Special Article

Molecular Mechanism of Herbs in Human Lung Cancer Cells

Tanawan Kummalue MD (Honors), MSc*

** Department of Clinical Pathology, Faculty of Medicine, Siriraj Hospital*

Herbs have been considered natural and valuable sources for anticancer drug discovery. Herbal medicine has been prescribed in many countries over centuries for treating various diseases including infectious and malignant diseases. Nowadays, many of the drugs that have been used for treatment of malignant diseases are derived from natural products such as Taxol, a natural product isolated initially from Pacific Yew (Taxus brevifolia). This review article describes research on molecular mechanisms, especially cytotoxic effect of natural products from plant sources, primarily preclinical studies, involving human lung cancer cells in vitro for providing more knowledge and issues for potential drug development from medicinal herbs in the future.

Keywords: *Antiproliferative effect, Herbs, Drug development, Plant-derived compounds*

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Lung cancer is the most frequent cause of cancer-related death and accounts for more than a million deaths yearly worldwide with non-small cell lung cancer (NSCLC) accounting for 75-85% of lung cancer[1,2]. In Thailand, lung cancer is the second most common cancer in men after liver cancer, with an estimated incidence rate of 25.9 per 100,000 whereas an estimated rate of lung cancer in Thai women is 10.0 per 100,000 after cervical, breast and liver cancer[3]. The pathogenesis of lung cancer involves the accumulation of multiple molecular abnormalities, particularly with the exposure to smoking. These alterations include the genetic mutations, chromosomal changes with consequent inactivation of tumor suppressor genes and overactivity of signal transduction cascades. p53, a prototype tumor suppressor gene and most common genetic lesion in human cancers, acts as a transcription factor regulating a member of downstream genes including p21, MDM2, GADD45, and BAX. Although not consistently associated with prognostic significance, p53 mutations play a key role in tumor development by dysregulation of cell cycle control and apoptosis. p53 mutation as well as high Bcl2 and low BAX expression occur in most small cell lung cancer. An important signal transduction pathway, the RAS proto-oncogene family especially KRAS, can be inactivated in some lung cancers by point-mutations, leading to inappropriate signaling for cell proliferation. In contrast to p53 mutations, KRAS mutations are most commonly seen in non-small cell lung cancer especially adenocarcinoma[4,5]. Molecular studies of lung cancer have provided new avenues for early diagnosis and therapeutic strategies, however, certain patients are still plagued by rapid disease recurrence and progression, and there has been no significant improvement in their overall survival. Therefore, it remains a disease with poor prognosis and the primary cause of cancer-related deaths in both men and women despite recent advances made in drug development. The development or presence of resistance to chemotherapeutic agents is a major obstacle to the effective treatment of lung cancer. Identifying the molecular determinants of sensitivity and resistance to chemotherapy is expected to improve the therapeutic efficacy.

Herbs have been considered valuable sources for anticancer drug discovery[6]. Herbal medicine, recorded in many countries, e.g., Chinese pharmacopoeia, has been prescribed for many diseases over centuries and began to be matched by increasing scientific attention[7].

Correspondance to : Kummalue T, Department of Clinical Pathology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Based on recent scientific research on herbs, herbal therapies have been considered alternative treatments for malignancies[8]. The different components in herbs may have synergistic activities or buffering toxic effects and extracts from a mixture of herbs might have more therapeutic or preventive activities than the herbs alone. However, several studies have demonstrated that extracts from several herbal medicines or mixtures have an anticancer potential and could inhibit cancer cell proliferation in vitro or in vivo[9,10]. For example, the lead compound, Taxol, a natural product isolated initially from the Pacific Yew (*Taxus brevifolia*) in the late 1980s destroys the spindle, leading to a loss of chromosome segregation with consequent inhibition of cell division and cell death[11]. Interestingly, it is likely that most of the herbal medicines or mixtures exert their antitumor activities via the apoptotic process.

