Topical Review Article

A Systematic Review of Iran's Medicinal Plants With Anticancer Effects

Journal of Evidence-Based Complementary & Alternative Medicine
2016, Vol. 21(2) 143-153

DOI: 10.1177/2156587215600873
cam.sagepub.com
SAGE

Majid Asadi-Samani, PhD Candidate[1], Wesam Kooti, MSc[2], Elahe Aslani, MSc[3], and Hedayatollah Shirzad, PhD[1]

Abstract

Increase in cases of various cancers has encouraged the researchers to discover novel, more effective drugs from plant sources. This study is a review of medicinal plants in Iran with already investigated anticancer effects on various cell lines. Thirty-six medicinal plants alongside their products with anticancer effects as well as the most important plant compounds responsible for the plants' anticancer effect were introduced. Phenolic and alkaloid compounds were demonstrated to have anticancer effects on various cancers in most studies. The plants and their active compounds exerted anticancer effects by removing free radicals and antioxidant effects, cell cycle arrest, induction of apoptosis, and inhibition of angiogenesis. The investigated plants in Iran contain the compounds that are able to contribute effectively to fighting cancer cells. Therefore, the extract and active compounds of the medicinal plants introduced in this review article could open a way to conduct clinical trials on cancer and greatly help researchers and pharmacists develop new anticancer drugs.

Keywords

cancer, cytotoxicity, medicinal plants, phytochemicals

Received June 21, 2015. Received revised July 21, 2015. Accepted for publication July 22, 2015.

Introduction

Cancer is a main reason for mortality involving more than one-third of the global population in some way. Cancer is the cause of more than 20% of the whole mortality worldwide.[1] According to the report of the International Agency for Research on Cancer[2] of the World Health Organization published in 2014, the global incidence of cancer has been approximately 14 million new cases and is projected to register 19.3 million in 2025. According to this report, lung cancer was the most prevalent cancer (13%) in 2012 followed by breast cancer (11.9%), colon cancer (9.7%), and prostate cancer (7.9%). In Iran, the mean rate of cancer incidence has been 7.134 per 100 000 population, 85 000 individuals are estimated to acquire cancer and nearly 55 000 individuals die due to cancer per year.[2,3]

Meanwhile, there are a variety of therapeutic approaches to treat cancer, including surgery, chemotherapy, radiation therapy, hormone therapy, and immunotherapy. Despite being highly efficient, surgery is not always practical under any circumstances. For radiotherapy, systemic radiotherapy is variously conducted, including external radiation therapy, brachiotherapy, and internal radiation therapy in view of the source and site of tumor and the type of cells with several side effects, alongside therapeutic effect, for the patient such as poisoning as the most significant one leading to variation in skin health as alopecia and destruction of epithelial cells (scaling) and epithelial moisture (dermis revealing and skin secretion of serous fluid) and potentially mouth ulcers and complications, bone marrow suppression, and development of anemia, leukopenia, and thrombocytopenia.[4] Chemotherapy drugs, including antimetabolites (such as methotrexate), passive material of DNA (such as cisplatin and doxorubicin), antitubulin agents (such as taxis), and hormones that are most frequently used cause unwanted effects, including hair loss, bone marrow suppression, drug resistance, gastric ulcer, neurological dysfunction, and cardiac toxicity.[5-7]

In view of the above complications of the therapies currently considered for cancer, high costs of conventional therapies, and growing incidence of cancer in both developed and developing countries, it seems necessary to develop more novel approaches with higher efficiency so that the disease intensity could be declined. In this regard, there is considerable scientific and

[1] Student Research Committee, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
[2] Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran
[3] Department of Biology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran

Corresponding Author:
Hedayatollah Shirzad, PhD, Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.
Email: shirzadeh@yahoo.com

commercial interest in developing new anticancer agents from natural sources and the research aimed to develop new anticancer drugs has been turned into a significant research area.[8] In fact, naturally derived combinations have been under pharmacists' focus to synthesize new drugs and treat diseases due to availability, less frequent side effects and drug interactions, and cheapness.[9,10]

Plants produce a wide spectrum of chemical compounds with apparently no direct contribution to their growth and development, namely secondary metabolites. Terpenes, nitrogen-containing, and phenolic compounds are 3 main classes of these compounds with various biological properties in plants that are used for a wide variety of diseases including cancers,[11,12] neurological disorders,[13] chronic inflammation and lesions, particularly due to diabetes,[14,15] atherosclerosis,[16,17] cardiovascular diseases,[18,19] and wounds.[20] In addition, these natural products have been used alongside radiotherapy.

This article is a review of Iran's medicinal plants that have been already examined for anticancer effects, and also seeks to offer their main compounds and mechanisms of anticancer activities. This review article could open a way to develop new anticancer drugs for prevention and treatment of cancers.

Materials and Methods

In this systematic review, to collect data, different combinations of keywords *medicinal plants*, *anticancer*, *Iran*, *cytotoxicity*, *cell line*, and *phytochemical compounds* and their Persian equivalents were entered into databases consisting of Magiran, SID, and Iran Medex, as well as, international databases of Web of Knowledge, PubMed, and Scopus. The articles only in English and Persian languages published between 1976 and March, 2015 were only searched. Then, the articles on application of Iran's medicinal plants for prevention and treatment of cancers were selected, and those demonstrating anticancer effects of these plants and/or their compounds were reported.

Results

From the findings, 36 medicinal plants in Iran with studies conducted on their anticancer effects were reported (Table 1). Despite the fact that lung cancer has been the most prevalent cancer in 2014, little research has been conducted on the effects of medicinal plants on this cancer. Most studies have addressed breast cancer (Table 2). In most conducted studies, no clear mechanism of the plant effect has been offered. However, some compounds of the plants have been reported to be possibly responsible for anticancer effects. In addition, in some of the studies some compounds were extracted from the plants and the effect of these compounds on various cell lines were studied. Phenolic and alkaloid compounds were demonstrated to have anticancer effects on various cancers in most studies.

Discussion

The available therapeutic approaches to treat cancers are mostly accompanied with undesirable side effects (gastrointestinal disorders, kidney damage, etc). The present study indicated that the studied medicinal plants in Iran contain the compounds engaging specifically in fighting cancer cells and inhibiting growth and destruction of tumor cells only by affecting cancer cells.

These compounds mainly include alkaloids and phenolic and monoterpene compounds. Vinblastine, vincristine, curcumin, myrtucommulone, taxol, boswellic acids, and umbelliprenin, quercetin, catechin, cucurbitacin, kaempferol, thymol, carvacrol, 1,8-cineole, α-pinene, myrecene, β-sitosterol were some compounds with reported anticancer effects in most works. Alkaloids are nitrogen-containing compounds with plant origin, which often have a complex structure, high molecular weight, and show physiological activity in humans. Alkaloids cause cell cycle arrest in metaphase stage by preventing the formation of microtubules and hence could prevent cancer.[172]

Cancers and most difficult-to-cure diseases are associated with high level of oxidative stress.[173-175] Oxidative stress is a phenomenon which may cause damage to various physiological and biochemical processes. Overproduction of such free radicals may also cause oxidative damage to biomolecules such as DNA, lipids, and proteins.[176-178] This process eventually may lead to many chronic diseases, including cancer, atherosclerosis, diabetes, aging, and other degenerative diseases in humans.[179-181] Most of medicinal plants with anticancer property have antioxidant activity due to phenolic compounds. Therefore, these plants may, at least in part, exert their anticancer effects by counteracting free radicals. Antioxidant property of phenolic compounds (including flavonols and flavonoids) is due to the presence of hydroxyl groups.[182,183] Actually, medicinal plants with antioxidant activity play a crucial role in scavenging free radicals. They also are able to reduce the toxicity of toxic agents which induce oxidative stress.[184-188] If this is true, other plants with antioxidant property are likely to have anticancer activity, which should be further investigated.

On the other hand, the ability to induce apoptosis is an important marker for cytotoxic antitumor agents. Studies have shown that cytotoxic effect of alkaloids and phenols against different tumors is mediated through apoptosis.

