	rats	1.77 g/kg	
S.N.-H_2O	P.O.	rats	> 12 g/kg	(3.25 – 3.90 g/kg)
	I.P.	rats	3.56 g/kg	

Method : Litchfield and Wilcoxon method.
S.N.-Alc : 95% Alcohol extracts of Szu-Ni-San.
S.N.-H_2O: Distilled water extracts of Szu-Ni-San.
Dose : Crude extracts.

Table 2. Effects of Szu-Ni-San on swelling of Rat Hind Paw Induced by Carrageenin

Drug Dose (g/kg) P.O.		Swelling Ratio			
		1 hr.	2 hr.	3 hr.	4 hr.
Control		19.85 ± 2.16	26.40 ± 3.01	31.54 ± 2.47	35.61 ± 3.86
S.N.-Alc.	0.25	16.96 ± 1.73	21.77 ± 0.71	25.13 ± 0.67	28.46 ± 1.06
		(15.56)	(17.54)	(20.32)	(20.08)
S.N.-Alc.	0.50	13.15 ± 1.07*	19.76 ± 1.41	23.36 ± 1.87*	26.17 ± 2.59*
		(33.75)	(25.15)	(25.94)	(26.51)
S.N.-H_2O	0.25	18.94 ± 2.43	25.24 ± 3.52	30.65 ± 3.02	35.09 ± 4.08
		(3.27)	(4.39)	(2.90)	(1.46)
S.N.-H_2O	0.50	16.33 ± 0.58	23.05 ± 1.22	26.62 ± 1.00	28.66 ± 0.69
		(17.73)	(12.69)	(15.60)	(19.52)
Aspirin	0.15	13.65 ± 1.02*	15.90 ± 1.10**	17.15 ± 1.23***	17.11 ± 1.95**
		(31.23)	(39.77)	(45.62)	(51.59)

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$
(Compare to control)
( ) : % of inhibition

Table 3. Effects of Szu-Ni-San on Swelling of Rat Hind Paw Induced By Formalin

Drug Dose (g/kg) P.O.		Swelling Ratio			
		1 hr.	2 hr.	3 hr.	4 hr.
Control		41.22 ± 1.77	48.00 ± 2.47	55.78 ± 4.44	70.20 ± 2.43
S.N.-Alc.	0.25	36.50 ± 3.44	42.61 ± 4.80	47.56 ± 5.94	52.02 ± 3.76*
		(11.45)	(11.23)	(14.74)	(25.89)
S.N.-Alc.	0.50	22.07 + 1.11**	25.68 + 1.58***	31.38 + 2.82**	40.36 + 2.81***
		(46.45)	(46.50)	(43.74)	(42.50)
S.N.-H_2O	0.25	40.37 ± 2.49	47.19 ± 1.57	54.94 ± 1.08	64.37 ± 2.55
		(2.06)	(1.68)	(1.51)	(8.30)
S.N.-H_2O	0.50	36.28 ± 1.43)	43.29 ± 2.22	46.77 ± 2.88	51.17 ± 3.88*
		(11.98)	(9.81)	(16.15)	(27.10)
Aspirin	0.15	25.12 ± 2.31**	29.50 ± 3.14**	34.32 ± 2.55**	42.56 ± 3.16**
		(39.05)	(38.54)	(38.47)	(39.37)

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$
(Compare to control)
( ) : % of inhibition

Table 4. Effects of Szu-Ni-San on Swelling of Rat Hind Paw Induced by 5-HT

Drug Dose (g/kg) P.O.		Swelling Ratio			
		0.5 hr.	1.5 hr.	1.5 hr.	2.0 hr.
Control		52.92 ± 1.62	57.79 ± 3.34	48.50 ± 3.55	45.41 ± 4.35
S.N.-Alc	0.25	42.48 ± 2.24**	44.66 ± 1.79**	36.16 ± 2.18*	32.54 ± 2.32*
		(19.72)	(22.72)	(25.44)	(28.34)
S.N.-Alc	0.50	34.35 ± 2.28***	34.29 ± 2.34***	28.33 ± 1.71***	25.58 ± 1.85**
		(35.09)	(40.66)	(41.58)	(43.67)
S.N.-H_2O	0.25	52.78 ± 4.55	57.49 ± 8.01	48.23 ± 1.70	40.15 ± 2.26
		(0.26)	(0.52)	(0.56)	(11.58)
S.N.-H_2O	0.50	40.73 ± 3.26	43.14 ± 5.79	36.55 ± 4.01	32.02 ± 4.48
		(23.03)	(25.35)	(24.03)	(29.48)
Aspirin	0.15	39.50 ± 2.34**	42.42 ± 3.12**	36.61 ± 1.95**	33.01 ± 2.26**
		(25.35)	(26.59)	(24.63)	(29.48)

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$
(Compare to control)
( ) : % of inhibition

Table 5. Szu-Ni-San (0.5g/kg) on the Carrageenin-induced Paw Edema in Adrenalectomized Rats

