PREVENTION OF THE EXPERIMENTAL GASTRIC ULCER IN THE RAT BY SOME FOLK MEDICINAL PLANTS IN TAIWAN

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INTRODUCTION

The use of medicinal plants in China is one without interruption for thousands of years. Even today, the Chinese medicine is still popular in Taiwan. The purpose of this paper was to collect the crude drugs which have some reputation as remedies of stomach pain in Taiwan and to find the experimental evidence supporting the effectiveness of these crude drugs. The results of preliminary pharmacological screening is reported in this paper.

METHODS AND MATERIALS

Twelve crude drugs had been collected and their origin had been identified. These drugs include;

Root of Alpinia speciosa K. Schum. (月桃)[8]。

Whole plant of Araceae. Typhonium divaricatum (Linn) DECNE. (犁頭草)[7]。

Stem and leaves of Bischofia trifoliata Hook. (重陽木)[7]。

Root of Canarium album Raeusch. (橄欖根)[7]。

Raw fruit of Carica papaya Linn. (番木瓜)[8]。

Trunk of Citrus medica L. var. Sarcodactylis Swingle. (佛手柑)[7]。

Leaves of Cordyline terminalis (L.) Kunth. (朱蕉)[7]。

Leaves and branches of Crataeva religiosa Forst F. (三脚別)[7]。

Whole plant of Duchenea indica (Andr) Focke. (蛇莓)[7]。

Trunk and branches of Drynaria Fortunei J. Sm; polypodium Fortunei Kuntz. (石岩薑)[8]。

Rhizomes of Glycyrrhiza Uralensis Fisher et De Candolle. (甘草)[8]。

Trunk and branches of Rhus semialata MURR. var. roxburghii DC. (埔鹽)[7]。

Naringen (table 2 and table 4) is a flavonoid glycoside, mp. 168–170°C, isolated from the rhizomes of Drynaria Fortunei. Sm.[17]

The crude extract was administered to the experimental rats intraperitoneally or orally with a stomach tube. The dosage was expressed as the corresponding weight of the crude drug.

Induction of stress ulcer:

The rats weighing about 200 grams were refrained from taking food for 24 hours before the experiment. The rat was fixed on a board and immersed in water up to the level of breast at 25°C for 3,5 and 7 hours. After the stress, the animal was killed and the stomach was carefully incised.

Haemorrhage and erosion of the mucosa of glandular portion of the stomach developed in almost all animals. The inside haemorrhagic areas were photographed and the degree of ulcer was evaluated by the diameter of ulcer and haemorrhage. Score of 5 was given to ulcer area larger than 2 mm in diameter, 2 to the ulcer with diameter between 1 and 2 mm, and 1 to those with diameter less than 1 mm. The degree of ulceration

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was compared by the sum of the scores of each animal and was expressed as "total ulcer count".

Induction of reserpine ulcer:

The rats were injected subcutaneously with 5 mg/kg of reserpine and kept away from food for 24 hours, and then the rats were sacrificed. 5 g/kg of extracts were administered intraperitoneally every 12 hours before the rats were killed. The degree of ulceration was compared by "total ulcer count".

RESULTS

Effect of stress time on the induction of ulcer:

As shown in table 1, the severity of stress ulcer is parallel to the duration of immersion of rats in water. Death occurred if the rats were stressed for more than 24 hours. Three hours of stress already produced an obvious ulcerogenic effect in the present experiment. Whereas, the rats produced no or little ulcer if the animals were fasted for 3 days.

Effect of crude extracts intraperitoneally administered:

All of the extracts were administered intraperitoneally (5 g/kg) to the rats which were then stressed in water for 3 hours. The last five extracts in table 2 including Glycyrrhiza uralensis Fisher et De Candolle, Typhonium divaricatum (Linn) Decne, Rhus semialata MURR var Roxburghii DC, Alpinia speciosa K Schum, and Bischofia trifilliata Hook are found effective against acute stress ulcer (t test, $p<.01$).

Table 1. Effect of time on the rats stress ulcer

Time stressed	No. of animals	Total ulcer count±S. E.
3 hours	6	62.1 ±17.1
5 hours	10	83.8 ±11.4
7 hours	7	89.67±10.5

Table 2. Effects of crude extracts intraperitoneally administered.

