

Inhibitory Effects of Herbal Extracts on Cyclooxygenase Activity of Prostaglandin H₂ Synthase from Sheep Seminal Vesicle

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Abstract – Prostaglandin H₂ synthase is the pharmacological target site of non-steroidal antiinflammatory drugs. Inhibitory effects on cyclooxygenase activity of the synthase by extracts prepared from herbal medicines and wild plants in Korea have been estimated. Sixteen species out of 612 species exhibited more than 50% of inhibition on the enzyme activity. The active extracts prepared from *Carex humilis*, *Celastrus orbiculatus*, *Eugenia caryophyllata*, *Gleditsia japonica* var. *koraiensis*, *Glycyrrhiza grabra*, *Glycyrrhiza uralensis*, *Gyrophora exculenta*, *Lespedeza maximowiczii*, *Morus alba*, *Persicaria conspicua*, *Prunus salicina*, *Pterocarya stenoptera*, *Rheum undulatum*, *Vitis amurensis*, and *Vitis coignetiae* have been sequentially washed with methylene chloride, ethyl acetate, *n*-butanol. Among the solvent fractions of the active herbal extracts, the ethyl acetate fraction of *Carex humilis* exhibited the highest inhibitory effect on the cyclooxygenase activity of prostaglandin H₂ synthase.

Key words – Cyclooxygenase activity, prostaglandin H₂ synthase, herbal extract, *Carex humilis*.

Introduction

Prostaglandin H₂ synthase (EC 1.14.99.1) catalyzes the committed step of metabolic pathway of arachidonic acid to form prostaglandins, prostacycline, and thromboxanes (Shimizu and Wolfe, 1990). The enzyme possesses two enzymatic activities, a cyclooxygenase (COX) which catalyzes the bis-dioxygenation of polyunsaturated substrate such as arachidonic acid to form prostaglandin G₂, and a peroxidase which catalyzes the conversion of prostaglandin G₂ to

prostaglandin H₂ (Marnett *et al.*, 1988; Ruf *et al.*, 1992). The prostaglandin H₂ synthase is a glycosylated membrane-bound protein with unusual subcellular distributions in the endoplasmic reticulum, nuclear envelope, and plasma membrane within the same cell (Hedin *et al.*, 1987; Otto *et al.*, 1993; Regier *et al.*, 1993). The enzyme purified from endoplasmic reticulum of sheep seminal vesicle is a heme protein with homodimer of 70-kDa subunits, where heme is required for both COX and peroxidase activities (DeWitt *et al.*, 1990; Hemler *et al.*, 1976).

Recently it has become apparent that mammalian cells contain two related, but

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unique, isozymes of prostaglandin H₂ synthase, referred to as COX-1 and COX-2 (Simmons *et al.*, 1991). The two isozymes are approximately 60% identical, and 75% similar at the amino acid sequence level (Hla and Neilson, 1992; Yokoyama and Tanabe, 1989). However, amino acid residues believed to be important for the enzyme function including heme ligand sites, EGF homology domain, glycosylation sites, and aspirin acetylation site are conserved among the isozymes (see references cited in Smith and DeWitt, 1994). Furthermore, COX-1 and COX-2 are essentially identical for their enzyme kinetic parameters, maximal catalytic activity (V_{max}) and affinity (K_m) for arachidonic acid as a substrate (Meade *et al.*, 1993). The two isozymes, COX-1 and COX-2 are encoded in different genes whose regulation and expression are quite different. COX-1 is a constitutively expressed enzyme that is present in most tissues, although the level of expression varies among cell types and increases two- to four-fold following hormonal or growth factor stimulation (DeWitt and Meade, 1993). COX-2 is nearly undetectable in most tissue except prostate, brain, testis and lung under normal physiological conditions, but its expression can be dramatically increased during inflammation or following stimulation with growth factors, cytokines, phorbol esters or hormones (DeWitt, 1991). Although the exact physiological roles of the two isozymes are not definitively elucidated, it is hypothesized that COX-1 is a "housekeeping" enzyme that produces prostaglandins that regulate normal cellular processes, and COX-2 produces prostaglandins involved in inflammation, mitogenesis and/or ovulation (Jonat *et al.*, 1990, Smith *et al.*, 1989).

Prostaglandins, prostacycline, and thromboxanes formed from arachidonic acid are autocrine and paracrine regulators of normal cellular function (Curtis-Prior, 1988). Several pathophysiological conditions including

pain, fever, inflammation, hypertension, and thrombosis can be evoked by dysregulation of the metabolic pathway of arachidonic acid, where prostaglandin H₂ synthase is a rate-limiting enzyme (Curtis-Prior, 1988). The prostaglandin H₂ synthase is the pharmacological target site of nonsteroidal antiinflammatory drugs (DeWitt *et al.*, 1993). The drugs have characteristic inhibitory effects on COX activity of the synthase but do not appreciably inhibit the peroxidase activity (Shimokawa and Smith, 1993).

As a part of our screening studies to identify the antiinflammatory agents with analgesic, antipyretic and/or antithrombic effects, inhibitory effects on the COX activity by extracts prepared from herbal medicines and wild plants in Korea have been estimated in this study. Sixteen out of 612 kinds of the herbal extracts exhibited more than 50% of inhibition on the enzyme activity at their final concentration of 100 µg/ml. Some of the active extracts have been subjected to sequential fractionation with methylene chloride, ethyl acetate, *n*-butanol, and polar residue. Among the solvent fractions of the active herbal extracts, the highest inhibitory effect on COX activity has been identified in ethyl acetate fraction of *Carex humilis*.

Experimental

General chemicals – Arachidonic acid, indomethacin, dexamethasone, and hemoglobin were purchased from Sigma Chem. Co. Sheep seminal vesicles were obtained from Pel-Freez Biol., Tris from Kodak International Biotech. Inc., and phenol from Boehringer Mannheim.

Herbal extracts – Herbal medicines were obtained from a drug store (Dongyak Yakup Co.), and wild plants were collected at the hills and mountains near Cheongju of Korea. The plants were taxonomically identified with respect to morphology, and voucher specimens were deposited at the herbarium

of Chungbuk National University. Each of the dried plants was sliced, and then extracted twice with 80% MeOH at room temperature. The extract solution was evaporated under reduced pressure at 50 °C, and then completely dried by lyophilization. Some of the MeOH extracts were subjected to sequential fractionations with methylene chloride, ethyl acetate, and then *n*-butanol as follows. The MeOH extract was resuspended in more than 10 volume of water, and then extracted several times with methylene chloride until colored constituents were not transferred to the methylene chloride layer. The aqueous layer remaining after the methylene chloride extractions was sequentially extracted with ethyl acetate, and then *n*-butanol as described above. The methylene chloride, ethyl acetate, *n*-butanol fractions and the final aqueous layer after the *n*-butanol extraction were evaporated under reduced pressure, and then completely dried by lyophilization. The dried MeOH extract and solvent fractions were used as samples.

COX assay—The enzyme activity was measured at 37 °C by monitoring O₂ consumption using a Clark-type oxygen electrode (YSI, USA) (DeWitt, *et al.*, 1990; Meade *et al.*, 1993). Enzyme reactions were initiated by adding microsomal fraction prepared from sheep seminal vesicle to a reaction mixture of 3 ml of 0.1 M Tris-HCl, pH 8.0, containing 100 μM arachidonic acid, 1 mM phenol, 25 μM of hemoglobin, and a designated concentration of herbal extract. Sheep seminal vesicles stored at -80 °C were sliced, and then homogenized with a Polytron homogenizer in 5 to 10 volume of 0.1 M Tris-HCl, pH 8.0, containing 1 mM phenol. The homogenate was centrifuged at 10,000×*g* for 10 min, and the resulting supernatant was centrifuged at 100,000×*g* for 1 hr. The microsome pellet was resuspended in 0.1 M Tris-HCl, pH 8.0, containing 1 mM phenol to make 1 to 10 mg per ml of protein con-

centration. Specific activities of the resulting enzyme sources were usually 15,000 to 40,000 units per mg of microsomal protein, where one unit of COX activity is defined as the amount of enzyme which catalyzes the consumption of 1 nmol of O₂ per min in the assay solution at 37 °C. The microsomal fraction with 10,000 units of COX activity was used for each assay.

Statistics—Inhibitory effect of each herbal extract on the COX activity was represented as % of inhibition = [(control Oxy - sample Oxy)/control Oxy] × 100, where "Oxy" means the initial rate of O₂ consumption by enzyme only (control) or enzyme plus herbal extract (sample). Data were collected as mean ± standard error from 2 to 5 independent tests, and significance of the data was analyzed by the Student's *t*-test.