Phenolic compounds exhibit anticancer effects through affecting cell proliferation processes (eg, through the G2/M cell cycle arrest and inhibition of topoisomerase II), apoptosis, angiogenesis, and the impact on the routes of phosphoinositide 3-kinase (PI3-K) and protein kinase B (Akt). Studies have demonstrated that inhibition of PI3-K activity inhibits phosphorylation of Akt and mammalian target of rapamycin (mTOR), which leads to reduced activity of nuclear factor-κB (NF-κB). Through this mechanism, transcription and synthesis of the cell cycle-driving proteins are inhibited and thus the growth of cancer cells is reduced and the cell death increases.[189-192] For example, quercetin, a phenolic compound in plants, prevents the activation of the transcription factor NF-κB through inhibiting Akt and Ikka-a phosphorylation and hence the anticancer activity is exerted.[193] Curcumin, as a major pigment in turmeric, induces apoptosis in transformed rodent and human cells in inhibition of the culture of formation of cyclooxygenase metabolite.[69-72]

Table 1. Anticancer Effects of Various Iranian Medicinal Plants.

Scientific Name	Part(s) Used	Important Compounds	Mechanisms	References
Ferula assa-foetida	Shoot, resin	Coumarin compounds (especially sesquicoumarins), sulfur-containing compounds, and β-sitosterol and oleic acid	Inhibition of mutagenesis, DNA destruction and cancer cells proliferation; increase of proteolytic enzymes activity	21–24
Thymus vulgaris	Shoot	Thymol and carvacrol	Cell cycle arrest	25–27
Thymbra spicata	Shoot	Thymol and carvacrol	Inhibition of DNA destruction	28–30
Taverniera spartea	Shoot	Isoflavonoid compounds and saponins	Induction of necrosis and apoptosis	31, 32
Peganum harmala	Seed	Alkaloids	Induction of apoptosis (by caspase activation and increase of proteolytic enzymes activity)	33–35
Viola tricolor	Shoot	Flavonoids (especially rutin and quercetin)	Cell cycle arrest	36–38
Achillea wilhelmsii	Shoot	Phenolic compounds (especially flavonoids and monoterpens such as 1,8-cineole and α-pinene)	Induction of apoptosis	39–43
Mentha pulegium	Shoot	Pulegone, menthone, piperitone, limonene, isomenthone, octen-3-ol	Induction of apoptosis	44–46
Ammi visnaga	Shoot	Visnadine, cimifugin, khellol, β-sitosterol, kaempferol, quercetin	Cell cycle arrest	47–50
Camellia sinensis	Leaf	Epicatechin, epigallocatechin, epigallocatechin gallate, epigallocatechin-3-gallate	Inhibition of cancer cells proliferation (by inhibit of 5-α reductase enzyme activity)	20, 51–55
Avicennia marina	Leaf	Flavonoids (especially naphthoquinone compounds such as 3-chlorodeoxylapachol)	Antioxidant effects; induction of apoptosis	56–58
Silybum marianum	Seed	Flavonoids (especially silymarin)	Antioxidant effects; cell cycle arrest	59, 60
Artemisia absinthium L	Root, shoot	Artemisinin, quercetin, isorhamnetin, limonene, myrecene, linalool, α-pinene, β-pinene, artesunate	Inhibition of cancer cells proliferation (decrease in response to nuclear receptors); inhibition of angiogenesis and cell migration; induction of apoptosis	61–64
Curcuma longa	Rhizome	Curcumin	Inhibition of cancer cells proliferation (by adjusting gene expression); inhibition of angiogenesis; induction of apoptosis	65–72
Crocus sativus L	Stigma	Phenolic compounds (especially quercetin)	Inhibition of cancer cells proliferation (inhibits DNA synthesis)	73–76
Zingiber officinale	Rhizome	Flavonoids (especially kaempferol, catechin, fisetin, and quercetin)	Induction of apoptosis	66, 77, 78
Olea europae	Leaf, fruit	Oleic acid, pinoresinol, oleuropein, acidic triterpenes, oleanolic acid, maslinic acid	Inhibition of cancer cells proliferation (inhibition of HER2 gene expression); inhibition of angiogenesis; induction of apoptosis	52, 79–81
Taxus baccata L	Leaf	Taxol	Cell cycle arrest	82–84
Nigella sativa	Seed	Thymoquinone, dinitroquinone	Cell cycle arrest; induction of apoptosis	85–90
Allium sativum L	Fruit	Allicin, ajoene	Cell cycle arrest; induction of apoptosis	91–101
Lepidium sativum	Shoot	Vitamins (A, B, C and E), isothiocyanate, α-linolenic acid, glucosinolates	Antioxidant effects; cell cycle arrest	102–104
Trigonella foenum-graceum L	Shoot	Flavonoids and alkaloids (such as gingerol, cedrene, zingerone, vanillin, and eugenol)	Antioxidant effects; induction of apoptosis	105–108
Glycyrrhiza glabra	Root	Glycyrrhizin	Inhibition of cancer cells proliferation (bcl-2 phosphorylation); morphological changes in cancer cells and induction of apoptosis	109–112
Physalis alkekengi	Fruit	Physalins	Induction of apoptosis	113–116
Lagenaria siceraria Standl	Shoot, fruit	Vitamins (B group and C), saponins, cucurbitacin	Cell cycle arrest	117–121
Ferula gummosa	Shoot	Sesquiterpenes and coumarins	Cell cycle arrest; induction of apoptosis	122–130
Boswellia serrata	Resin	Boswellic acid	Inhibition of cancer cells proliferation (distribution in the biosynthesis of nucleic acids and proteins); decrease of cells viability (increase of reactive oxygen species production); induction of apoptosis (by activation of caspases)	131–133

(continued)

Table 1. (continued)

Scientific Name	Part(s) Used	Important Compounds	Mechanisms	References
Urtica dioica L	Leaf	Phenolic compounds	Antioxidant effects; cell cycle arrest	134–138
Ammi majus	Shoot, seed	Coumarin compounds (especially psoralens)	Cell cycle arrest; induction of apoptosis	139, 140
Rosa damascena	Petal	Phenolic compounds (such as gallic acid, catechin, and epicatechin)	Antioxidant effects; DNA protection	141–144
Astragalus cystosus	Shoot	Lectins, flavonoids and terpenoids	Cell cycle arrest; induction of apoptosis	145–148
Myrtus communis	Leaf	Polyphenols, myrtucommulone, semi-myrtucommulone, 1,8-cineole, α-pinene, myrtenyl acetate, limonene, linalool, α-terpinolene	Antioxidant effects, induction of apoptosis (DNA fragmentation and activation caspases)	149–155
Vinca rosea	Shoot	Vincristine, vindoline, vinflunine, vinblastin, catharantin	Antioxidant effects; inhibition of cancer cells proliferation (effect on microtubules)	156–159
Citrullus colocynthis	Fruit	Cucurbitacin, quercetin, β-sitosterol	Cell cycle arrest; induction of apoptosis	160–164
Polygonum aviculare	Shoot	Tannins, saponins, flavonoids and alkaloids	Antioxidant effects; cell cycle arrest; induction of apoptosis	165–168
Astroudaucus orientalis	Root, shoot	α-pinene, α-thujene, α-copaene, fenchyl-acetate, myrecene, sabinene	Cell cycle arrest; induction of apoptosis	169–171

Table 2. Effect of Iranian Medicinal Plants on Different Cancers.

