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Note

Anti-inflammatory Activity of the Major Constituents of *Lonicera japonica*

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Previously, we reported that the *n*-butanol fraction of *Lonicera japonica* showed anti-inflammatrory activity in mice and rats. Several constituents such as loniceroside A and B, flavonoids and iridoids were isolated from this fraction. In this investigation, the anti-inflammatory activity of the major constituents of *L. japonica* was studied. Loniceroside A, lonicerin and loganin showed anti-inflammatory activity comparable to aspirin.

Key works : *Lonicera japonica*, *n*-butanol fraction, Anti-inflammatory activity, Loniceroside A, Lonicerin, Loganin

INTRODUCTION

The flowers or whole plants of *Lonicera japonica* have been used as antidote, diuretics, tonics, antipyresis and anti-inflammatory agents (Shanghai, 1985). However, the reports concerning anti-inflammatory activity *L. japonica* have been few. In a recent paper, we reported the anti-inflammatory and the analgesic activities of the water extract of *L. japonica* and its *n*-butanol (BuOH) fraction obtained by the modified extraction method. The BuOH fraction showed higher activity than the water extract prepared by the method described in the ancient literature (Lee et al., 1994). Therefore, the anti-inflammatory activity of the several major constituents of *L. japonica* was studied in this investigation.

MATERIALS AND METHODS

Croton-oil, arachidonic acid (AA), heavy mineral oil, prednisolone and aspirin were purchased from Sigma Chem. Co. (USA). Desiccated *Mycobacterium butyricum* was obtained from Difco Lab. The other reagents used were of the highest purity available. Loniceroside A and lonicerin were isolated from the BuOH fraction of *L. japonica* (Son *et al.*, 1994a; Son *et al.*, 1994b). Loganin was also isolated and the chemical structure was confirmed by comparison of the spectral data with the reported data (Kawai *et al.*, 1988). Hederagenin was obtained by acid hydrolysis of Loniceroside A and B according to the procedure of Son *et al.* (1994a). The chemical structures of the constituents are shown in Fig. 1. Anti-inflammatory activity : Male ICR mice and Sprague-Dawley (SD) rats obtaind from the Animal Center (Seoul National University) were maintained under the conditions of 22±1°C, 12 h/12 h (L/D) cycle feeding with pellet chaw and water *ad libitum*. Animals were used after acclimation of at least 7 days. All compounds were orally administered to experimental animals. Ear edema assay was carried out using mice (19-21 g) according to the slightly modified method (Kim *et al.*, 1993) of the original procedure of Tonnelli *et al.* (1963). Ear edema were measured using dial thickness gauge 1 hr after 2.5% AA treatment or 5 hr after 2% croton-oil treatment to ears of mice. Adjuvant-induced arthritis (AIA) was carried out according to the procedure of Kubo *et al.* (1984) using *Mycobacterium butyricum* (0.6 mg/rat) suspended in mineral oil. Loniceroside A and prednisolone were administered orally to rats (190-210 g) once daily for 20 consecutive days. Data were represented in mean±S.E. Statistical significance was evaluated using Student t-test.

RESULTS AND DISCUSSION

In order to elucidate anti-inflammatory activity of

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Table I. Anti-inflammatory activity of the components of *L. japonica*

Group	Dose (mg/kg)	Thickness increased [a] (mm)	Thickness increased [b] (mm)
Control	-	0.26±0.02 (-)	0.24±0.01 (-)
Prednisolone	10	0.13±0.02*** (52)	0.15±0.02*** (36)
Aspirin	100	0.23±0.02** (13)	0.18±0.02** (25)
Hederagenin	100	0.15±0.03*** (42)	0.18±0.01*** (23)
Loniceroside A	100	0.17±0.02*** (34)	0.18±0.02** (23)
Lonicerin	100	0.16±0.02*** (39)	NT
Loganin	100	0.21±0.02** (20)	0.19±0.02* (19)

[a]Croton-oil induced ear edema, [b]AA induced ear edema, n=8, Data in parenthesis represented % inhibition of ear edema., NT : Not tested * : P < 0.05, ** : P < 0.01, *** : P < 0.001, Significantly different from control.

