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Anti-allergic Activity of Oriental Medicinal Herbs

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ABSTRACT : The effects of extracts from various Oriental medicinal herbs on mast-cell-mediated allergic reactions were investigated in this study. Out of these extracts, the medicinal herb *Atractylodis rhizoma alba* exhibited the most potent activity in the cells, with IC_{50} values of 20.5 ㎍/㎖ by DNP-BSA and 33.04 ㎍/㎖ by compound 48/80. Similar to the in vitro activity, *Atractylodis rhizoma alba* inhibited compound-48/80-induced systemic anaphylaxis by 31.3% at 300 ㎎/㎏ in mice. It also suppressed the secretion of TNF-α, a major pro-inflammatory cytokine in the cells. These results may suggest that *Atractylodis rhizoma alba* shows anti-allergic activity in compound 48/80-induced anaphylactic mice through the inhibition of mast cells.

Key word **:** *Atractylodis rhizoma alba*, mast cells, anti-allergic activity

INTRODUCTION

Many Oriental herbs, including *Atractylodis rhizoma alba*, are used as traditional folk remedies for various diseases in Asian countries. Specially, various medicinal herbs have been reported to have anti-allergic activity in vitro and in vivo (Nagai *et al.*, 2004; Makino *et al.*, 2003; Kim *et al.*, 2003; Lee *et al.*, 2004a, b). However, active constituents and mechanisms of action of most herbs are largely unknown, and few have been investigated for their pharmacologic activity or in-vivo animal models. Therefore, a systematic examination of these herbal remedies must be conducted.

Mast cells and blood basophils are responsible for a variety of allergic disorders, such as allergic rhinitis, dermatitis, asthma, and food allergies, as well as catastrophic anaphylactic reactions to insect stings and some drugs. These cells respond to IgE-directed antigens via the high-affinity receptor for IgE, FcεRI, by releasing granules that contain preformed inflammatory mediators and by generating inflammatory lipids and cytokines including TNF-α (Kay 2001a, b). In the allergic condition, mast cells are activated by the multivalent binding of an antigen to immunoglobulin E (IgE) that is bound to its multimeric receptor, FcεRI. The ensuing aggregation of these receptors results in the rapid phosphorylation by Lyn kinase of the tyrosine residues in the immunoreceptor-tyrosine-based activation motifs (ITAMs) of the β and γ subunits of FcεRI, which in turn results in the recruitment and activation of the protein tyrosine kinase Syk. Syk is responsible for the activation of a large number of downstream-signaling molecules and, in this manner, regulates degranulation and the generation of inflammatory mediators (Rivera 2002). In this study, we used RBL-2H3 mast cells, one of common mast cells, to screen the anti-allergic activity of various medicinal herbs.

Atractylodis rhizoma alba, known as Baek-Chul in Korea, is a dried root or rhizome of *Atractyldes japonica* Koidzumi or *Atractyldes ovata* Koidzumi (Compositae). The major constituent of *Atractylodis rhizoma alba* is atractylon. The extract of the dried root is known to be used as crude drugs mainly for the treatment of stomach disorders and for diuretic properties in Korean, Japanese and Chinese traditional medicines (Yamamoto and Sabashi, 1992; Hikino *et al.*, 1964). However, the effects of *Atractylodis rhizoma alba* on the degranulation of mast cells and on in-vivo anti-allergic activity have not yet been tested.

In this study, we aimed to screen which extracts from various Oriental medicinal herbs have in-vitro anti-allergic activity and then measured whether extracts having the in-vitro activity had in-vivo anti-allergic activity using compound 48/80-induced anaphylactic animal mice. *Atractylodis rhizoma alba* exhibited potent in-vivo anti-allergic activity through the inhibition of mast cells. The results suggested that further studies with *Atractylodis rhizoma alba* is necessary for potential utility in the treatment of allergic diseases.

MATERIALS AND METHODS

Reagents

DNP-specific monoclonal IgE and DNP-BSA, Arabic gum, tween 80 and compound 48/80 were purchased from Sigma Chemical Co. (St Louis, MO). The minimal essential medium

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(MEM) and other cell-culture reagents were obtained from GIBCO/Life Technologies, Inc. (Rockville, MD). The antibodies were purchased from the following sources: antibodies against TNF-α from Santa Cruz Biotechnology Inc. (Santa Cruz, CA).