Apoptosis or programmed cell death has an essential role in controlling cell numbers in many developmental and physiological settings and in chemotherapy-induced tumor cell killing. It is a genetically regulated biological process guided by the ratio of proapoptotic and antiapoptotic proteins. Apoptosis is impaired in many human tumors suggesting that disruption of apoptotic function contributes substantially to the transformation of a normal cell to a tumor cell. The apoptotic cell is characterized by loss of cell volume, plasma membrane blebbing, nuclear condensation, chromatic aggregation and endonucleocytic degradation of DNA into nucleosomal fragments. These cell changes occur after a cascade of cell-signaling and caspase-mediated events that regulate proapoptotic and antiapoptotic proteins and are triggered by two major pathways: the death-receptor-induced extrinsic pathway and the mitochondria apoptosome-mediated apoptotic intrinsic pathway. Both of these pathways lead to caspase activation and cleavage of specific cellular substrates. The receptor- triggered-apoptosis pathway includes ligands and their receptors such as FAS, TNF, and TRAIL as well as downstream molecules such as caspases and Bcl-2 family members. The mitochondria-apoptosome-mediated pathway includes apoptotic stimuli induced by radiation therapy and chemotherapy, mitochondria, apoptosome and key effector caspases. Caspases are activated in a cascade-like fashion. Initiator or upstream caspases (caspases 8, 9, and 10) can activate effectors or downstream caspases, including caspases 3, 6, and 7, which lead to induction of apoptosis. Crosstalk also exists between the two apoptotic pathways. For example, FAS is linked to the mitochondria-apoptosome-mediated that is mediated through the activation of caspase 8 to cleave the BID protein resulting in the release of cytochrome c from mitochondria. The inhibitors of apoptotic proteins including XIAP and cIAPs, surviving, the P13K/AKT/NFkB pathway and heat shock proteins (HSPs), can interact with caspases and cause inhibition of apoptosis[12,13]. A diagram demonstrating the apoptotic pathway is shown in Fig. 1.

This is a selective review highlighting herbal medicine based on molecular mechanism associated with human lung cancer cells in vitro. The knowledge of the mechanism will provide the understanding to the anticancer activities of these medicinal herbs and will lead to the potential to develop novel anticancer agents from plants.

Based on the knowledge of the apoptotic process, the author classified the mechanisms of these medicinal herbs into two groups: herbs induced apoptosis via inactivation of tumor suppressor gene p53 (direct DNA damage) and those promote apoptosis via activation of death signaling molecules (other proteins activation).

Herbs induce apoptosis via tumor suppressor gene p53

Bupleurum falcatum

Saikosaponin D, one of the major components of *Bupleurum falcatum* which could be extracted from other species of Bupleurum and from related genuses, is used for the treatment of various liver diseases in traditional Chinese medicine[14]. It can inhibit the proliferation in the lung cancer cell line, A549, with the IC50 value at 10.18 $\pm$ 0.09 M. By using flow cytometry and PI staining, Saikosaonin D 10 M increased the population of cells in the G1 phase from 34.7% to 53.9%. Marked induction of p53 and p21/WAF1 protein was observed in a dose-dependent manner, indicating that the Saikosaponin D-mediated cell cycle arrest might operate through the induction of p21/WAF1 protein on a p53-dependent event in A549 cells. The caspase 8 activity increased at 12 hours and reached maximum induction at 24 hours in 20 M Saikosaponin D treated A549 cells[15].

Curcuma longa

Curcumin, a phenolic compound of the rhizome of the plant *Curcuma longa* has anti-inflammatory, antioxidant and anticancer activities. A549 and H1299 human lung cancer cell lines were used for the present study and found that the growth inhibitory effect of curcumin was concentration dependent in

