Full Length Research Paper

In vitro cytotoxic screening of 300 selected Chinese medicinal herbs against human gastric adenocarcinoma SGC-7901 cells

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Accepted 21 February, 2012

Natural products have traditionally provided a rich source of drugs for many diseases, including cancer, and plants are an important source of novel natural products. Only a fraction of the diversity of the biosphere has been tested for biological activity and novel cancer therapeutics remains to be discovered. The present study was undertaken to evaluate the cytotoxic activity of the crude ethanolic extracts of 300 species of herbal plants traditionally used in China for the treatment of a variety of diseases. MMT assay was used to examine *in vitro* cytotoxic activity of these extracts on human gastric adenocarcinoma SGC-7901 cells and splenocytes (normal cells). Extracts which exhibited cytotoxicity at 100 μ M were considered active. 33 of these raw ethanolic extracts demonstrated growth inhibitory activity on SGC-7901 cells. Interestingly, of the 33 active extracts on cancer cells, nine showed less toxicity against the normal spleen cells. Furthermore, four hundred natural compounds were screened against SGC-7901 cells. Of the 400 natural compounds, 18 significantly inhibited proliferation of SGC-7901 cells. These results indicate the potential use of traditional Chinese medicinal herbs as antineoplastic agents and suggest that further studies evaluating their mechanism(s) of action and the isolation of active anti-tumor compounds are warranted.

Key words: Traditional Chinese medicines (TCM), SGC-7901 cells, natural compounds, cytotoxic activity.

INTRODUCTION

Through the history of civilization, the humans have relied on natural products as a primary source of medicine. It is estimated that 80% of the global population rely on plant derived medicines to address their health care needs (Gurib-Fakim, 2006). Of the 250,000 to 500,000 known plant species, very few have been investigated for their pharmacological qualities, and compounds of significant medicinal value may still remain undiscovered in many plant species. Gastric cancer is the second most common cause of global cancer-related mortality (738,000 deaths, 9.7%) and it is the fourth most frequently diagnosed cancer (Ferlay et al., 2010). The rate of incidents of gastric cancer is comparatively higher in Eastern Asia and 65 to 70% of new cases of deaths were reported from gastric cancer in less-developed countries (Hernandez et al., 2010; Parkin, 2001). In 2005, the incidence rate of gastric cancer (0.3 million deaths and 0.4 million new cases) ranked third among the most common cancers in China (Yang et al., 2005). Locally, advanced or metastatic stomach cancer has a poor prognosis with a low long-term survival of only 11.5% (Tetzlaff et al., 2008). Currently, surgery is one of the most common treatments of gastric cancer but survival rate of patients with gastric cancer is less than 33%. Gastric cancer is often diagnosed at an advanced stage when a cure is not possible and treatment is palliative with the intent of improving the guality and guantity of life.

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New therapeutic options are desperately needed for the treatment of gastric cancer. Thus, there is an immense need to identify novel and promising agents for the cure and treatment of gastric cancer. In the last few decades, several researchers have identified numerous dietary and botanical natural compounds which possess chemopreventive potential and antioxidant properties (Amin et al., 2009; Gong et al., 2012; Pal et al., 2012). Plants are one of the most important source for anticancer agents (Cragg and Newman, 2005). David Newman and Gordon Cragg (Newman and Cragg, 2007) found that of 155 FDA-approved small molecule anticancer drugs, 47% were either natural products or analogues inspired by them. The traditional Chinese medicine (TCM) has held and still holds an important position in primary health care in China and has been recently recognized by Western countries as a fertile source for revealing novel lead molecules for modern drug discovery. Although TCM has been used for thousands of years in China and has made great contributions to human health, only a fraction of them has been tested for biological activity and novel cancer therapeutics remains to be discovered. It is necessary to identify the biological activities of herbal plants. Therefore, in the present study cytotoxic properties of ethanol extracts of 300 medicinal plants and 400 natural products were screened against human gastric cancer SGC-7901 cells. Of the 300 ethanolic extracts, 33 extracts were active and interestingly, of the 33 active extracts on cancer cells, nine showed less cytotoxicity against the normal spleen cells. Of the 400 natural compounds, 18 significantly inhibited proliferation of SGC-7901 cells.

