

## Screening of Korean Medicinal Plants for Antitumor Activity

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**Abstract** □ Potential antitumor activity of sixteen Korean medicinal plants was tested against leukemia SN 36, murine tumor model. Survival studies by measuring life span indicated that *Morus alba* (*Moraceae*), *Verbascum phlomoides* (*Scrophulariaceae*), *Curcuma longa* (*Zingiberaceae*), *Torilis japonica* (*Umbelliferae*), *Bupleurum falcatum* (*Umbelliferae*) and *Codonopsis pilosula* (*Campanulaceae*) exhibited significant antitumor activity with the dose-schedule employed in the experiment. Methanol(70%) extracts of *Platycodon grandiflorum* (*Campanulaceae*), *Bupleurum longeradiatum* (*Umbelliferae*) and *Asiasarum sieboldii* (*Aristolochiaceae*) showed rather potent toxicity.

**Keywords** □ Screening of antitumor activity-leukemia SN 36-*Morus alba* (*Moraceae*).

Our efforts for searching biologically active substances obtained from plant origin have been made in the authors' laboratories for years<sup>1)</sup>. Up to present, more than two hundreds Korean medicinal plants have been evaluated for their biological activities such as antimicrobial, antitumor activities and behavioral effects.

In the present report, 16 Korean medicinal plants were extracted with methanol and these methanol extracts were tested for their antitumor activity against animal model of

tumor, leukemia SN-36.

Among them, the extracts of *Morus alba* (*Moraceae*), *Bupleurum falcatum* (*Umbelliferae*), and *Codonopsis pilosula* (*Campanulaceae*) exhibited potent antitumor activities.

### MATERIALS AND METHODS

#### *Plant Samples and Methanol Extracts*

All plants, traditionally used in Korea as folkloric medicine, were purchased from local herb drug stores in Seoul, and then they were taxonomically identified by the botanist in our institute. Plants were extracted with methanol under reflux condition, and the extracts were prepared under reduced pressure at 30°C.

#### *Animals and Tumor Line*

The leukemia SN-36 has been maintained in our laboratory for years. Female, dd strain mice were *i. p.* injected with  $1 \times 10^5$  tumor cells on day 0. Test groups of mice received *i. p.* several different doses of extracts once daily for six days from day 1. Control group mice only received *i. p.* physiological saline alone once daily for 6 days.

Drinking water containing streptomycin (50mg/l) were supplied for all mice throughout the experiment. Dose-schedule employed

in this experiment was shown in Table I.

## RESULTS AND DISCUSSION

Total 16 species belonging to 10 families were evaluated against leukemia SN-36 of murine tumor. Average survival time of control group consisting of 10 mice appeared to be  $12 \pm 2$  day.

The survival rate of test mice was compared with that of average life span of control group, and data were shown in Table II.

When the average survival days of test mice were reduced more than 20% of that of control group mice, the extracts were considered to be toxic with respect to the dose-schedule

**Table I: Protocols of antitumor tests**

Day	0	1	2	3	4	5	6
Control	Tumor inoculation				← Saline →		
					← Extracts →		
Test	$1 \times 10^5$ cells per mouse			200 mg/kg/mouse/day	100mg/kg/mouse/day		30/mg/kg/mouse/day

1. Types of tumor: leukemia SN-36, ascites.
2. Animals: dd strain,  $20 \pm 2g$ , female.
3. Route of administration: intraperitoneal injection with total MeOH extracts once daily for 6 days.
4. Number of mice per cage: 10 mice.
5. Observation periods: 50 days.
6. Drinking water contained streptomycin, 50mg/l

