Anticancer Properties of Different Species of *Salvia*

Farklı *Salvia* Türlerinin Antikanser Özellikleri

Review Article

Işıl Yıldırım* and Türkan Kutlu
İnönü University, Faculty of Science and Arts, Department of Chemistry Chemistry, Malatya, Turkey.

ABSTRACT

Historically, thousands of different species of plant have been reported as being useful for the treatment of cancer. *Salvia* species think among these plants. *Salvia*; "sage" are derived from the Latin salvere referring to remedy properties arrogate to the various *Salvia* species. *Salvia* is the largest genus of plants in the mint family, Lamiaceae. In this review we performed to report the anticancer features of different species of *salvia*

Key Words
Salvia, Anticancer activity.

ÖZET

Tarih boyunca binlerce farklı bitki türünün kanser tedavisinde kullanımı rapor edilmiştir. *Salvia* türleri de bu bitkiler arasındadır. Adaçayı, çeşitli *salvia* türlerine atıfta bulunmak için latincede salvare kelimesinden türemiştir. *Salvia* Lamiaceae ailesinin en geniş bitki türüdür. Bu derlemede farklı *salvia* türlerinin anti kanser özelliği hakkında bilgi verme amaçlanmıştır.

Anahtar Kelimeler
Salvia, Anti kanser aktivite.

Article History: Received: Jan 26, 2015; Revised: May 26, 2015; Accepted: June 06, 2015; Available Online: Jul 25, 2015.

DOI: 10.15671/HJBC.20154312548

Correspondence to: I. Yıldırım, İnönü University, Faculty of Science and Arts, Department of Chemistry, Malatya, Turkey.
Tel: +90 537 569 8699 Fax: +90 422 341 0037 E-Mail: isilyld@hotmail.com

INTRODUCTION

Cancer; also known as a malignant tumor or malignant neoplasm, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body [1,2]. Recently; Cancer researchers have been tended to herbal medicine in treat cancer. Because they have therapeutic properties. *Salvia* species are among these plants. *Salvia* belongs to Lamiaceae family. In this review we performed to report the anticancer features of different species of *salvia*.

The information Literature

In a work; *Salvia absconditiflora* were investigated anti- tumor effect on the MCF-7 and MDA-MB-231 breast cancer cell lines. Cell proliferation was inhibited 50% by different IC_{50} values calculated in different assays and different time intervals [3].

From isolated *S. acetabulosa essential oil* inhibited the vitality of amelanotic melanoma (C32) and large cell carcinoma COR-L23 cell lines with IC_{50} values of 6.3 and 6.5 μg/mL. From isolated *S. leriifolia* exhibited a strong inhibitory activity on renal adenocarcinoma ACHN, large cell carcinoma COR-L23, amelanotic melanoma C32, and malignant melanoma A375 with IC_{50} values of 6.8, 7.5, 9.1, and 12.5 μg/mL seriatim. Nevertheless both *S. acetabulosa* and *S. leriifolia* were not executing anti-proliferative activity against human skin fibroblast 142BR [4].

Aqueous extracts of *Salvia chinensis* specify anti-proliferative activity. Results indicate the potential use of traditional Chinese medicinal herbs as antineoplastic agents [5].

In a work; investigated of anticancer effect of *Salvia cryptantha* against breast cancer as *in viro* and *in vivo*. Consequently; this plant had been exhibited antitumor activity [6].

Etanolic extract of *Salvia dominica*, *Salvia hierosolymitana*, *Salvia indica* leaves and other plants were evaluated for their anti-proliferative activity on a breast cancer cell line (MCF7). This extracts were exhibited high cytotoxic activity [7].

From *Salvia* isolated different terphenoids emceed forceful anti-proliferative activity against the prostate cancer cell lines (PC3) with IC_{50} of 3.9 ± 0.1, 6.2±0.1 and 2.8±0.1 μM, in oreder of , and cervical cancer cell lines (HeLa) with Ic_{50} of 8.0±0.3, 2.6±0.1 and 2.7±0.1 μM, respectively [8].