MATERIALS AND METHODS

Chemicals and reagents

Cell culture medium reagents (DMEM) and MTT [3'-(4, 5 dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide], trypan blue dye, and dimethyl sulfoxide (DMSO) were purchased from Sigma. Fetal bovine serum (FBS) was purchased from the Hangzhou Sijiqing Biological Engineering Materials Co., Ltd.

Preparation of the crude herbal plant extracts

The herbal plants were crushed and extracted in Soxhlet extractor with alcohol (95%) for more than 12 cycles to achieve maximum extraction of its ingredients. The ethanol extract was hemi dried using rotary evaporator and then dissolved in 80% methanol. After centrifugation at 12000 rpm for 15 min, the supernatant was separated and filtered with 0.18 µm filter paper. Starting from the first peak to the end of the last peak, the extracted material was divided into 80 fractions on the basis of time (30 s per fraction) using high performance liquid chromatography (HPLC). The fractions were dried and dissolved in dimethyl sulfoxide (DMSO) to Obtain a 20 mM stock solution. These fractions were subjected to screening for cytotoxicity against human gastric adenocarcinoma SGC-7901 cells, analyzed by MTT assay and cells were microscopically examined to detect morphological changes.

Cell culture

Human gastric adenocarcinoma SGC-7901 cells were cultured in DMEM nutrients mixture supplemented with 10% FBS and antibiotics at 37°C in a humidified atmosphere with 5% CO₂ and 95% air. Cells were seeded in 10 cm culture dish and allowed to grow approximately 70% confluence before experimentation.

Cell proliferation assay

The cytotoxic effects of the ethanolic extracts of Chinese herbs and natural compounds on the cells were determined by MTT assay as we previously described (Rasul et al., 2011, 2012a; Shawi et al., 2011). Briefly, SGC-7901 cells were seeded at a density of 1×10^4 cells per well in 96-well plates and were allowed to grow overnight. Cells were incubated with 100 µM of ethanolic extracts (20 mM dissolved in DMSO) of herbs in 96 well plates and with various concentrations of single compounds. After incubation for 24 h, growth of cells was determined by adding 10 µl MTT (5 mg/ml in phosphate buffered saline) to each well and incubated for 4 h. After removal of the medium, 150 µl DMSO was added to each well and shaken carefully. The absorbance was read at a wavelength of 570 nm in a plate reader (ELX 800, BIO-TEK Instruments Inc.). The growth curve was plotted against mean values which were calculated using the following equation:

 $I\% = [A_{570} (control) - A_{570} (treated)] / A_{570} (control) *100$

Analysis of toxicity on murine splenocytes

In order to observe cytotoxic effects of costunolide on normal cells, splenocytes were isolated from mouse as we previously described (Rasul et al., 2012b). Splenocytes were cultured in 96 well plates, incubated with 100 μ M of positive fractions of ethanolic extract of herbs for 24 h. Cells were stained with 0.4% trypan blue, observed and photographed under microscopy.

RESULTS

Traditional Chinese medicine (TCM) is widely used for the treatment of cancer (Deng et al., 2006; Xu et al., 2006). Giving the important roles of Chinese herbs in anticancer activity, the ethanol extracts of Chinese herbs were screened against human gastric adenocarcinoma SGC-7901 cells. In our search for plant derived natural products with cytotoxic activity, we prepared crude extracts from three hundreds selected Chinese herbs. Several reasons contribute to the selection of these plants in our studies, such as: (1) SFDA approved herbs that contain therapeutic ingredients for a broad spectrum of human diseases, thousands of years history and best Pharmacological profiles, and (2) their greater distribution in many tropical and subtropical countries. For construction of the traditional Chinese medicines (TCM) fraction library, crude herbal extracts were first prepared by 95% ethanol extraction on Soxhlet reflux apparatus followed by automated fractionation of the extracts using preparative HPLC. Throughout the screening, herbal ethanol extract was divided into 78 fractions by preparative HPLC and each fraction was dissolved in