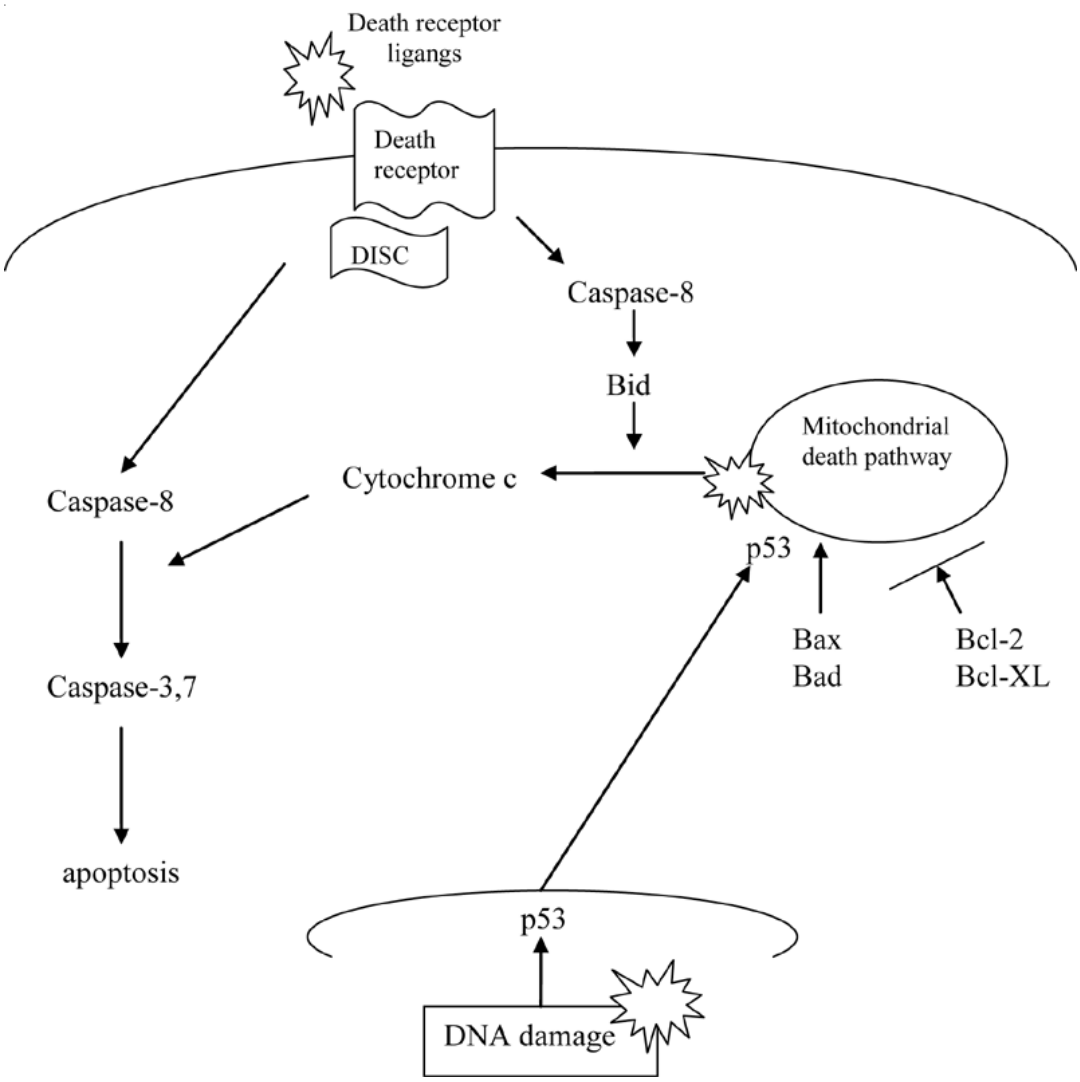

Fig. 1 Multiple pathways of apoptosis. Binding of ligands to death receptor such as Fas causes activation of the death inducing signaling complex (DISC) and direct activation of caspases, resulting in apoptosis. Another initial event is by directly damaging DNA or by producing oxidative injury to mitochondria. In response, p53 is activated and induces pro-apoptotic proteins including Bax which can occur through proteolysis, dephosphorylation and several other mechanisms. Cross-talk between the death receptor and mitochondrial pathway is provided by Bid, which causes release of cytochrome c from mitochondria. Alternatively, p53 directly targets mitochondria, initiating cytochrome c release

both cell lines. The IC50s at 24 hours exposure of curcumin were 50 and 40 M in A549 and H1299 cells, respectively. Determination of PARP cleavage in curcumin treated H1299 cells by flow cytometry, at 24 hours, a concentration at 100 M of curcumin induced PARP cleavage in approximately 90% of treated cells. Induction of apoptosis by curcumin involved several pathways. RT-PCR was performed and found that a decrease in expression of p53, bcl-2 and bcl-XL was observed. Bax and caspase genes remained unchanged up to the 60 M of curcumin but showed a decrease in expression levels at 80-160 M[16].