Wafica S. Itani et al., found that combining the three bioactive compounds of S. *libanotica* essential oil, Linalyl acetate (Ly) Terpeniol (Te) and Camphor (Ca) caused significant growth suppression of HCT116 p53+/+ cells in PreG1 (64% at 48 hours). In p53-/- cells, Ly + Te + Ca caused cell accumulation in PreG1 and G2/M phases [9].

Methanolic extract of *Salvia eremophil*, *Salvia macrosiphon*, *Salvia reuterana*, *Salvia santolinifolia* be labour cytotoxic effect on the Raji lymphoma cell line. This extracts More than 50% of Raji cells growth was inhibited [10].

In a work; the investigated of the anti-proliferative activity of ethanolic extracts of *Salvia menthifolia* on DBTRG-05MG cell line. Consequently; *Salvia menthifolia* towards this extremely aggressive human glioblastoma cell line. Suggested that a natural source of anti-tumor agents [11].

According to a study published in the 2011; Investigated of anticancer activity of *Salvia officinalis* essential oil against HNSCC cell line (UMSCC1). Consequently; *Salvia officinalis* essential oil to inhibit human HNSCC cell growth. And it has been suggested as therapeutic potential [12].

In a work publis in the 2013; methanol extracts prepared from *Salvia officinalis L.*, on a non-Hodgkin's B-cell lymphoma (Raji) and human leukemic monocyte lymphoma (U937), Human acute myelocytic leukemia (KG-1A) and Human Umbilical Vein Endothelial (HUVEC) cell lines. Consequently; The *Salvia officinalis L.* extract was found dose and time-dependently inhibits the proliferation of lymphoma and leukemic cells possibly via an apoptosis-dependent pathway [13].

Isolated from *Salvia radula* of betulafolientriol oxide and salvigenin inhibit 50% of cancer cells [14].

In a study published in the 2014, *Salvia atropatana*, *Salvia sclarea* Salvia *sahendica*, *Salvia hydrangea*, *Salvia xanthocheila*, *Salvia macrosiphon*, *Salvia glutinosa*, *Salvia chloroleuca* and *Salvia ceratophylla* species for their antioxidant and anti-proliferative activities. *S. ceratophylla* ex/hibited the strongest anticancer activity against C32 cells with an IC_{50} value of 20.8 μg/mL, while *S. glutinosa* exhibited an IC_{50} value of 29.5 μg/mL against ACHN cell line [15]

According to a study publish in the 2006, evaluation of anticancer activity of methanolic extract of *Salvia dominica L*. leaves, *Salvia lanigera* Desf. Aerial parts, *Salvia menthaefolia* Ten roots, *Salvia palaestina* Benth. aerial parts, *Salvia sclarea* L. roots and *Salvia spinosa* L. aerial parts on the glioblastoma (DBTRG-05MG, T98G, U-87MG), colorectal adenocarcinoma (WiDr and HT-29), prostate adenocarcinoma (MDA Pca2b), choriocarcinoma (JEG-3), endometrium adenocarcinoma (HEC-1A) and B lymphoblast (CIR). According to results, the genus *Salvia* could be considered a natural resource of potential antitumor agents [16].

Recently; shown that the oil extract of *Salvia triloba* has effect chemopreventive abilities in the DMBA/TPA mouse model of skin carcinogenesis [17].

S. xanthocheila, S. aegyptiaca, *S. aethiopis*, *S. atropatana*, *S. eremophila*, *S. hypoleuca*, *S. limbata, S. nemorosa, S. santolinifolia, S. sclarea, S. syriaca*, in localizated in Iran. As used this plants extract appraised cytotoxic activity on HL60, K562 cells, Mcf-7 cells [18]

In a work; it was that mechanisms of actions and cell signaling pathways of anticancer of diterpenoids from Salvia species were determined [19].

Reported that hydrophilic phenolic acids of *Salvia miltiorrhiza Bunge* has anticancer effect [20].

In a work aimed that to investigate the antitumor activty of Chi-Shen extract (CSE) from the water-soluble compounds of *Salvia miltiorrhiza* on HepG2 cells (hepatocellular carcinoma cell line). Consequently; demonstrated that CSE was able to inhibit the proliferation of HepG2 cells and cause apoptosis [21].

