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Induction of Quinone Reductase, an Anticarcinogenic Marker Enzyme, by Medicinal Herb Extracts

Chong-Suk Kwon*, Ji Hyeon Kim*, Kun Ho Son*, Young-Kyoon Kim, Jeong Soon Lee, Jin Kyu Lim and Jong-Sang Kim†**

Department of Animal Science and Biotechnology, Kyungpook National University, Daegu 702-701, Korea
**Department of Food Science and Nutrition, Andong National University, Andong 760-749, Korea*
***Department of Forest Resources, Kookmin University, Seoul 136-702, Korea*

Abstract

To search for novel cancer preventive agents, we assessed the quinone reductase (QR)-inducing activities of medicinal herb extracts in cultured murine hepatoma cells (hepa1c1c7 cells). Among 216 herb extracts tested in this study, 8 kinds of herbal extracts were found to induce QR activity in hepa1c1c7 cells by more than 2-fold when used at the concentration of 25 μg/mL. The methanol extracts of *Aster koraiensis* NK and *Pulsatilla koreana* Nakai induced QR by 252 and 223%, respectively, at the concentration of 25 μg/mL. Most of the herbal extracts with QR inducing-activity increased the enzyme activity in a typical dose-dependent manner. The QR activity in BP^{r}c1 cells was induced more than 50% by the extracts of *Pulsatilla koreana* Nakai, *Inula helenium, Physalis alkekengi var. francheti (Masters)* Makino, *Chrysanthemum zawadskii var. latilobum* Kitamura, *Artemisia keiskeana* Miquel, *Chrysanthemum boreale* Makino. In conclusion, *Pulsatilla koreana* Nakai, *Aster koraiensis* N.K, and *Chrysanthemum zawadskii var. latilobum* Kitamura, which showed relatively high QR induction, merit further animal study to evaluate their potential as cancer preventive agents.

Key words: medicinal herb, quinone reductase, cancer prevention, hepa1c1c7, BP^{r}c1

INTRODUCTION

Induction of phase 2 enzymes such as quinone reductase (QR; NAD(P)H:(quinone-acceptor) oxidoreductase (EC1.6.99.2)), and glutathione S-transferase (GST) is closely associated with the prevention of chemical carcinogenesis (1). Phase 2 enzymes are involved in detoxification of carcinogens, bioactiviation of some anticancer drugs, stabilization of tumor suppressor(s), and prevention of oxidative damage caused by various chemicals. Accordingly, there has been considerable interest in screening natural products for their capacity to induce quinone reductase activity, and many diverse chemical agents such as oxidizable diphenols, isothiocyanates, and even hydrogen peroxide have been found to do so (2). Thus it is anticipated that the plant kingdom may be a rich source of QR inducers awaiting discovery. Biochemical studies have already demonstrated that the NQO1 gene, encoding QR, contains 2 distinct regulatory elements in its 5′-flanking region, one of which is an antioxidant responsive element (ARE), also called the EpRE (electrophile response element), and the other a xenobiotic response element (XRE) called the AhRE. QR induction through the XRE involves the binding of a ligand to the aromatic hydrocarbon receptor, AHR. The aryl hydrocarbon (Ah) receptor (AhR) is a member of the basic helix-loop-helix PER-ARNT-SIM (PAS) transcription factor family and translocates to the nucleus upon binding to Arnt (3). The AHR/Arnt dimer interacts with the DNA sequences known as XREs to regulate QR expression. Both NQO1 and CYP1A1 genes can be induced by TCDD and polycyclic aromatic hydrocarbons, while the induction of NQO1 is largely dependent upon the ability of bifunctional inducers such as dye, Sudan I and β-naphthoflavone to first undergo conversion to oxidative labile metabolites through a functional P450-dependent mechanism. However, it seems that some compounds, known as monofunctional inducers, induce only QR without affecting the expression of phase I enzymes. It is known that some pro-carcinogens, such as benzo(a) pyrene, are ultimately converted into carcinogenic agents by the action of phase I enzymes. Accordingly, BP^{r}c1 cells, a mutant defective in *Ah* receptor function, may be a good model system for screening for substances that induce phase II enzymes alone. The 1,2-dithiol-3-thiones, a class of five-membered cyclic sulfur compounds which have chemotherapeutic and chemoprotective properties, have been reported to elevate quinone reductase and glutathione levels in BP^{r}c1 cells as well as hepa1c1c7

†Corresponding author. E-mail: vision@knu.ac.kr
Phone: +82-53-950-5752, Fax: +82-53-950-6750

ells (2).