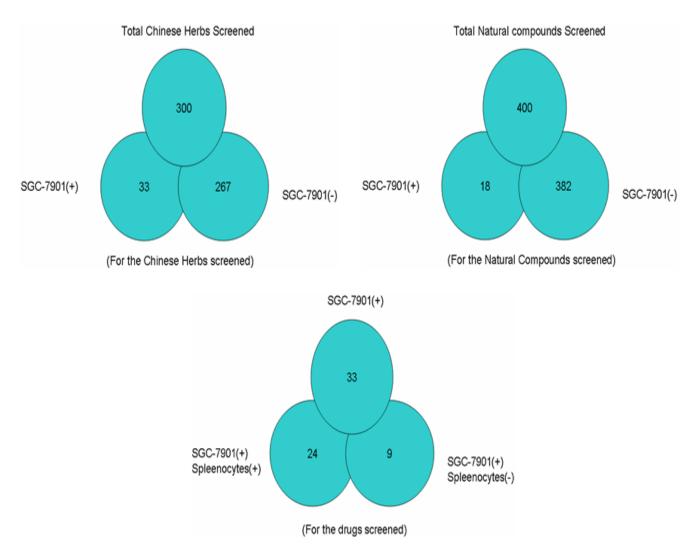


Figure 1. The summary of results of screening of Chinese herbs and natural compounds for cytotoxic activity against human gastric adenocarcinoma SGC-7901. The positive cytotoxic Chinese herbs against freshly isolated normal mouse spleen cells.

DMSO (20 mM solution suppose average compounds molecular weight is 500 dalton) in 96 cells plates. A final concentration of 100 µM was used to screen for cytotoxic activity against human gastric adenocarcinoma SGC-7901 cells. Positive fractions, possessing anticancer activities were found and the herbs showing activity in the form of clusters (successive positive fractions) were considered as anticancer positive herbs. Of the 300 raw ethanolic extracts, 33 demonstrated growth inhibitory activities on SGC-7901 cells. Interestingly, of the 33 active extracts on cancer cells, nine showed less cytotoxicity against the normal spleen cells. Furthermore, 400 natural compounds were screened against SGC-7901 cells. Of the 400 natural compounds, 18 significantly inhibited proliferation of SGC-7901 cells (Figure 1). The detail of the Chinese and Latin names and positive fractions of these 33 cytotoxic active extracts on human gastric adenocarcinoma SGC-7901 cells are shown in Table 1. We tested the toxicity of positive

fractions of these 33 cytotoxic active extracts on freshly isolated mouse splenocytes to exclude fractions toxic to normal cells. The results indicated 24 herbs showed remarkable toxicity and nine herbs have less effects on mouse splenocytes. Blue color refer to the Chinese herb which showed less cytotoxic activities against normal splenocytes cells in comparison to the human gastric adenocarcinoma SGC-7901 cells (Table 1).

Furthermore, 400 natural compounds were screened against SGC-7901 cells. Of the 400 natural compounds, 18 significantly inhibited proliferation of SGC-7901 cells. Complete dose-response curves were generated and IC_{50} values were calculated for these natural compounds against human gastric adenocarcinoma SGC-7901 cells (Table 2). The results in Table 2 show that natural compounds have different IC_{50} values such as Artesunate (44.7±5.3), Isoalantolactone (37.9±3.4), Cucurbitacin-II a (17.9±3.4), Tubeimiside-1 (20.7±1.3), 20(S)-Ginsenoside (20.4±3.6), Evodiamine (11.7±1.9), Chelerythrine (18.4±2.6),