In a study investigated that antitumor activity of *Salvia menthifolia* ten of methanolic extraction on the DBTRG-05MG cell line (human glioblastoma cell line) In a result corrected that this *salvia* species is a natural source of anti-tumor agents [22].

Bauer *et al*. determined that Carnosol and Carnosic Acids from *Salvia officinalis* Inhibit Microsomal Prostaglandin E2 Synthase-1, which Prostaglandin E2 (PGE2), the most relevant eicosanoid promoting inflammation and tumorgenesis, is formed by cyclooxygenases (COXs). Consequently; identify that *Salvia officinalis* may critically contribute to the anti-inflammatory and anti-carcinogenic properties [23].

According to a work published in the 2011; *Salvia leriifolia* extracts and isolated constituents were evaluated for their cytotoxic activity against a panel of human cancer cell lines, including renal adenocarcinoma (ACHN), amelanotic melanoma (C32), colorectal adenocarcinoma (Caco-2), lung large cell carcinoma (COR-L23), malignant melanoma (A375), lung carcinoma (A549), and hepatocellular carcinoma (Huh-7D12) cells. In a result suggested that this components a selective activity against tumor cells [24].

Abu-Dahap *et al*., studied the anti-proliferative activity of crude ethanol extracts from *S. ceratophylla L., S. dominica L., S. hormium L., S. hierosolimitana Boiss., S. indica L., S. spinosa L., S. syriaca L., S. fruticosa* Mill. (syn. *S. triloba* L.) and *S. verbeneca* grown in Jordan against human tumor models of breast cancer; MCF-7, T47D, ZR-75-1, and BT 474. Results exhibited as a potential source for novel anticancer therapy [25].

According to a work published in the 2014; investigated of antioxidant and anti-proliferative activities of *Salvia sclarea, Salvia atropatana,*

Salvia sahendica, Salvia hydrangea, Salvia xanthocheila, Salvia macrosiphon, Salvia glutinosa, Salvia chloroleuca and *Salvia ceratophylla* species. Consequently *S. ceratophylla* exhibited the strongest activity against C32 cells with an IC_{50} value of 20.8 μg/mL, while *S. glutinosa* exhibited an IC_{50} value of 29.5 μg/mL against ACHN cell line [26].

Reported that The acetone extract of *Salvia officinalis L*. exhibited the most potent cytotoxicity (IC_{50} = 14 to 36 μg/mL) against three different cancer cell lines (B16F10, MCF-7 and HeLa) [27].

It has been shown that the oil extract of *Salvia triloba* has potential chemo-preventive talent in the DMBA/TPA mause of model skin carcinogenesis [28].

Reported that the ethanol crude extracts of S triloba showed anti-proliferative activity to MCF7 with IC_{50} values, and 25.25 μg/mL [29].

Itani *et al.,* investigated of anticancer effect of *Salvia libanotica* essential oil on colon carsinoma. Consequently to be that sage oil component as promising chemotherapeutic agents against colon cancer [30].

The Salvia libanotica essential oil has potential to prevent the proliferation of skin papillomas induced by 7,12 dimethylbenz[a]anthracene (DMBA)- and 12-O-tetradecanoylphorbol-13-acetate (TPA) in mice [31].

In a work; anti-proliferative activty of *Salvia officinalis L*. essential oil were determined against Human melanoma (A375, M14, and A2058) cell lines [32].

Reported that *S. leriifolia* exhibited a strong inhibitory activity on renal adenocarcinoma ACHN, large cell carcinoma COR-L23, amelanotic melanoma C32, and malignant melanoma A375 with IC_{50} values of 6.8, 7.5, 9.1, and 12.5 μg/mL respectively. *S. acetabulosa* inhibited the viability of C32 and COR-L23cell lines with IC_{50} values of 6.3 and 6.5 μg/mL. However, both *S. acetabulosa* and *S. leriifolia* couldn't exert anti-proliferative activity against human skin fibroblast 142BR [33]. *S. officinalis* oil was able to inhibit the growth of renal cell adenocarcinoma with IC_{50} of 100.70 μg/mL. The oil was unable to react with human breast cancer cell (MCF-7) and hormone dependent prostate carcinoma cell [34].

