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Anti-allergy Activity of Cinnamomi Cortex

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Abstract – The anti-allergy activity of *Cinnamomum cassia* cortex extract and its fractions were investigated in mice. The extract exhibited potent anaphylactic shock and Arthus reaction. Among the fractions obtained in the successive fractionation with n-hexane, butanol and acetone, the butanol insoluble portion was shown to have the activities.

Keywords – *Cinnamomum cassia,* Lauraceae, anti-allergy activity

Introduction

Cinnamomum cassia Blume (Lauraceae) is a medicinal plant which has been used as a stomachic, carminative, sedative, antipyretic, antispasmodic or analgesic in Oriental Medicine (Huh,1613; Namba, 1993). The aqueous extract of *C. cassia* was reported to inhibit increased excretion of protein in urine of nephritic rats (Yagi, *et al* 1980). Anti-ulcer actions have been ascribed to this extract (Akira, *et al* 1986). The aqueous extract was also reported on the inhibitory actions of complement dependent reactions including reversed cutaneous anaphylaxis, Forssman cutaneous vasculitis and nephrotoxic serum nephritis classified as type II and the Arthus reaction classified as type III. However, the extract was not affected in passive cutaneous anaphylaxis (type I) and contact dermatitis (type IV) (Nagai, *et al.*, 1982). The pharmacological studies on Cinnamomi Cortex were reported on its components of cinnamaldehyde which had the depressive and sedative, hypotensive, and anti-ulcer actions.

To pursue active components, we have screened some Oriental plant drugs for anti-allergic activity with type I and type III models classified by Coombs and Gell (Cooms *et al.*, 1968). This paper deals with the anti-allergic effect of Cinammomi Cortex extract and the fractions evaluated by systemic anaphylaxis (Type I) model and Arthus reaction (Type III) model.

Experimental

Plant material – The dry cortex of *C. cassia* was purchased from the Oriental herb market in Seoul.

Extraction and separation – The powdered cortex (1.08 kg) was refluxed three times 4 hr with 80% MeOH in a water bath. The MeOH extract was evaporated to dryness and the dry residue (128.5 g) was partitioned in succession between H_2O and n-hexane (hexane fraction A, 2.0g, 7% per MeOH extract) and then n-butanol. During the fractionation procedure with n-butanol, the insoluble material was obtained by filtration (fraction C, 9.23 g, 31%), and the aqueous layer was concentrated and dried to give water fraction B (5.06 g, 17%). The concentrated butanol extract was dissolved with acetone and then filtered. The filtrate was concentrated to give acetone soluble fraction D (10.13 g, 34%) and the acetone insoluble part was dried to give fraction E (3.28 g, 11%).

Animals – Male ICR mice weighing 20 to 25 g were used. The mice were bred in the animal house of Natural Products Research Institute and adapted to animal room over 1 week. Mice were housed in each cage maintained at a temperature of 23±2°C, 12 hr-lighting period. They were fed commercial pellet food (Samyang Yuji Co. Ltd.) and tap water *ad libitum.*

Test sample preparation – The samples were prepared as a solution or suspension in 1% CMC saline. The doses were administered orally in a volume of 10 ml/kg of body weight of mice.

Systemic anaphylaxis – The method was employed according to Amir *et al.* (1991). Mice were given an i.p. injection of 8 mg/kg compound 48/80, a mast cell degranulator. Test substances were i.p. administered 1hr before injection of compound 48/80. Mortality rate was determined 60 min after induction of

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shock.

Arthus reaction – This test was performed according to the method by Takahashi *et al.* (1986). Mice were sensitized by the i.p. injection of sheep red blood cell (SRBC). Two weeks after sensitization, the mice were challenged by s.c. injection on the right footpad with 0.05 ml of SRBC in phosphate buffer saline (PBS, pH 7.4). The extent of the swelling of the footpad was measured using plethysmometer (Ugo Basile, Italy) before, 90 min and 180 min after challenge.

Statistical analysis – The data were analyzed statistically by Students *t*-test. P values of 0.05 or less were considered significant.

Results and Discussion

The anti-allergic effect of a 80% MeOH extract and various fractions from Cinnamomi Cortex originating from *C. cassia* were investigated by using experimental models of two allergic responses of Type I and III models.

Acute anaphylaxis, or anaphylactic shock is believed to be caused by chemical mediators such as histamine and leukotrienes being released from mast cell.