S/N	Chinese name	Latin name	Positive fraction	SGC-7901 cell	Spleen cell
1	天花粉	Radix trichosanthis	E6-E11; F2-F5	+	-
2	狼毒	Radix euphorbiae fischerianae	F4-F10; G2-G5	+	+
3	甘草	Glycyrrhiza uralensis	F3-F11; G2-G5	+	-
4	艾叶	Artemisia argyi	D7-D11; E2-E11; F2-F11	+	-
5	辛夷	Flos magnoliae	E2-E4; G8-G11	+	-
6	防风	Radix saposhnikoviae	G4,G6-G10	+	+
7	白头翁	Radix pulsatillae	E2-E11; F9-F11; G2-G6	+	+
8	白芷	Radix angelicae dahuricae	F11, G2-G6	+	+
9	旋覆花	Flos inulae	D2-D11; E2-E11; F2-F4	+	+
10	桔梗	Radix platycodi	E3-E8	+	+
11	天仙藤	Caulis aristolochiae	E4-E6,E10; F2-F6,G2-G10	+	-
12	麦冬	Radix ophiopogonis	F10,F11; G2-G11; H2-H8	+	+
13	甘松	Radix et rhizome nardostachyos	F3,F6,F7; G2- G11; H2,H3	+	+
14	丁香	Flos syzygii aromatici	F2,F4,F6,F10	+	+
15	香加皮	Cortex periplocae	F4,F9-F11; H5	+	+
16	猪牙皂	Fructus gleditsiae abnormalis	F2-F11; G2-G6	+	+
17	木香	Radix aucklandiae	F5-F11; G2-G8	+	-
18	小三七	Radix notoginseng	F0,F11; G2-G10	+	+
19	竹黄	Shiraia bambusicola	A9-A11; B2-B6; C5,C8	+	-
20	苦丁茶	llex latifolia	F3,F8	+	+
21	苦丁香	Cucumis melo var	E2-E11; F2-F11; G2-G11	+	+
22	皂角	Fructus gleditsiae	E8,E11; F3-F11; G2-G10	+	+
23	炮姜	Rhizoma zingiberis preparata	F7-F11; G2	+	+
24	鹅不食草	Herba centipedae	E4-E8	+	+
25	降香	Lignum dalbergiae Odoriferae	F3-F8,F11	+	+
26	香附	<u>Rhizoma cyperi</u>	F4-F10; G6	+	-
27	干姜	<u>Rhizoma zingiberis officinalis</u>	E7-E11; F2-F11; G2-G4	+	-
28	广枣	Fructus choerospondiatis	H5,H6,H8,H9	+	+
29	过江龙	Caulis entadae	D9-D11	+	+
30	黄蜀葵根	Radix abelmoschi	E7-E9; F2,F7,F8,H2,H3	+	+
31	海桐皮	Cortex erythriniae	F9-F11; G2-G10	+	+
32	苦参	Sophora flavescens	E4-E11; F2-F8	+	-
33	夏枯草	Spica prunellae	E10,E11,F2,F3	+	+

 Table 1. List of 33 cytotoxic extracts of Chinese herbs with their positive fractions (herbs were screened by high throughput strategy) against human gastric adenocarcinoma SGC-7901 cells.

S/N	English name	Chinese name	M.W	IC₅₀ (µM)
1	Artesunate	青蒿琥酯	384.43	44.7±5.3
2	Isoalantolactone	异土木香内酯	232.318	37.9±3.4
3	Cucurbitacin II a	雪胆素甲(雪胆甲素)	574.702	17.9±3.4
4	Tubeimiside-1	土贝母苷甲	1319.43	20.7±1.3
5	20(S)-Ginsenoside Rh2	20(S)-人参皂苷Rh2	622.6	18.9±1.3
6	Shikonin	左旋紫草素	288.295	19.7±0.9
7	Cepharanthin	千金藤素	606.707	20.4±3.6
8	Evodiamine	吴茱萸碱	303.358	11.7±1.9
9	Chelerythrine	白屈菜红碱	348.36	18.4±2.6
10	Patchouli alcohol	百秋李醇	222.366	29.3±3.8
11	Dracorhodin perchlorate	血竭素高 氯酸盐	366.75	54.9±4.3
12	Resveratrol	白藜芦醇	390	16.4±2.7
13	Podophyllotoxin	鬼臼毒素	414.405	19.4 <u>+</u> 2.7
14	Oridonin	冻凌草甲素	364.43	18.4±0.7
15	Curcumin	姜黄素	368.38	28.7±2.3
16	Magnolol	厚朴酚	266.33	64.9±4.3
17	Costunolide	木香烃内酯	232.32	37.7±3.3
18	Pseudolaric acid	土荆皮乙酸	430.491	8.7±1.9