Target Organ	Study Design	Scientific Name	Reference(s)
Lung	Clinical trial	*Astragalus cystosus*	146
	Cell line: A549	*Lagenaria siceraria* Standl	117
		Ferula gummosa (Umbelliprenin)	122
		Rosa damascena	141
		Curcuma longa	68
	Cell line: SK-Mes-1	*Thymbra spicata*	28
	Cell line: QU-DB	*Curcuma longa*	67
Breast	Mouse	*Silybum marianum*	60
		Trigonella foenum-graceum L	106
	Cell line: BT-20	*Avicennia marina* (3-chlorodeoxylapachol)	58
	Cell line: MDA-MB231	*Avicennia marina*	57
		Zingiber officinale	78
	Cell line: BT474	*Olea europae*	52
		Taverniera spartea	32
	Cell line: T47D	*Astrodaucus orientalis*	169
		Camellia sinensis	54
		Curcuma longa	67
		Ammi visnaga	48
	Cell line: MDA-MB468	*Taxus baccata* L	83, 84
	Cell line: MCF-7	*Polygonum aviculare*	167
		Lagenaria siceraria Standl	119
		Crocus sativus L	75
		Zingiber officinale	77
		Allium sativum L (diallyl disulfide)	95, 98
		Vinca rosea (Alkaloids)	156
		Glycyrrhiza glabra (glycyrrhizin)	112
		Rosa damascena	141
		Lepidium sativum	104
		Ammi majus	139
		Citrullus colocynthis (Cucurbitacin)	164
		Taverniera spartea	32
		Myrtus communis	149–151
		Ferula gummosa	123
	Cell line: 4T1	*Glycyrrhiza glabra*	110
		Silybum marianum	60

(continued)

Table 2. (continued)

Target Organ	Study Design	Scientific Name	Reference(s)
Prostate	Clinical trial; Mouse; Cell line: LNCaP, hPCPs	*Urtica dioica*	134–136
	Mouse	*Thymus vulgaris*	25
	Cell line: DU-145	*Taverniera spartea*	32
		Camellia sinensis	54
	Cell line: PC-3	*Ferula szowitsiana* (Umbelliprenin)	126
		Allium sativum L (diallyl disulfide)	96
		Taverniera spartea	32
	Cell line: PC-3M	*Curcuma longa*	66
		Zingiber officinale	66
Cervix	Cell line: HeLa	*Ammi majus*	139
		Rosa damascena	142
		Polygonum aviculare	165, 166
		Physalis alkekengi	113, 116
		Astragalus cystosus	145
		Taxus baccata L	84
		Peganum harmala	32, 33
		Viola tricolor	36
		Boswellia serrata	129
		Curcuma longa (Curcumin)	70
	Cell line: PA1	*Ferula szowitsiana* (Umbelliprenin)	126
Head	Clinical trial	*Thymus vulgaris*	26
Colon	Cell line: RKO, SW480, HCT116	*Olea europae* (pinoresinol)	79
	Cell line: HT-29, SW480, HCT116	*Crocus sativus* L	74
	Cell line: HCT-116	*Nigella sativa* (Thymoquinone)	88
	Cell line: HT-29	*Artemisia absinthium* L	62
		Achillea wilhelmsii	39
		Allium sativum L	93
	Cell line: DLD-1	*Ferula szowitsiana* (Umbelliprenin)	126
Larynx	Cell line: KB	*Avicennia marina* (3-chlorodeoxylapachol)	58
	Cell line: Hep-2	*Citrullus colocynthis*	160
		Curcuma longa	65
		Allium sativum L	94
Liver	Cell line: HepG2	*Astragalus cystosus* (saponines and flavonoids)	147, 148
		Ferula assa-foetida	21
		Crocus sativus L	73, 76
		Citrullus colocynthis (Cucurbitacin)	163
Skin	Cell line: A431	*Vinca rosea*	156
	Cell line: SK-MEL-28	*Ferula gummosa*	122
Blood cells	Cell line: K562	*Mentha pulegium*	44
		Artemisia absinthium L (Artesunate)	64
		Lepidium sativum	103
		Taxus baccata L	84
	Cell line: Jurkat T-CLL, Raji B-CLL	*Ferula szowitsiana* (Umbelliprenin)	125
Kidney	Cell line: ACHN	*Nigella sativa*	86
Bladder	Cell line: ECV-304	*Lepidium sativum*	102
Stomach	Cell line: AGS	*Ferula gummosa*	124

Conclusion

The investigated medicinal plants in this article could be a key to identifying the compounds with anti-cancer effects; therefore, if their compounds are examined, they might help to develop new, more efficient drugs, in addition to contributing to identifying the main mechanisms involved in cancer.

Author Contributions

All the authors wrote the first draft of the manuscript equally. MAS and HS revised and edited the last version.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work has been extracted from the PhD thesis of Majid Asadi-Samani and it has been funded by Deputy of Research and Technology of Shahrekord University of Medical Sciences.

Ethical Approval

As this review did not involve any human or animal subjects, ethical approval was not required.

References

1. Agarwal N, Majee C, Chakraborthy G. Natural herbs as anticancer drugs. *Int J PharmTech Res*. 2012;4:1142-1153.
2. International Agency for Research on Cancer. *World Cancer Report 2014*. Lyon, France: IARC Press; 2014.
3. Mousavi SM, Gouya MM, Ramazani R, Davanlou M, Hajsadeghi N, Seddighi Z. Cancer incidence and mortality in Iran. *Ann Oncol*. 2009;20:556-563.
4. Smeltzer SC, Bare BG, Hinkle JL, Cheever KH. *Brunner and Suddarth's Textbook of Medical Surgical Nursing*. 12th ed. Philadelphia, PA: Lippincott Williams & WIlkins; 2010:205-231.
5. Nussbaumer S, Bonnabry P, Veuthey JL, Sandrine F. Analysis of anticancer drugs: a review. *Talanta*. 2011;85:2265-2289.
6. Monsuez J, Charniot JC, Vignat N, Artigou JY. Cardiac side-effects of cancer chemotherapy. *Int J Cardiol*. 2010;144:3-15.
7. Dropcho EJ. The neurologic side effects of chemotherapeutic agents. *Continuum*. 2011;17:95-112.
8. Kinghorn AD, Farnsworth NR, Soejarto DD, et al. Novel strategies for the discovery of plant-derived anticancer agents. *Pharm Biol*. 2003;41:53-67.
9. Sakarkar DM, Deshmukh VN. Ethnopharmacological review of traditional medicinal plants for anticancer activity. *Int J PharmTech Res*. 2011;3:298-308.
10. Nussbaumer S, Bonnabry P, Veuthey JL, Sandrine F. Analysis of anticancer drugs: a review. *Talanta*. 2011;85:2265-2289.
11. Shirzad H, Taji F, Rafieian-Kopaei M. Correlation between antioxidant activity of garlic extracts and WEHI-164 fibrosarcoma tumor growth in BALB/c mice. *J Med Food*. 2011;14:969-974.
12. Azadmehr A, Hajiaghaee R, Afshari A, et al. Evaluation of in vivo immune response activity and in vitro anti-cancer effect by *Scrophularia megalantha*. *J Med Plants Res*. 2011;5:2365-2368.
13. Rabiei Z, Rafieian-Kopaei M, Heidarian E, Saghaei E, Mokhtari S. Effects of *Zizyphus jujube* extract on memory and learning impairment induced by bilateral electric lesions of the nucleus Basalis of Meynert in rat. *Neurochem Res*. 2014;39:353-360.
14. Baradaran A, Madihi Y, Merrikhi A, Rafieian-Kopaei M, Nasri H. Serum lipoprotein (a) in diabetic patients with various renal function not yet on dialysis. *Pak J Med Sci*. 2013;29:354-357.
15. Behradmanesh S, Horestani MK, Baradaran A, Nasri H. Association of serum uric acid with proteinuria in type 2 diabetic patients. *J Res Med Sci*. 2013;18:44-46.
16. Madihi Y, Merrikhi A, Baradaran A, et al. Bioactive components and the effect of hydroalcoholic extract of *Vaccinium myrtillus* on postprandial atherosclerosis risk factors in rabbits. *Pak J Med Sci*. 2013;29:384-389.
17. Setorki M, Nazari B, Asgary S, Azadbakht L, Rafieian-Kopaei. Antiatherosclerotic effects of verjuice on hypocholesterolemic rabbits. *Afr J Pharm Pharmacol*. 2011;5:1038-1045.
18. Khosravi-Boroujeni H, Sarrafzadegan N, Mohammadifard N, et al. White rice consumption and CVD risk factors among Iranian population. *J Health Popul Nutr*. 2013;31:252-261.
19. Sadeghi M, Khosravi-Boroujeni H, Sarrafzadegan N, et al. Cheese consumption in relation to cardiovascular risk factors among Iranian adults—IHHP Study. *Nutr Res Pract*. 2014; 8: 336-341.
20. Asadi SY, Parsaei P, Karimi M, et al. Effect of green tea (*Camellia sinensis*) extract on healing process of surgical wounds in rat. *Int J Surg*. 2013;11:332-337.
21. Sadooghi SD, Nezhad-Shahrokh-Abadi Kh, Zafar Balanezhad S, Baharara J. Investigating the cytotoxic effects of ethanolic extract of *Ferula assa-foetida* resin on HepG2 cell line. *Feyz*. 2013;17: 323-330.
22. Hofbauer R, Frass M, Gmeiner B, Kaye AD, Frost EA. Effects of *Ferula assa-foetida* extract on neutrophil migration at the cellular level. *Heart Dis*. 2001;3:14-17.
23. Escribano J, Alonso GL. Crocin, sofranol and picocrocine from *Ferula assa-foetida* inhibit the growth of human cancer cell in vitro. *Cancer Lett*. 1996;100:23-30.
24. Nakagawa H, Tsuta K, Kiuchi K, et al. Growth inhibitory effects of diallyl disulfide on human breast cancer cell lines. *Carcinogenesis*. 2001;22:891-897.
25. Keramati K, Sanai K, Babakhani A, Rakhshan M, Vaezi Gh, Haeri A. Effect of hydroalcoholic extract *Thymus vulgaris* induced prostate cancer injection DMBA in Wistar rats. *J Pazhuhesh*. 2011;35:135-140.
26. Sertel S, Eichhorn T, Plinkert PK, Efferth T. Cytotoxicity of *Thymus vulgaris* essential oil towards human oral cavity squamous cell carcinoma. *Anticancer Res*. 2011;31:81-87.
27. Keeforer-Ring K, Thompson JD, Linhart YB. Beyond six scents: defining a seventh *Thymus vulgaris* chemotype new to southern France by ethanol extraction. *Flavour Frag J*. 2009;24:117-122.
28. Sabzali S, Arman R, Panahi J, Havasian MR, Haghani K, Bakhtiyari S. Investigation on the inhibitory effects of hydroalcoholic extract of *Thymbra spicata* on the growth of lung cancer cell line SK-Mes-1. *J Ilam Univ Med Sci*. 2014;22:153-158.
29. Aydın E, Türkez H, Keleş MS. The effect of carvacrol on healthy neurons and N2a cancer cells: some biochemical, anticancerogenicity and genotoxicity studies. *Cytotechnology*. 2014;66:149-157.
30. Dirican E, Turkez H, Toğar B. Modulatory effects of *Thymbra spicata* L. different extracts against the mercury induced genotoxicity in human lymphocytes in vitro. *Cytotechnology*. 2012; 64:181-186.
31. Abegaz BM, Ngadjui BT, Bezabih M, Mdee LK. Novel natural products from marketed plants of eastern and southern Africa. *Pure Appl Chem*. 1999;71:919-926.
32. Khalighi-Sigaroodi F, Jeddi-Tehrani M, Ahvazi M, et al. Cytotoxicity evaluation of *Taverniera spartea* on human cancer cell lines. *J Med Plants*. 2014;2:114-128.
33. Forouzandeh F, Salimi S, Naghsh N, Zamani N, Jahani S. Evaluation of anti-cancer effect of *Peganum harmala* L hydroalcholic extract on human cervical carcinoma epithelial cell line. *J Shahrekord Univ Med Sci*. 2014;16:1-8.
34. Shahverdi AR, Ostad SN, Khodaee S, et al. Antimicrobial and cytotoxicity potential of *Peganum harmala* smoke. *Pharmacogn Mag*. 2008;4:236-240.
35. Jiménez J, Riverón-Negrete L, Abdullaev F, Espinosa-Aguirre J, Rodríguez-Arnaiz R. Cytotoxicity of the β-carboline alkaloids