Animals

Male ICR mice (aged 4 weeks) were purchased from the Dae Han Experimental Animal Center (Daejon, Korea), and ten mice were placed in each cage in a laminar airflow cabinet where a temperature of 22 ± 1 ℃ and a relative humidity of 55 ± 10% were maintained throughout the study. The animal study was done by the institutional guideline at Duksung Women's University.

Preparation of *Atractylodis rhizoma alba* and other crude extracts

The *Atractylodis rhizoma alba* and other herbal extracts were imported from China, and prepared by the Korea Research Institutes of Bioscience and Biotechnology as follows. Briefly, the dried herbs (100 g) were extracted with 1000 ㎖ of ethanol at 50℃ by use of an ultrasonic cleaner (Branson Ultrasonics Corporation) and the extracted materials were concentrated with a speed bag (Biotron corporation) at 40℃ for 24 hr. The concentrated extract was stored −4℃. The yield of extraction was about 15% (w/w). The ethanol extract was purchased from the Korea Research Institutes of Bioscience and Biotechnology for this study. The extracts were dissolved in DMSO for in vitro assay and suspended in 5% arabic gum for in vivo animal studies.

Cell culture and measurement of degranulation

RBL-2H3 cells were grown as monolayers in MEM with Earle's salts, supplemented with glutamine, antibiotics, and 10% fetal-bovine serum (FBS). In each experiment, the cells were harvested through trypsinization, were transferred to 24-well (2×10^5 cells/0.4 ㎖/well) cluster plates (Ali *et al.*, 1990), and were incubated overnight in a complete growth medium with 25-ng/㎖ DNP-specific IgE for stimulation by antigen or 30 μM quercetin for stimulation by compound 48/80 in complete growth medium. Next day, the cultures were washed and the required buffered solution was added (0.2 ㎖/well). Experiments on intact cells were performed in a PIPES-buffered medium (25-mM PIPES, pH 7.2, 159-mM NaCl, 5-mM KCl, 0.4-mM $MgCl_2$, 1-mM $CaCl_2$, 5.6-mM glucose, and 0.1% fatty-acid-free fraction V from bovine serum). Unless stated otherwise, the cultures were incubated for 30 min with or without crude extracts before adding stimulants, 25-ng/㎖ antigen (DNP-BSA), or 10-㎍/㎖ compound 48/80 for 10 min. The secretion of granules was determined through the measurement of the release of the granule marker β-hexosaminase with the use of a colorimetric assay, through which the release of p-nitrophenol from p-nitrophenyl-N-acetyl-β-D-glucosaminide was measured (Ozawa *et al.*, 1993). The values were expressed as percentages of intracellular β-hexosaminidase that were released into the medium. The IC_{50} values, the concentration necessary to obtain 50% inhibition of the response, were calculated through nonlinear regression analysis using the GraphPad software (San Diego, CA, USA).

Compound-48/80-induced Systemic Anaphylaxis

Systemic anaphylaxis was induced by the mast-cell degranulator compound 48/80 (Alfonso *et al.*, 2000; Hong *et al.*, 2003). Each mouse was given an intraperitoneal injection of 8 ㎎/㎏ of compound 48/80 in saline. *Atractylodis rhizoma alba* extracts were suspended in 5% arabic gum and were administered orally in doses of 30-300 ㎎/㎏ 1 hour before the injection of compound 48/80 to induce anaphylactic shock. The survival rate was monitored for 1 hr after the injection of compound 48/80.

Analysis of TNF-α secretion

The cells were transferred to 24-well (2×10^5 cells/0.4 ㎖/well) cluster plates (Ali *et al.*, 1990), and were incubated overnight with 25-ng/㎖ DNP-specific IgE. The cells were stimulated by 25 ng/㎖ Antigen (DNP-BSA) for 24 hours. The media containing TNF-α secreted from the cells were concentrated using Ultrafiltration system (Amicon, MWCO 10,000 Da), and then the concentrates were denatured by boiling at 95 for 5 min in a 2x Laemmli buffer (Laemmli 1970). The proteins were separated with the use of SDS-PAGE and were transferred to nitrocellulose membranes (Schleicher and Schuell, BA85). After blocking in TTBS buffer (10 mM Tris-HCl, pH 7.5, 150 mM NaCl, 0.05% Tween 20) containing 5% skimmed milk powder, the membrane was incubated with individual monoclonal or polyclonal antibodies. The immunoreactive proteins were detected with the use of horse-radish peroxidase-coupled secondary antibodies and through enhanced chemiluminescence, according to the manufacturer's (Amersham Pharmacia Biotech) instructions.