Salvia santolinifolia, *Salvia eremophil*, *Salvia macrosiphon*, *Salvia reuterana*, methanolic extracts of the plants were prepared and their cytotoxic effect determined on the Raji lymphoma cell line In result this extrcts more than 50% of Raji cells growth was inhibited by 21 μg/mL of this extract. *S. macrosiphon* extract also showed a strong inhibitory effect on this tumor cell line (IC_{50}= 77±1 μg/mL) [35].

In a work; cytotoxic properties of total methanol extract of *Salvia chloroleuca* were investigated on MCF-7, a breast carcinoma cell line. results exhibited a mechanism whereby *S. chloroleuca* induces apoptosis of MCF-7 human breast cells through a ROS-mediated pathway [36].

Russo and co-worker in their study the growth-inhibitory and pro-apoptotic effects of the essential oils from Sw and Sc S. verbenaca were evaluated in the human melanoma cell line M14, testing cell vitality, cell membrane integrity, genomic DNA fragmentation and caspase-3 activity. Both the essential oils were able to inhibit the growth of the cancer cells examined inducing also apoptotic cell death, but the essential oil from cultivated samples exhibited the major effects [37].

In a study publish in the 2014 year; the *Salvia miltiorrhiza* were informed to anticancer property [38].

In a study with *Salvia dominica*, its extracts exhibited potent anti-proliferative activity [39].

Sridharan *et al.,* investigate of antitumor potential of *Salvia leucantha Cav* (EESL) ethanolic extact on Ehrlich Ascites Carcinoma cell lines. Consequently; suggested that *Salvia leucantha Cav* has dominant anticancer [40].

According to published in the 2015 year, polysaccharides from *Salvia chinensis* (PSSC)

suppressed in vivo proliferation of H22 cells with undetectable toxic effects on tumor-bearing mice, PSSC alleviated tumor transplantation-induced CD4+ T cell apoptosis and dysregulation of serum cytokine profiles, which elevated cytotoxic activities of natural killer and CD8+ T cells. PSSC reduced serum levels of prostaglandin E2 (PGE2). Injection of exogenous PGE2 completely abrogated the antitumor immunostimulatory activity of PSSC. Cyclic adenosine monophosphate (cAMP) is the second messager of PGE2. In CD4+ T cells, PSSC substantially declined intracellular cAMP. This event elevated protein levels of JAK3, enhancing STAT5 phosphorylation and STAT5-depedent expression of anti-apoptotic genes. Cyclooxygenase-2 is the key enzyme mediating biosynthesis of PGE2. PSSC suppressed the transcription and translation of cyclooxygenase-2 in tumor associated macrophages [41].

Reported that Tanshinone IIA, extracted from the dried root of *S. miltiorrhiza*, is one of the potential anticancer components [42].

Wang and colleagues, Neo-tanshinlactone isolated from *S. miltiorrhiza* have property to in vitro against several human cancer cell lines, significant inhibition against two human breast cancer cell lines [43].

Hu and cowekers investigated the antihepatocellular carcinoma effects of Chi-Shen extract (CSE) from the water-soluble compounds of *Salvia miltiorrhiza* In a result identified that CSE was able to inhibit the proliferation of HepG2 cells and cause apoptosis [44].

In a work; the anti-proliferative and pro-apoptotic effects of water extracts of *Salvia fruticosa* (SF) and *Salvia officinalis* (SO) and of their main phenolic compound rosmarinic acid (RA) were evaluated in two human colon carcinoma-derived cell lines, HCT15 and CO115, which have different mutations in the MAPK/ERK andPI3K/Akt signalling pathways [45].

In a study; evaluated Induction of apoptosis and inhibition of proliferation in colon cancer cells the effect of *Salvia fruticosa* (SF) and *Salvia officinalis* (SO) water extracts and their main phenolic compound rosmarinic acid (RA) in two human colon carcinoma-derived cell lines, HCT15 and CO115, which have different profiles of constitutive activation of PI3K/Akt and MAPK/ERK pathways. Findings suggest that sage extracts inhibit proliferation in HCT15 cells due to their inhibition on KRAS with a consequent MAPK/ERK pathway down regulation and endorse the use of sage on anticancer therapy/prevention [46].