harmine and harmaline in human cell assays in vitro. *Exp Mol Pathol*. 2008;60:381-389.
36. Mortazavian SM, Ghorbani A, Ghorbani Hesari T. Effect of hydro-alcoholic extracts of *Viola tricolor* and its fractions on proliferation of cervix carcinoma cells. *Iran J Obstet Gynecol Infertil*. 2012;15:9-16.
37. Vukics V, Kery A, Bonn GK, Guttman A. Major flavonoid components of heartsease (*Viola tricolor* L.) and their antioxidant activities. *Anal Bioanal Chem*. 2008;390:1917-1925.
38. Kanadaswami C, Lee L, Lee PP, et al. The antitumor activities of flavonoids. *In Vivo*. 2005;19:895-910.
39. Dalali Isfahani L, Monajemi R, Amjad L. Cytotoxic effects of extract and essential oil leaves of *Achillea wilhelmsii* C. Koch on colon cancers cells. *Exp Anim Biol*. 2013;1:1-6.
40. Kazemi M, Rostami H. Chemical composition and biological activities of Iranian *Achillea wilhelmsii* L. essential oil: a high effectiveness against Candida spp. and Escherichia strains. *Nat Prod Res*. 2015;29:286-288.
41. Azadbakht M, Semnani K, Khansari N. The essential oils composition of *Achillea wilhelmsii* C. Koch leaves and flowers. *J Med Plants*. 2003;2:55-59.
42. Sharma H, Parihar L, Parihar P. Review on cancer and anticancerous properties of some medicinal plants. *J Med Plants Res*. 2011; 5:1818-1835.
43. Dokhani Sh, Cottrell T, Khajeddin J, Mazza G. Analysis of aroma and phenolic components of selected Achillea species. *Plant Food Hum Nutr*. 2005;60:55-62.
44. Aslani E, Naghsh N, Ranjbar M. Cytotoxic effect of *Mentha pulegium* plants before flowering on human chronic myelogenous leukemia K562 cancer category. *J Arak Univ Med Sci*. 2014;16:1-10.
45. Vian MA, Fernandez X, Visinoni F, Chemat F. Microwave hydrodiffusion and gravity, a new technique for extraction of essential oils. *J Chromatogr A*. 2008;1190:14-17.
46. Morton LW, Caccetta RA, Puddey IB, Croft KD. Chemistry and biological effects of dietary phenolic compounds: relevance to cardiovascular disease. *Clin Exp Pharmacol Physiol*. 2000;27: 152-159.
47. Ghareeb AM, Zedan TH, Gharb LA. Antibacterial and antifungal activities of *Ammi visnaga* extracts against pathogenic microorganisms. *Iraqi J Sci*. 2011;52:30-36.
48. Mohammed ZY, Nada SM, Al-Halbosiy MM, Abdulfattah SY, Abdul-Hameed B. Cytotoxic effects of *Ammi visnaga* volatile oil on some cancer cell lines. *J Biotechnol Res Cent*. 2014;8:5-7.
49. Abduljalil TZ, Saour K, Nasser AM. Phytochemical study of some flavonoids present in the fruits of two Ammi L. species wildly grown in Iraq. *Iraqi J Pharm Sci*. 2010;19:48-57.
50. Vanachayangkul P, Byer K, Khan S, Butterweck V. An aqueous extract of *Ammi visnaga* fruits and its constituent's khellin and visnagin prevent cell damage caused by oxalate in renal epithelial cells. *Phytomedicine*. 2010;17:653-658.
51. Adhami V, Ahmad N, Mukhtar H. Molecular targets for green tea in prostate cancer prevention. *J Nutr*. 2003;133:2417-2424.
52. Hosain zadegan H, Ezzet por B, Abdollah por F, Motamedy M, Rashidipor M. Study of cytotoxic activity of olive and green tea extracts on breast tumor cell line. *J Ardabil Univ Med Sci*. 2010;10:287-294.
53. Carmen C, Reyes A, Rafael G. Beneficial effects of green tea—a review. *J Am Coll Nutr*. 2006;25:79-99.
54. Ravindranath MH, Saravanan TS, Monteclaro CC, et al. Epicatechins purified from green tea (*Camellia sinensis*) differentially suppress growth of gender-dependent human cancer cell lines. *Evid Based Complement Alternat Med*. 2006;3:237-247.
55. Ravindranath MH, Ramasamy V, Moon S, Ruiz C, Muthugounder S. Differential growth suppression of human melanoma cells by tea (*Camellia sinensis*) epicatechins (ECG, EGC and EGCG). *Evid Based Complement Alternat Med*. 2009;6:523-530.
56. Sharaf M, El-Ansari MA, Saleh NA. New flavonoids from *Avicennia marina*. *Fitoterapia*. 2000;71:274-277.
57. Momtazi borojeni A, Behbahani M, Sadeghi-aliabadi H. Evalution of cytotoxic effect of some extracts of *Avicennia marina* against MDA-MB231 human breast cancer cell line. *Pharm Sci*. 2011;16:229-238.
58. William PJ, Lobo-Echeverri T, Mi Q, et al. Antitumour activity of 3-chlorodeoxylapachol, a naphthoquinone from *Avicennia germinans* collected from an experimental plot in southern Florida. *J Pharm Pharmacol*. 2005;57:1101-1108.
59. Gazák R, Walterová D, Kren V. Silybin and silymarin—new and emerging applications in medicine. *Curr Med Chem*. 2007;14: 315-338.
60. Shariatzadeh SM, Hamta A, Soleimani M, Fallah Huseini H, Samavat S. The cytotoxic effects of Silymarin on the 4T1 cell line derived from BALB/c mice mammary tumors. *J Med Plants*. 2014;4:55-65.
61. Gordanian B, Behbahani M, Carapetian J, Fazilati M. Cytotoxic effect of *Artemisia absinthium* L. grown at two different altitudes on human breast cancer cell line MCF7. *Res Med*. 2012;36:124-131.
62. Chen HH, Zhou HJ, Fang X. Inhibition of human cancer cell line growth and human umbilical vein endothelial cell angiogenesis by artemisinin derivatives in vitro. *Pharm Res*. 2003;48:231-236.
63. Haghi G, Safaei A, Safai Ghomi J. Identification and determination of flavonoids in leaf, dried aqueous and dried hydroalcoholic extract of *Artemisia absinthium* by HPLC. *Iran J Pharm Res*. 2004;3:89-90.
64. Zhou HJ, Wang WQ, Wu GD, Lee J, Li A. Artesunate inhibits angiogenesis and down regulates vascular endothelial growth factor expression in chronic myeloid leukemia K562 cells. *Vascul Pharmacol*. 2007;47:131-138.
65. Ayyadurai N, Valarmathy N, Kannan S, Jansirani D, Alsenaidy A. Evaluation of cytotoxic properties of *Curcuma longa* and *Tagetes erecta* on cancer cell line (Hep2). *Afr J Pharm Pharmacol*. 2013; 7:736-739.
66. Kurapati KR, Samikkannu T, Kadiyala DB, et al. Combinatorial cytotoxic effects of *Curcuma longa* and *Zingiber officinale* on the PC-3M prostate cancer cell line. *J Basic Clin Physiol Pharmacol*. 2012;23:139-146.
67. Ranjbari J, Alibakhshi A, Arezumand R, et al. Effects of *Curcuma longa* extract on telomerase activity in lung and breast cancer cells. *Zahedan J Res Med Sci*. 2014;16:1-6.
68. Mohammad P, Nosratollah Z, Mohammad R, Abbas A, Javad R. The inhibitory effect of *Curcuma longa* extract on telomerase activity in A549 lung cancer cell line. *Afr J Biotechnol*. 2010;9: 912-919.