RESULTS

Activity of *Atractylodis rhizoma alba* and other herbal extracts as assessed from degranulation of RBL-2H3 cells by antigen and compound 48/80

We utilized RBL-2H3 mast cells for *in vitro* assay to assess anti-allergic activity. RBL-2H3 cells were stimulated by DNP-

Table 1. Effects of natural products on the antigen-induced degranulation in mast cells.

Name of the Herbal drug	Plant name	Voucher specimen number	Family	Percent inhibition of degranulation[a]
Puerariae Flos	*Pueraria thunbergiana*	DS-001	Leguminosae	59.4
Chrysanthemi Flos	*Chrysanthemum indicum*	DS-002	Compositae	35.0
Glycyrrhizae Radix	*Glycyrrhiza uralensis*	DS-003	Leguminosae	86.7
Angelicae koreanae Radix	*Angelicae koreana*	DS-004	Umbelliferae	45.1
Liriopis Tuber	*Liriope platyphylla*	DS-005	Liliaceae	9.7
Polygalae Radix	*Polygala tenuifolia*	DS-006	Polygalaceae	14.0
Rhemaniae Radix	*Rehmannia glutinosa var. purpurea*	DS-007	Scrophulariaceae	9.5
Cinnamomi Ramulus	*Cinnamomum cassia*	DS-008	Lauraceae	93.1
Drynariae Rhizoma	*Drynaria fortunei*	DS-010	polypodiaceae	20.7
Sophorae Fructus	*Sophora flavescens*	DS-012	Leguminosae	81.0
Sophorae Flos	*Sophora flavescens*	DS-013	Leguminosae	80.7
Dianthi Herba	*Dianthus chinensis*	DS-015	Caryophyllaceae	79.1
Chrisanthemi sibirici Herba	*Chrysanthemum zawadskii var. latilobum*	DS-016	Asteraceae	93.4
Euonimi Lignum Suberalatum	*Euonymus alatus*	DS-017	Celastraceae	36.9
Citri unshiu Pericarpium	*Citrus reticulata*	DS-018	Rutaceae	14.7
Citri tangerinae Semen	*Citrus reticulate*	DS-019	Rutaceae	−5.7
Cibotii Rhizoma	*Cibotium barometz*	DS-020	Dicksoniaceae	22.1
Platycodi Radix	*Platicodon grandiforum*	DS-022	Campanulaceae	−23.8
Trachelospermi Caulis	*Trachelospermum jasminoides*	DS-023	Apocyanaceae	63.4
Arisaematis Rhizoma	*Arisaema amurense var. serratum*	DS-024	Araceae	24.6
Phragmitis Rhizoma	*Phragmites communis*	DS-025	Gramineae	−22.6
Aloe	*Aloe*	DS-026	Liliaceae	−41.9
Salviae Radix	*Salvia miltiorrhiza*	DS-027	Labiatae	66.0
Angelicae Sinensis Radix	*Angelica gigas*	DS-028	Umbelliferae	11.1
Angelicae Gigantis Radix	*Angelica gigas*	DS-029	Umbelliferae	27.2
Angelicae Gigantis Radix	*Angelica gigas*	DS-030	Umbelliferae	22.1
Angelicae Gigantis Radix	*Angelica gigas*	DS-031	Umbelliferae	−23.6
Aconiti Tuber	*Aconitum carmichaeli*	DS-032	Buttercup family	84.8
Persicae Semen	*Prunus persica*	DS-034	Amygdalaceae	27.8
Persicae Semen	*Prunus persica*	DS-035	Amygdalaceae	32.5
Araliae Cordatae Radix	*Aralia continentalis*	DS-036	Ginseng Family	25.6
Eucomiae Cortex	*Eucommia ulmoides*	DS-037	Eucommiaceae	20.2
Eucomiae Folium	*Eucommia ulmoides*	DS-038	Eucommiaceae	16.1
Eucomiae Ramulus	*Eucommia ulmoides*	DS-039	Eucommiaceae	39.8
Eucomiae Cortex	*Eucommia ulmoides*	DS-040	Eucommiaceae	13.3
Polygonati Officinalis Rhizoma	*Polygonatum odoratum var. pluriflorum*	DS-041	Liliaceae	16.1
Aristolchiae Fructus	*Aristolochia contorta*	DS-042	Aristolochiaceae	79.3
Cannabis Semen	*Cannabis sativa*	DS-043	Moraceae	44.7
Nux-Vomica	*Strychnos nux-vomica*	DS-044	Loganiaceae	15.1
Ephedrae Herba	*Ephedra sinica*	DS-045	Ephedraceae	63.0
Ephedrae Radix	*Ephedra sinica*	DS-046	Ephedraceae	89.9
Codonopsitis Radix	*Codonopsis pilosula*	DS-047	Campanulaceae	−19.7
Viticis Fructus	*Vitex rotundifolia*	DS-048	Verbenaceae	21.9
Liriopis Tuber	*Liriope platyphylla*	DS-049	Liliaceae	−1.9
Chaenomelis Fructus	*Chaenomeles sinensis*	DS-050	Rosaceae	13.9
Fraxini Cortex	*Fraxinus rhynchophylla*	DS-052	Oleaceae	15.4
Saussureae Radix	*Saussurea lappa*	DS-053	Compositae	75.2
Saussureae Radix	*Saussurea lappa*	DS-054	Compositae	86.1
Actinidiae Caulis	*Actinidia arguta*	DS-056	Actinidiaceae	43.6