Tripterygium wilfordii Hook F

Extracts of *Tripterygium wilfordii* Hook F have long been used in Chinese traditional medicine for centuries for the treatment of inflammatory and auto-immune disorders such as rheumatoid arthritis[17,18].

Given its effectiveness, more rigorous attempts were made to identify the biological active compound in the 1970s and PG490 (triptolide) and PG490-88 (a semisynthetic compound derived from PG490) were isolated and extracted from this plant[19]. These semisynthetic compounds inhibited growth of several human cancer-derived cell lines including breast, prostate, lung and leukemic cell lines grown in culture. Interestingly, the inhibitory effect of PG490 on the growth of tumor cells in culture were enhanced in the presence of other inducers of apoptosis such as tumor necrosis factor-α and chemotherapeutic agent[20,21].

When combined with a chemotherapeutic agent, PG490 enhanced apoptosis through signaling pathways involving both p53 and p21. PG490 acts in synergy with the topoisomerase II inhibitor, doxorubicin, to induce apoptosis of cultured HT1080 cells (fibrosarcoma cells) by inhibiting doxorubicin-induced upregulation of p21/WAFI but induced p53. PG490-88 is a water-soluble product of PG490 which now has been studied in the phase I trial for solid tumors[22,23].

Flavonoid compounds

Flavonoids are a broadly distributed class of plant pigments, universally present in vascular plants and responsible for much of the coloring in nature[24]. They are strong antioxidants that occur naturally in foods and can inhibit carcinogenesis in rodents[25].

Acacetin

Acacetin (5,7-dihydroxy-4'-methoxyflavone), a flavonoid compound, has been reported to possess anti-peroxidative, anti-inflammatory and antiplasmodial effects[26-28]. The proliferation inhibitory effect of acacetin was observed to be in a dose dependent manner with A549 human lung cancer cell lines. Its IC50 value was 9.46 μM. The effect of acacetin on cell cycle progression of A549 with 5 μM increased the population of the G1 phase from 34.7 to 42.6%. DNA fragmentation of A549 was found at 12 hours and maximized at 48 hours after exposure of A549 cells to acacetin with 5 and 10 μM. The level of p53, p21, Fas and Fas ligand were assayed by using the ELISA kit and found that acacetin increased the expression of p53 and p21/WAF1 proteins in A549 cells[29]. Results on the Fas ligand assay indicated that FasL, mFasL and sFasL increased in a dose-dependent manner.

Isoliquiritigenin

Isoliquiritigenin (ISL), a flavonoid found in licorice and shallot, is a potent anti-oxidant with anti-inflammatory, antiplatelet aggregation and cancer-preventing properties[30,31].

The ISL inhibited the proliferation of A549 cells with IC50 value at 27.14 mol/L. Compared with the control group, 20 mol/L ISL increased the population of cells in the G1 phase from 26.3 to 45.8%. DNA fragmentation was found after the addition of ISL at the level of 20 and 40 mol/L at 12 hours and maximal at 48 hours. The number of cells undergoing apoptosis at 48 hours increased approximately 3.2 fold with ISL 20 mol/L and 7.1 fold with 40 μmol/L. The expression of p53 and p21/WAF1 protein was assayed by ELISA and showed a marked induction of p53 and p21/WAF1 protein with a maximum level at 12 and 24 hours respectively. Maximum Fas was detected at 24 hours with a similar result as Fas ligand[32].