69. Hosseinimehr SJ. A review of preventive and therapeutic effects of curcumin in patients with cancer. *J Clin Excell*. 2014;2:50-63.
70. Anand P, Sundaram C, Jhurani S, Kunnumakkara AB, Aggarwal BB. Curcumin and cancer: an ''old-age'' disease with an ''age old'' solution. *Cancer Lett*. 2008;267:133-164.
71. Shafaghati N, Hedayati N, Hosseinimehr SJ. Protective effects of curcumin against genotoxicity induced by 131-iodine in human cultured lymphocyte cells. *Pharmacogn Mag*. 2014;10:106-110.
72. Sarkar FH, Li Y, Wang Z, Padhye S. Lesson learned from nature for the development of novel anti-cancer agents: implication of isoflavone, curcumin, and their synthetic analogs. *Curr Pharm Des*. 2010;16:1801-1812.
73. Nejad Shahrokhabadi Kh, Tavakkol Afshari J, Rakhshandeh H, Barouk A. Study of cytotoxicity effect of total saffron extract on hepatocarcinoma cell line (HepG2) [in Persian]. *Med Sci J Islamic Azad Univ Tehran Med Branch*. 2009;19:154-159.
74. Aung HH, Wang CZ, Ni M, Fishbein A, Mehendale SR, Xie JT. Crocin from *Crocus sativus* possesses significant anti-proliferation effects on human colorectal cancer cells. *Exp Oncol*. 2007;29:175-180.
75. Mousavi M, Baharara J, Asadi-Samani M. Anti-angiogenesis effect of *Crocus sativus* L. extract on matrix metalloproteinase gene activities in human breast carcinoma cells. *J HerbMed Pharmacol*. 2014;3:101-105.
76. Rahimi Fard N, Haji Mahdipour H, Hedayati MH, Esmaili M. Evaluation of cytotoxic effects of aqueous-methanolic saffron extract on Vero, HeLa and Hep2 cell lines using MTT assay method. *Iran J Med Microbiol*. 2011;4:59-65.
77. Moheghi N, Tavakkol Afshari J, Brook A. The cytotoxic effect of *Zingiber officinale* in breast cancer (MCF7) cell line. *Horizon Med Sci*. 2011;17:28-34.
78. Rahman S, Salehin F, Iqbal A. In vitro antioxidant and anticancer activity of young *Zingiber officinale* against human breast carcinoma cell lines. *BMC Complement Altern Med*. 2011;11:76.
79. Fini L, Hotchkiss E, Fogliano V, et al. Chemopreventive properties of pinoresinol-rich olive oil involve a selective activation of the ATM-p53 cascade in colon cancer cell lines. *Carcinogenesis*. 2008;29:139-146.
80. Menendez JA, Vazquez-Martin A, Oliveras-Ferraros C, et al. Extra-virgin olive oil polyphenols inhibit HER2 (erbB-2)-induced malignant transformation in human breast epithelial cells: relationship between the chemical structures of extra-virgin olive oil secoiridoids and lignans and their inhibitory activities on the tyrosine kinase activity of HER2. *Int J Oncol*. 2009;34:43-51.
81. Rub M, Juliana C, Elvira I, Hern V, Ruiz-Gutierrez M, Luisa N. Acidic triterpenes compromise growth and survival of 20 astrocytoma cell lines by regulating reactive oxygen species accumulation. *Cancer Res*. 2007;67:3741-3751.
82. Khazir J, Mir BA, Mir SA, Cowan D. Natural products as lead compounds in drug discovery. *J Asian Nat Prod Res*. 2013;15:764-788.
83. Hamta A, Parvini P. Study of cytotoxic effects of taxol and rosemary extracts on cancerous cells derived from DMBA-induced breast cancer in SD rats. *Cell Tissue Res*. 2011;2:117-126.
84. Sadeghi-Aliabadi H, Alavi M, Asghari Gh, Mirian M. Cytotoxic evaluation of different extracts of *Taxus baccata* against MDA-MB-468, HeLa and K562 cancer cell lines. *J Isfahan Med Sch*. 2013;31:1508-1517.
85. Asadi-Samani M, Kafash-Farkhad N, Azimi N, Fasihi A, Alinia-Ahandani E, Rafieian-Kopaei M. Medicinal plants with hepato-protective activity in Iranian folk medicine. *Asian Pac J Trop Biomed*. 2015;5:146-157.
86. Tabasi NS, Khajavi-Rad A, Mahmoudi M, et al. The effects of *Nigella sativa* ethanolic extract on proliferation and apoptosis of renal cell carcinoma ACHN cell line. *J Shahrekord Univ Med Sci*. 2010;12:7-14.
87. Ait Mbarek L, Ait Mouse H, Elabbadi N, et al. Anti-tumor properties of blackseed (*Nigella sativa* L.) extracts. *Braz J Med Biol Res*. 2007;40:839-847.
88. Gali-Muhtasib H, Diab-Assaf M, Boltze C, et al. Thymoquinone extracted from black seed triggers apoptotic cell death in human colorectal cancer cells via a p53-dependent mechanism. *Int J Oncol*. 2004;25:857-866.
89. Shoeib AM, Elgayyar M, Dudrich P, Bell J. In vitro inhibition of growth and induction of apoptosis in cancer cell lines by thymoquinone. *Int J Oncol*. 2003;22:107-13.
90. Muhtasib H, Roessner A, Schneider R. Thymoquinone: a promising anti-cancer drug form natural sources. *Int J Biochem Cell Biol*. 2006;38:1249-1253.
91. Lamm DL, Riggs DR. The potential application of *Allium sativum* (garlic) for the treatment of bladder cancer. *Urol Clin North Am*. 2000;27:157-162.
92. Shirzad H, Taji F, Pourgheysari B, Raisi S, Rafieian-Kopaei M. Comparison of antitumour activities of heated and raw garlic extracts on fibrosarcoma in mice. *J Babol Univ Med Sci*. 2012;14:77-83.
93. Robert V, Mouille B, Mayeur C, Michaud M, Blachier F. Effects of the garlic compound diallyl disulfide on the metabolism, adherence and cell cycle of HT-29 colon carcinoma cells: evidence of sensitive and resistant sub-populations. *Carcinogenesis*. 2001;22:1155-1161.
94. Hadjzadeh MAIR, Tavakol Afshari J, Ghorbani A, Shakeri MT. The effects of aqueous extract of garlic (*Allium sativum* L.) on laryngeal cancer cells (Hep-2) and L929 cells in vitro. *J Med Plants*. 2006;2(18):41-48.
95. Nakagawa H, Tsuta K, Kiuchi K, Senzaki H, Tanaka K, Tsubura A. Growth inhibitory effects of diallyl disulfide on human breast cancer cell lines. *Carcinogenesis*. 2001;22:891-897.
96. Arunkumar A, Vijayababu MR, Srinivasan N, Aruldhas MM, Arunakaran J. Garlic compound, diallyl disulfide induces cell cycle arrest in prostate cancer cell line PC-3. *Mol Cell Biochem*. 2006;288:107-113.
97. Oommen S, Anto RJ, Srinivas G, Karunagaran D. Allicin (from garlic) induces caspase-mediated apoptosis in cancer cells. *Eur J Pharmacol*. 2004;485:97-103.
98. Colić M, Vucević D, Kilibarda V, Radicević N, Savić M. Modulatory effects of garlic extracts on proliferation of T-lymphocytes in vitro stimulated with concanavalin A. *Phytomedicine*. 2002;9:117-124.
99. Ahmed N, Laverick J, Sammons J, Zhang H, Maslin DJ, Hassan HT. Ajoene, a garlic-derived natural compound, enhances chemotherapy-induced apoptosis in human myeloid leukaemia