Table 1. Continued.

Name of the Herbal drug	Plant name	Voucher specimen number	Family	Percent inhibition of degranulation[a]
Buddleiae Flos	*Buddleja officinalis*	DS-057	Loganiaceae	79.4
Menthae Herba	*Mentha arvensis L. var piperascens*	DS-058	Labiatae	98.6
Sterculiae Scaphigerae Semen	*Sterculia scaphigera*	DS-059	Sterculiaceae	17.6
Potulacae Grandiflorae Herba	*Portulaca oleracea*	DS-060	Polyporaceae	70.7
Peucedani Japonici Radix	*Peucedanum japonicum*	DS-061	Umbelliferae	24.5
Torreyae Semen	*Torreya nucifera*	DS-062	Torreyaceae	12.1
Sinapis Semen	*Brassica juncea*	DS-063	Cruciferae	6.7
Chelidoni Herba	*Chelidonium major*	DS-064		88.4
Amomi Cardamomi Fructus	*Santalum album*	DS-065	Santalaceae	66.1
Pulsatillae Radix	*Pulsatilla koreana*	DS-066	Ranunculaceae	22.3
Imperatae Rhizoma	*Hordenum vulgare*	DS-067	Gramineae	2.8
Cynanchi Radix	*Cynanchum atratum*	DS-068	Asclepiadaceae	71.6
Stemonae Radix	*Stemona japonica*	DS-069	Stemonaceae	27.9
Ampelopsis Radix	*Ampelopsis japonica*	DS-070	Vitaceae	82.6
Paeoniae Radix alba	***Paeonia lactiflora***	DS-071	Ranunculaceae	29.1
Paeoniae Radix alba	***Paeonia lactiflora***	DS-072	Ranunculaceae	29.5
Angelicae Dahuricae Radix	*Angelica dahurica*	DS-073	Umbelliferae	93.4
Pharbitidis Semen	*Pharbitis nil*	DS-076	Convolvulacea	60.6
Atractylodis Rhizoma alba	*Atractylodes japanica*	DS-078	Compositae	99.4
Dolichoris Semen	*Dolichos lablab*	DS-080	Legminosae	11.3
Dolichoris Semen	*Dolichos lablab*	DS-081	Legminosae	19.9
Polygoni Multiflori Radix alba	*Polygonum multiflorum*	DS-082	Polyporaceae	16.7
Polygoni Multiflori Radix alba	*Polygonum multiflorum*	DS-083	Polyporaceae	39.5
Lilie Bulbus	*Lilium longiflorum*	DS-084	Liliaceae	37.7
Hoelen	*Pachyma* ***hoelen***	DS-085	Polyporaceae	26.9
Rubi Fructus	*Rubia cordifolia*	DS-086	Rubiaceae	7.4
Rubi Fructus	*Rubia cordifolia*	DS-087	Rubiaceae	15.2
Zedoariae Rhizoma	*Curcuma zedoaria*	DS-088	Zingiberaceae	64.6
Tritici Immatri Semen	*Triticum aestivum*	DS-089	Graminae	-4.8
Spirodelae Herba	*Spirodela polyrhiza*	DS-090	Lemnaceae	43.8
Tokoro Rhizoma	*Dioscorea tokoro*	DS-091	Dioscoreaceae	17.4
Arecae Pericarpium	*Areca catechu*	DS-092	Palmae	80.7
Belamcandae Rhizoma	*Areca catechu*	DS-093	Palmae	78.2
Luffae Fructus Retinervus	*Luffa cylindrical*	DS-094	Cucurbitaceae	17.7
Quisqalis Fructus	*Quisqualis indica var. vilosa*	DS-095	Combretaceae	10.4
Codonopsitis Lanceolatae Radix	*Codonopis lanceolata*	DS-096	Campanulaceae	7.9
Adenophorae Radix	*Adenophora triphylla var. japonica*	DS-097	Campanulaceae	7.8
Torilidis Fructus	*Cnidium monieri*	DS-098	Umbelliferae	82.7
Crataegi Fructus	*Crataegus pinnatifida Bunge var. typica*	DS-099	Rosaceae	11.3
0.1% DMSO				2.1
PP2				92.5