Treatment	No. of animals	Dose (g/kg) I. P.	Total ulcer count±S. E.
Control	6	Saline	62.1 ±17.1
Canarium album Raeuseh	5	5g/kg	59.5 ±14.6
Citrus medica L. var. Sarcodactylis	5	5g/kg	53.0 ±12.6
Swinble Duchenea indica (Andr) Focke	5	5g/kg	42.5 ±12.5
Crataeva religiosa Forst. F	5	5g/kg	39.4 ±13.7
Carica papaya Linn	5	5g/kg	33.1 ± 4.2
Cordyline terminalis (L.) Kunth.	5	5g/kg	28.3 ±11.3
Drynaria Fortunei J. Sm.	5	5g/kg	27.25±12.2
Naringenin	5	5mg/kg	35.0 ±10.6
Glycyrrhiza uralens is Fisher et De Caadolle	5	5g/kg	#21.5 ± 9.1
Typhonium divaricatum (Linn) DECNE	5	5g/kg	#20.6 ± 7.0
Rhus semialata MURR var, roxburghii DC.	5	5g/kg	#12.1 ± 6.3
Alpinia speciosa K. Schum	5	5g/kg	# 7.2 ± 5.4
Bischofia trifoliata Hook	5	5g/kg	# 6.0 ± 4.5

# $P < 0.01$, (t test).

As shown in Fig 1, 3 hours of stress is enough to produce the obvious ulcerogenic effect in the control rat stomach, Fig. 2 demonstrated the protective effect of Alpinia extract against acute stress ulcer.

The raw fruit juice of papaya is said to be effective for the treatment of peptic ulcer in Taiwan. The anti-ulcer activity of Carica papaya Linn is not strong enough in this experiment (tables 2, 3 and 4).

Table 3. Effect of crude extracts orally administered.

Treatment	No. of animals	Dose (g/kg oral)	Total ulcer count±S. E.
Control	10	15g/kg	83.8 ±11.4
Citrus medica L. var Sarcodactylis Swingle	5	15g/kg	72.25±13.7
Cordyline terminalis L. Kunth.	5	15g/kg	64.67±12.6
Carica papaya Linn.	5	15g/kg	64.60± 6.5
Canarium album Raeusch.	5	15g/kg	63.67±11.3
Crataeva religiosa Forst, F.	5	15g/kg	57.7 ±20.7
Duchenea indica (Andr), Focke.	5	15g/kg	49.5 ±11.3
Drynaria Fortunei J. Sm.	5	15g/kg	37.8 ± 6.4
Rhus semialata MURR var. roxburghii DC.	5	15g/kg	#26.25± 4.2
Glycyrrhiza uralensis Fisher et De Candolle.	6	15g/kg	#25.0 ± 7.2
Alpinia speciosa K. Schum.	6	15g/kg	#19.4 ± 6.8
Typhonium divaricatum (Linn), DECNE.	6	15g/kg	#18.6 ± 5.6
Bischofia trifoliata Hook.	6	15g/kg	#12.0 ± 4.2

# $p < 0.01$, (t test).

Table 4. Effects of crude extracts (5g/kg I. P.) on reserpine (5 mg/kg S. C.) ulcer.

Treatment	No. of animals	Dose (g/kg I. P.)	Total ulcer count±S. E.
Control	5	Saline	39.0 ±11.5
Cordyline terminalis (L) Kunth	5	5g/kg	37.5 ±13.5
Bischofia trifoliata Hook	5	5g/kg	30.5 ±10.5
Duchenea indica (Andr) Focke	5	5g/kg	28.0 ±16.0
Crataeva religiosa Forst. F.	5	5g/kg	27.6 ±15.3
Carica papaya Linn	5	5g/kg	26.3 ±13.0
Naringenin	5	5g/kg	24.5 ± 8.5
Citrus medica L. var Sarcodactylis Swingle	5	5g/kg	17.67± 9.4
Drynaria Fortunei J. Sm.	5	5g/kg	17.0 ± 8.5
Rhus semialata MURR var. roxburghii DC.	5	5g/kg	14.1 ± 7.0
Canarium album Raeusch	5	5k/kg	13.2 ± 7.3
Glycyrrhiza Uralensis Fisher et De Candolle	5	5g/kg	#10.4 ± 4.5
Alpinia speciosa K. Schum	5	5g/kg	# 5.6 ± 1.8
Typhonium divaricatum (Linn) DECNE	5	5g/kg	# 4.8 ± 2.0
Typhonium divaricatum (Linn) DECNE	5	5g/kg	# 4.8 ± 2.0

# $p < 0.02$, (t test).

Effect of crude extracts orally administered:

The effect of the extracts administered orally through a stomach tube (15 g/kg) was then studied. The extracts were given orally to the rats every 2.5 hours before the rats were killed. Table 3 show that Rhus semialata MURR var roxburghii DC, Glycyrrhiza uralensis Fisher et De Condolle, Alpinia speciosa K Schum, Typhonium divaricatum (Linn) Decne, Bischofia trifoliata Hook are found effective orally against stress ulcer (t test, $p<.01$).