Results and Discussion

The COX activity of prostaglandin H₂ synthase is a target site for pharmacological actions of nonsteroidal antiinflammatory drugs (DeWitt *et al.*, 1993). As a standard assay, inhibitory effects of antiinflammatory

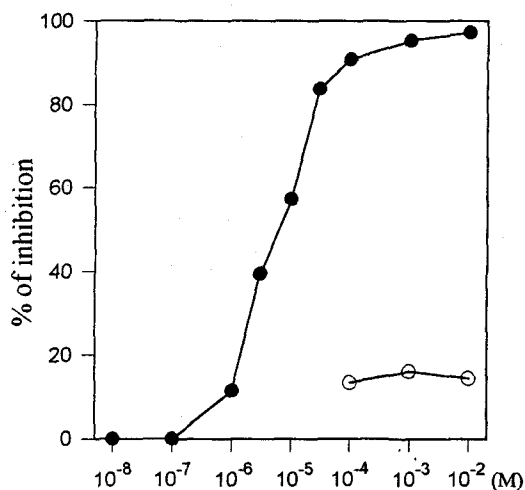


Fig. 1. Inhibition on COX activity by indomethacin (solid circle) and dexamethasone (open circle). Standard error was within 10% of the mean of triplicates.

drugs, indomethacin and dexamethasone, on the enzyme activity were estimated (Fig. 1). Indomethacin, a kind of nonsteroidal anti-inflammatory drugs, inhibited the COX activity in a dose-dependent pattern, but dexamethasone, a kind of steroidal anti-inflammatory drugs, did not. Indomethacin significantly inhibited the COX activity at concentrations higher than 1 mM, while it showed more than 90% of inhibition at concentrations higher than 100 μ M. However, indomethacin with less than 0.1 μ M as the final concentration did not inhibit the COX activity at all. Dexamethasone with 0.1 mM to 10 mM exhibited less than 20% of non-specific inhibition on the enzyme activity.

Inhibitory effects of 612 kinds of herbal ex-

tracts on the COX activity were estimated (Table 1). None of the herbal extracts with 10 μ g/ml exhibited more than 50% of inhibition on the enzyme activity. At the concentration of 100 μ g/ml, sixteen extracts exhibited more than 50% of inhibition on the COX activity. The active extracts were prepared from underground part of *Carex humilis*, branch and leaf of *Celastrus orbiculatus*, flos of *Eugenia caryophyllata*, branch and leaf of *Gleditsia japonica* var. *koraiensis*, branch and leaf of *Glycyrrhiza grabra*, radix of *Glycyrrhiza uralensis*, fungus of *Gyrophora exculenta*, aerial part of *Lespedeza maximowiczii*, aerial part and cortex of *Morus alba*, whole plant of *Persicaria*

Table 1. Inhibition on COX activity by total MeOH extracts.

Plant (part of use) / Family	% of Inhibition	
	10 μ g/ml	100 μ g/ml
<i>Abies holophylla</i> (b.l.) / Pinaceae	5	23
<i>Abutilon avicennae</i> (a.p.) / Malvaceae	11	1
<i>Acalypha australis</i> (w.p.) / Euphorbiaceae	18	20
<i>Acanthopanax gracilistylus</i> (b.l.) / Araliaceae	< 0	20
<i>Acanthopanax gracilistylus</i> (cortex) / Araliaceae	< 0	< 0
<i>Acanthopanax boreanum</i> (b.l.) / Araliaceae	< 0	11
<i>Acanthopanax sessitiflorus</i> (b.l.) / Araliaceae	< 0	13
<i>Acer ginnala</i> (b.l.) / Aceraceae	7	26
<i>Acer mono</i> (b.l.) / Aceraceae	< 0	3
<i>Acer pseudo-sieboldianum</i> (b.l.) / Aceraceae	3	8
<i>Achillea sibirica</i> (a.p.) / Compositae	7	9
<i>Aconitum koreanum</i> (tuber) / Ranunculaceae	13	7
<i>Aconitum koreanum</i> (w.p.) / Ranunculaceae	< 0	2
<i>Acorus calamus</i> var. <i>angustatus</i> (w.p.) / Araceae	9	< 0
<i>Acorus gramineus</i> (rhizoma) / Araceae	3	8
<i>Actaea asiatica</i> (a.p.) / Ranunculaceae	< 0	< 0
<i>Actinidia arguta</i> (b.l.) / Actinidiaceae	12	22
<i>Actinidia arguta</i> var. <i>rufinervis</i> (b.l.) / Actinidiaceae	13	16
<i>Actinidia polygama</i> (b.l.) / Actinidiaceae	< 0	< 0
<i>Adenocaulon himalaicum</i> (a.p.) / Compositae	< 0	< 0
<i>Adenophora trachelioides</i> (radix) / Campanulaceae	22	31
<i>Adenophora triphylla</i> var. <i>japonica</i> (w.p.) / Campanulaceae	< 0	< 0
<i>Aeschynomame indica</i> (w.p.) / Leguminosae	10	9
<i>Aesculus turbinata</i> (b.l.) / Hippocastanaceae	26	45
<i>Agastache rugosa</i> (a.p.) / Labiatae	< 0	8
<i>Agastache rugosa</i> (herba) / Labiatae	< 0	< 0
<i>Agrimonia pilosa</i> (herba) / Rosaceae	25	35
<i>Agrimonia pilosa</i> (w.p.) / Rosaceae	< 0	16
<i>Agrostis clavata</i> var. <i>nukabo</i> (w.p.) / Gramineae	< 0	0

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Aiinsliaea acerifolia</i> (w.p.) / Compositae	< 0	< 0
<i>Ailanthus altissima</i> (b.l.) / Simaroubaceae	7	10
<i>Akebia quinata</i> (caulis) / Lardizabalaceae	21	< 0
<i>Alangium platanifolium</i> var. <i>macrophyllum</i> (b.l.) / Alangiaceae	5	16
<i>Albizia julibrissin</i> (b.l.) / Leguminosae	8	27
<i>Albizia julibrissin</i> (cortex) / Leguminosae	< 0	< 0
<i>Alisma orientale</i> (rhizoma) / Alismataceae	< 0	< 0
<i>Allium cepa</i> (bulbus) / Liliaceae	< 0	< 0
<i>Alopecurus aequalis</i> var. <i>simplicifolium</i> (w.p.) / Gramineae	14	< 0
<i>Alpinia oxyphylla</i> (fructus) / Zingiberaceae	12	25
<i>Amaranthus mangostanus</i> (a.p.) / Amaranthaceae	< 0	8
<i>Ambrosia artemisiifolia</i> var. <i>elatior</i> (a.p.) / Compositae	18	17
<i>Ambrosia artemisiifolia</i> var. <i>elatior</i> (u.p.) / Compositae	< 0	26
<i>Amomum cardamomum</i> (fructus) / Zingiberaceae	15	< 0
<i>Amomum tsao-ko</i> (fruit) / Zingiberaceae	11	37
<i>Amomum villosum</i> (semen) / Zingiberaceae	1	12
<i>Ampelopsis brevipedunculata</i> var. <i>heterophylla</i> (b.l.) / Vitaceae	< 0	7
<i>Amphicarpaea edgeworthii</i> var. <i>perma</i> (a.p.) / Leguminosae	3	6
<i>Anemarrhena asphodeloides</i> (rhizoma) / Liliaceae	< 0	< 0
<i>Anemarrhena asphodeloides</i> (w.p.) / Liliaceae	14	3
<i>Angelica dahurica</i> (a.p.) / Umbelliferae	9	< 0
<i>Angelica dahurica</i> (radix) / Umbelliferae	20	< 0
<i>Angelica decursiva</i> (w.p.) / Umbelliferae	2	16
<i>Angelica gigas</i> (a.p.) / Umbelliferae	< 0	< 0
<i>Angelica gigas</i> (radix) / Umbelliferae	< 0	< 0
<i>Angelica koreana</i> (a.p.) / Umbelliferae	< 0	< 0
<i>Angelica koreana</i> (rhizoma) / Umbelliferae	3	6
<i>Angelica sieboldii</i> (w.p.) / Umbelliferae	7	13
<i>Aquilaria agallocha</i> (lignum) / Thymelaceae	7	< 0
<i>Aralia continentalis</i> (radix) / Araliaceae	< 0	< 7
<i>Aralia elata</i> (b.l.) / Araliaceae	5	10
<i>Arctium lappa</i> (semen) / Compositae	9	4
<i>Arctium lappa</i> (u.p.) / Compositae	17	4
<i>Areca catechu</i> (pericarpium) / Palmae	7	30
<i>Areca catechu</i> (semen) / Palmae	31	33
<i>Arisaema consanguineum</i> (rhizoma) / Araceae	12	18
<i>Aristolochia contorta</i> (a.p.) / Aristolochiaceae	11	4
<i>Armoracia lapathifolia</i> (w.p.) / Cruciferae	8	< 0
<i>Artemisia argyi</i> (folium) / Compositae	< 0	< 0
<i>Artemisia capillaris</i> (a.p.) / Compositae	17	25
<i>Artemisia capillaris</i> (a.p.) / Compositae	18	12
<i>Artemisia iwayomogi</i> (b.l.) / Compositae	3	27
<i>Artemisia japonica</i> (a.p.) / Compositae	22	21
<i>Artemisia keiskeana</i> (w.p.) / Compositae	< 0	< 0
<i>Artemisia montana</i> (a.p.) / Compositae	10	26
<i>Artemisia princeps</i> (a.p.) / Compositae	22	36
<i>Artemisia selengensis</i> (a.p.) / Compositae	5	9
<i>Artemisia sirversiana</i> (a.p.) / Compositae	13	13