According to a work publish in the 2012; The cytotoxic effect of *Salvia mirzayanii*, *Salvia macrosiphon*, *Salvia multicaulis* were studied against HepG2 Cells. In a result the extracts of *S. macrosiphon* and *S. multicaulis* had no significant cytotoxic effects against HepG2 cells [47].

In a work; the cytotoxic activity of the *Salvia verticillata* L essential oil was investigated against HT-29 (colon adenocarcinoma), Caco-2 (colorectal adenocarcinoma), T-47D (breastductalcarcinoma) and NIH-3T3 (Swiss mouse embryo fibroblast) cell lines. Consequently essential oil of *S. verticillata* showed higher cytotoxic effect on Caco-2 cell line [48].

Tanshinones are the major bioactive compounds of *Salvia miltiorrhiza* Bunge (Danshen) roots. In a work the antitumor effects of tanshinones on the highly invasive human lung adenocarcinoma cell line, CL1-5. Consequently; determined that Tanshinone I significantly inhibited migration, invasion, and gelatinase activity in macrophage-conditioned medium-stimulated CL1-5 cells in vitro and also reduced the tumorgenesis and metastasis in CL1-5-bearing severe combined immune deficient mice [49].

According to a work publish in 2015 bioactive compounds isolated from the roots of *Salvia sahendica* Boiss and Buhse using bioassay-guided procedures and their biological effects against MCF-7 breast carcinoma cells. In comparison with other solvents, the hexane-based extraction resulted in the most potent anti-cancer activity were exhibited [50].

CONCLUSION

Plants, therapeutic purposes are among the latest trends in the world. Because plants are including a lot of metabolites. These metabolites are exhibit a lot pharmacological effect such as antioxidant, antimicrobial, antifungal, antibacterial, anti-inflammatory etc. also they have protect a lot of disease such as cancer, cardiovascular disease etc. Literature inform correct that *salvia* species effect of especially cancer a lot of illness. Frequent use of its, will be useful.