Table 2. MMT assay results of the cytotoxic activities of various compounds against human gastric adenocarcinoma SGC-7901 cells with their IC_{50} values for 24 h.

M.W, Molecular weight; IC_{50} , the half maximal inhibitory concentration.

Patchoulialcohol (29.3 \pm 3.8), Dracorhodin perchlorate (54.9 \pm 4.3), Resveratrol (16.4 \pm 2.7), Podophyllotoxin (19.4 \pm 2.7), Oridonin (18.4 \pm 0.7), Magnolol (64.9 \pm 4.3), Costunolide (37.7 \pm 3.3), and Pseudolaric acid (8.7 \pm 1.9) against human gastric adenocarcinoma SGC-7901 cells.

To the best of our knowledge, inhibitory effects of Isoalantolactone, Tubeimiside-1, Patchouli alcohol, Dracorhodin perchlorate, and Magnolol on human Gastric adenocarcinoma SGC-7901 cells has been reported for the first time.

DISCUSSION

With an increasing cancer rate globally, there is an urgent quest for the improvement of therapeutic activity and selectively of anticancer agents. Herbs are an important source for drug development. Of the 300 raw ethanolic extracts, 33 demonstrated growth inhibitory activities on SGC-7901 cells. Interestingly, of the 33 active extracts on cancer cells, nine showed less cytotoxicity against the normal spleen cells (Table 1).

To survey the detail of studies on these herbs, search in PubMed was done. Few studies were reported on *Radix trichosanthis*. Im et al. (2003) reported that *Radix Trichosanthis* inhibits the melanogenesis in B16 cells. *Radix Euphorbiae fischerianae* is a perennial herbaceous plant distributed widely in northeast mainland China. The dried plant roots, named 'lang-du' in traditional Chinese medicine, are used as a remedy for the treatment of edema, ascites, and cancer (Wang et al., 2010). There have been a number of reports on isolation of compounds from the roots of *E. fischeriana* (Liu et al., 1997). Furthermore, Wang et al. (2006) reported the isolation of seven new diterpenoids and two known compounds from the dried roots of *E. fischeriana*.

Accumulating evidence from epidemiological studies indicates that hexane/ethanol extracts of *Glycyrrhiza uralensis* exhibit anti-inflammatory, anti-oxidative stress activities (Wu et al., 2011), inhibit the metastatic capacity of prostate cancer cells (Park et al., 2010), induce G1 cycle arrest (Seon et al., 2012) and apoptosis in cancer cells (Seon et al., 2010). Results indicated that crude saponins acquired from the *Platycodi Radix*, root of *Platycodon grandiflorum*, inhibits HT-29 cell proliferation by inducing apoptosis (Kim et al., 2008). Platycodin D has direct cytotoxic effect on human leukemia cells and suppresses telomerase activity and is also involved in suppressing PMA-enhanced NF-kB activation (Ahn et al., 2006; Shin et al., 2009).

The Aristoloside, water extract of *Caulis aristolochiae manshuriensis*, inhibited the growth of mouse mammary tumors (Nagasawa et al., 1997; Wu et al., 1994) and enhanced growth of mammary glands and lactation in

mouse (Nagasawa et al., 1997; Wu et al., 1995). *Radix* ophiopogonis is a well known TCM and several compounds are derived from it (Zhu et al., 1989). There have been a number of reports on the potential of the extracts and its derived compounds possessing anti-myocardial ischemic activity (Feng et al., 2008; Li et al., 1996; Zheng et al., 2007; Zheng et al., 2009) and anti-diabetic activity (Ding et al., 2012; Kako et al., 1995; Lin et al., 2011).