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Arthraxon hispidus</i> (w.p.) / Gramineae	4	12
<i>Arundinella hirta</i> (a.p.) / Gramineae	< 0	< 0
<i>Asarum heterotropoides</i> var. <i>mendshuricum</i> (radix) / Aristolochiaceae	< 0	< 0
<i>Asarum sieboldii</i> (w.p.) / Aristolochiaceae	12	1
<i>Asparagus cochinchinensis</i> (radix) / Liliaceae	28	12
<i>Asparagus schoberioides</i> (w.p.) / Liliaceae	< 0	< 0
<i>Aster ageratoides</i> (a.p.) / Compositae	< 0	7
<i>Aster pinnatifidus</i> (w.p.) / Compositae	< 0	< 0
<i>Aster scaber</i> (w.p.) / Compositae	< 0	< 0
<i>Aster tataricus</i> (a.p.) / Compositae	< 0	< 0
<i>Aster yomena</i> (a.p.) / Compositae	4	6
<i>Astragalus membranaceus</i> (radix) / Leguminosae	2	15
<i>Astragalus membranaceus</i> (a.p.) / Leguminosae	< 0	3
<i>Athyrium yokoscense</i> (a.p.) / Aspidiaceae	< 0	< 0
<i>Atractylodes japonica</i> (a.p.) / Compositae	7	34
<i>Atractylodes japonica</i> (rhizoma) / Compositae	< 0	< 0
<i>Belamcanda chinensis</i> (a.p.) / Iridaceae	< 0	21
<i>Benincasa hispida</i> (semen) / Cucurbitaceae	4	< 0
<i>Berberis amurensis</i> (b.l.) / Berberidaceae	< 0	< 0
<i>Berberis koreana</i> (b.l.) / Berberidaceae	7	< 0
<i>Berberis poiretii</i> (b.l.) / Berberidaceae	< 0	< 0
<i>Betula davurica</i> (b.l.) / Betulaceae	7	1
<i>Bidens bipinnata</i> (a.p.) / Compositae	21	26
<i>Bidens cernua</i> (w.p.) / Compositae	< 0	16
<i>Bidens tripartita</i> (w.p.) / Compositae	< 0	< 0
<i>Bilderdykia dentata-alata</i> (a.p.) / Polygonaceae	< 0	< 0
<i>Biota orientalis</i> (semen) / Cupressaceae	8	< 0
<i>Boehmeria nivea</i> (a.p.) / Urticaceae	27	35
<i>Boehmeria sieboldiana</i> (a.p.) / Urticaceae	21	31
<i>Boehmeria spicata</i> (b.l.) / Urticaceae	< 0	15
<i>Boehmeria tricuspis</i> (a.p.) / Urticaceae	0	< 0
<i>Boehmeria tricuspis</i> (u.p.) / Urticaceae	7	< 0
<i>Boswellia carterii</i> (resin) / Burceraceae	14	11
<i>Brachybotrys paridiformis</i> (a.p.) / Borraginaceae	16	7
<i>Brassica alba</i> (semen) / Cruciferae	< 0	2
<i>Brassica campestris</i> subsp. <i>napus</i> var. <i>nippo-oleifera</i> (w.p.) / Cruciferae	6	3
<i>Bulbostylis barbata</i> (w.p.) / Cyperaceae	< 0	10
<i>Bupleurum falcatum</i> (radix) / Umbelliferae	9	19
<i>Buxus microphylla</i> var. <i>koreana</i> (b.l.) / Buxaceae	< 0	< 0
<i>Caesalpinia sappan</i> (lignum) / Leguminosae	7	28
<i>Callicarpa japonica</i> (b.l.) / Verbenaceae	6	6
<i>Calystegia soldanella</i> (a.p.) / Convolvulaceae	< 0	15
<i>Campanula glomerata</i> var. <i>dahurica</i> (a.p.) / Campanulaceae	11	13
<i>Campanula takesimana</i> (w.p.) / Campanulaceae	< 0	5
<i>Cannabis sativa</i> (a.p.) / Moraceae	12	15
<i>Capsella bursa-pastoris</i> (w.p.) / Cruciferae	8	33
<i>Caragana sinica</i> (b.l.) / Leguminosae	3	37
<i>Cardamine lyrata</i> (w.p.) / Cruciferae	< 0	12

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Carduus crispus</i> (a.p.) / Compositae	7	< 0
<i>Carex humilis</i> (u.p.) / Cyperaceae	20	95
<i>Carex kobomugi</i> (a.p.) / Cyperaceae	6	< 0
<i>Carex kobomugi</i> (u.p.) / Cyperaceae	< 0	22
<i>Carex maackii</i> (w.p.) / Cyperaceae	1	42
<i>Carex siderostica</i> (w.p.) / Cyperaceae	< 0	< 0
<i>Carpesium divaricatum</i> (w.p.) / Compositae	< 0	10
<i>Carthamus tinctorius</i> (flos) / Compositae	20	16
<i>Cassia tora</i> (a.p.) / Leguminosae	6	18
<i>Catalpa ovata</i> (b.l.) / Bignoniaceae	13	5
<i>Cayratia japonica</i> (a.p.) / Vitaceae	< 0	8
<i>Cedrus deodara</i> (b.l.) / Pinaceae	< 0	< 0
<i>Celastrus flagellaris</i> (b.l.) / Celastraceae	28	28
<i>Celastrus orbiculatus</i> (b.l.) / Celastraceae	< 0	60
<i>Celastrus stephanotifolius</i> (b.l.) / Celastraceae	6	< 0
<i>Centipeda minima</i> (w.p.) / Compositae	< 0	< 0
<i>Cersis chinensis</i> (b.l.) / Leguminosae	< 0	39
<i>Chaenomeles sinensis</i> (b.l.) / Rosaceae	3	36
<i>Chamaecyparis obtusa</i> (b.l.) / Cupressaceae	< 0	36
<i>Chelidonium majus</i> var. <i>asiaticum</i> (a.p.) / Papaveraceae	< 0	< 0
<i>Chelidonium speciosa</i> (a.p.) / Papaveraceae	< 0	5
<i>Chenopodium virgatum</i> (w.p.) / Chenopodiaceae	2	< 0
<i>Chenopodium album</i> var. <i>centrorubrum</i> (a.p.) / Chenopodiaceae	< 0	< 0
<i>Chenopodium glaucum</i> (a.p.) / Chenopodiaceae	< 0	6
<i>Chrysanthemum indicum</i> (a.p.) / Compositae	< 0	< 0
<i>Chrysanthemum indicum</i> (flos) / Compositae	< 0	< 0
<i>Chrysanthemum zawadskii</i> var. <i>latilobum</i> (w.p.) / Compositae	< 0	< 0
<i>Chyranthes japonica</i> (a.p.) / Amaranthaceae	< 0	8
<i>Cimicifuga heracleifolia</i> (a.p.) / Ranunculaceae	< 0	6
<i>Cimicifuga heracleifolia</i> (rhizoma) / Ranunculaceae	19	6
<i>Cinnamomum cassia</i> (cortex) / Lauraceae	< 0	< 0
<i>Cinnamomum japonicum</i> (b.l.) / Lauraceae	< 0	7
<i>Cirsium pendulum</i> (a.p.) / Compositae	20	2
<i>Cistanche salsa</i> (herba) / Orobanchaceae	< 0	22
<i>Citrus aurantus</i> var. <i>tachibana</i> (Fructus) / Rutaceae	< 0	< 0
<i>Clematis apiifolia</i> (a.p.) / Ranunculaceae	1	< 0
<i>Clematis chinensis</i> (radix) / Ranunculaceae	27	< 0
<i>Clematis fusca</i> var. <i>violacea</i> (b.l.) / Ranunculaceae	< 0	< 0
<i>Clematis heracleifolia</i> var. <i>dauidiana</i> (w.p.) / Ranunculaceae	11	11
<i>Clematis mandshurica</i> (a.p.) / Ranunculaceae	< 0	8
<i>Clematis trichotoma</i> (a.p.) / Ranunculaceae	7	< 0
<i>Clerodendron trichotomum</i> (b.l.) / Verbenaceae	8	5
<i>Clinopodium chinense</i> (a.p.) / Labiatae	12	7
<i>Cnidium monnieri</i> (fruit) / Umbelliferae	3	< 0
<i>Cnidium officinale</i> (rhizoma) / Umbelliferae	5	27
<i>Cocculus trilobus</i> (a.p.) / Menispermaceae	< 0	18
<i>Coix lachryma-jobi</i> var. <i>ma-yuen</i> (semen) / Gramineae	22	22