References

1. World Health Organization, February 2014. Retrieved 10 June 2014.
2. National Cancer Institute. Retrieved 10 June 2014.
3. S. Yılmaz., Cell proliferation was inhibited 50 % by different IC50 values calculated in different assays and different time intervals, Doctora thesis. 2013.
4. M.R. Loizzo, F. Menichini, R. Tundis, M. Bonesi, F. Nadjafi, A.M. Saab, N.G. Frega, F. Menichini., Comparative Chemical Composition and Antiproliferative Activity of Aerial Parts of *Salvia leriifolia* Benth. and *Salvia acetabulosa* L. Essential Oils Against Human Tumor Cell In Vitro Models, J Med Food., 13 (2010) 62-9.
5. M. Shoemaker, B. Hamilton, S.H. Dairkee, I. Cohen M.J. Campbel., In vitro anticancer activity of twelve Chinese medicinal herbs, Phytotherapy Research. 19 (2005) 649–651.
6. H. Özer, A. Altun, S. Unver-Saraydın, S. Soylu, S. Göktaş, E. tuncer, D.S. İnan, B. Köksal, T. Kaya Temiz, B. Tepe, M. Şen, K. Karadayı, M. Turan., antitumor effects of *salvia abscondifflora* Greuter&Burdet Syn.*Salvia Crytantha* Montbret&aucher ex Benth. on breast cancer, Indian journal of traditional knowledge. 12 (2013) 390-397.
7. R. Abu-Dahab, F. Afifi., Antiproliferative activity of selected medicinal plants of Jordan against a breast adenocarcinoma cell line (MCF7), Scientia Pharmaceutica. 75 (2007) 121-136 .
8. M.I. Choudheary, A. Hussain, A. Adhikari, B.P. Marasini, S. Sattar, A. Wahab., Anticancer and α-chymotrypsin inhibiting diterpenes and triterpenes from *Salvia leriifolia*, Phytochemistry Letters. 6 (2013) 139–143.
9. W.S. Itani, S.H. El-Banna, S.B. Hassan, R.L. Larsson, A. Bazarbachi, H.U. Gali-Muhtasib., Anti-colon cancer components from Lebanese sage (*Salvia libanotica*) essential oil, Cancer Biol Ther., 7 (2008) 1765-73.
10. Z. Amirghofran, F. Zand, K. Javidnia, R. Miri., The Cytotoxic Activity of Various Herbals against Different Tumor Cells: An in vitro Study, Iranian Red Crescent Medical Journal., 12 (2010) 260-265.
11. G. Fiore, P. Massereli, M. Sajeva, F.G. Franchi., Anti-tumor activity of the methanolic extracts of *Salvia menthifolia*, Rev. Bras. Farmacogn. Braz. J. Pharmacogn., 22 (2012) 381-388.
12. S. Sertel, T. Eichhorn, P.K. Plinkert, T. Efferth., Anticancer activity of *Salvia officinalis* essential oil against HNSCC cell line. (UMSCC1). HNO. 59 (2011) 1203-8.
13. F.Z. Shahneh, S. Valiyari, B. Baradan, J. Abdolalizadeh, A. Bandehagh, A. Azadmehr, R. Hajiaghee., Inhibitory and Cytotoxic Activities of *Salvia Officinalis* L. Extract on Human Lymphoma and Leukemia Cells by Induction of apoptosis, Advanced Pharmaceutical Bulletin. 3 (2013) 51-55.
14. G.P.P. Kamatou, R.L. Van-Zyl, , H. Davids, F.R. Van Heerden, A.C.U. Lourens, A.M. Viljoen., Antimalarial and anticancer activities of selected South African *Salvia* species and isolated compounds from S. radula, South African Journal of Botany. 74 (2008) 238-243.
15. M.R. Loizzo, M. Abouali, P. Salehi, A. Sonboli, M. Kanani, F. Menichini, R. Tundis., In vitro antioxidant and antiproliferative activities of nine *Salvia* species, Natural Product Research: Formerly Natural Product Letters. 28 (2014) 2278-2285.
16. G. Fiore, C. Nencini, F. Cavallo, A. Capasso, A. Bader, G. Giorgi, L. Micheli, In vitro Antiproliferative Effect of Six *Salvia* species on human tumor cell lines, Phytotherapy Research. 28 (2006) 701-703.
17. A. Gali-Muhtasif., Anticancer and medicinal properties of essential oil and extracts of East Mediterranean sage (*Salvia triloba*), Lead Molecules from Natural Products: Discovery and New Trends. 171-183.
18. O. Firuzi, R. Miri, M. Asolalahi, S. Eslami, A.R. Jassibi., Cytotoxic, Antioxidant and Antimicrobial Activities and Phenolic Contents of Eleven *Salvia* Species from Iran, Iranian Journal of Pharmaceutical Research. 12 (2013) 801-810.
19. M. Akaberi, S. Mehri, M. İranshahi., Multiple pro-apoptotic targets of abietane diterpenoids from *Salvia* species, Fitoterapia. 100 (2015) 118–132
20. X. Chen, J. Guo, J. Bao, J. Lu, Y. Wang., The anticancer properties of *Salvia* miltiorrhiza Bunge (Danshen): a systematic review, Med Res Rev., 34(4) (2014) 768-94.
21. S. Hu, S.M. Che, X.K. Li, R. Qın, Z.N. Mei., Antitumor effects of Chi-Shen extract from *Salvia miltiorrhiza* and *Paeoniae radix* on human hepatocellular carcinoma cells, Acta Pharmacology. 28 (2007) 1215–1223.
22. G. Fiore, P. Maseralli, M. Sajeva, G.G. Franchi., Anti-tumor activity of the methanolic extracts of *Salvia menthifolia*, Brazilian Journal of Pharmacognosy. 22 (2012)381-388.
23. J. Bauer, S. Kuehenl, J.M. Rollinger, O. Secherer, H. Northoff, H. Stupner, O. Werz, A. Koebarle., Carnosol and Carnosic Acids from *Salvia officinalis* Inhibit Microsomal Prostaglandin E2 Synthase-1, The Journal of Pharmacology and Experimental Therapeutics 342 (2012) 169–176.
24. R. Tundis, M.R. Loizzo, F. Menichini, M. Bonesi, C. Colica, F. Menichini., In vitro cytotoxic activity of extracts and isolated constituents of *Salvia leriifolia* Benth. against a panel of human cancer cell lines, Chemistry Biodiversty. 8 (2011) 1152–1162.
25. R. Abu-Dahap, F. Affif, V. Kasabri, L. Majdalavi, R. Naffa., Comparison of the antiproliferative activity of crude ethanol extracts of nine salvia species grown in Jordan against breast cancer cell line models, Pharmagonosy magazine. 8 (2012) 319-324.