CD34-positive resistant cells. *Anticancer Res*. 2001;21: 3519-3529.
100. Shirzad H, Zamanzad B, Shahabi G. Expression of NC-2 receptor on MCL cells and its natural cytotoxicity against cancer cells. *Kuwait Med J*. 2009;41:112-116.
101. Shirzad H, Burton R, Smart Y, Rafieian-Kopaei M, Shirzad M. Natural cytotoxicity of NC-2+ cells against the growth and metastasis of WEHI-164 fibrosarcoma. *Scand J Immunol*. 2011;73:85-90.
102. Al-Fatimi M, Friedrich U, Jenett-Siems K. Cytotoxicity of plants used in traditional medicine in Yemen. *Fitoterapia*. 2005;76: 355-358.
103. Aslani E, Naghsh N, Ranjbar M. Cytotoxic effects of hydro-alcoholic extracts of cress (*Lepidium sativum*)—made from different stages of the plant—on k562 leukemia cell line. *Hormozgan Med J*. 2015;18:411-419.
104. Mahassni SH, Al-Reemi RM. Apoptosis and necrosis of human breast cancer cells by an aqueous extract of garden cress (*Lepidium sarivum*) seeds. *Saudi J Biol Sci*. 2013;20:131-139.
105. Alsemari A, Alkhodairy F, Aldakan A, et al. The selective cytotoxic anti-cancer properties and proteomic analysis of *Trigonella Foenum-Graecum*. *BMC Complement Altern Med*. 2014;14:114.
106. Amin A, Alkaabi A, Al-Falasi S, Daoud SA. Chemopreventive activities of *Trigonella foenum graecum* (fenugreek) against breast cancer. *Cell Biol Int*. 2005;29:687-694.
107. Hasanzadeh E, Rezazadeh SH, Shamsa SF, Dolatabadi R, Zarringhalam J. Review on phytochemistry and therapeutic properties of fenugreek (*Trigonella foenum-graceum*). *J Med Plants*. 2010;2:1-18.
108. Sur P, Das M, Gomes A, et al. *Trigonella foenum graecum* (fenugreek) seed extract as an antineoplastic agent. *Phytother Res*. 2001;15:257-259.
109. Hamta A, Shariatzadeh SMA, Soleimani Mehranjani SMA, Fallah Huseini H, Hosseinabadi F. The cytotoxic effects of *Glycyrrhiza glabra* L. root extract on 4T1 cell line derived from BALB/c mice mammary tumors. *J Med Plants*. 2014;2:92-103.
110. Harwansh RK, Patra KC, Pareta SK, Singh J. Pharmacological studies on *Glycyrrhiza glabra*. *Pharmacol Online*. 2011;2: 1032-1038.
111. Baltina LA. Chemical modification of glycyrrhizic acid as a route to new bioactive compounds for medicine. *Curr Med Chem*. 2003;10:155-171.
112. Rossi T, Castelli M, Zandomeneghi G, Ruberto A, Benassi L, Magnoni C. Selectivity of action of glycyrrhizin derivatives on the growth of MCF-7 and HEP-2 cells. *Anticancer Res*. 2003; 23:3813-3818.
113. Luo C-F, Kong J, Wang H, Liu H, Chen C, Shao S-H. Ethanol extracts of *Physalis alkekengi* Linn induced the apoptosis of human esophageal carcinoma cells. *Chin J Clin Lab Sci*. 2012; 12:21.
114. Torabzadeh P, Dezfulian M. Study of cytotoxicity effects of aqueous extract of *Physalis alkekengi* against u937 cell line. *Q J Anim Physiol Dev*. 2013;6:15-25.
115. Kawai M, Ogura T, Nakanishi M, et al. Structure of Physalin M isolated from *Physalis alkekengi* var. francheti. *Bull Chem Soc Jpn*. 2006;61:2696-2698.
116. Li X, Zhao J, Yang M, et al. Physalins and withanolides from the fruits of *Physalis alkekengi* L. var. franchetii (Mast.) Makino and the inhibitory activities against human tumor cells. *Phytochem Lett*. 2014;10:95-100.
117. Shokrzadeh M, Parvaresh A, Shahani S, Habibi E, Zalzar Z. Cytotoxic effects of *Lagenaria siceraria* Standl. extract on cancer cell line. *J Mazandaran Univ Med Sci*. 2013;23:225-230.
118. Saha P, Kundu Sen S, Bala A, Mazumder UK, Haldar PK. Evaluation of anticancer activity of *Lagenaria siceraria* aerial parts. *Int J Cancer*. 2011;3:244-253.
119. Ghosh K, Chandra K, Ojha AK, Sarkar S, Islam SS. Structural identification and cytotoxic activity of a polysaccharide from the fruits of *Lagenaria siceraria* (Lau). *Carbohydr Res*. 2009;344: 693-698.
120. Tyagi N, Sharma G, Hooda V. Phytochemical and pharmacological profile of *Lagenaria siceraria*: an overview. *Int Res J Pharm*. 2012;3:1-4.
121. Shah B, Seth A. pharmacognostic studies of the *Lagenaria siceraria* (molina) standley. *Int J PharmTech Res*. 2010;2:121-124.
122. Valiahdi SM, Iranshahi M, Sahebkar A. Cytotoxic activities of phytochemicals from Ferula species. *DARU*. 2013;21:39-45.
123. Eslami Jadidi B, Dehpouri A, Nemati F, Rezaei B. Cytotoxicity effects of the *Ferula gummosa* extract on the cancer cell line MCF7. *J Anim Biol*. 2013;5:1-7.
124. Gharaei R, Akrami H, Heidari S, Asadi MH, Jalili A. The suppression effect of *Ferula gummosa* Boiss. extracts on cell proliferation through apoptosis induction in gastric cancer cell line. *Eur J Integr Med*. 2013;5:241-247.
125. Ziai SA, Gholami O, Iranshahi M, Zamani AH, Jeddi-Tehranid M. Umbelliprenin induces apoptosis in CLL cell lines. *Iran J Pharm Res*. 2012;11:653-659.
126. Barthomeuf C, Lim S, Iranshahi M, Chollet P. Umbelliprenin from *Ferula szowitsiana* inhibits the growth of human M4Beu metastatic pigmented malignant melanoma cells through cell-cycle arrest in G1 and induction of caspase-dependent apoptosis. *Phytomedicine*. 2008;15:103-111.
127. Jalali HT, Petronilho S, Villaverde JJ, et al. Assessment of the sesquiterpenic profile of *Ferula gummosa* oleo-gum-resin (galbanum) from Iran contributes to its valuation as a potential source of sesquiterpenic compounds. *Ind Crops Prod*. 2013;44:185-191.
128. Iranshahi M, Masullo M, Asili A, et al. Sesquiterpene coumarins from *Ferula gumosa*. *J Nat Prod*. 2010;73:1958-1962.
129. Forouzandeh S, Naghsh N, Salimi S, Jahantigh D. Cytotoxic effect of *Boswellia serrata* hydroalcholic extract on human cervical carcinoma epithelial cell line. *Med Lab J*. 2014;8:7-13.
130. Chashoo G, Singh SK, Sharma PR, et al. A propionyloxy derivative of 11-keto-boswellic acid induces apoptosis in HL-60 cells mediated through topoisomerase I and II inhibition. *Chem Biol Interact*. 2011;189:60-71.
131. Bhushan S, Kumar A, Malik F, et al. A triterpenediol from *Boswellia serrata* induces apoptosis through both the intrinsic and extrinsic apoptotic pathways in human leukemia HL-60 cells. *Apoptosis*. 2007;12:1911-1926.
132. Huang MT, Badmaev V, Ding Y, Liu Y, Xie JG, Ho CT. Anti-tumor and anti-carcinogenic activities of triterpenoid, β-boswellic acid. *Biofactors*. 2000; 13:225-230.