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Coix lachryma-jobi</i> var. <i>mayuen</i> (a.p.) / Gramineae	3	7
<i>Colocasia antiquorum</i> var. <i>esculenta</i> (a.p.) / Araceae	< 0	< 0
<i>Commelina communis</i> (w.p.) / Commeliaceae	3	8
<i>Commiphora molmol</i> (resin) / Burceraceae	< 0	< 0
<i>Coptis chinensis</i> (rhizoma) / Ranunculaceae	< 0	15
<i>Corchorus capsularis</i> (a.p.) / Sterculiaceae	< 0	4
<i>Cornus controversa</i> (b.l.) / Cornaceae	< 0	17
<i>Cornus officinalis</i> (fructus) / Cornaceae	10	6
<i>Corydalis yanhusuo</i> (tuber) / Fumariaceae	7	< 0
<i>Corylus heterophylla</i> var. <i>thunbergii</i> (b.l.) / Betulaceae	26	27
<i>Crataegus pinnatifida</i> (b.l.) / Rosaceae	15	< 0
<i>Crataegus pinnatifida</i> (fructus) / Rosaceae	< 0	< 0
<i>Croton tiglium</i> (semen) / Euphorbiaceae	17	19
<i>Cucurbita moschata</i> (stem) / Cucurbitaceae	4	1
<i>Curcuma longa</i> (rhizoma) / Zingiberaceae	21	36
<i>Curcuma zedoaria</i> (rhizoma) / Zingiberaceae	3	15
<i>Cuscuta australis</i> (a.p.) / Convolvulaceae	8	3
<i>Cuscuta japonica</i> (a.p.) / Convolvulaceae	< 0	< 0
<i>Cynomorium songaricum</i> (herba) / Cynomoliaceae	< 0	8
<i>Cyperus amuricus</i> (w.p.) / Cyperaceae	7	17
<i>Cyperus nipponicus</i> (w.p.) / Cyperaceae	7	16
<i>Cyperus rotundus</i> (rhizoma) / Cyperaceae	17	30
<i>Cyrtomium fortunei</i> (a.p.) / Osmundaceae	4	< 0
<i>Datura stramonium</i> (w.p.) / Solanaceae	< 0	< 0
<i>Desmodium oldhami</i> (w.p.) / Leguminosae	5	< 0
<i>Desmodium oxyphyllum</i> (a.p.) / Leguminosae	9	< 0
<i>Deutzia parviflora</i> (b.l.) / Saxifragaceae	7	7
<i>Deutzia prunifolia</i> (b.l.) / Saxifragaceae	< 0	< 0
<i>Dianthus chinensis</i> (a.p.) / Caryophyllaceae	12	17
<i>Dicentra spectabilis</i> (a.p.) / Papaveraceae	< 0	< 0
<i>Dictamnus dasycarpus</i> (a.p.) / Rutaceae	3	23
<i>Digitaria sanguinalis</i> (a.p.) / Gramineae	< 0	17
<i>Dioscorea batatas</i> (radix) / Dioscoreaceae	< 0	< 0
<i>Dioscorea batatas</i> (semen) / Dioscoreaceae	9	4
<i>Dioscorea quinqueloba</i> (w.p.) / Dioscoreaceae	12	< 0
<i>Dioscorea tokora</i> (a.p.) / Dioscoreaceae	3	< 0
<i>Disporum viridescens</i> (a.p.) / Liliaceae	7	10
<i>Dolichos lablab</i> (semen) / Leguminosae	< 0	< 0
<i>Dryopteris crassirhizoma</i> (w.p.) / Polypodiaceae	< 0	15
<i>Duchesnea chrysantha</i> (w.p.) / Rosaceae	4	< 0
<i>Elaeagnus umbellata</i> (b.l.) / Elaeagnaceae	< 0	6
<i>Eleusine indica</i> (w.p.) / Gramineae	17	< 0
<i>Elsholtzia ciliata</i> (w.p.) / Labiatae	6	4
<i>Elsholtzia splendens</i> (w.p.) / Labiatae	< 0	< 0
<i>Ephedra sinica</i> (herba) / Ephedraceae	< 0	11
<i>Epimedium grandiflorum</i> (herba) / Berberidaceae	4	7

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Equisetum arvense</i> (w.p.) / Equisetaceae	< 0	< 0
<i>Equisetum hyemale</i> (a.p.) / Equicetaceae	12	8
<i>Erigerum annuus</i> (w.p.) / Compositae	< 0	5
<i>Erigerum canadensis</i> (w.p.) / Compositae	< 0	2
<i>Eriobotrya japonica</i> (folium) / Rosaceae	13	38
<i>Eucommia ulmoides</i> (b.l.) / Eucommiaceae	< 0	13
<i>Eucommia ulmoides</i> (cortex) / Eucommiaceae	20	11
<i>Eugenia caryophyllata</i> (flos) / Myrtaceae	10	95
<i>Euonymus alatus</i> (b.l.) / Celastraceae	< 0	< 0
<i>Euonymus alatus</i> for. <i>ciliata-dentatus</i> (b.l.) / Celastraceae	< 0	4
<i>Euonymus japonica</i> (b.l.) / Celastraceae	< 0	14
<i>Euonymus pauciflorus</i> (b.l.) / Celastraceae	14	14
<i>Euonymus planipes</i> (b.l.) / Celastraceae	5	29
<i>Eupatorium chinensis</i> for. <i>tripartitum</i> (a.p.) / Compositae	12	17
<i>Eupatorium chinensis</i> var. <i>simplicifolium</i> (w.p.) / Compositae	< 0	8
<i>Eupatorium fortunei</i> (a.p.) / Compositae	< 0	11
<i>Eupatorium lindleyanum</i> (a.p.) / Compositae	6	< 0
<i>Euphorbia jolkini</i> (a.p.) / Euphorbiaceae	< 0	4
<i>Euphorbia kansui</i> (radix) / Euphorbiaceae	< 0	< 0
<i>Euphorbia pekinensis</i> (a.p.) / Euphorbiaceae	13	< 0
<i>Euphorbia pekinensis</i> (radix) / Euphorbiaceae	< 0	< 0
<i>Euphorbia supina</i> (w.p.) / Euphorbiaceae	6	22
<i>Euphorbia longana</i> (fructus) / Saphindaceae	< 0	< 0
<i>Evodia officinalis</i> (fructus) / Rutaceae	9	4
<i>Festuca myuros</i> (a.p.) / Gramineae	5	5
<i>Festuca ovina</i> (w.p.) / Gramineae	< 0	< 0
<i>Foeniculum vulgare</i> (fructus) / Umbelliferae	5	< 0
<i>Forsythia koreana</i> (b.l.) / Oleaceae	< 0	3
<i>Forsythia koreana</i> (fructus) / Oleaceae	< 0	3
<i>Forsythia viridissima</i> (fructus) / Oleaceae	< 0	13
<i>Fraxinus sieboldiana</i> (b.l.) / Oleaceae	< 0	7
<i>Fritillaria verticillata</i> (tuber) / Liliaceae	< 0	< 0
<i>Galium verum</i> var. <i>asiaticum</i> (a.p.) / Rubiaceae	19	11
<i>Gardenia jasminoides</i> (fruit) / Rutaceae	< 0	38
<i>Gastrodia elata</i> (rhizoma) / Orchidaceae	11	< 0
<i>Gentiana scabra</i> (radix) / Gentianaceae	8	< 0
<i>Gentiana uchiyamai</i> (w.p.) / Gentianaceae	4	< 0
<i>Geranium nepalense</i> subsp. <i>thunbergii</i> (w.p.) / Geraniaceae	1	23
<i>Geranium sibiricum</i> (a.p.) / Geraniaceae	< 0	25
<i>Geum aleppicum</i> (a.p.) / Rosaceae	10	5
<i>Geum japonicum</i> (w.p.) / Rosaceae	< 0	< 0
<i>Ginkgo biloba</i> (folium) / Ginkgoaceae	20	28
<i>Glechoma hederacea</i> var. <i>longituba</i> (a.p.) / Labiatae	3	7
<i>Gleditsia japonica</i> var. <i>koraiensis</i> (b.l.) / Leguminosae	18	60
<i>Gleditsia sinensis</i> (spina) / Leguminosae	< 0	< 0
<i>Glycyrrhiza grabra</i> (b.l.) / Leguminosae	14	62
<i>Glycyrrhiza uralensis</i> (radix) / Leguminosae	4	51
<i>Gossipium nanking</i> (semen) / Malvaceae	13	19