Effect of crude extracts on reserpine ulcer:

The rats were injected subcutaneously with 5 mg/kg of reserpine and kept away from food for 24 hours. The extracts were administered intraperitoneally every 12 hours before the rats were killed.

As shown in table 4, the ulcer count of reserpine is much less than stress ulcer, though severe symptoms appeared in all animals. Glycyrrhiza uralensis Fisher et De Candolle, Alpinia speciosa K Schum, and Typhonium divaricatum (Linn) DECNE are also found effective to reserpine ulcer ($p<.02$).

DISCUSSION

Takagi and Watanabe (1963) demonstrated the induction of experimental stress ulcer when rats were immersed in water of 25°C for 20 hours.[16] In our experiment, the rats were stressed for 3 hours under the same condition, but the rats were kept away from food for 24 hours before the experiment, is enough to produce the obvious ulcerogenic effect, whereas the rats produced no or little ulcer if the animals were fasted for 3 days.

The best-known ingredient of licorice is glycyrrhizin, which has anti-inflammatory action and salt retaining action like mineralocorticoids (Cornforth and Long, 1957)[2]. Although the anti-inflammatory action may contribute to the anti-ulcer activity of licorice, it does not represent the whole activity of the plant.[16] (Takagi and Watanabe 1963). Our experiment as shown in tables 2 and 3, confirmed that the crude extracts of Glycyrrhiza uralensis Fisher et De Condolle is effective against stress ulcer of the rats.

Other extracts such as Typhonium divaricatum (Linn) DECNE, Rhus semialata MURR var roxburghii DC, Alpinia speciosa K. Schum, and Bischofia trifoliata Hook, are found more effective against stress ulcer of the rats than Glycyrrhiza uralensis Fisher et De Candolle. Their anti-ulcer activity need further investigation.

Naringen is a flavonoid glycoside mp. 168-170°C, isolated from the rhizomes of Drynaria Fortunei. Sm.[17] As shown in table 2 and table 3, the anti-ulcer activity of naringen is inferior to its mother plant.

The weak anti-ulcer activity of Carica papaya Linn as shown in tables 2, 3 and 4 in this paper indicates the opposite evidence to the effectiveness of raw papaya juice for the treatment of peptic ulcer.

5 mg/kg of reserpine is close to the lethal dose of rat. But the ulcer count of reserpine ulcer is much less than stress ulcer in the control group of rats. In the case of licorice extract, Takagi and Watanabe (1963) emphasizes the utility of the licorice extract for treating gastric ulcer without cholinergic ill effects because it has little anti-acetylcholine action and it does not inhibits the spontaneous motility of rat stomach in situ. The mechanism of anti-ulcer activity of extracts which prove effective to stress ulcer or reserpine ulcer may be different from each other. The further studies of the anti-ulcer activity of Typhonium divaricatum (Linn) DECNE, Rhus semialata MURR var. roxburghii DC, Alpinia speciosa K. Schum, and Bischofia trifoliata Hook, will be continued in this laboratory.

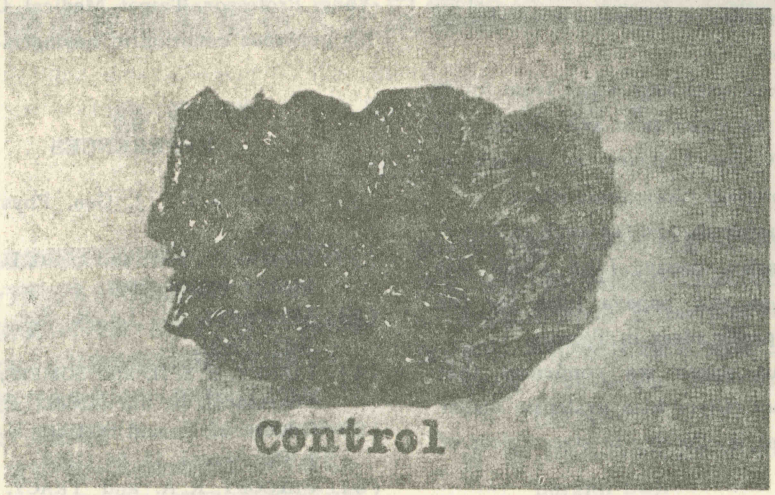

Fig. 1. Haemorrhage and erosion of the mucosa of the stomach developed in the control rat which was immersed in water for 3 hours.