This study was performed to investigate the cancer preventive potential of some medicinal herbal extracts by valuating their QR inducting activity in both mouse epatoma cells (hepa1c1c7) and its mutant (BP^rc1).

MATERIALS AND METHODS

Materials

All cell culture reagents and fetal bovine serum were obtained from Gibco BRL (Gaitherburg, MD, USA). Hepa1c1c7 and BP^rc1 cells were from American Type Culture Collection (Rockville, MD, USA). All other chemicals were of reagent grade.

Preparation of herbal extract

Ten grams of each dried herb was extracted with 100 mL methanol at room temperature overnight, and extract was evaporated *in vacuo* to yield a residue. The dry extract was stored at -70°C and re-dissolved in dimethylsulfoxide (DMSO) prior to use.

Cell culture

Hepa1c1c7 and its mutant (BP^rc1) cells were plated at density of 3×10^5 or 5×10^5 cells/plate in 10 mL of α-MEM supplemented with 10% FBS. The plates were incubated for 3~4 days in a humidified incubator in 5% CO_2 at 37°C. Cells were cultured for 48 hrs, followed by exposure to various concentrations of herbal extract for another 24 hrs.

Enzyme assays

QR activity was measured by a spectrophotometric assay in which the rate of reduction of 2,6-dichlorophenolindophenol was monitored at 600 nm (4). Briefly, cells were plated, grown, and exposed to different concentrations of herbal extract for 24 hr before harvesting. The cells were washed with ice-cold 0.15 M KCl-10 mM potassium phosphate (pH 7.4), removed from the plates by scraping with rubber policeman, and disrupted for 5 sec using an ultrasonic cell disrupter (50W, Kontes, Vineland, NJ, USA). Cell homogenates were centrifuged at 12,000 rpm for 5 min in a microcentrifuge (VS-15000 CFN11, Vision, Seoul, Korea). QR activity was assayed by measuring the rate of oxidation of 2,6-dichlorophenolindophenol at 600 nm in the assay system containing 25 mM Tris-HCl (pH 7.4), 0.7 mg crystalline bovine serum albumin at pH 7.4, 0.01% Tween 20, 5 µM FAD, 0.2 mM NADH, 0 or 10 µM dicoumarol, and 200 µL cell extract in a final volume of 3.0 mL. QR induction was expressed as the ratio of the QR activity (2,6-dichlorophenolindophenol reduced/min) in the presence and absence of the assay sample.

RESULTS

A number of studies have suggested that the induction of phase 2 detoxification enzymes such as QR is a relevant mechanism for cancer prevention (1-5). This study evaluated the QR induction activities of 216 kinds of medicinal herbs growing on Korean peninsula. Among the 216 herbal extracts tested in this study, 45 induced QR activity in hepa1c1c7 cells by more than 30% at the concentration of 25 µg/mL (Table 1). In particular, *Aster koraiensis* N.K, *Pulsatilla koreana* Nakai, *Dendrobium moniliforme (L.) Sw., Anglelica gigas, Physalis alkekengi var. francheti (Masters)* Makino, *Chrysanthemum zawadskii var. latilobum* Kitamura, *Chrysanthemum indicum* L., and *Artemisia keiskeana* Miquel showed 2-fold or higher induction ratio of the enzyme. These herbal extracts caused QR induction in a typical dose-dependent manner. For instance, the methanol extracts of *Aster koraiensis* N.K at 10, 25, 50 µg/mL induced QR activity by 172, 226, 249% relative to control, respectively (Fig. 1).

The 45 herbal extract that exhibited significant QR induction in hepa1c1c7 cells were then evaluated for QR induction activity in BP^rc1 cells defective in the aryl hydrocarbon nuclear translocator (Arnt). QR activity in BP^rc1 cells was significantly induced by 13 of the herbal extracts including: *Aster koraiensis* N.K, *Pulsatilla koreana* Nakai, *Dendrobium moniliforme* L.Sw., *Inula helenium, Physalis alkekengi var. francheti* (Masters) Makino, *Chrysanthemum zawadskii var. latilobum* Kitamura, *Cichorium intybus* L., *Chrysanthemum indicum* L., *Artemisia keiskeana* Miquel, *Artemisia melini, Xanthium strumarium* L., *Inula*