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Gyrophora exculenta</i> (fungus) / Gysophoraceae	25	58
<i>Helianthus annuus</i> (a.p.) / Compositae	< 0	5
<i>Hemerocallis fulva</i> (w.p.) / Liliaceae	4	13
<i>Hemerocallis fulva</i> var. <i>kwanso</i> (w.p.) / Liliaceae	< 0	< 0
<i>Hepatica asiatica</i> (w.p.) / Ranunculaceae	7	< 0
<i>Heracleum moellendorffii</i> (w.p.) / Umbelliferae	7	18
<i>Hibiscus mutabilis</i> (a.p.) / Malvaceae	12	26
<i>Hibiscus trionum</i> (w.p.) / Malvaceae	< 0	< 0
<i>Hordeum vulgare</i> (semen) / Gramineae	16	23
<i>Hosta japonica</i> var. <i>lancifolia</i> (w.p.) / Liliaceae	13	< 0
<i>Houttuynia cordata</i> (w.p.) / Saururaceae	10	13
<i>Humulus japonicus</i> (w.p.) / Moraceae	16	7
<i>Humulus lupulus</i> (a.p.) / Cannabiaceae	< 0	24
<i>Hydrangea serrata</i> for. <i>acuminata</i> (w.p.) / Saxifragaceae	7	12
<i>Hypericum ascyron</i> (w.p.) / Guttiferae	8	10
<i>Hypericum erectum</i> (w.p.) / Guttiferae	< 0	23
<i>Hypochaeris ciliata</i> (a.p.) / Compositae	< 0	< 0
<i>Ilex macropoda</i> (b.l.) / Aquifoliaceae	< 0	< 0
<i>Impatiens balsamina</i> (a.p.) / Balsaminaceae	2	9
<i>Impatiens noli-tangere</i> (a.p.) / Balsaminaceae	15	16
<i>Impatiens textori</i> (a.p.) / Balsaminaceae	< 0	< 0
<i>Imperata cylindrica</i> var. <i>koenigii</i> (w.p.) / Gramineae	< 0	< 0
<i>Indigofera kirilowii</i> (b.l.) / Leguminosae	11	4
<i>Inula britannica</i> var. <i>chinesis</i> (a.p.) / Compositae	< 0	< 0
<i>Iris ensata</i> var. <i>spontanea</i> (a.p.) / Araceae	< 0	< 0
<i>Iris ensata</i> var. <i>spontanea</i> (u.p.) / Araceae	< 0	4
<i>Iris nertschinskia</i> (w.p.) / Iridaceae	< 0	10
<i>Isodon excisus</i> (w.p.) / Labiatae	< 0	7
<i>Isodon japonicus</i> (a.p.) / Labiatae	11	7
<i>Isodon japonicus</i> (w.p.) / Labiatae	< 0	< 0
<i>Ixeris dentata</i> (a.p.) / Compositae	7	19
<i>Ixeris polycephala</i> (w.p.) / Compositae	2	16
<i>Juglans sinensis</i> (b.l.) / Juglandaceae	9	15
<i>Juniperus chinensis</i> (b.l.) / Cupressaceae	1	21
<i>Kalopanax pictus</i> (b.l.) / Araliaceae	13	< 0
<i>Kalopanax septemlobus</i> (cortex) / Araliaceae	14	< 0
<i>Kerria japonica</i> (b.l.) / Rosaceae	< 0	< 0
<i>Kummerowia stipulacea</i> (w.p.) / Leguminosae	4	16
<i>Kummerowia striata</i> (w.p.) / Leguminosae	12	22
<i>Kyllinga brevifolia</i> var. <i>leiolepis</i> (w.p.) / Cyperaceae	< 0	1
<i>Lactuca indica</i> var. <i>laciniata</i> for. <i>indivisa</i> (w.p.) / Compositae	10	4
<i>Lactuca triangulata</i> (w.p.) / Compositae	< 0	< 0
<i>Lathyrus davidii</i> (a.p.) / Leguminosae	< 0	< 0
<i>Lathyrus japonica</i> (a.p.) / Leguminosae	< 0	< 0
<i>Leonurus sibiricus</i> (a.p.) / Labiatae	< 0	< 0
<i>Lespedeza cuneata</i> (a.p.) / Leguminosae	8	11
<i>Lespedeza cyrtobotrya</i> (a.p.) / Leguminosae	1	< 0
<i>Lespedeza maximowiczii</i> (a.p.) / Leguminosae	19	56

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Lespedeza pilosa</i> (b.l.) / Leguminosae	21	10
<i>Lespedeza tetraloba</i> (a.p.) / Leguminosae	10	3
<i>Ligularia jaluensis</i> (a.p.) / Compositae	< 0	< 0
<i>Ligusticum tenuissimum</i> (radix) / Umbelliferae	23	23
<i>Ligustrum obusifolium</i> (b.l.) / Oleaceae	< 0	< 0
<i>Lilium tigrinum</i> (u.p.) / Liliaceae	< 0	< 0
<i>Lindera erythrocarpa</i> (b.l.) / Lauraceae	14	26
<i>Lindera obtusiloba</i> (b.l.) / Lauraceae	16	40
<i>Lindera strychnifolia</i> (radix) / Lauraceae	15	16
<i>Liriodendron tulipifera</i> (b.l.) / Magnoliaceae	14	31
<i>Liriope graminifolia</i> (tuber) / Liliaceae	4	< 0
<i>Liriope spicata</i> (w.p.) / Liliaceae	5	2
<i>Lobelia chinensis</i> (a.p.) / Campanulaceae	< 0	< 0
<i>Lonicera japonica</i> (caulis) / Caprifoliaceae	< 0	21
<i>Lonicera japonica</i> (flos) / Caprifoliaceae	17	< 0
<i>Loranthus parasiticus</i> (b.l.) / Loranthaceae	< 0	< 0
<i>Lycium chinense</i> (b.l.) / Solanaceae	6	9
<i>Lycium chinense</i> (fructus) / Solanaceae	< 0	< 0
<i>Lycium chinense</i> (radicis cortex) / Solanaceae	7	< 0
<i>Lycoris koreana</i> (a.p.) / liliaceae	1	21
<i>Lycoris squamigera</i> (u.p.) / Nymphaeaceae	< 0	< 0
<i>Lyndera erythrocarpa</i> (b.l.) / Lauraceae	6	21
<i>Lysimachia davurica</i> (w.p.) / Primulaceae	28	35
<i>Lythrum salicaria</i> (w.p.) / Lythraceae	26	7
<i>Maackia amurensis</i> (b.l.) / Leguminosae	18	13
<i>Machilus thunbergii</i> (cortex) / Lauraceae	6	33
<i>Magnolia kobus</i> (b.l.) / Magnoliaceae	< 0	< 0
<i>Magnolia liliflora</i> (flos) / Magnoliaceae	11	8
<i>Magnolia salicifolia</i> (b.l.) / Magnoliaceae	< 0	2
<i>Magnolia sieboldii</i> (b.l.) / Magnoliaceae	6	3
<i>Malus asiatica</i> (b.l.) / Rosaceae	3	13
<i>Malus baccata</i> (b.l.) / Rosaceae	< 0	6
<i>Malus pumila</i> var. <i>dulcissima</i> (b.l.) / Rosaceae	< 0	15
<i>Melampyrum roseum</i> (a.p.) / Scrophulariaceae	< 0	< 0
<i>Melandryum firmum</i> (w.p.) / Caryophylliaceae	< 0	< 0
<i>Melilotus suaveolens</i> (a.p.) / Leguminosae	15	26
<i>Mentha arvensis</i> (herba) / Labiatae	< 0	8
<i>Mentha arvensis</i> var. <i>piperascens</i> (w.p.) / Labiatae	17	3
<i>Metaplexis japonica</i> (a.p.) / Asclepiadaceae	< 0	< 0
<i>Microstegium vimineum</i> (w.p.) / Gramineae	1	< 0
<i>Mirabilis jalapa</i> (a.p.) / Nyctaginaceae	8	6
<i>Miscanthus sacchariflorus</i> (a.p.) / Compositae	1	13
<i>Miscanthus sinensis</i> (a.p.) / Gramineae	< 0	2
<i>Morus alba</i> (a.p.) / Moraceae	5	76
<i>Morus alba</i> (cortex) / Moraceae	12	70
<i>Mosla dianthera</i> (w.p.) / Labiatae	< 0	< 0
<i>Mosla punctulata</i> (w.p.) / Labiatae	< 0	9
<i>Nelumbo nucifera</i> (semen) / Nymphaeaceae	3	39