[a]Percent inhibition of degranulation was determined by the measurement of the release of the granule marker β-hexosaminase in the media as described in Materials and Methods. The degranulation by antigen was 32 ± 2.3% in the RBL-2H3 mast cells. 0.1% DMSO and 10 μM PP2 were used as the negative or positive control, respectively.

BSA or compound 48/80. RBL-2H3 mast cells were primed with 25-ng/㎖ DNP-specific IgE or 30 μM quercetin overnight before stimulation with DNP-BSA antigen or compound 48/80. We measured the inhibitory activities on degranulation with the ethanol extracts of approximately 100 Oriental medicinal herbs (Table 1). As reported previously, *Glycyrrhizae radix* (Kim *et al.*, 2001), and *Chrisanthemi sibirici herba* (Lee *et al.*, 2004b) strongly inhibited degranulation in the cells. *Atractylodis rhizoma alba* also significantly suppressed degranulation (Fig. 1) in a dose-dependent manner induced by compound 48/

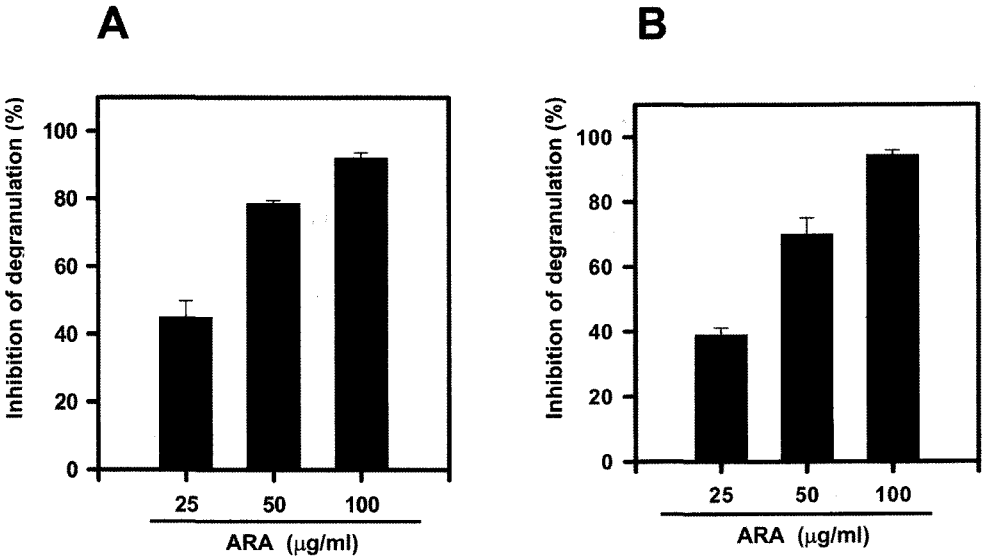

Fig. 1. *Atractylodis rhizoma alba* inhibits degranulation in a dose-dependent manner. RBL-2H3 cells were incubated overnight in 24-well cluster plates with 25-ng/mℓ DNP-specific IgE or 30-μM quercetin in complete growth medium. The medium was replaced with a PIPES-buffered medium that contained the indicated concentration of *Atractylodis rhizoma alba* before stimulation with 25-ng/mℓ DNP-BSA (A) or 10-μg/mℓ compound 48/80 (B) for measurement of release of β-hexosaminidase. The values are the mean ± S.E.M. from three independent experiments.

Table 2. Protective activity of *Atractylodis rhizoma alba* on compound 48/80-induced anaphylaxis in mice.

Dose (mg/kg)[a]	Compound 48/80 (8 mg/kg)[b]	Survival rate (%)[c]
Vehicle	+	0.0
20	+	0.0