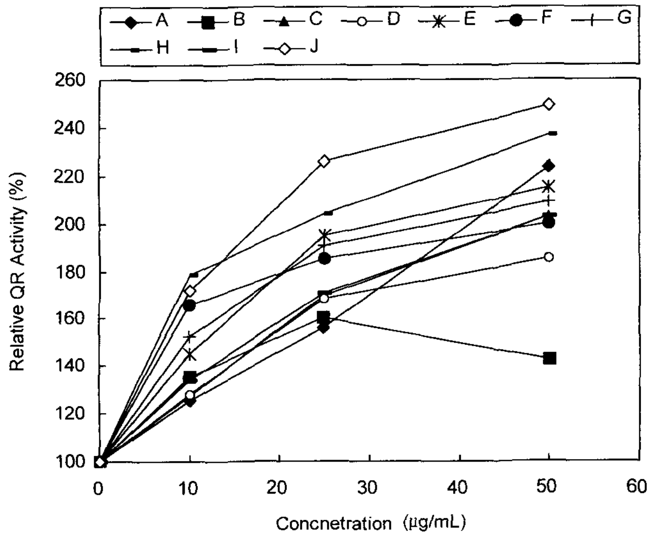


Fig. 1. Dose-response relationship of QR activity in hepa1c1c7 cells. Cells were exposed to different concentrations of herbal extracts for 24 hrs prior to QR assay.
A: *Physalis alkekengi var. francheti* (Masters) Makino, B: *Pulsatilla koreana* Nakai, C: *Chrysanthemum zawadskii var. latilobum* Kitamura, D: *Inula helenium*, E: *Chrysanthemum indicum* L., F: *Angelica gigas*, G: *Artemisia keiskeana* Miquel, H: *Xanthium strumarium* L., I: *Forsythiae fructus*, J: *Aster koraiensis* N.K.

Table 1. Quinone reductase induction in hepa1c1c7 and BP^{r}c1 cells by methanol extracts from medicinal herbs[1)]

Sample (methanol extract)	Part used	% QR Induction	
		Hepa1c1c7	BP^{r}c1
Acanthopanax sessiliflorus (R.M) Seem	leaf	47.14	
Acanthopanax sessiliflorus (R.M) Seem	fruit	49.47	
Achillea sibirica Ledeb	whole	147.26	
Achyranthes japonica (Miq). N.	aerial part	122.46	
Aconitium carmichaehi	whole	105.83	
Acorus calamus L.	leaf	90.24	
Actinidia arguta Planch	leaf	129.22	
Adenophora triphylla var. j.H	root	111.51	
Agastache rugosa (Fisch. et Meyer) O.K.	aerial part	117.38	
Agrimonia pilosa Ledeb	whole	103.32	
Akebia quinata Decne	leaf	108.11	
Allium senescens L.	whole	113.30	
Allium thunbergi G. Don	whole	103.48	
Allium thunbergi G. Don	leaf	123.76	
Allium tuberosum Roth	whole	107.14	
Allium victorialis L. var. platyphyllum H.M.	root	85.03	
Althaea rosea L.C.	whole	127.61	
Aneilema keisak	whole	138.91	97.82
Anemarrhena asphodeloides Bunge	whole	102.80	
Angelica dahurica (Fisch.) Benth. et Hooker f.	whole	127.22	
Angelica gigas	fruit	232.50	122.09
Angelica tenuissima Nakai	whole	157.39	
Anglelica autiloba	leaf	126.19	
Anglelica gigas	whole	122.02	
Anglelica gigas	leaf	149.91	
Aquilegia buergeriana S. et Z. var. O.K.	whole	104.96	
Aralia continentalis Kitagawa	fruit	142.77	120.82
Aralia continentalis Kitagawa	leaf	124.50	
Aralia continentalis Kitagawa	seed	116.81	
Aralia elata	leaf	83.79	
Arctium lappa L.	aerial part	115.95	
Arisaema amurense Max. for. serratum K.N.	fruit	94.20	
Artemisia capillaris Thunb.	whole	134.26	100.84
Artemisia keiskeana Miquel	whole	205.77	156.49
Artemisia melini	aerial part	147.43	143.49
Artemisia princeps var. orientalis	aerial part	107.44	
Artemissiae capillaris Herba	leaf	127.22	
Aruncus dioicus (Walt.) Fern var. K.H.	whole	64.77	
Asparagi Tuber	whole	118.84	
Asparagus oligoclonos Max	stem	96.09	
Asparagus oligoclonos Max	whole	120.09	
Aster koraiensis N.K.	whole	252.37	143.61
Aster scaber Thunb.	whole	108.50	
Aster tataricus L.	whole	128.80	
Astragalus membranaceus	whole	144.50	
Atractylodes japonica Koidz	whole	123.33	
Belamcanda chinensis L.DC.	fruit	103.39	
Campsis grandiflora (Thunb.) K. Schumann	leaf	112.78	
Canavalia gladiata DC.	aerial part	107.32	
Canavalia gladiata DC.	fruit	91.72	
Caragana sinica	whole	107.35	