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Nicotiana tabacum</i> (a.p.) / Solanaceae	< 0	5
<i>Oenanthe javanica</i> (a.p.) / Umbelliferae	6	3
<i>Oenothera lamarckiana</i> (a.p.) / Oenotheraceae	< 0	41
<i>Oenothera lamarckiana</i> (u.p.) / Oenotheraceae	< 0	13
<i>Oenothera odorata</i> (w.p.) / Oenotheraceae	< 0	22
<i>Oplismanus undulatifolius</i> (w.p.) / Gramineae	< 0	10
<i>Orixa japonica</i> (a.p.) / Rutaceae	7	< 0
<i>Orostachys japonicus</i> (a.p.) / Pinaceae	17	9
<i>Osmunda japonica</i> (a.p.) / Osmundaceae	28	24
<i>Osterium sieboldii</i> (a.p.) / Ranunculaceae	< 0	< 0
<i>Pachyma hoelen</i> (sclerotia) / Polyporaceae	< 0	< 0
<i>Paederia scandens</i> (a.p.) / Rubiaceae	< 0	< 0
<i>Paeonia albiflora</i> (radix) / Ranunculaceae	< 0	14
<i>Paeonia suffruticosa</i> (cortex) / Paeoniaceae	30	32
<i>Panax ginseng</i> (radix) / Araliaceae	< 0	1
<i>Parthenocissus tricuspidata</i> (b.l.) / Vitaceae	6	41
<i>Patrinia scabiosaeifolia</i> (w.p.) / Valerianaceae	18	11
<i>Pedicularis resupinata</i> (w.p.) / Scrophulariaceae	2	< 0
<i>Perilla frutescens</i> (herba) / Labiatae	< 0	< 0
<i>Persicaria conspicua</i> (w.p.) / Polygonaceae	10	55
<i>Persicaria filiforme</i> (w.p.) / Polygonaceae	< 0	11
<i>Persicaria hydropiper</i> (w.p.) / Polygonaceae	10	13
<i>Persicaria lapathifolia</i> (a.p.) / Polygonaceae	7	4
<i>Persicaria perfoliata</i> (a.p.) / Polygonaceae	12	28
<i>Persicaria posumbu</i> var. <i>laxiflora</i> (a.p.) / Polygonaceae	18	35
<i>Persicaria senticosa</i> (a.p.) / Polygonaceae	3	8
<i>Persicaria sieboldii</i> (a.p.) / Polygonaceae	4	14
<i>Persicaria thunbergii</i> (w.p.) / Polygonaceae	9	< 0
<i>Persicaria viscosa</i> (w.p.) / Polygonaceae	< 0	11
<i>Petasites japonica</i> (w.p.) / Compositae	12	1
<i>Peucedanum japonicum</i> (a.p.) / Umbelliferae	3	3
<i>Peucedanum japonicum</i> (radix) / Umbelliferae	< 0	< 0
<i>Peucedanum praeruporum</i> (radix) / Umbelliferae	21	7
<i>Peucedanum terebinthaceum</i> (w.p.) / Umbelliferae	< 0	< 0
<i>Pharbitis nil</i> (a.p.) / Convolvulaceae	< 0	6
<i>Pharbitis nil</i> (semen) / Convolvulaceae	< 0	< 0
<i>Phaseolus nipponensis</i> (a.p.) / Leguminosae	7	5
<i>Phaseolus radiatus</i> (w.p.) / Leguminosae	22	5
<i>Phaseolus vulgaris</i> (a.p.) / Leguminosae	< 0	< 0
<i>Phellodendron amurense</i> (b.l.) / Rutaceae	< 0	7
<i>Phellodendron amurense</i> (cortex) / Rutaceae	25	20
<i>Philadelphus schrenckii</i> (b.l.) / Saxifragaceae	9	18
<i>Phlox paniculata</i> (a.p.) / Polemoniaceae	10	< 0
<i>Phlox subulata</i> (w.p.) / Polemoniaceae	< 0	< 0
<i>Phragmites communis</i> (a.p.) / Gramineae	< 0	< 0
<i>Phragmites japonica</i> (a.p.) / Gramineae	5	18
<i>Phryma leptostachya</i> var. <i>asiatica</i> (b.l.) / Phrymaceae	14	24

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Phthairospermum japonicum</i> (w.p.) / Scrophulariaceae	< 0	< 0
<i>Phyllostachys nigra</i> var. <i>henonis</i> (stem) / Gramineae	< 0	< 0
<i>Phyllostachys pubescens</i> (b.l.) / Gramineae	< 0	< 0
<i>Phyteuma japonicum</i> (a.p.) / Campanulaceae	< 0	< 0
<i>Phytolacca americana</i> (a.p.) / Phytolaccaceae	< 0	< 0
<i>Phytolacca esculenta</i> (radix) / Phytolaccaceae	6	1
<i>Picea abies</i> (b.l.) / Pinaceae	5	35
<i>Picrasoma altissima</i> (b.l.) / Simaroubaceae	14	31
<i>Picris hieracioides</i> var. <i>glabrescens</i> (w.p.) / Compositae	15	4
<i>Pilea mongolica</i> (a.p.) / Uriticaceae	< 0	< 0
<i>Pinellia ternata</i> (tuber) / Araceae	18	12
<i>Pinus densiflora</i> (b.l.) / Pinaceae	23	< 0
<i>Pinus koraiensis</i> (b.l.) / Pinaceae	< 0	4
<i>Pinus parviflora</i> var. <i>pentaphylla</i> (b.l.) / Pinaceae	< 0	< 0
<i>Pinus strobus</i> (b.l.) / Pinaceae	< 0	22
<i>Plantago asiatica</i> (semen) / Plantaginaceae	5	< 0
<i>Platanus occidentalis</i> (b.l.) / Platanaceae	10	35
<i>Platycarya strobilacea</i> (b.l.) / Juglandaceae	22	23
<i>Platycodon grandiflorum</i> (radix) / Campanulaceae	< 0	< 0
<i>Platycodon grandiflorum</i> (w.p.) / Campanulaceae	< 0	18
<i>Pleuropterus cilinervis</i> (a.p.) / Polygonaceae	27	30
<i>Pleuropterus multiflorum</i> (radix) / Polygonaceae	< 0	< 0
<i>Poa sphondylodes</i> (w.p.) / Gramineae	< 0	< 0
<i>Polygala tenuifolia</i> (radix) / Polygalaceae	< 0	4
<i>Polygonatum odoratum</i> var. <i>pluriflorum</i> (w.p.) / Liliaceae	< 0	7
<i>Polygonatum sibiricum</i> (a.p.) / Liliaceae	< 0	< 0
<i>Polygonatum sibiricum</i> (rhizoma) / Liliaceae	21	17
<i>Polygonum aviculare</i> (w.p.) / Polygonaceae	< 0	35
<i>Polystichum tripterum</i> (w.p.) / Aspidiaceae	< 0	< 0
<i>Poncirus trifoliata</i> (b.l.) / Rutaceae	4	24
<i>Poncirus trifoliata</i> (fructus) / Rutaceae	4	22
<i>Populus davidiana</i> (b.l.) / Salicaceae	12	15
<i>Populus maximowiczii</i> (b.l.) / Salicaceae	< 0	1
<i>Populus tomentiglandulosa</i> (b.l.) / Salicaceae	< 0	< 0
<i>Portulaca oleracea</i> (a.p.) / Portulacaceae	1	26
<i>Potentilla chinensis</i> (herba) / Rosaceae	18	28
<i>Potentilla chinensis</i> (u.p.) / Rosaceae	9	9
<i>Potentilla freyniana</i> (a.p.) / Rosaceae	10	19
<i>Potentilla paradoxa</i> (a.p.) / Rosaceae	21	< 0
<i>Prunella vulgaris</i> (herba) / Labiatae	< 0	28
<i>Prunus armeniaca</i> var. <i>ansu</i> (b.l.) / Rosaceae	< 0	< 0
<i>Prunus armeniaca</i> var. <i>ansu</i> (semen) / Rosaceae	11	4
<i>Prunus ishidoyana</i> (b.l.) / Cornaceae	< 0	18
<i>Prunus leveilleana</i> var. <i>pendula</i> (b.l.) / Rosaceae	< 0	< 0
<i>Prunus mume</i> (b.l.) / Rosaceae	18	28
<i>Prunus persica</i> (b.l.) / Rosaceae	10	< 0
<i>Prunus persica</i> (semen) / Rosaceae	3	8
<i>Prunus salicina</i> (b.l.) / Rosaceae	20	63