133. Poeckel D, Werz O. Boswellic acids: biological actions and molecular targets. *Curr Med Chem*. 2006;13:3359-3369.
134. Durak I, Biri H, Devrim E, Sözen S, Avcı A. Aqueous extract of *Urtica dioica* makes significant inhibition on adenosine deaminase activity in prostate tissue from patients with prostate cancer. *Cancer Biol Ther*. 2004;3:855-857.
135. Konrad L, Müller HH, Lenz C, Laubinger H, Aumüller G, Lichius JJ. Antiproliferative effect on human prostate cancer cells by a stinging nettle root (*Urtica dioica*) extract. *Planta Med*. 2000;66:44-47.
136. Safarinejad MR. *Urtica dioica* for treatment of benign prostatic hyperplasia: a prospective, randomized, double-blind, placebo-controlled, crossover study. *J Herbal Pharmacother*. 2005;5: 1-11.
137. Aydin M, Aslaner A, Zengin A. Using *Urtica dioica* in esophageal cancer: a report of a case. *Internet J Surg*. 2005;7(2).
138. Pinelli P, Ieri F, Vignolini P, Bacci L, Baronti S, Romani A. Extraction and HPLC analysis of phenolic compounds in leaves, stalks, and textile fibers of *Urtica dioica* L. *J Agric Food Chem*. 2008;56:9127-9132.
139. Nemati F, Eslami Jadidi B, Talebi Darabi M. Investigation cytotoxic effects of *Ammi majus* extract on MCF-7and Hela cancer cell line [in Persian]. *J Anim Biol*. 2013;5:59-66.
140. Shokoohinia Y, Hosseinzadeh L, Alipour M, Mostafaie A, Mohammadi-Motlagh H-R. Comparative evaluation of cytotoxic and apoptogenic effects of several coumarins on human cancer cell lines: osthole induces apoptosis in p53-deficient H1299 cells. *Adv Pharmacol Sci*. 2014;2014:8.
141. Zu Y, Yu H, Liang L, et al. Activities of ten essential oils towards *Propionibacterium acnes* and PC-3, A-549 and MCF-7 cancer cells. *Molecules*. 2010;15:3200-3210.
142. Zamiri-Akhlaghi A, Rakhshandeh H, Tayarani-Najaran Z, Mousavi SH. Study of cytotoxic properties of *Rosa damascena* extract in human cervix carcinoma cell line. *Avicenna J Phytomed*. 2011;1:74-77.
143. Baydar NG, Baydar H. Phenolic compounds, antiradical activity and antioxidant capacity of oil-bearing rose (*Rosa damascena* Mill.) extracts. *Ind Crops Prod*. 2013;41:375-380.
144. Kalim MD, Bhattacharyya D, Banerjee A, Chattopadhyay S. Oxidative DNA damage preventive activity and antioxidant potential of plants used in Unani system of medicine. *BMC Complement Altern Med*. 2010;10:77.
145. Aldaghi L, DehpoorJoybari A, Nemati F, Mirdashti R, Akrami R. The effects of cytotoxicity of *Astragalus cystosus* on the Hela cells by using MTT method. *J Sabzevar Univ Med Sci*. 2014;20: 603-610.
146. Cassileth BR, Rizvi N, Deng G, et al. Safety and pharmacokinetic trial of docetaxel plus an Astragalus-based herbal formula for non-small cell lung cancer patients. *Cancer Chemother Pharmacol*. 2009;65:67-71.
147. Auyeung K, Law P, Ko JK. Astragalus saponins induce apoptosis via an ERK-independent NF-κB signaling pathway in the human hepatocellular HepG2 cell line. *Int J Mol Med*. 2009; 23:189-196.
148. Hu YW, Liu CY, Du CM, Zhang J, Wu WQ, Gu ZL. Induction of apoptosis in human hepatocarcinoma SMMC-7721 cells in vitro by flavonoids from *Astragalus complanatus*. *J Ethnopharmacol*. 2009;123:293-301.
149. Ogur R. Studies with *Myrtus communis* L.: anticancer properties. *J Intercult Ethnopharmacol*. 2014;3:135-137.
150. Sumbul S, Ahmad MA, Asif M, Akhtar M. *Myrtus communis* Linn—A review. *Indian J Nat Prod Resour*. 2011;2:395-402.
151. Mothana RA, Kriegisch S, Harms M, Wende K, Lindequist U. Assessment of selected Yemeni medicinal plants for their in vitro antimicrobial, anticancer, and antioxidant activities. *Pharm Biol*. 2011;49:200-210.
152. Alipour G, D ashti S, Hosseinzadeh H. Review of pharmacological effects of *Myrtus communis* L. and its active constituents. *Phytother Res*. 2014;28:1125-1136.
153. Asgarpanah J, Ariamanesh A. Phytochemistry and pharmacological properties of *Myrtus communis* L. Indian J Tradit Knowl. 2015;14:82-87.
154. Tretiakova I, Blaesius D, Maxia L, et al. Myrtucommulone from *Myrtus communis* induces apoptosis in cancer cells via the mitochondrial pathway involving caspase-9. *Apoptosis*. 2008;13: 119-131.
155. Aidi Wanes W, Mhamdi B, Sriti J, et al. Antioxidant activities of the essential oils and methanol extracts from myrtle leaf. *Food Chem Toxicol*. 2010;48:1362-1370.
156. Khazaei Poul Y, Majd A, Labibi F, Moini Zanjani T. Cytotoxic effect of methanolic extracts of vegetative and reproductive parts of *Vinca rosea* on A431, a human skin squamous carcinoma cell line. *J Physiol Pharmacol*. 2014;18:364-372.
157. Roepkea J, Salima V, Wua M, et al. Vinca drug components accumulate exclusively in leaf exudates of Madagascar periwinkle. *Proc Natl Acad Sci U S A*. 2010;107:15287-15299.
158. Siddiqui S, Ismail Z, Saidan N. Simultaneous determination of secondary metabolites from *Vinca rosea* plant extractives by reverse phase high performance liquid chromatography. *Pharmacogn Mag*. 2011;7:92-96.
159. Jayakumar D, Mary SJ, Santhi RJ. Evaluation of antioxidant potential and antibacterial activity of *Calotropis gigantea* and *Vinca rosea* using in vitro model. *Indian J Sci Technol*. 2010; 3:720-723.
160. Tavakkol Afshari J, Rakhshandeh H, Zamani AR, Mahdavi Shahri N, Ghazezadeh L, Norozi M. Cytotoxicity effects of *Citrullus colocynthis* on Hep2 and L929 cell lines. *Hakim Res J*. 2005;8:47-54.
161. Hatam NA, Whiting DA, Yousif NJ. Cucurbitacin glycosides from *Citrullus colocynthis*. *Phytochemistry*. 1989;28: 1268-1271.
162. Wasfi IA. Some pharmacological studies on *Citrullus colocynthis*. *J Herbs Spices Med Plants*. 1994;2:65-79.
163. Ayyad S-EN, Abdel-Lateff A, Alarif WM, Patacchioli FR, Badria FA, Ezmirly ST. In vitro and in vivo study of cucurbitacins-type triterpene glucoside from *Citrullus colocynthis* growing in Saudi Arabia against hepatocellular carcinoma. *Environ Toxicol Pharmacol*. 2012;33:245-251.
164. Tannin-Spitz T, Grossman S, Dovrat S, Gottlieb HE, Bergman M. Growth inhibitory activity of cucurbitacin glucosides isolated from *Citrullus colocynthis* on human breast cancer cells. *Biochem Pharmacol*. 2007;73:56-67.