The extract (100 mg/kg, i.p.) significantly inhibited systemic anaphylaxis induced by compound 48/80 by 87%, whereas cromolyn inhibited by 50% (Table 1).

Table 1. Effects of Cinnamomi Cortex extracts on systemic anaphylaxis induced by compound 48/80 in mice

Treatment	Dose (mg/kg, i.p.)	No. of Animals	Mortality (%)
Saline	--	8	88
C. Cortex ext.	100	8	13
Cromolyn	100	8	50

The Arthus reaction may be defined as a local area of tissue necrosis resulting from immune complex usually elicited in the skin. Because of the excess of antibodies the antigen diffuses into the vascular wall, large immune complexes are formed, which precipitate locally and trigger the inflammatory reaction. In contrast to IgE-mediated type I reactions, which appear immediately, the Arthus lesion develops over a few hours and reaches a peak 4 to 10 hours after injection when it can be seen as an area of visible edema with severe hemorrhage followed occasionally by ulceration. In Arthus reaction in mice which is a model of type III allergic reaction, the extract suppressed the symptoms of Arthus reaction in an early stage. The extract at 1,000 mg/kg p.o. inhibited significantly Arthus reaction by 28%, whereas cromolyn at 100 mg/kg i.p. inhibited by about 30% (Table 2).

Among the fractions, fraction C, the butanol insoluble fraction elicited most potent inhibition of anaphylactic shock by 100% at a dose of 18.1 mg/kg p.o. and of Arthus reaction by 22.1% at a dose of 244.7 mg/kg p.o. as shown in Table 3 and 4, respectively. It is noted that the doses of the fractions administered in mice were proportional to the yields

Table 3. Effect of various fractions obtained from methanol extract of Cinnamomi Cortex on systemic anaphylaxis induced by compound 48/80 in mice

Treatment	Dose (mg/kg, i.p.)	No. of Animals	Mortality (%)
Saline	--	8	100
A	7.8	8	75
B	9.7	8	50
C	18.1	8	0
D	12.4	8	75
E	38.9	8	50
Cromolyn	100	8	25

Table 2. Effects of Cinnamomi Cortex extract on Arthus reaction induced by sheep red blood cell in mice

Treatment	Dose (mg/kg, p.o.)	No. of Animals	Increase percent in volume (M.±S.E.)	
			90 min	180 min
Saline	--	7	145.1± 8.9	152.5± 6.5
C. Cortex ext.	500	6	123.0±11.7 (15.2)	138.2± 4.3 (9.4)
	1000	6	104.3± 5.2** (28.1)	115.6±10.2** (24.2)
Cromolyn	100(i.p.)	6	100.3± 6.6** (30.9)	110.0±12.6** (27.9)

Significantly different from the saline group (*; $p<0.05$, **; $p<0.01$)
The figures in parentheses indicate inhibition ratio (%)

Table 4. Effect of various fraction obtained from methanol extracts of Cinnamomi Cortex on Arthus reaction induced by SRBC in mice

Treatment	Dose (mg/kg, p.o.)	No. of Animals	Increase percent in volume (M.±S.E.)	
			90 min	180 min
Saline	--	6	120.4± 8.1	164.8±12.9
A	68.5	5	97.0±11.4 (19.5)	135.0±11.3 (18.1)
B	171.2	5	103.7± 7.8 (13.9)	133.8±16.3 (18.8)
C	244.7	5	93.9± 7.3* (22.1)	130.8±17.8 (20.6)
D	342.5	5	108.8±13.7 (9.6)	154.4±22.9 (6.3)
E	108.6	5	120.5± 5.7 (-0.0)	173.5± 7.2 (-5.3)

Significantly different from the saline group (*; $p<0.05$, **; $p<0.01$)
The figures in parentheses indicate inhibition ratio (%)

obtained from the extract. This make it possible that the active component(s) contained in the extract can be pursued.

In conclusion, the butanol insoluble fraction of the extract has shown to be potent inhibition of Type I and Type III allergic reaction in *in vivo* experiments. Thus, it is described that the anti-allergic components might be contained in the butanol insoluble fraction and the characterization of pure active compounds responsible for the anti-allergic action of the fraction and the detailed mechanism of the anti-allergic action of the fraction remained to be further investigated.

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