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Prunus sargentii</i> (b.l.) / Rosaceae	13	11
<i>Psoralea corylifolia</i> (semen) / Leguminosae	1	42
<i>Pteridium aquilinum</i> var. <i>latiusculum</i> (a.p.) / Polypodiaceae	18	1
<i>Pterocarya stenoptera</i> (b.l.) / Juglandaceae	6	98
<i>Pueraria thumbergiana</i> (a.p.) / Leguminosae	13	10
<i>Pueraria thumbergiana</i> (radix) / Leguminosae	2	8
<i>Pulsatilla koreana</i> (a.p.) / Ranunculaceae	< 0	< 0
<i>Quamoclit angulata</i> (a.p.) / Convolvulaceae	< 0	1
<i>Quamoclit pennata</i> (a.p.) / Convolvulaceae	< 0	2
<i>Quercus acutissima</i> (b.l.) / Fagaceae	< 0	< 0
<i>Quercus aliena</i> (b.l.) / Fagaceae	< 0	< 0
<i>Quercus mongolica</i> (b.l.) / Fagaceae	4	2
<i>Quercus dentata</i> (b.l.) / Fagaceae	19	19
<i>Ranunculus sceleratus</i> (a.p.) / Ranunculaceae	15	36
<i>Ranunculus tachiroei</i> (a.p.) / Ranunculaceae	< 0	< 0
<i>Ranunculus tachiroei</i> (u.p.) / Ranunculaceae	< 0	10
<i>Ranunculus chinensis</i> (a.p.) / Ranunculaceae	< 0	3
<i>Raphanus sativus</i> (semen) / Cruciferae	18	< 0
<i>Rehmannia glutinosa</i> (rhizoma) / Scrophulariaceae	1	6
<i>Reynoutria elliptica</i> (a.p.) / Polygonaceae	28	28
<i>Rhamnus davurica</i> (b.l.) / Rhamnaceae	29	14
<i>Rhapontica uniflora</i> (a.p.) / Compositae	< 0	17
<i>Rheum undulatum</i> (rhizoma) / Polygonaceae	< 0	57
<i>Rhododendron mucronulatum</i> (b.l.) / Ericaceae	15	18
<i>Rhododendron schlippenbachii</i> (a.p.) / Ericaceae	4	26
<i>Rhododendron yedoense</i> var. <i>poukha-nense</i> (b.l.) / Ericaceae	< 0	< 0
<i>Rhus chinensis</i> (b.l.) / Anacardiaceae	< 0	9
<i>Rhus verniciflua</i> (fructus) / Anacardiaceae	7	45
<i>Ricinus communis</i> (w.p.) / Euphorbiaceae	< 0	2
<i>Rorippa islandica</i> (w.p.) / Cruciferae	< 0	< 0
<i>Rosa laevigata</i> (fructus) / Rosaceae	28	17
<i>Rosa multiflora</i> (b.l.) / Rosaceae	< 0	14
<i>Rubia akane</i> (a.p.) / Rubiaceae	6	8
<i>Rubus coreanus</i> (fructus) / Rosaceae	< 0	< 0
<i>Rubus crataegifolius</i> (w.p.) / Rosaceae	< 0	10
<i>Rubus parvifolius</i> (a.p.) / Rosaceae	< 0	4
<i>Rubus phoenicolasius</i> (a.p.) / Rosaceae	< 0	< 0
<i>Rumex longifolius</i> (w.p.) / Polygonaceae	< 0	18
<i>Salix floderusii</i> (b.l.) / Salicaceae	< 0	< 0
<i>Salix gilgiana</i> (b.l.) / Salicaceae	< 0	< 0
<i>Salix glandulosa</i> (b.l.) / Salicaceae	1	11
<i>Salix hallaisanensis</i> (w.p.) / Salicaceae	< 0	< 0
<i>Salvia chanroenica</i> (w.p.) / Labiatae	< 0	18
<i>Salvia plebeia</i> (w.p.) / Labiatae	< 0	11
<i>Sambucus williamsii</i> var. <i>coreana</i> (b.l.) / Caprifoliaceae	< 0	10
<i>Sanguifolia officinalis</i> (w.p.) / Rosaceae	< 0	6
<i>Sanguisorba hakusanensis</i> (w.p.) / Rosaceae	< 0	< 0

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Sanguisorba longifolia</i> (a.p.) / Rosaceae	5	15
<i>Sanguisorba officinalis</i> (radix) / Rosaceae	< 0	23
<i>Sasa borealis</i> (a.p.) / Gramineae	< 0	< 0
<i>Saussurea lappa</i> (radix) / Compositae	< 0	< 0
<i>Saxifraga manshuriensis</i> (a.p.) / Saxifragaceae	< 0	< 0
<i>Schizandra chinensis</i> (semen) / Magnoliaceae	< 0	8
<i>Schizonepeta tenuifolia</i> (herba) / Labiatae	6	18
<i>Scirpus wichurai</i> (a.p.) / Cyperaceae	23	32
<i>Scrophularia buergeriana</i> (w.p.) / Scrophulariaceae	3	21
<i>Scrophularia ningpoensis</i> (radix) / Scrophulariaceae	6	4
<i>Scutellaria baicalensis</i> (a.p.) / Labiatae	12	6
<i>Scutellaria baicalensis</i> (radix) / Labiatae	14	6
<i>Secale cereale</i> (w.p.) / Gramineae	11	< 0
<i>Securinega suffruticosa</i> (b.l.) / Euphorbiaceae	15	31
<i>Sedum Zokuriense</i> (w.p.) / Crassulaceae	19	21
<i>Sedum aizoon</i> (w.p.) / Crassulaceae	< 0	12
<i>Sedum erythrostichum</i> (a.p.) / Crassulaceae	9	11
<i>Sedum sarmentosum</i> (w.p.) / Crassulaceae	< 0	3
<i>Sedum verticillatum</i> (a.p.) / Crassulaceae	< 0	< 0
<i>Senecio intergrifolius</i> var. <i>spathulatus</i> (w.p.) / Compositae	< 0	< 0
<i>Serratula coronata</i> var. <i>insularis</i> (w.p.) / Compositae	< 0	14
<i>Sesamum indicum</i> (w.p.) / Pedaliaceae	15	15
<i>Setaria chodrachne</i> (w.p.) / Gramineae	< 0	< 0
<i>Setaria glauca</i> (w.p.) / Gramineae	< 0	4
<i>Setaria viridis</i> (a.p.) / Gramineae	18	8
<i>Siegesbeckia glabrescens</i> (a.p.) / Compositae	11	< 0
<i>Siegesbeckia pubescens</i> (a.p.) / Compositae	1	4
<i>Silene armeria</i> (a.p.) / Caryophyllaceae	< 0	< 0
<i>Siphonostegia chinensis</i> (a.p.) / Scrophulariaceae	< 0	2
<i>Sium sauve</i> (a.p.) / Umbelliferae	< 0	8
<i>Smilax china</i> (u.p.) / Liliaceae	15	13
<i>Smilax sieboldii</i> (b.l.) / Liliaceae	< 0	< 0
<i>Solanum nigrum</i> (herba) / Solanaceae	< 0	< 0
<i>Sophora flavescens</i> (a.p.) / Leguminosae	12	8
<i>Sophora flavescens</i> (fructus) / Leguminosae	< 0	< 0
<i>Sophora japonica</i> (fructus) / Leguminosae	< 0	< 0
<i>Sparganium stoloniferum</i> (rhizoma) / Sparganiaceae	< 0	12
<i>Spiraea blumei</i> (b.l.) / Rosaceae	< 0	12
<i>Spiraea japonica</i> (b.l.) / Rosaceae	4	17
<i>Spiraea prunifolia</i> (b.l.) / Rosaceae	23	15
<i>Spiraea salicifolia</i> (b.l.) / Rosaceae	10	24
<i>Staphylea bumalda</i> (b.l.) / Staphyleaceae	6	1
<i>Stellaria alsine</i> var. <i>undulata</i> (w.p.) / Caryophyllaceae	13	3
<i>Stellaria aquatica</i> (a.p.) / Caryophyllaceae	< 0	12
<i>Stephania tetrandra</i> (radix) / Menispermaceae	9	< 0
<i>Stephandra incisa</i> (b.l.) / Rosaceae	2	2
<i>Stewartia koreana</i> (b.l.) / Theaceae	< 0	< 0
<i>Streptolirion cordifolium</i> (a.p.) / Commelinaceae	< 0	18