Table 1. Continued

Sample (methanol extract)	Part used	% QR Induction	
		Hepa1c1c7	BP^rc1
Cassia tora L.	whole	113.19	
Cassiae Semen	aerial part	140.26	76.82
Cedrela sinensis A. Juss.	leaf	86.97	
Chelidonium majus var. asiaticum (Hara) Ohw	whole	131.34	70.18
Chloranthus japonicus Sieb	aerial part	122.79	
Chrysanthemum boreale (Makino) Makino	whole	145.88	159.78
Aralia elata	leaf	83.79	
Arctium lappa L.	aerial part	115.95	
Arisaema amurense Max. for. serratum K.N.	fruit	94.20	
Artemisia capillaris Thunb.	whole	134.26	100.84
Artemisia keiskeana Miquel	whole	205.77	156.49
Artemisia melini	aerial part	147.43	143.49
Artemisia princeps var. orientalis	aerial part	107.44	
Artemissiae capillaris Herba	leaf	127.22	
Aruncus dioicus (Walt.) Fern var. K.H.	whole	64.77	
Asparagi Tuber	whole	118.84	
Asparagus oligoclonos Max	stem	96.09	
Asparagus oligoclonos Max	whole	120.09	
Aster koraiensis N.K.	whole	252.37	143.61
Aster scaber Thunb.	whole	108.50	
Aster tataricus L.	whole	128.80	
Astragalus membranaceus	whole	144.50	
Atractylodes japonica Koidz	whole	123.33	
Belamcanda chinensis L.DC.	fruit	103.39	
Campsis grandiflora (Thunb.) K. Schumann	leaf	112.78	
Canavalia gladiata DC.	aerial part	107.32	
Canavalia gladiata DC.	fruit	91.72	
Caragana sinica	whole	107.35	
Cassia tora L.	whole	113.19	
Cassiae Semen	aerial part	140.26	76.82
Cedrela sinensis A. Juss.	leaf	86.97	
Chelidonium majus var. asiaticum (Hara) Ohw	whole	131.34	70.18
Chloranthus japonicus Sieb	aerial part	122.79	
Chrysanthemum boreale (Makino) Makino	whole	145.88	159.78
Chrysanthemum cinerariae folium	whole	103.57	
Chrysanthemum indicum L.	aerial part	211.73	130.92
Chrysanthemum zawadskii var. latilobum Kitamura	whole	204.76	171.72
Cichorium intybus L.	whole	140.27	154.38
Cirsium japonicum	whole	70.46	
Cnidium officinale	aerial part	133.88	88.38
Codonopsis pilosula (Fr.) Nannf.	aerial part	105.15	
Coix lacryma-jobi L. var. M.S	aerial part	119.92	
Commelina communis L.	flower	115.60	
Commelina communis L.	leaf	100.16	
Convallaria keiskei Miq	whole	72.57	
Convallaria keiskei Miq	root	81.43	
Cyperi rotundus	whole	83.36	
Cyperus rotundus	seed	103.78	
Dendrobium moniliforme (L.) Sw.	whole	206.26	141.75
Dianthus chinensis L.	whole	114.97	
Dianthus superbus var. I.W.	aerial part	118.09	