26. M.R. Loizzo, M. Abuali, P. Salehi, A. Sonboli, M. Kanani, F. Menichini, R. Tundis., In vitro antioxidant and antiproliferative activities of nine *Salvia* species, Natural Product Research: Formerly Natural Product Letters. 24 (2014) 2278-2285.
27. J. Alzeer, B.R. Vumiddi, R. Arefeh, W. Rimawi, H. Saleem, N.W. Luedtke., The influence of extraction solvents on the anticancer activities of Palestinian medicinal plants Journal of Medicinal Plant Research. 8 (2014) 408-415.
28. H. Gali-Muhtasif., Anticancer and medicinal property of essential oil and extract of east Mediterranean sage (*Salvia triloba*), Leads molecule from Natural Product. (2006) 169-180.
29. J.Z. Al-Kalaldeh, R. Abu-Dahab, F.U. Afifi.,"Volatile oil composition and antiproliferative activity of *Laurus nobilis*, *Origanum syriacum*, *Origanum vulgare*, and *Salvia triloba* against human breast adenocarcinoma cells," Nutrition Research. 30 (2010) 271–278.
30. W.S. Itani, S.H. El-Banna, S.B. Hassan, L.R. Larson, A. Bazarbach, H.U. Gali-Muhtsip., Anti colon cancer components from Lebanese sage (*Salvia libanotica*) essential oil, Cancer Biology & Therapy. 7 (2008) 1765-1773.
31. H.U. Gali-Muhtasib, N.I. Affara., Chemopreventive effects of sage oil on skin papillomas inmice, Phytomedicine. 7 (2000) 129–136.
32. A. Russo, C. Formisano, D. Rigano, F. Senatore, S. Delfine, V. Cardile, S. Roselli, M. Bruno., Chemical composition and anticancer activity of essential oils of Mediterranean sage (*Salvia officinalis* L.) grown in different environmental conditions, Food and Chemical Toxicology. 55 (2013) 42–47.
33. M.R. Loizzo, F. Menichini, R. Tundis, M. Bonesi, F. Nadjafi, A.M. Saab, N.G. Frega, F. Menichini., Comparative Chemical Composition andAntiproliferative Activity of Aerial Parts of *Salvia leriifolia* Benth. and *Salvia acetabulosa* L. Essential Oils Against Human Tumor Cell in vitro Models. J Med Food., 13 (2010) 62-9.
34. M.R. Loizzo, R. Tundis, F. Menichini, A.M. Saab, G.A. Statti, F. Menichini., Cytotoxic Activity of Essential Oils from Labiatae and Lauraceae Families Against in vitro Human Tumor Models. Anticancer Res. 27 (2007) 3293-3299.
35. Z. Amirghofran, F. Zand, K. Javidnia, R. Mirri., The Cytotoxic Activity of Various Herbals against Different Tumor Cells: An in vitro Study, Iranian Red Crescent Medical Journal. 12 (2010) 260-265.
36. Z. Tayarani-Najaran, J. Asili, A. Aiobi, S.A. Emami., Growth Inhibition and Apoptosis Induction of *Salvia chloroleuca* on MCF-7 Breast Cancer Cell Line, Iranian Journal of Pharmaceutical Research. 12 (2013) 789-799.
37. A. Russo, V. Cardile, A.C.E. Graziano, C. Formisano, D. Rigano, M. Canzoneri, M. Bruno, F. Senatore, Comparison of essential oil components and in vitro anticancer activity in wild and cultivated *Salvia verbenaca*. Natural Product Research., (2014) 1-11.