100	+	12.5
300	+	31.3
300	−	100.0

[a]Administered p.o. in 200 μl/20 g mouse 1 h before the i.p. injection of compound 48/80. *Atractylodis rhizoma alba* was suspended in 5% Arabic gum. Eight mice were tested for each of the indicated doses.
[b] Administered i.p. in 200 μl/20 g mouse.
[c] Measured 1 h after injection of compound 48/80, values are the means of two independent experiments.

80 as well as antigen. IC_{50} values for antigen and compound 48/80 were 20.5 μg/mℓ and 33.04 μg/mℓ, respectively. These results indicated that *Atractylodis rhizoma alba* may have a potent anti-allergic activity *in vivo* animal model.

Atractylodis rhizoma alba inhibit compound 48/80-mediated anaphylaxis in mice

Next, to measure in-vivo anti-allergic activity of *Atractylodis rhizoma alba*, we used the compound 48/80-mediated anaphylactic animal model. Compound 48/80 successfully induced anaphylactic death within 1 hr after intraperitoneal injection of 8 mg/kg to ICR mice. As shown in Table 2, compound 48/80-induced anaphylactic death was dose-dependently inhibited by *Atractylodis rhizoma alba*. The anaphylatic death was inhibited by 31.3% in mice given by 300 mg/kg of *Atractylodis rhizoma alba*.

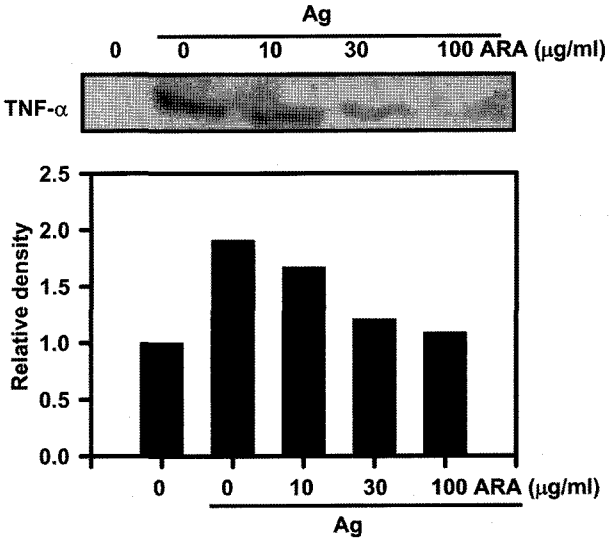

Fig. 2. Effects of *Atractylodis rhizoma alba* on the secretion of TNF-α. The cells were transferred to 24-well (2×10^5 cells/0.4 mℓ/well) cluster plates, and were incubated overnight with 25-ng/mℓ DNP-specific IgE. Then, the cells were stimulated by 25-ng/mℓ Antigen (DNP-BSA) for 24 hours. The media containing TNF-α secreted from the cells were concentrated using Ultrafiltration system (Amicon, MWCO 10,000 Da), and then the concentrates were subjected to Western blotting analysis.