Table 1. Continued

Sample (methanol extract)	Part used	% QR Induction	
		Hepa1c1c7	BP^rc1
Dictamnus dasycarpus Turcz	whole	126.59	
Dioscorea batatas Decne.	leaf	55.05	
Dioscorea nipponica Makino	aerial part	134.30	69.86
Disporum sessile subsp. Flavens kitagawa	whole	131.05	
Duchesnea chrysantha (Zoll. et Morr.) Miq.	aerial part	120.73	
Ecinopsis setifer Iijin	whole	129.94	
Elsholtzia splendes	whole	99.96	
Epomedium koreanum Nakai	aerial part	104.94	
Equisetum hyemale L.	whole	114.17	
Euphorbia pekinensis	stem	95.02	
Euphorbia pekinensis	leaf	118.99	
Ficus carica L.	leaf	113.15	
Ficus carica L.	aerial part	144.14	72.57
Foeniculi vulgare	aerial part	107.46	
Foeniculum vulgare	aerial part	108.99	
Forsythiae Fructus	whole	181.12	144.55
Galium verum var. *asiaticum* Nakai	whole	133.15	66.60
Geranium sibiricum L.	whole	137.61	111.04
Geranium sibiricum L.	aerial part	110.67	
Geum japonicum Thunb.	aerial part	104.42	
Glycyrrhizae Radix	seed	161.25	108.54
Glycyrrhizae uralensis	whole	118.22	
gondrea	aerial part	103.57	
Gossypium indicum Lam.	leaf	118.40	
Gynostemma pentaphyllum	leaf	83.53	
Hemerocallis fulva L.	whole	148.66	132.38
Hemerocallis fulva L.	root	75.32	
Hemerocallis fulva var. kwanso Regel	whole	104.68	
Hemerocallis lilioasphodelus	whole	108.20	
Hemerocallis lilioasphodelus	root	111.21	
Hibiscus manihot L.	flower	108.62	
Hibiscus manihot L.	leaf	87.10	
Hibiscus manihot L.	whole	104.52	
Hibiscus manihot L.	aerial part	96.74	
Hibiscus manihot L.	fruit	117.28	
Hibiscus mutabilis L.	whole	76.73	
Hosta lancifolia	leaf	91.44	
Hosta plantaginea Aschers	whole	96.26	
Houttuynia cordata Thunb	aerial part	89.44	
Impatiens textori Miquel	aerial part	98.93	
Inula britannica var. chinensis Regel	aerial part	87.81	
Inula helenium	aerial part	191.77	166.02
Inula helenium	whole	153.22	168.37
Iris koreana Nakai	whole	96.16	
Iris pallassii Fischer var. C.F.	leaf	85.07	
Iris sanguinea Hornem	whole	133.05	93.26
Ixeridium dentatum T.T.	whole	151.03	117.52
Ixeris dentata (Thunb.) Nakai	whole	109.54	
Jasminum nudiflorum Lindl	aerial part	117.41	
Leonurus sibiricus L.	whole	110.00	
Leonurus sibiricus L.	aerial part	92.97	

Table 1. Continued

Sample (methanol extract)	Part used	% QR Induction	
		Hepa1c1c7	$BP^{r}c1$
Ligularia fischeri (Ledeb.) Turcz	leaf	91.20	
Ligusticum chuanxiong	whole	124.65	
Lilium leichtlinii	whole	126.99	
Lilium tigrinum Ker-Gawi.	aerial part	115.51	
Liriope platyphylla Wang et Tang	leaf	128.71	
Liriope platyphylla Wang et Tang	whole	94.98	
Liriope platyphylla Wang et Tang L.	fruit	67.21	
Lonicera japonica Thunb	aerial part	100.83	
Lonicera japonica Thunb	fruit	99.91	
Lotus corniculatus var. japonicus	whole	136.34	85.33
Lycium chinense Miller	aerial part	141.99	98.57
Lycium chinense Miller	fruit	104.89	
Lycium chinense Miller	leaf	95.42	
Lysimachia barystachys Bunge	aerial part	86.94	
Lysimachia davurica	whole	120.86	
Menispermum dauricum DC.	aerial part	115.88	
Mentha arvensis var. piperascens Malinv	whole	112.09	
Menthae Herba	whole	110.94	
Metaplexis japonica (Thunb.) Makino	aerial part	144.63	118.77
Morus bombysis	leaf	111.01	
Oenothera odorata Jacq.	whole	112.59	
Osmunda japonica Thunb.	aerial part	109.84	
Ostericum koreanum (Max.) Kitagawa	whole	91.29	
Paeonia suffruticosa Andrews	whole	124.37	
Paeonia suffruticosa Andrews	flower	162.57	88.18
Patarinia scabiosaefolia Fischer	whole	122.70	
Patrinia villosa (Thunb.) Juss	whole	121.60	
Perilla frutescens	whole	141.02	
Persicaria filiformis T.N.	aerial part	113.13	
Petasites japonicus (Sieb. et Zucc.) Maxim	whole	113.85	
Peucedanum japonicum	whole	136.49	122.35
Peucedanum japonicum T.	leaf	142.04	77.46
Physalis alkekengi	whole	83.99	
Physalis alkekengi var. francheti (Masters) Makino	leaf	233.79	197.79
Phytolacca americana L.	aerial part	116.99	
Pimpinella brachycarpa K.N.	aerial part	121.15	
Plantago asiatica L.	whole	104.45	
Plantago asiatica L.	aerial part	97.52	
Plantago asiatica L.	seed	101.22	
Platycodon grandiflorum J.A.DC	whole	124.42	
Pleuroptems multiflorus Turez	whole	124.86	
Pleuropterus multiflorus Turez.	leaf	101.22	
Polyganatum stenophyllum	root	88.39	
Polygonatum stenophyllum	whole	100.69	
Polygonatum stenophyllum	root	100.53	
Polymni sonchifolia	leaf	122.00	
Potentilla discolor Bunge	flower	104.37	
Pteridium aquilinum var. latiusculum	whole	125.13	
Pulsatilla koreana Nakai	whole	223.72	183.08
Rehmanniae glutinosa	leaf	103.01	
Reynoutria elliptica (Koidz.) Migo	leaf	93.10	