Stilbenoids

Natural stilbenoids, including resveratrol which is originally identified as a phytoalexin abundant in grapes, peanuts, pines and other Leguminosae family plants, have been reported to exhibit a variety of important biological effects such as a protective role in atherosclerosis and coronary heart diseases[33]. Many studies have also demonstrated the potential of natural stilbenoids to mediate the strong antioxidant, anti-mutagenic, anti-inflammatory or potent cancer chemopreventive effects in carcinogenesis[34].

In addition, resveratrol inhibited the growth of several human cancer cell lines, including human oral squamous carcinoma, promyelocytic leukemia, breast, prostate and colon cancer cells[35]. The growth inhibitory potential of stilbenoids was determined in cultured A549 cells; one of these stilbenoids, 3, 4, 5-trimethoxy-4'-bromo-sis-stilbene (BCS) exhibited a remarkable growth inhibitory effect against A549 lung cancer cells with a IC50 value 0.03 M. When treated cells were analyzed for the cell cycle; the G2/M phase was accumulated in a time-dependent manner of up to 16 hours and then subsequently increased in the sub-G1 phase, indicative of apoptotic peaks during incubation time. Apoptosis of treated cells was confirmed by the DNA ladder pattern. Western blotting was performed and it was found that the p53 protein level was increased after 8 hours incubation with BCS 0.2 μM in a time dependent manner and the level of p21 was remarkably enhanced after 16 hours up to 48 hours incubation. The present study suggested that BCS is a potent inhibitor of the growth of lung cancer cells. Induction of apoptosis related to cell cycle arrest at the G2/M phase with a p53 and p21 dependent pathway[36].

Herbs promote apoptosis via death signaling molecules

Angelica sinensis

The root of *Angelica sinensis*, also known as "Danggui", is a popular herbal medicine and has been widely used in China for gynecological diseases for a long time. Bio-based assay for extracts of *Angelica sinensis* showed that the acetone extract (AE-AS) was dose-dependent in antiproliferative effects on A549, HT29, DBTRG-05MG and J5 human cancer cells. The IC50 value of AE-AS on mentioned cancer cells ranged from 35-50 μg/ml after 24 hours of treatment. After 72 hours of exposure, AE-AS at the dose of 40 μg/ml significantly reduced A549 cell proliferation to 24 ± 3.2% of control. In cell cycle analysis of A549 cells stained with PI, AE-AS significantly altered the G1 to S progression and decreased the number of cells in the S phase. Interestingly, AE-AS induced the apoptosis with condensation of chromatin in the nucleus of A549 cells as confirmed by Hoechst 33342 DNA staining and annexin V staining. By using specific fluorogenic peptide substrates and Western blotting, the molecular apoptotic pathway of AE-AS treated cells was found to be induced by activation of caspase 9 and 3 which was mediated via the suppression of Bcl-2 and cdk4 expression rather than p53 or Bax[37].

Bupleurum scorzonerifolium

The acetone extract of *Bupleurum scorzonerifolium* (AE-BS) showed a dose-dependently antiproliferative effect on the proliferation of A549 human lung cancers. The IC50 of AE-BS on A549 cells was 59 ± 4.5 g/ml on day 1. The IC50 of AE-BS for W138 human normal lung fibroblast cells was significantly higher than that for A549 cells (150 ± 16 g/ml, $p < 0.01$). After 72 hours of exposure, AE-BS (60 g/ml) significantly reduced A549 cells proliferation to 33 ± 3.2% of control. In TUNEL assay, A549 cells treated with AE-BS showed typical morphologic features of apoptosis, and the percentage of apoptotic cells was approximately 38% on day 1. Using the TRAP assay in A549 cells treated with extracts of AE-BS for 1, 2, and 3 days, the telomerase activity was reduced significantly to 25% after treating the cells for 3 days. This observation suggested that AE-BS inhibits telomerase resulting in telomere shortening, repressed proliferation and altered cell cycle leading to apoptosis[38,39].