Previous studies demonstrated that aqueous extracts of *Artemisia argyi* showed cytotoxic effects on various cancer cells (Shoemaker et al., 2005). Several flavones were isolated from the methanolic extracts of the aerial parts of *A. argyi* (Seo et al., 2003). Eupatilin and Jaceosidin are important constituents of *A. argyi* and it is reported that these compounds inhibit the proliferation of different cancer cells (Jeong et al., 2007; Kim et al., 2007; Shawi et al., 2011). *Flos magnoliae* is one of the traditional Chinese medicine; epimagnolin and fargesin are compounds isolated from the ethanol extract of *Flos magnoliae* (Chen et al., 1988). *Flos magnoliae* induces apoptosis of RBL-2H3 cells (Kim et al., 2003).

Radix saposhnikoviae is one of the important ingredient of Chinese herbal formula (RCM-101) which inhibits inducible NO production (Lenon et al., 2008). Acid Saposhnikovia polysaccharide (A-SPS), potential main active ingredient of Saposhnikovia polysaccharide, has strong antioxidant activity and can be applied as a potential natural antioxidant in food and medicine industry (Zhang et al., 2008). Polyacetylenic alcohols such as panaxynol and heptadeca-1,8-diene-4,6-diyne-3,10-diol were identified from Saposhnikoviae Radix and all these inhibited the growth of a human gastric adenocarcinoma MK-1 cells (Saita et al., 1995). Radix Angelicae dahuricae has been shown to possess anti-inflammatory and anti-noceptive activities (Kang et al., 2008). The bioactive components of Radix Angelicae dahuricae have been confirmed to be coumarins (Park et al., 2009; Xie et al., 2010; Zheng et al., 2010).

Caulis entadae, a well known TCM herb and recently it is reported that the methanol extract of *Caulis entadae* showed the antimicrobial and antioxidant properties and four compounds were isolated (Teke et al., 2011). *Shiraia bambusicola*, a fungus grows on bamboos. The phytochemical 11, 11 dideoxyverticillin was derived from the fungus *Shiraia bambusicola*, a potent small molecule compound capable of potently inhibiting tyrosine kinase activity, especially that of epidermal growth factor receptor (EGFR), in both molecular and cellular models. This compound also exhibits cytotoxicity against a broad spectrum of cancer cell lines *in vitro*, and has been shown to suppress angiogenesis and reduce secretion of VEGF from tumor cells (Chen et al., 2005b; Zhang et al., 2005) and induces G2/M arrest (Chen et al., 2005a).

Ilex latifolia (Aquifoliaceae), a primary component of "kudingcha", has been used in Chinese folk medicine to treat various kinds of diseases including headaches,

inflammatory diseases, and cardiac ischemic injury (Lau et al., 2002). Ilex latifolia also was reported to have protective effects against cardiac ischemic injury and to increase the blood flow in the coronary arteries (Pirker and Goodman, 2010). Furthermore, many antioxidant molecules were isolated from Ilex latifolia (Huang et al., 2001a; Huang et al., 2001b; Negishi et al., 2004). Ilex latifolia protect against ischemic brain injury (Kim et al., 2011). Cortex periplocae is the dry root of the traditional Chinese herb Periploca Sepium Bunge used for treatment of rheumatoid arthritis and reinforcement of bones and tendons in traditional medicine. Extracts and compounds derived from Cortex periplocae inhibits the proliferation of various cancer cells such as colon carcinoma cell line SW480 (Du et al., 2009; Zhao et al., 2010) and lung carcinoma (Lu et al., 2010).