Table 1. Continued

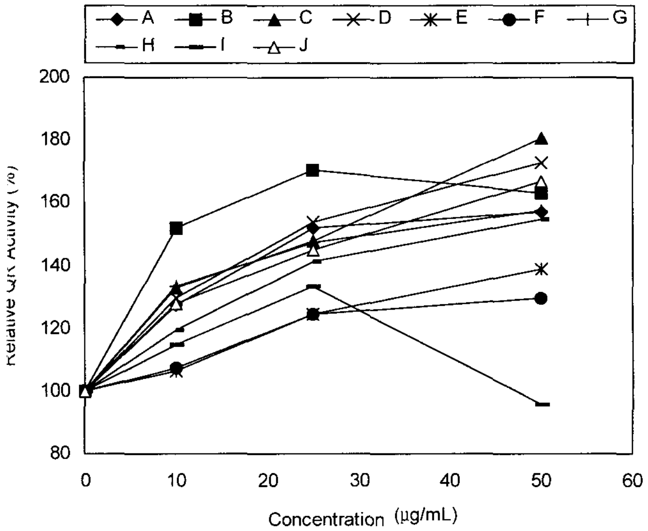
Sample (methanol extract)	Part used	% QR Induction	
		Hepa1c1c7	BP[r]c1
Reynoutria elliptica (Koidz.) Migo	leaf	110.75	
Reynoutria elliptica (Koidz.) Migo	root	95.83	
Rheum undelatum L.	leaf	107.10	
Rhodea japonica Roth	leaf	105.97	
Rhododendron mucronulatum T.	whole	114.34	
Rubus crataegifolius Bunge	whole	103.33	
Rumex acetocella L.	whole	92.40	
Rumex crispus L.	whole	106.98	
Ruta graveolens	aerial part	139.23	118.77
Salvia plebeia	whole	141.16	124.96
Sanguisorba officinalis L.	seed	78.17	
Saururus chinensis (Lour) Baill	whole	144.37	90.33
Schisandra chinensis Baill	leaf	98.30	
Scilla chinensis	aerial part	86.62	
Scilla chinensis	seed	99.53	
Scutellaria baicalensis George	aerial part	95.71	
Sedum aizoon	whole	132.18	96.53
Sedum kamtschaticum Fischer	aerial part	109.17	
Sedum kamtschaticum Fisher	leaf	134.82	76.21
Sedum sarmentosum Bunge	whole	108.33	
Sedum spectrabile	whole	88.63	
Selaginella tamariscina	leaf	110.17	
Selaginella tamariscina	whole	148.53	98.95
Sophora flavescens Ait	whole	117.06	
Symphytum officinale L.	whole	93.79	
Symphytum officinale L.	root	98.31	
Syneilesis palmata (Thunb.) Maxim.	aerial part	122.04	
Taraxacum platicarpum	aerial part	94.99	
Trachelospermum asiaticum var. I.N.	whole	144.44	97.75
Veronica linariaefolia Pall.	whole	144.24	96.51
Veronica rotundavar. Subintegra	whole	159.48	117.13
Viola mandshurica W. Becker	aerial part	109.61	
Viola mandshurica W.B.	whole	149.44	91.73
Vitis coignetiae Pulliat	leaf	95.40	
Washabia japonica	aerial part	99.75	
Washabia japonica	leaf	82.85	
Xanthium strumarium L.	whole	160.27	154.60
Zanthoxylum schinifolium S. et Z.	leaf	95.55	
Zanthoxylum schinifolium S. et Z.	whole	186.84	110.29
Zingiber mioga (Thunb.) Roscoe	whole	130.90	
Zizyphus jujuba	fruit	86.91	