**Table II: Antitumor screening of Korean medicinal plants**

Korean name	Plant name	Part in use	Dose (mg/kg)	Average survival days ( $M \pm S. D.$ )	Increased life span (Percent of control)
Control		Physiological saline		$12 \pm 2$	100
Sa In	<i>Amomum xanthioides</i> (Zingiberaceae)	Fructus	200	$12.9 \pm 3$	107.5
			100	$15.4 \pm 3$	128.3
			30	$22.7 \pm 5$	189.2
Yang Gang	<i>Alpinia officinarum</i> (Zingiberaceae)	Rhizoma	200	$14.5 \pm 2$	120.8
			100	$15.8 \pm 2$	131.7
			30	$12.8 \pm 2$	106.7
Ul Gum	<i>Curcuma longa</i> (Zingiberaceae)	Rhizoma	200	$21.3 \pm 4$	177.5
			100	$19.7 \pm 4$	164.2
			30	$11.0 \pm 2$	91.7
Shi Namu	<i>Evodia danielii</i> (Rutaceae)	Fructus	200	$15.7 \pm 3$	130.8
			100	$15.0 \pm 4$	125.0
			30	$12.1 \pm 2$	100.9
Mullein	<i>Verbascum phlomoides</i> (Scrophulariaceae)	Flos	200	$21.9 \pm 6$	182.5
			30	$11.6 \pm 2$	96.7
Gil Gyeong	<i>Platycodon grandiflorum</i> (Campanulaceae)	Radix	200	$5.3 \pm 1$	Toxic
			100	$8.6 \pm 0$	Toxic
			30	$11.1 \pm 2$	No activity
Sang Beck	<i>Morus alba</i> (Moraceae)	Cortex	200	$41.6 \pm 4$	346.7
		Radix	100	$22.8 \pm 5$	190.0
			30	$23.8 \pm 6$	198.3
San Jak Yak	<i>Paeonia obovata</i> (Ranunculaceae)	Cortex	200	$18.8 \pm 5$	156.7
		Radix	100	$10.9 \pm 1$	No activity

			30	11.9 ± 2	No activity
Shi Ra Ja	<i>Anethum graveolens</i> ( <i>Umbelliferae</i> )	Fructus	200	10.3 ± 2	85.8
			100	17.7 ± 3	147.5
			30	12.6 ± 2	No activity
Sa Sang Ja	<i>Torilis japonica</i> ( <i>Umbelliferae</i> )	Fructus	200	12.4 ± 2	No activity
			100	11.1 ± 2	No activity
			30	17.8 ± 6	185.8
Gae Shi Ho	<i>Bupleurum longeradiatum</i> ( <i>Umbelliferae</i> )	Radix	200	6.4 ± 1	Toxic
			100	8 ± 1	Toxic
			30	10.2 ± 1	85
Oh Mi Ja	<i>Schizandra chinensis</i> var. <i>typica</i> ( <i>Magnoliaceae</i> )	Fructus	200	13.2 ± 2	110
			100	14.9 ± 3	124
			30	14.9 ± 3	124
			30	14.2 ± 3	117.5
Shi Ho	<i>Bupleurum fasciatum</i> ( <i>Umbelliferae</i> )	Radix	200	21.3 ± 9	177.5
			100	29.0 ± 9	241.7
			30	20.1 ± 3	167.5
Man Sam	<i>Codonopsis pilolula</i> ( <i>Campanulaceae</i> )	Radix	200	15.6 ± 3	130
			100	27.1 ± 8	226
Se Shin	<i>Asiasarum sieboldii</i> ( <i>Aristolochiaceae</i> )	Radix	200	1.1 ± 0	Toxic
			100	4.8 ± 2	Toxic
			30	10.0 ± 2	83.3
San Jo In	<i>Zizyphus vulgaris</i> var. <i>spinosa</i> ( <i>Rhamnaceae</i> )	Semen	200	14.4 ± 3	128.3
			100	12.8 ± 2	No activity
			30	12.9 ± 2	No activity

employed in the present experiment.

The murine tumor, leukemia SN-36 appeared to possess about 17~20 hrs doubling time which is approximately same doubling time as leukemia 1210 during active growth. One advantage of this experimental tumor system, unlikely leukemia 1210, it can be inoculated easily and propagated into non genetically inbred mice. As the data shown in Table II, the most active extract appeared to be root skin of *Morus alba*.

More than 300% of increased life span could be obtained in this experiment. But no mice could survive for 50 days.

Among 16 plants so far tested *Morus alba* (*Moraceae*), *Curcuma longa* (*Zingiberaceae*),

*Amomum xanthioides* (*Zingiberaceae*), *Bupleurum falcatum* (*Umbelliferae*) appeared to exhibit potent antitumor activities under the dose-schedule employed.

In addition, *Torilis japonica* (*Umbelliferae*) and *Codonopsis pilosula* (*Campanulaceae*) at the lower doses employed in this experiment exhibited higher survival rates. If the less amount of dose is administered, there will be a possibility that antitumor activity will be increased. The extracts of *Bupleurum longeradiatum* (*Umbelliferae*) and *Asiasarum sieboldii* (*Aristolochiaceae*) showed potent toxicity rather than antitumor activity.

Fractionation of methanol extracts obtained from the plants possessing significant antitu-

mor activity is now being undertaken for further study in our laboratory.

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