***Coxi lachryma* (or Adlay seed)**

This grass crop has long been used not only in traditional Chinese medicine but also as a nourishing food. The seed of Adlay has been reported to be used for anti-inflammatory, stomachic, diuretic and antispastic effect in vivo for treatment of warts, rheumatism and neuralgia. The methanolic extract of the adlay seed was tested and found that it inhibited the proliferation of A549 cells in a dose-dependent manner with the IC55-IC65 at 100 μg/ml. It inhibited progression of G1/S transition in the cell cycle with the suppression of cyclin A expression but not cyclin D1 or cyclin E. The induction of apoptosis was investigated by studying the degradation of PARP. PARP is the first identified in vivo substrate for caspases and its degradation is a typical marker for apoptosis. Time dependent degradation of PARP from 116-85 kDa was found in A549 cells treated with 300 μg/ml of methanolic extract[40].

Lithospermum radix

-hydroxyisovalerylshikonin (-HIVS), a compound isolated from the oriental traditional medicinal herb *Lithospermum radix*, is a ATP non-competitive inhibitor of protein tyrosine kinases, such as EGFR, and it induces apoptosis in various human cancer cell lines. When DMS114 cells, human lung cancer cells, were exposed to -HIVS, the cells displayed morphological changes characteristic of apoptosis, such as condensed and fragmented nuclei as confirmed by the DNA ladder pattern and cell-death detection ELISA kit (Roche). The level of expression of TRAP1 in DMS114 cells treated with -HIVS was reduced and the effect was dose-dependent. Treatment of DMS114 cells with -HIVS 10 M increased the amount of cytochrome c in cytosol and suppressed the expression of TRAP1 in mitochondria. These results were consistent with the reduction of tyrosine phosphorylation of proteins in DMS114 cells. The suppression of expression of TRAP1 by -HIVS was inhibited in the presence of the antioxidant N-acetyl cysteine (NAC). These findings indicated that ROS might be an important regulator of the expression of TRAP1[41].

Thalictrum acutifolium

Thalictrum acutifolium has been used for a long time, with well-documented efficacy in cancer therapy in China. From the roots of this herb, the purified compound, a bisalkaloid, acutiaporberine, was isolated. This alkaloid could inhibit the growth of several cell lines in vitro. In 95-D, metastatic lung cancer cell lines, acutiaporberine induced apoptosis at the concentration of 0.06 mol/ml for 22 hours. At this level of treatment, condensation of nuclear chromatin in the early phase of apoptosis was observed and the DNA ladder began to appear at the time of 24 hours. When a

population of cells which contains apoptotic cells is stained with PI and measured by flow cytometry, the percentage of cells undergoing apoptosis increased with the increase of the drug concentration and the incubation time with the highest percentage of apoptosis reaching 42.36%. A high expression of bcl-2 and bax proteins in the treated cells as confirmed by Western blotting suggested that the apoptotic process was induced by bcl-2 gene but p53 independent[42].

Morphological changes compatible with apoptosis (chromatin condensation, nuclear fragmentation and apoptotic bodies) of PLA-801, human non-small lung cancer cell line, treated with acutiaporberine at the concentration of 0.06 mol/ml were observed. The percentage of cells undergoing the apoptosis reached the highest percentage of 58 when treated with 0.11 mol/ml of acutiaporberine for 48 hours. DNA fragmentation was found when treated with acutiaporberine at 0.06 or 0.11 mol/ml for 48 hours. From the Western blotting analysis, c-myc and bax gene expression was up-regulated when cells were treated with acutiaporberine for 24 hours[43].