[1)]Concentration of sample in cultured cells was 25 μg/mL.

helenium, Chrysanthemum boreale Makino (Table 1). Most of the extracts induced QR in a dose-dependent manner (Fig. 2). At the concentration of 25 μg/mL, the methanol extract of *Pulsatilla koreana* Nakai showed the highest QR induction ratio which was 170%. Also, QR activity in BP[r]c1 cells was upregulated the most highly by the extract of *Chrysanthemum zawadskii var. latilobum* Kitamura when the concentration was increased to 50 μg/mL.

DISCUSSION

Several plant extracts are known to induce detoxifying



'ig. 2. Dose-response relationship of QR activity in BP^{r}c1. Cells were exposed to different concentrations of herbal extract or 24 hrs prior to QR assay.
A: *Physalis alkekengi var. francheti* (Masters) Makino, B: *Pulsatilla koreana* Nakai, C: *Chrysanthemum zawadskii var. latilobum* Kitamura, D: *Inula helenium*, E: *Chrysanthemum indicum* L., F: *Angelica gigas*, G: *Artemisia keiskeana* Miquel, H: *Xanthium strumarium* L., I: *Forsythiae fructus*, J: *Aster koraiensis* N.K.

nzymes such as quinone reductase and glutathione-S-ransferase. Induction of phase 2 detoxifying enzymes usually is closely associated with cancer prevention mainy due to rapid removal of potential carcinogens from the ody. In our continuing search for novel chemopreventive agents, herbal extracts were screened for QR induction apacity in hepa1c1c7 and BP^{r}c1 cells. Identification of QR inducers is also a way to screen for more general nduction of detoxifying enzymes since the specific acivity of QR rises concomitantly with other phase 2 letoxification enzymes in many animal tissues in response o chemopreventive agents (5). This study examined QR nduction potential of the methanol extracts of 216 species of plants growing in Korean peninsula. About 20% of them showed QR induction in hepa1c1c7 cells by more han 30%, compared to control cells, while 10% of test samples caused a significant induction of QR in BP^{r}c1.

Aster koraiensis N.K., *Xanthium strumarium* L., and *Physalis alkekengi var. francheti* (*Masters*) Makino all exhibited relatively strong QR-inducing activity. Aster species have been used as diuretics and expectorants in folk medicine and are reported to contain astersaponin, shionone, and quercetin (6). Quercetin is a well-known QR inducer and is probably responsible for QR induction by the methanol extract of *Aster koraiensis* N.K. (7). *Xanthum strumarium* L. is reported to be effective in relieving symptoms of arthritis and rhinitis (6). However, little is known about the bioactive components in this medicinal herb. *Physalis alkekengi* has been reported to contain calystegins with glycosidase inhibitory properties (8) and is suspected to be an estrogen antagonist, although its structure has not been revealed (9). However, no previous study has reported detoxification activity of the plant. The most extensive screening of plants for chemopreventive activity was performed by Tawfiq and coworkers (10), using an assay which measures the induction of QR activity in murine cells challenged with solutions of potential inducers. They found that extracts of some brassicas, legumes (peas), lettuces, red pepper, grapefruit and some herbs including basil, tarragon and rosemary were inducers of QR activity. More recently, we also examined the QR inducing activities of 30 kinds of Korean vegetables and found that *Arctium lappa* (Burdock), *Brassica juncea* (Mustard leaf), *Pteridium aguilinum* (Bracken) and *Chrysanthemum coronarium* (Crown daisy) caused a significant induction of quinone reductase activity with a limited increase in arylhydrocarbon hydroxylase activity (11).

In summary, *Pulsatilla koreana* Nakai, *Chrysanthemum zawadskii var. latilobum* Kitamura, and *Aster koraiensis* N.K exhibited relatively high QR induction in both cell lines deserve further animal study to evaluate chemopreventive potential.

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