Animal	Drug P.O.	Swelling Ratio					
		1 hr.	2 hr.	3 hr.	4 hr.	5 hr.	6 hr.
Adrenalectomized	Control	23.90±1.06	27.37±1.80	32.85±1.77	37.52±4.10	38.70±4.60	32.61±3.80
	S.N.-Alc	20.23±0.98* (15.37)	23.41±1.37 (14.17)	25.93±1.29* (21.06)	27.93±1.37 (25.56)	29.92±1.14 (22.69)	26.08±1.23 (20.02)
Sham Operated	Control	17.48±0.67	19.38±0.70	22.98±1.06	22.20±0.69	17.37±1.02	14.10±1.68
	S.N.-Alc	12.60±0.85*** (27.92)	14.02±7.53*** (27.65)	15.52±0.45*** (32.46)	15.27±0.93*** (31.22)	12.98±0.74** (25.27)	10.88±1.0** (22.84)

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * P 0.05 ** P 0.01 *** P 0.00i
(Compare to control)
( ) : % of inhibition

Table 6. Effects of Szu-Ni-San on the Increased Vascular Permeability Induce by Histamine-Phosphate

Dose (g/kg) (P.O.)		Evan's blue (X 10^{-6} g)	% inhibition
Control		12.76 ± 0.58	
S.N.-Alc.	0.25	12.73 ± 0.83	0.24
S.N.-Alc.	0.50	9.06 ± 0.88**	28.66
S.N.-H_2O	0.25	12.63 ± 0.16	1.00
S.N.-H_2O	0.50	9.97 ± 0.49*	21.49
Aspirin	0.15	8.79 ± 0.64**	31.11

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$ ** $P < 0.01$
(Compare to control)

Table 7. Effects of Szu-Ni-San on the Increased Vascular Permeability Induced by Acetic Acid

Dose (g/kg) (P.O.)		Evan's Blue (X 10^{-6} g)	% Inhibition
Control		16.28 ± 0.62	
S.N.-Alc.	0.25	13.20 ± 1.23*	18.92
S.N.-Alc.	0.50	10.51 ± 0.51***	35.44
S.N.-H_2O	0.25	15.10 ± 0.82	7.19
S.N.-H_2O	0.50	13.04 ± 1.17*	19.90
Aspirin	0.15	9.82 ± 1.24***	39.68

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$ *** $P < 0.001$
(Compare to control)

Table 8. Analgesic Effects of Szu-Ni-San on Writhing Symptom of the Mice

Drug	Dose (g/kg) P.O.	No. of Writhing (for 10 min.)	% Protection
Control	——	25.50 ± 1.13	——
S.N.-Alc.	0.25	22.50 ± 1.53	11.76
S.N.-Alc.	0.50	16.70 ± 1.14***	34.51
S.N.-H_2O	0.25	24.80 ± 1.48	2.74
S.N.-H_2O	0.50	19.30 ± 0.96**	24.31
Aspirin	0.20	16.33 ± 1.82***	35.96

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: ** $P < 0.01$ *** $P < 0.001$
(Compare to control)

Table 9. Analgesic Effects of Szu-Ni-San in Mice (Hot Plate Method: 55.0 ± 0.2°C)

Drug	Dose (g/kg) P.O.	Onset (Sec.)
Control	———	5.00 ± 0.46
S.N.-Alc.	0.25	6.53 ± 0.60
S.N.-Alc.	0.50	6.97 ± 0.60*
S.N.-H_2O	0.25	5.37 ± 0.59
S.N.-H_2O	0.50	6.04 ± 0.24
Aspirin	0.20	5.49 ± 0.60

Statistical Evaluation: Student's t-test
Data: Mean ± S.E.
Significant: * $P < 0.05$
(Compare to control)

Table 10. Hypothermic Effects of Szu-Ni-San

Drugs	Dose P.O.	Before Administration	Time After Administration 1 hr.	2 hr.	3 hr.	4 hr.
Control		37.65 ± 0.05	37.55 ± 0.07	37.46 ± 0.07	37.60 ± 0.12	37.65 ± 0.14
S.N.-Alc.	0.50	37.75 ± 0.09	37.48 ± 0.07	37.65 ± 0.08	37.68 ± 0.08	37.73 ± 0.09
S.N.-Alc.	1.00	37.60 ± 0.08	37.15 ± 0.15*	37.35 ± 0.12	37.38 ± 0.19	37.60 ± 0.19
S.N.-H_2O	0.50	37.61 ± 0.09	37.51 ± 0.12	37.48 ± 0.16	37.58 ± 0.19	37.68 ± 0.12
S.N.-H_2O	1.00	37.66 ± 0.05	37.45 ± 0.12	37.43 ± 0.09	37.50 ± 0.13	37.58 ± 0.12

Statistical Evaluation: Student's t-test Data: Mean ± S.E.
Significant: * $P < 0.05$
(Compare to control)