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Styrax japonica</i> (b.l.) / Styracaceae	8	13
<i>Styrax obassia</i> (b.l.) / Styracaceae	30	34
<i>Symphytum officinale</i> (a.p.) / Boraginaceae	< 0	< 0
<i>Symplocos chinensis</i> for. <i>pilosa</i> (b.l.) / Symplocaceae	11	< 0
<i>Syneilesis palmata</i> (w.p.) / Compositae	5	< 0
<i>Synurus exelsus</i> (a.p.) / Compositae	< 0	< 0
<i>Syringa woifii</i> (b.l.) / Oleaceae	< 0	< 0
<i>Taraxacum mongolicum</i> (herba) / Compositae	< 0	< 0
<i>Taraxacum platycarpum</i> (w.p.) / Compositae	6	< 0
<i>Taxus cuspidata</i> (b.l.) / Taxaceae	< 0	17
<i>Teucrium japonicum</i> (a.p.) / Labiatae	5	< 0
<i>Thalictrum aquilegifolium</i> (w.p.) / Ranunculaceae	< 0	2
<i>Thalictrum filamentosum</i> var. <i>tenerum</i> (a.p.) / Ranunculaceae	29	17
<i>Thalictrum minus</i> var. <i>hypoleucum</i> (a.p.) / Ranunculaceae	1	16
<i>Thuja orientalis</i> (b.l.) / Cupressaceae	< 0	22
<i>Torilis japonica</i> (b.l.) / Umbelliferae	7	30
<i>Tradescantia reflexa</i> (w.p.) / Commelinaceae	< 0	14
<i>Trichosanthes kirilowii</i> (a.p.) / Cucurbitaceae	< 0	< 0
<i>Trichosanthes kirilowii</i> (radix) / Liliaceae	< 0	< 0
<i>Trichosanthes kirilowii</i> (semen) / Cucurbitaceae	< 0	< 0
<i>Trifolium repens</i> (a.p.) / Leguminosae	< 0	8
<i>Trigonotis peduncularis</i> (w.p.) / Boraginaceae	12	27
<i>Tussilago fartara</i> (w.p.) / Compositae	< 0	3
<i>Ulmus davidiana</i> (b.l.) / Ulmaceae	3	27
<i>Ulmus parvifolia</i> var. <i>coreana</i> (b.l.) / Ulmaceae	< 0	< 0
<i>Uncaria rhynchophylla</i> (ramulus) / Rubiaceae	9	24
<i>Urtica angustifolia</i> (a.p.) / Urticaceae	3	< 0
<i>Vaccinium koreanum</i> (b.l.) / Ericaceae	< 0	< 0
<i>Veronica persica</i> (a.p.) / Scrophulariaceae	< 0	< 0
<i>Veronicastrum sibiricum</i> (a.p.) / Scrophulariaceae	< 0	24
<i>Viburunum sargentii</i> (b.l.) / Caprifoliaceae	< 0	< 0
<i>Vicia amoena</i> (a.p.) / Leguminosae	14	< 0
<i>Vicia bungei</i> (a.p.) / Leguminosae < 0	< 0	
<i>Vinca major</i> (w.p.) / Apocynaceae	< 0	< 0
<i>Viola patrinii</i> (w.p.) / Violaceae	< 0	< 0
<i>Viola verecunda</i> (w.p.) / Violaceae	< 0	< 0
<i>Viola yedoensis</i> (w.p.) / Violaceae	< 0	< 0
<i>Vitex rotundifolia</i> (fructus) / Verbenaceae	32	30
<i>Vitis amurensis</i> (a.p.) / Vitaceae	18	98
<i>Vitis coignetiae</i> (b.l.) / Vitaceae	3	55
<i>Weigela subsessilis</i> (b.l.) / Caprifoliaceae	10	28
<i>Wistaria floribunda</i> (b.l.) / Leguminosae	5	8
<i>Xanthium strumarium</i> (folium) / Compositae	< 0	12
<i>Youngia denticulata</i> (w.p.) / Compositae	2	14
<i>Youngia japonica</i> (a.p.) / Compositae	5	18
<i>Youngia smalliana</i> (a.p.) / Liliaceae	< 0	2
<i>Yungia chelidonifolia</i> (w.p.) / Compositae	< 0	< 0

Table 1. Continued

Plant (part of use) / Family	% of Inhibition	
	10 µg/ml	100 µg/ml
<i>Zanthoxylum bungeanum</i> (pericarpium) / Rutaceae	< 0	7
<i>Zanthoxylum schinifolium</i> (b.l.) / Rutaceae	2	26
<i>Zingiber officinale</i> (rhizoma) / Zingiberaceae	< 0	< 0
<i>Zizyphus vulgaris</i> var. <i>inermis</i> (fructus) / Rhamnaceae	11	< 0
<i>Zizyphus vulgaris</i> var. <i>spinosa</i> (semen) / Rhamnaceae	< 0	6

Inhibitory effects on COX activity are represented as % of inhibition compared to the control, where sample was treated at 10 µg/ml or 100 µg/ml as the final concentration. Abbreviations are aerial part (a.p.), branch and leaf (b.l.), underground part (u.p.), and whole plant (w.p.).

Table 2. Inhibition on COX activity by solvent-fractionated extracts.

Plant (part of use)	dose (µg/ml)	% of inhibition			
		MC	EtOAc	BuOH	Residue
<i>Carex humilis</i> (u.p.)	100	28 ± 1*	95 ± 1*	27 ± 3*	< 0
<i>Celastrus orbiculatus</i> (b.l.)	100	19 ± 4*	75 ± 2*	23 ± 3*	< 0
<i>Eugenia caryophyllata</i> (flos)	100	88 ± 1*	19 ± 6*	10 ± 4*	< 0
<i>Gleditsia japonica</i> var. <i>koraiensis</i> (b.l.)	100	48 ± 6*	28 ± 5*	20 ± 2*	< 0
<i>Glycyrrhiza uralensis</i> (radix)	100	83 ± 1*	76 ± 2*	33 ± 3*	11 ± 4
	50	63 ± 1*	58 ± 3*	21 ± 2*	< 0
<i>Morus alba</i> (cortex)	100	73 ± 3*	73 ± 3*	48 ± 2*	1 ± 4
	50	55 ± 2*	62 ± 1*	27 ± 1*	1 ± 1
<i>Persicaria conspicua</i> (w.p.)	100	55 ± 2*	83 ± 2*	49 ± 6*	14 ± 2
	50	31 ± 2*	60 ± 2*	35 ± 2*	3 ± 2
<i>Prunus salicina</i> (b.l.)	100	7 ± 2*	24 ± 4*	21 ± 2*	6 ± 3
<i>Pterocarya stenoptera</i> (b.l.)	100	47 ± 5*	8 ± 7*	10 ± 4*	6 ± 3
<i>Rheum undulatum</i> (rhizoma)	100	58 ± 3*	73 ± 3*	43 ± 3*	< 0
	50	24 ± 4*	60 ± 2*	31 ± 3*	< 0
<i>Vitis amurensis</i> (a.p.)	100	84 ± 3*	50 ± 3*	40 ± 3*	5 ± 2
	50	38 ± 1*	44 ± 2*	15 ± 2*	7 ± 2

The herbal extracts were sequentially fractionated with methylene chloride (MC), ethyl acetate (EtOAc), and then *n*-butanol (BuOH). The residue is an aqueous layer after *n*-butanol extraction. Data are represented as mean ± standard error, and significance of them is $p < 0.01$ (*). The sample was treated with 50 µg/ml or 100 µg/ml as the final concentration. Abbreviations are aerial part (a.p.), branch and leaf (b.l.), underground part (u.p.), and whole plant (w.p.).

conspicua, branch and leaf of *Prunus salicina*, branch and leaf of *Pterocarya stenoptera*, rhizoma of *Rheum undulatum*, aerial part of *Vitis amurensis*, and branch and leaf of *Vitis coignetiae*.

Some of the active extracts were subjected to further sequential fractionation with methylene chloride, ethyl acetate, *n*-butanol, and polar residue. Inhibitory effects of each of the solvent fractions on COX activity were estimated (Table 2). Ethylacetate fractions of *Carex humilis*, *Celastrus orbiculatus*, *Persicaria conspicua* and *Rheum undulatum*

exhibited their highest inhibition on COX. Methylene chloride fractions of *Eugenia caryophyllata* and *Vitis amurensis* and both methylene chloride and ethyl acetate fractions of *Glycyrrhiza uralensis* and *Morus alba* showed highest activity, *Gleditsia japonica* var. *koraiensis*, *Prunus salicina*, and *Pterocarya stenoptera* seem to be significantly reduced in their inhibitory effects on COX by the sequential solvent fractionation. None of the extracts exhibited more than 50% of inhibition in their *n*-butanol and polar residue fractions at the concentration of

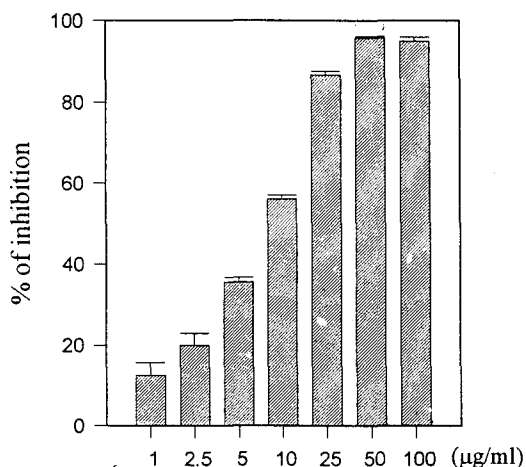


Fig. 2. Dose-dependent inhibition on COX activity by the ethyl acetate fraction of underground part of *Carex humilis*.

100 µg/ml. The highest inhibition on COX activity was identified in the ethyl acetate fraction of *Carex humilis* among the solvent fractions of 11 herbal extracts in this study.

The ethyl acetate fraction of *Carex humilis* exhibited dose-dependent inhibition on the enzyme activity as shown in Fig. 2., where 50% of inhibition (IC_{50}) was identified at about 10 µg/ml. To identify the inhibitor(s) on COX activity, activity-directed fractionations of heral extract prepared from underground part of *Carex humilis* (Cyperaceae) are now in progress.

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