Effect of *Atractylodis rhizoma alba* on the secretion of TNF-α

It is intriguing to us whether ARA inhibits the secretion of TNF-α, a major inflammatory cytokine from the mast cells. ARA dose-dependently and significantly suppressed the secretion of TNF-α (Fig. 2).

DISCUSSION

In many Asian countries, folk herb medicines have been used to cure various diseases without proving the pharmacological activity. As part of systematic investigation of some of their herbal medicines we have investigated that various medicinal herbs including *Atractylodis rhizoma alba* may be a valuable anti-allergic medication. In the present study, we measured the anti-allergic effects of various plant extracts using in- vitro and in-vivo animal model. Among them, *Atractylodis rhizoma alba* was identified for the first time as a potent plant extract to treat allergic diseases. We showed that *Atractylodis rhizoma alba* pretreatment significantly suppressed compound 48/80-induced systemic anaphylactic reaction in mice and inhibited degranulation induced by DNP-BSA and compound 48/80 in RBL-2H3 cells. *Atractylodis rhizoma alba* also inhibited the secretion of TNF-α by DNP-BSA.

Stimulation of mast cells with antigen initiates the activation of signal transduction pathways that lead to degranulation and generation of various inflammatory cytokines. Several studies demonstrate that compound 48/80 and other polybasic compounds can activate G proteins (Mousli *et al.*, 1990). Recently, Chadi *et al.* (2000) reported that compound 48/80 activated RBL-2H3 mast cell phospholipase D (PLD) via heterotrimeric GTP-binding proteins. Although compound 48/80 is still used as an experimental model in vivo (Alfonso *et al.*, 2000), the compound acts only on certain subtypes of mast cells, such as rat peritoneal mast cells, to induce the rapid release of inflammatory mediators. Rat mucosal mast cells and RBL-2H3 mast cells are not activated by the compound (Swieter *et al.*, 1993; Ogasawara *et al.*, 1997). However, as shown in this (Fig. 1B) and a previous study (Senyshyn *et al.*, 1998), RBL-2H3 cells become sensitive to compound 48/80 after treatment with 30 μM quercetin for 24 hr. The treatment with quercetin increased expression of Gi proteins by more than 7-fold in RBL-2H3 cells and it transformed the cell from an unresponsive to a compound 48/80-responsive phenyotype, thus providing a useful cell line for our experiments (Senyshyn *et al.*, 1998). The degranulation in RBL-2H3 cells was induced by compound 48/80 with the maximal response of approximately 17% release of granules. *Atractylodis rhizoma alba* strongly suppressed degranulation induced by DNP-BSA antigen or compound 48/80 (Fig. 1) at concentrations considerably lower than those reported for other anti-allergic medicinal herbs (Yi *et al.*, 2002; Hong *et al.*, 2003). However, the mechanism of inhibition of degranulation by *Atractylodis rhizoma alba* is unknown and we are currently investigating the effects of *Atractylodis rhizoma alba* on signaling pathways that lead to degranulation in the mast cells.

Stimulated mast cells also produce a variety of cytokines that include interleukins 1, 3, 4, 5, and 6 as well as TNF-α and granulocyte-macrophage colony-stimulating factor (Baugartner and Beaven 1996; Galli 1993). Typically, increased expression of cytokine protein is detectable 30 min and several hours after the addition of stimulant (Gordon *et al.*, 1990). Such cytokines, particularly TNF-α, are thought to mediate pathogenic inflammatory reactions at later stages of the allergic reaction (Galli 1993). Based on our finings that the secretion of TNFα was suppressed by *Atractylodis rhizoma alba*, we suggest that it may be useful of in the treatment of late-phase allergic symptoms as well as reactions to antigen challenge in allergic diseases. In summary, we report for the first time that *Atractylodis rhizoma alba* inhibited dose-dependently degranulation of RBL-2H3 cells by DNP-BSA antigen or compound 48/80 and effectively suppressed in-vivo anaphylatic reaction in mice. In addition, *Atractylodis rhizoma alba* inhibited the secretion of TNF-α in a dose-dependent manner. These findings indicate that *Atractylodis rhizoma alba* may be a potential candidate for treatment of various allergic diseases. However, further study should be necessary to identify the mechanism of action and the active components of *Atractylodis rhizoma alba*.

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