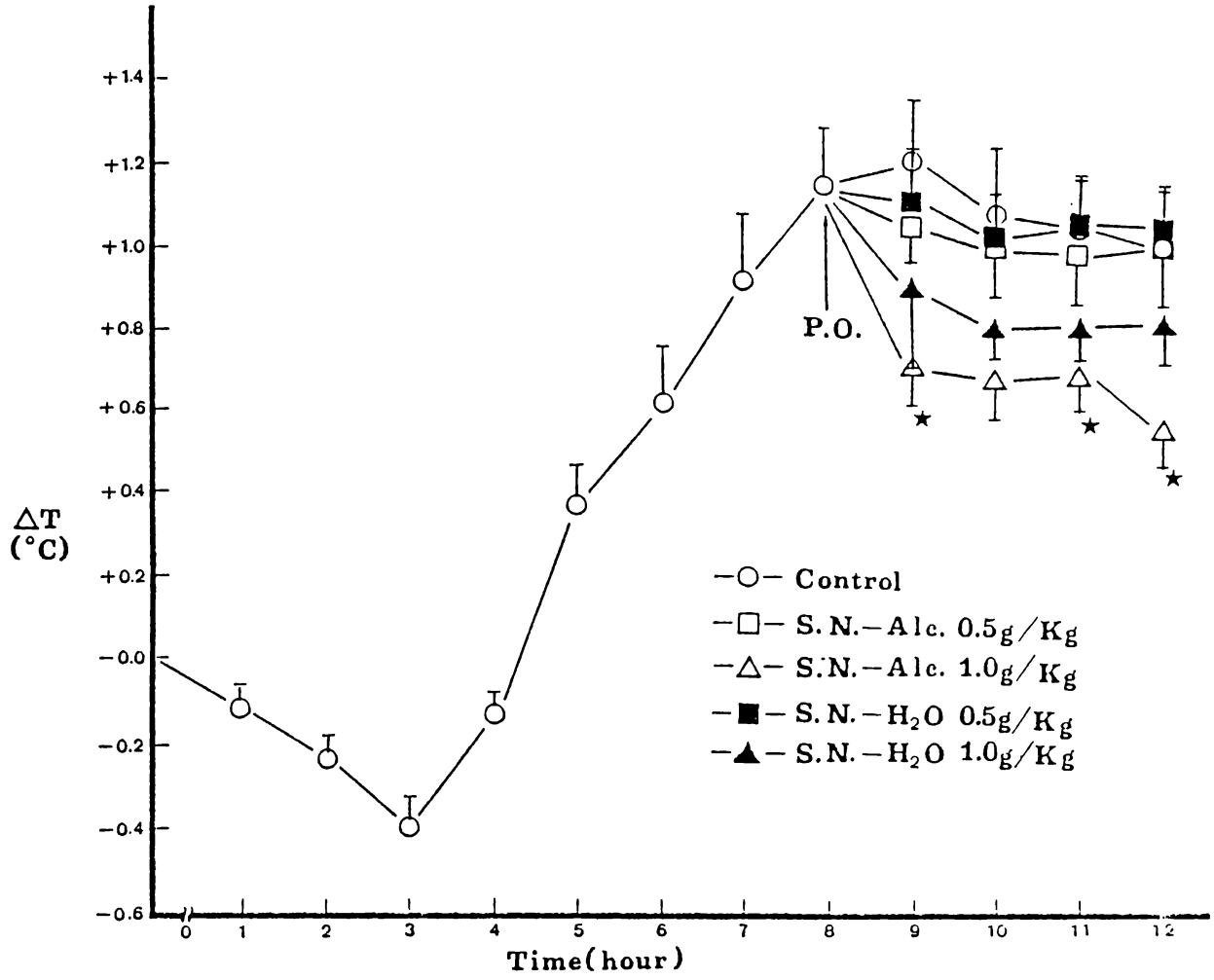

Fig. 1. Hyperthermic Patterns of Carrageenin and Antipyretic Effect of Szu-Ni-San. Vertical Bars Represent Mean ± S.E. (*$P < 0.05$)

四逆散抗炎作用之藥理學研究

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四逆散由等量柴胡、甘草、白芍、枳實組成。中醫臨床主治胃腸炎、乳腺炎、急性闌尾炎、肋間神經痛、脘腹痛等症。但至今未見其藥理學研究報告，故本研究探討其抗炎、鎮痛、解熱之藥理作用及作用機轉。

實驗結果顯示，四逆散酒精抽取物對Carrageenin，formalin，5-HT 誘發大白鼠後肢浮腫有抑制作用。對醋酸及histamine誘發末梢滲透具抑制作用。對熱板法、醋酸法具鎮痛作用。對正常大白鼠及carrageenin 誘發發熱大白鼠具解熱作用。但對切除腎上腺大白鼠的抗浮腫作用有顯著降低的情形。其抗炎作用可能與aspirin 相似，爲抑制5-HT及histamine 作用，解熱作用可能與抑制PGE合成有關。