165. Banazadeh H, Delazar A, Habibi Roudkenar M, Rahmati Yamchi M, Sadeghzadeh Oscoui B, Mehdipour A. Effects of knotweet or polygonum aviculare herbal extract on proliferation of HeLa cell line. *Med J Mashhad Univ Med Sci*. 2012;54:238-241.
166. Mohammad R, Hossein B, Davood F, Farnaz T, Ali F, Yuse R. The apoptotic and cytotoxic effects of *Polygonum avicular* extract on Hela-S cervical cancer cell line. *Afr J Biochem Res*. 2011;5:373-378.
167. Habibi RM, Mohammadi RA, Delazar A, et al. Effects of *Polygonum aviculare* herbal extract on proliferation and apoptotic gene expression of MCF-7. *DARU*. 2011;19:326-331.
168. Salama HMH, Marraiki N. Antimicrobial activity and phytochemical analyses of *Polygonum aviculare* L. (Polygonaceae), naturally growing in Egypt. *Saudi J Biol Sci*. 2010;17:57-63.
169. Abdolmohammadi MH, Fouladdel Sh, Shafiee A, Amin Gh, Ghaffari SM, Azizi E. Antiproliferative and apoptotic effect of *Astrodaucus orientalis* (L.) drude on T47D human breast cancer cell line: potential mechanisms of action. *Afr J Biotechnol*. 2009; 8:4265-4276.
170. Razavi SM, Imanzadeh G, Dolati S, et al. Phytochemical prospection and biological activity of *Astrodaucus orientalis* (L.) Drude growing wild in Iran. *Pharmacologia*. 2011;2:299-301.
171. Nazemiyeh H, Razavi SM, Delazar A, et al. Distribution profile of volatile constituents in different parts of *Astrodaucus orientalis* (L.) Drude. *Rec Nat Prod*. 2009;3:126-130.
172. Kintzios SE, Barberaki MG. *Plants That Fight Cancer*. Boca Raton, FL: CRC Press; 2003:20-22.
173. Nasri H, Rafieian-Kopaei M. World Cancer Day 2014: ''increasing the awareness''. *Cell J*. 2014;16:383-34.
174. Karamati SA, Hassanzadazar H, Bahmani M, Rafieian-Kopaei M. Herbal and chemical drugs effective on malaria. *Asian Pac J Trop Dis*. 2014;4:599-601.
175. Bagheri N, Rahimian Gh, Salimzadeh L, et al. Association of the virulence factors of *Helicobacter pylori* and gastric mucosal interleukin-17/23 mRNA expression in dyspeptic patients. *EXCLI J*. 2013;12:5-14.
176. Baradaran A, Nasri H, Rafieian-Kopaei M. Oxidative stress and hypertension: possibility of hypertension therapy with antioxidants. *J Res Med Sci*. 2014;19:358-367.
177. Madihi Y, Merrikhi A, Baradaran A, et al. Impact of sumac on postprandial high-fat oxidative stress. *Pak J Med Sci*. 2013;29: 340-345.
178. Kafash-Farkhad N, Asadi-Samani M, Rafieian-Kopaei M. A review on phytochemistry and pharmacological effects of *Prangos ferulacea* (L.) Lindl. *Life Sci J*. 2013;10:360-367.
179. Bahmani M, Zargaran A, Rafieian-Kopaei M. Identification of medicinal plants of Urmia for treatment of gastrointestinal disorders. *Rev Bras Farmacogn*. 2014;24:468-480.
180. Rahimian G, Sanei MH, Shirzad H, et al. Virulence factors of *Helicobacter pylori* vacA increase markedly gastric mucosal TGF-β1 mRNA expression in gastritis patients. *Microb Pathog*. 2014;67-68:1-7.
181. Bahmani M, Rafieian M, Baradaran A, Rafieian S, Rafieian-Kopaei M. Nephrotoxicity and hepatotoxicity evaluation of *Crocus sativus* stigmas in neonates of nursing mice. *J Nephropathol*. 2014;3:81-85.
182. Lam RY, Woo AY, Leung PS, Cheng CH. Antioxidant actions of phenolic compounds found in dietary plants on low-density lipoprotein and erthrocytes in vitro. *J Am Coll Nutr*. 2007;26: 233-242.
183. Pahari B, Chakraborty S, Chaudhuri S, Sengupta B, Sengupta PK. Binding and antioxidant properties of therapeutically important plant flavonoids in biomembranes: Insights from spectroscopic and quantum chemical studies. *Chem Phys Lipids*. 2012;165:488-496.
184. Nasri H, Rafieian-Kopaei M. Tubular kidney protection by antioxidants. *Iran J Public Health*. 2013;42:1194-1196.
185. Baradaran A, Nasri H, Nematbakhsh M, Rafieian-Kopaei M. Antioxidant activity and preventive effect of aqueous leaf extract of Aloe Vera on gentamicin-induced nephrotoxicity in male Wistar rats. *Clin Ter*. 2014;165:7-11.
186. Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. *Pharm Biol*. 2013;51:1104-1109.
187. Asgari A, Rafieian-Kopaei M. Single or whole antioxidants in metal toxicities. *J Herbmed Pharmacol*. 2015;4:69-70.
188. Nasri H, Rafieian-Kopaei M. Protective effects of herbal antioxidants on diabetic kidney disease. *J Res Med Sci*. 2014;19: 82-83.
189. Memmott RM, Dennis PA. Akt-dependent and independent mechanisms of mTOR regulation in cancer. *Cell Signal*. 2009; 2:656-664.
190. Ramos S. Cancer chemoprevention and chemotherapy: dietary polyphenols and signalling pathways. *Mol Nutr Food Res*. 2008;52:507-526.
191. West KA, Castillo SS, Dennis AP. Activation of the PI3K/Akt pathway and chemotherapeutic resistance. *Drug Resist Updat*. 2002;5:234-248.
192. Van Aller GS, Carson JD, Tang W, et al. Epigallocatechin gallate (EGCG), a major component of green tea, is a dual phosphoinositide-3-kinase/mTOR inhibitor. *Biochem Biophys Res Commmun*. 2011;406:194-199.
193. Sun ZJ, Chen G, Hu X, et al. Activation of PI3K/Akt/IKK-α/NF-κB signaling pathway is required for the apoptosis-evasion-evasion in human salivary a denoid cystic carcinoma: its inhibition by quercetin. *Apoptosis*. 2010;15:850-863.