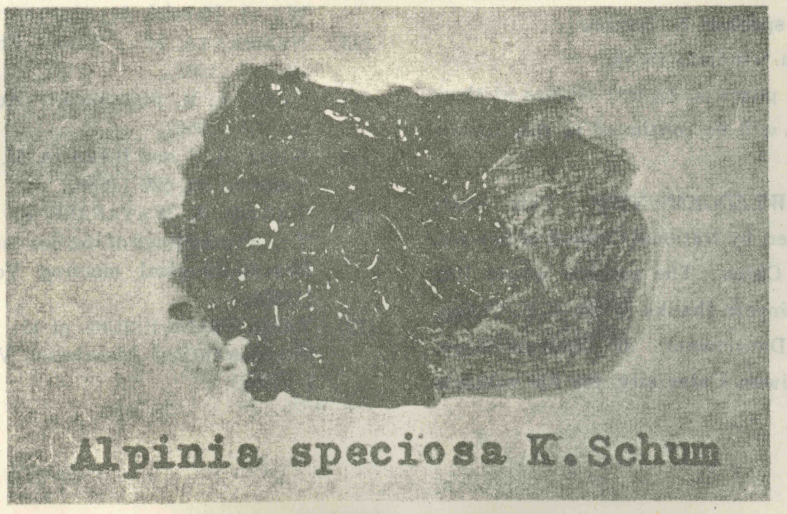

Fig. 2. Alpinia extracts (5 g/kg. i.p) is effective against the experimental stress ulcer. When the rat was immersed in water for 3 hours.

SUMMARY

1. Twelve crude drugs had been collected and the preliminary pharmacological screening had been done.

2. The rats were kept away from for 24 hours before the experiment and stressed in water of 25°C for 3 hours is enough to produce the obvious ulcerogenic effect.

3. This paper showed the weak anti-ulcer activity of Carica. papaya Linn which was widely used as raw papaya juice for the treatment of peptic ulcer in Taiwan.

4. In this paper we confirmed that Licorice extract (Glycrrhiza uralensis Fisher et De Candolle) is effective to stress ulcer of rats.

5. Naringen is a flavonoid glycoside mp. 168-170°C, isolated from the rhizomes of Drynaria Fortunei. Sm. Its anti-ulcer activity is inferior to its mother plant.

6. The extracts through the screening methods of stress ulcer and reserpine ulcer of rats, another four extracts had been shown their strong anti-ulcer activity in this paper.

e.g. Typhonium divaricatum (Linn) DECNE.
Rhus semialata MURR var. roxburghii Dc.
Alpinia speciosa K. Schum.
Bischofia trifoliata Hook.

The further pharmacological studies of these crude drugs will be continued in this laboratory.

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臺灣產民間藥對抗大花鼠實驗性胃潰瘍之研究

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(1970年5月8日受理)

1. 本篇共收集臺灣民間用於治療胃潰瘍之生藥十二種，希能給予藥理學上對抗潰瘍藥效之證明。

2. 大花鼠停食24小時後，固定於木板上，浸水齊胸於 25°C 水中 3 小時即能產生明顯的應力潰瘍。

3. 民間最流行之生木瓜汁，對胃潰瘍之療效，以本篇結果顯示，其抗潰瘍 (Stress ulcer and reserpine ulcer) 效果不佳。其他如敏感根、佛手柑片、朱蕉葉、三脚別、蛇莓等對於大花鼠之應力潰瘍之療效均差。

4. 本篇確證1963年高木與渡邊氏之報告即甘草抽出液對大花鼠有抗潰瘍之效。

5. Naringen 爲石岩薑 Drynaria Fortunei Sm 單離出之一種 flavonoid 結晶 mp. 168-170°C 其抗潰瘍之效果不如石岩薑本身之粗抽出液。

6. 本篇以 stress 及 reserpine ulcer 之方法，除甘草外，另有四種抗潰瘍效力較强之生藥爲：

　　犁頭草 (Typhonium divaricatum. Linn DECNE).

　　埔　鹽 (Rhus semialata MURR. var. roxburghii DC).

　　月　桃 (Alpinia speciosa K. Schum).

　　重陽木 (Bischofia trifoliata Hook).

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私立臺北醫學院藥理學科