38. X. Chen, J. Guo, J. Bao, J. Lu, Y. Wang., The anticancer properties of *Salvia miltiorrhiza Bunge (Danshen)*: A systematic review, Med Res Rev., 34 (2014) 768-94.
39. R. Abu-Dahab, F. Afifi., Antiproliferative activity of selected medicinal plants of Jordan against a breast adenocarcinoma cell line (MCF7), Scientia Pharmaceutica. 75 (2007) 121-136.
40. G. Sridharan, P. Brindha, R. Raja, R. Amutha-Priya. In-vitro and in-vivo cytotoxic effect of *salvia leucantha* cav. against each cell lines, International Journal of Pharmacy and Pharmaceutical Sciences. 4 (2012) 143-146.
41. G. Shu, W. Zhao, L. Yue, H. Su, M. Xiang. Antitumor immunostimulatory activity of polysaccharides from *Salvia chinensis* Benth, Journal of Etnopharmacology. 20 (2015) 237-47
42. L. Zhou, Z. Zuo, M.S.S. Chow. Danshen an overview of its chemistry Pharmacology pharmacokinetics and clinical use, J. Clin. Pharmacol., 45 (2005) 1345–1359.
43. X.H. Wang, K.F. Bastow, C.M. Sun, Y.L. Lin, H.J. Yu, M.J. Don, T.S. Wu, S. Nakamura, K.H. Lee. Antitumor Agents 239 Isolation structure elucidation total synthesis and anti–breast cancer activity of neotanshinlactone from *Salvia miltiorrhiza*, J. Med. Chem., 47 (2004) 5816–5819.
44. S. Hu, S.M. Chen, X.K. Li, R. Qin, Z.N. Mei., Antitumor effects of Chi-Shen extract from *Salvia miltiorrhiza* and *Paeoniae radix* on human hepatocellular carcinoma cells, Acta Pharmacology Sin., 28 (2007) 1215–1223.
45. C.P.R.F. Xavier, C. Lima, M. Fernandes-Ferreira, C. Pereira-Wilson. *Salvia Fruticosa*, *Salvia Officinalis*, and Rosmarinic Acid Induce Apoptosis and Inhibit Proliferation of Human Colorectal Cell Lines: The Role in MAPK/ERK Pathway, Nutrition and Cancer. 61 (2009) 564–571.
46. C.P.R.F. Xavier, C. Lima, M. Fernandes-Ferreira, C. Pereira-Wilson., Induction of apoptosis and inhibition of proliferation in colon cancer cells by *Salvia fruticosa*, *Salvia officinalis* and rosmarinic acid, Planta Med., (2008) 74 - PA19.
47. S.K. Azar, R.E. Mooen, H. Niknahad., Cytotoxicity of Juniperus excels and *Salvia mirzayanii* Extracts against HepG2 Cells, Iranian Journal of Pharmaceutical Sciences. 8 (2012) 241-247.
48. N.K. Dehaghi, S.N. Ostad, N. Maafi, S. Pedram, Y. Ajani, A. Hadjiakhoondi, M. Khanavi., Cytotoxic activity of the essential oil of *Salvia verticillata* L, Research Journal of Pharmacognosy (RJP). 1 (2014) 27-33.
49. C.Y. Lee, H.F. Sher, H.W. Chen, C.C. Liu, C.H. Chen, C.S. Lin, P.C. Yang, H.S. Tsay, J.J.W. Chen., Anticancer effects of tanshinone I in human non-small cell lung cancer, Molecular cancer therapeutics. 7 (2008) 3527-3538.
50. V. Kafil, M. Eskandandi, Y. Omidi, H. Nazemiyeh, J. Barar. Abietane diterpenoid of *Salvia sahendica* Boiss and Buhse potently inhibits MCF-7 breast carcinoma cells by suppression of the PI3K/AKT pathway, RSC Adv., 5 (2015) 18041-18050.