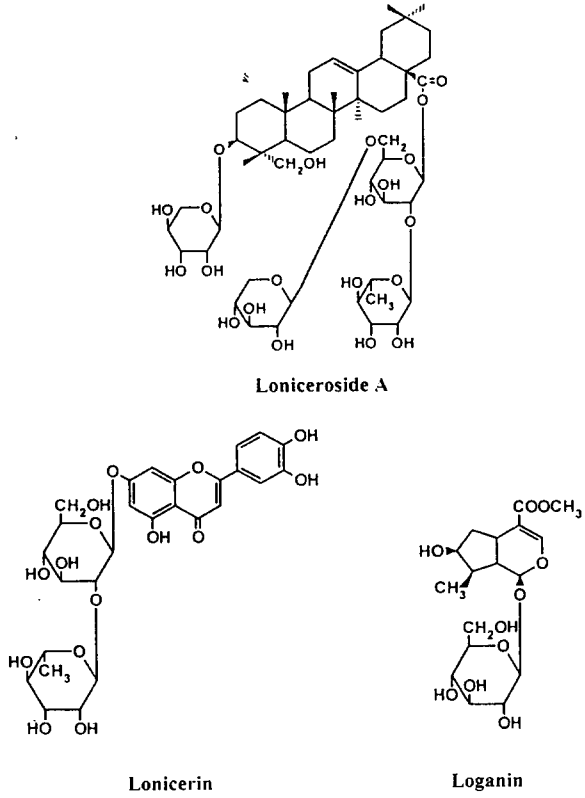

Fig. 1. Chemical structures of the major constituents

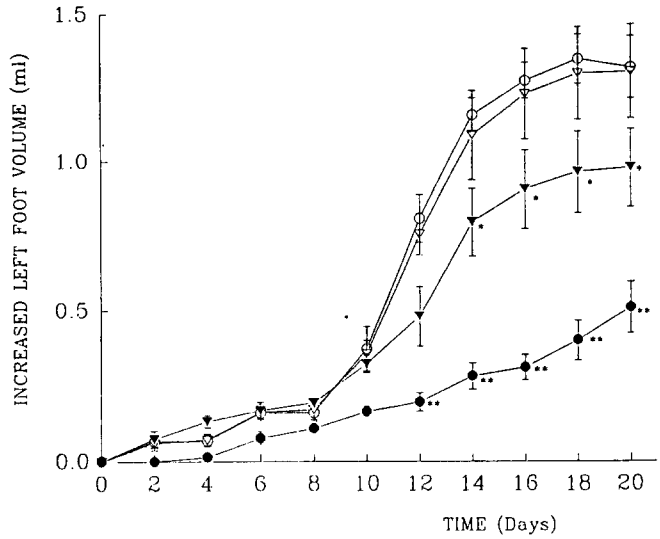

Fig. 2. Anti-arthritic activity of loniceroside A Control (○), Prednisolone : 20 mg/kg/day (●), Loniceroside A : 20 mg/kg/day (△), 100 mg/kg/day (▲), n=6, *P < 0.05, **P < 0.01, Significantly different from control.

the major constituents of *L. japonica*, the mouse ear edema test was used for an acute inflammatory model and the AIA test was used for a chronic inflammatory model. We isolated several compounds from *L. japonica* such as loniceroside A and B as the new compounds, several flavonoids including ochnaflavone and lonicerin, and iridoids (Son *et al.*, 1992; 1994a; 1994b). Among these compounds, loniceroside A, lonicerin and loganin were evaluated in this experiment. As represented in Table I, loniceroside A, lonicerin and loganin showed anti-inflammatory activity against mouse ear edema. Although far less potent than prednisolone, a steroidal anti-inflammatory drug, anti-inflammatory activities of these compounds were comparable to aspirin at the dose of 100 mg/kg. Hederagenin, an aglycone of loniceroside A, also showed anti-inflammatory activity in the same model. As shown in Fig. 2, loniceroside A (100 mg/kg/day) reduced adjuvant-induced arthritis in rats. Prednisolone used as a reference compound showed potent activity at a dose of 20 mg/kg/day. These findings demonstrate that loniceroside A exhibits anti-inflammatory activity against acute and chronic inflammation. And these results were well correlated with the previous findings of Bhargava *et al.* (1970) demonstrating that hederagenin possesses anti-inflammatory and anti-arthritic activities in rats. From our experimental results, it may be concluded that loniceroside A, lonicerin and loganin contribute to the anti-inflammatory activity of *L. japonica*.

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