Radix notoginseng is an important Chinese medicinal plant. Panax notoginseng saponins (PNS), the main active components of Radix Notoginseng (Gan and Zheng, 1992), are used for treating atherosclerosis (Wang et al., 2008), cerebral infarction (Yao and Li, 2001), and cerebral ischemia (Yao and Li, 2002). The major bioactive saponins of Radix Notoginseng are ginsenoside Rg₁, ginsenoside Rb₁, and notoginsenoside R₁. In addition, notoginsenoside R₁, a saponin unique to Panax notoginseng, has anti-thrombus activity (Chen et al., 2010). The chemical constituents and extracts of various parts of P. notoginseng have antiproliferative effects on SW480 human colorectal cancer cells (Wang et al., 2007, 2009). Rhizoma zingiberis preparata is one the important ingredient of CML-1, purified extract from a mixture of 13 oriental herbs, have been widely used for the treatment of inflammatory diseases in Asia (Eum et al., 2005) and inhibited the IkB/NF-kB signaling pathway (Mo et al., 2007).

Lignum dalbergiae Odoriferae is known as Jiang Xiang in China and used to move blood, to eliminate blood accumulation, and prevent bleeding (Guo et al., 2010). Rhizoma cyperi, the rhizome of Cyperus rotundus L., is a well known functional food and traditional herbal medicine in China and Korea. It has been reported that Cyperi rhizoma has antioxidant and free radical scavenging activities that play a major role in protection of neurodegenerative disorders (Lee et al., 2010). The phytochemical studies reveal that several compounds were isolated from *Rhizoma cyperiand* and identified as physicion, hexadecanoic acid. beta-sitosterol, stigmasterol, catenarin, and daucosterol (Wu et al., 2008).

The water soluble extracts of *Fructus* choerospondiatis contain several compounds (Zhang et al., 2001) and its flavonoids maintain the integrity of cytomembrane by scavenging free radicals and inhibiting lipid per-oxidation and protect cardiac muscle (Zhang et al., 2001). *Erythrina variegate* belongs to plant family *Leguminosae*, it is a folk medicine in China and has been mainly used as an antibacterial (Tanaka et al., 2010),

anti-inflammatory (Hegde et al., 1995), and antiosteoporosis agents (Zhang et al., 2007). Chemical and pharmacological studies reveal that alkaloid, isoflavone, isoflavanone, and oleanolic acid have been isolated from this herb and founded that possessed anticancer activity (Ghosal et al., 1972; Soto-Hernandez and Jackson, 1994; Xiaoli et al., 2006).

Sophora flavescens, a medicinal plant, is commonly found in Eastern Asia. Previous studies revealed that S. flavescens plant was used as traditional herbal medicine treatment of for the diarrhea. gastrointestinal hemorrhage, and eczema (Zhu, 1998). Chemical and pharmacological studies of S. flavescens have illustrated the isolation of alkaloids (Okuda et al., 1965; Sekine et al., 1993; Song et al., 1999), flavonoids (Ding et al., 2005; Kang et al., 2000a, 2000b; Kim et al., 2006; Kuroyanagi et al., 1999; Kyogoku et al., 1973; Lee et al., 2007; Liu et al., 2010; Oh et al., 2011; Shen et al., 2006; Son et al., 2003) and tritepenoid saponins (Ding et al., 2005, 1992). Spica prunellae is used an ingredient of Shikunshito-Kamiho (SKTK), a traditional Chinese medicine, SKTK which exerts anti-carcinogenic activity on experimental murine colorectal cancer (Yoo et al., 2001). Hot water extract of Flos inulae showed antioxidant, antiinflammatory, and anti-browning activities (Wu et al., 2010).

Cytotoxicity screening models provide important preliminary data for selection of Chinese medicinal herbs with potential anticancer properties for future work. In conclusion, several plants showed promising activities and further studies will be required and directed to the most active and specific plants in order to isolate the cytotoxic compounds. These results indicate the potential use of traditional Chinese medicinal herbs as antineoplastic agents and suggest that further studies evaluating their mechanism(s) of action and the isolation of active anti-tumor compounds are warranted.

ACKNOWLEDGMENTS

This work has been supported by Ministry of Education (MOE) of Pakistan and China Scholarship Council (CSC) of China for doctoral degree. The authors would like to acknowledge Muhammad Rauf for editing of figure.

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