Scutellaria barbata

Scutellaria barbata, a traditional Chinese herbal medicine native to southern China, is widely used as an anti-inflammatory and a diuretic in China. Extracts of *Scutellaria barbata* have been shown to have in vivo growth inhibitory effects on a number of cancers such as S180 mouse sarcoma, U14 cervical carcinoma, solid hepatoma, etc. The extract of *Scutellaria barbata* on human lung cancer cells, A549, exhibited a marked growth inhibitory effect in a dose-dependent manner. The IC50 was approximately 0.21 ± 0.04 mg/ml. To confirm the apoptosis, caspase 3/7 activity was assayed by using Apo-ONE Homogeneous Caspase-3/7 Assay kit and found that *Scutellaria barbata* treated cells increased A549 caspase3/7 activities. Apoptosis of A549 cells induced by *Scutellaria barbata* was analyzed by Annexin-V staining and demonstrated that treated cells with 0.5 mg/ml *Scutellaria barbata* extract for 48 hours resulted in a rate of cell apoptosis of 57.67%. The cDNA microarray experiment was performed to characterize the mechanism of *Scutellaria barbata* induced killing and found that two genes related to cell response to DNA damage, GADD45A and GIP, decreased dramatically. A total of 20 cell cycle genes were found to have changed after treatment indicated that the cell cycle was widely involved in the *Scutellaria barbata* treatment. Some enzyme activity (STK12,DUSP5 and TOPK), cell signal transduction (GIP, BMP2), nucleic acid binding (ATF3,HNRPD and SMARCF1)were also found to be affected[44].

Solanum incanum

A purified compound from the *Solanum incanum* herb, solamargine (SM), has been shown to inhibit the growth of human tumor cells, e.g. colon, prostate, breast and human hepatoma cells[45,46]. The IC50 of solamargine of A549 cells was 2.9 μM. After incubation with solamargine 9.6 μM for 18 hours, dramatic decreases in the percentage of G0/G1 and G2/M phases were approximately 2.6 and 7.1 fold higher than the untreated control. Apoptosis of solamargine induced A549 cells required TNFRs expression as confirmed by staining the cell nuclei with DAPI and TNFRs followed by FITC-conjugated IgG detection and anti-TNFRs antibodies. From Western blotting and flow cytometry, exposure of A549 cells to 4.8 μM solamargine resulted in down-regulation of Bcl-2 and Bcl-xl and up-regulation of Bax and caspase-3 expression. Thus, solamargine modulated the expression of TNFRs and mitochondria-related Bcl-2 family[47].

Conclusion

The finding of the molecular mechanism via apoptosis of these herbs recognized in human lung cancer cells is summarized in Table 1. Typically, normal p53 function plays a crucial role in inducing apoptosis and cell cycle checkpoints in human cells following DNA damage[48]. This has been further supported by the finding that p53 is the most commonly mutated tumor suppressor gene. Moreover, the chemosensitivity of cancer cells to chemotherapy agents is greatly influenced when the function of p53 is abrogated[49]. However, it appeared that the antiproliferative activities of herbs in human lung cancer cells is induced via an apoptotic system with or without p53 pathway. Some herbs were observed to have an interaction with the Fas/FasL system which is a key signaling transduction pathway of apoptosis in cells and tissues[50]. Ligation of Fas by agonistic antibody or its mature ligand induces receptor oligomerization and formation of a death-inducing signaling complex (DISC), followed by activation of caspase-8, then further activating a series caspase cascade resulting in cell apoptotic death[51]. FasL is a tumor necrosis factor related type II membrane protein[52]. However, the role of the Fas/FasL ligand system in the control of apoptosis in lung cancer is controversial[53].

Most herbs alter the cell cycle by increasing the proportion of cells in G1 phase in a dose dependent

Table 1. Summary of the molecular mechanism of medicinal herbs

Plants	Plant compound	Cell line affected	Mechanism of apoptosis
Angelica sinensis	Acetone extract	A549, HT29, J5DBTRG-05MG	Activation of caspase 9 and 3 mediated via the suppression of Bcl-2 and cdk 4 expression. No activation of caspase-8.
Bupleurum falcatum	Saikosaponin D	A549	Increasing the expression of p53 and p21/WAF1 proteins and induction of Fas/APO1.
Bupleurum scorzonerifolium	Acetone extract	A549	Inhibited telomerase activity.
Coxi lachryma (ลูกเดือย)	Methanolic extract	A549	Inhibition of cyclin A expression and activation via caspase cascade.
Curcuma longa (ขมิ้นชัน)	Curcumin	A549, HT1299	Decreased expression of p53, bcl-2 bcl-XL.
Lithospermum radix	-HIVS	DMS114	Decreased and suppressed the expression of TRAP1.
Tripterygium wilfordii Hook F	Triptolide and its derivatives	A549, H 358,CalU1, SKLu1,H23, HT1080	Induced apoptosis via p53 and p21 pathway.
Thalictrum acutifolium	Acutiaporberine	95-D, PLA-801	Inhibited expression of bcl-2 gene and activated expression of bax gene. p53 independent.
Scutellaria barbata	Ethanol extract	A549	Activation through caspase cascade. Increase caspase 3/7. Activation of cell cycle control genes such as STK6, MCM5, etc.
Solanum incanum	Solamargine	A549	Increased the release of cytochrome c. Decreased the bcl-2 and bcl-XL. Increased Bax and caspase-3 activity.
Plant pigments	Acacetin	A549	Via p53 pathway
Liliaceae plants	Isoliquiritigenin	A549	Via p53 pathway
Grapes, peanuts, pines and other Leguminosae family	Stilbenoids	A549	Via p53 pathway

manner. In addition, inhibition of lung cancer cells growth via the G2/M phase cell cycle arrest was also induced by some herbs. In fact, most of the drugs that affect the G2/M phase evoke the stabilization of microtubules, following induction of inhibition of microtubule disassembly and thus arresting the G2/M phase[54]. Overall, antiproliferative effects of herbs might be possibly dependent on cell types or the culture conditions.

The discovery of novel anticancer agents that will hopefully provide the desired degree of sensitivity for cancer cells have advanced significantly due to the increasingly acquired resistance to cancers. Such significant insensitivity of cancer cells to chemotherapy drugs results in low response rates and consequently in the failure of therapy. Therefore, the research and development of new and safe drugs has become necessary. To date, many of the chemotherapeutic agents are natural products or are derived from natural products. Interestingly, herbs have been used in the treatment of various cancers for a long period of time and their therapeutic effects involving anticancer properties have been scientifically evaluated both in vitro and in vivo. Therefore, it is hopeful that the search for novel natural agents is likely to provide more potent anticancer agents and the discovery of novel anticancer drugs from plants would be an important addition to cancer therapy in the future.

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สมุนไพรกับเซลล์มะเร็งปอด: กลไกการออกฤทธิ์

ธนวรรณ กุมมาลือ

สมุนไพรเป็นพืชทรัพยากรที่มีคุณค่าซึ่งเกิดขึ้นเองตามธรรมชาติโดยที่แพทย์แผนโบราณได้นำสมุนไพรมาใช้ในการรักษาโรคต่าง ๆ นานกว่าศตวรรษ สมุนไพรได้ถูกนำมาใช้ในการรักษาโรคหลายชนิด เช่น โรคติดเชื้อ และโรคมะเร็งเป็นต้น ในกว่าทศวรรษที่ผ่านมาได้มีความพยายามที่จะศึกษาสมุนไพรโดยการประยุกต์วิธีทางวิทยาศาสตร์เพื่อค้นหาตัวยาจากสมุนไพรที่มีฤทธิ์ในการรักษาโรคมะเร็งและได้ประสบความสำเร็จมาแล้ว ก็มีดังเช่นการค้นพบ Taxol ซึ่งได้มาจากต้น Pacific Yew มีชื่อทางวิทยาศาสตร์ว่า Taxus brevifolia บทความนี้เขียนขึ้นมาเพื่อรวบรวมข้อมูลเกี่ยวกับพืชสมุนไพรที่ได้ถูกนำมาศึกษาทางด้าน molecular และทดลองพบว่ามีฤทธิ์ในการฆ่า หรือ ยับยั้งการเจริญเติบโตของ human lung cancer cell lines เพื่อจะได้เป็นแนวทางความเข้าใจของการทำงานของพืชสมุนไพรต่าง ๆ และจะได้เป็นแนวทางสำหรับการค้นพบยาใหม่ ๆ จากพืชสมุนไพรต่อไปในอนาคต