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# Anti-Cancer Activity of Herbal Plants in Chaharmahal and Bakhtyari Districts, South-West of Iran

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## ABSTRACT

Traditionally plants were used to prevent and reduce the risk of cancer and many studies has proved that plants are one of the important sources of anticancer drugs [1]. Studies show that natural products involves in the development of approximately 75% of novel anticancer agents between 1981 and 2010 [2]. Thereby, investigation of natural products is one of the most important aspects to discover new compounds with possible anti-cancer activity. Ancient nation of Iran contained the most geographically diverse which can be divided into 12 separate geographic environments and boasts 5 major climates [3].This astounding diversity in Iran's geography allows Iran to host more than 7500 species of plants around 1800 of which are used in medicine. Many of Iran's most precious herbal treasures are plants found nowhere else in the world [3]. Here we are reviewing medicinal plant with anticancer activity in The folk herbal medicine among the ethnic communities Bakhtyari and Chaharmahali in Chaharmahal and Bakhtyari districts, South-West of Iran [4].

**Keywords:** Medicinal plants, Anti-cancer activity, South-West of Iran, Chemotherapy

# INTRODUCTION

Cancer is one of the main causes of death all over the world. The world health organization **(WHO)** estimates that 84 million people would die of cancer between 2005 and 2015 [5]. Cancer is characterized by a series of malignant diseases result in uncontrolled growth of abnormal cells, which affect different parts of the body and can result in death [6]. Internal and external factors can induce acquire abnormal functions by make changes to normal cells. Chemotherapy and systemic therapy are an important option in cancer treatment by removing all cancerous colonies within the patient's body [7].

There is considerable scientific in the discovery of new anticancer drugs from natural plants. The costs of the therapy with chemical and synthetic drugs are very high, and there is still no extremely effective drugs to treat most cancers [8]. 5000 species among More than 422000 species of flowering plants have been reported from all over the world for medicinal purposes [9]. Since ancient times, plants have been one of the first and most available resources usable for medicinal purpose. Plant materials such as leaf, root, flower and seed of medicinal plant can be used in the form of their extracts and chemical compounds to produce human drugs or veterinary medicine [10].

Iran has a unique meteorological conditions which contributed to more than 8000 plant species in the diversity [11], that's why the flora of this country is known as green gold to many Scientifics [12]. This astounding diversity in Iran's geography allows Iran to host more than 7500 species of plants around 1800 of which are used in medicine. Many of Iran's most precious herbal treasures are plants found nowhere else in the world [3] (Tables 1-12).

**Table 1:** *Teucrium Polium* L from Lamiaceae family with local name of Chez Koohi, Kalporeh**.**

| Cell Lines | Result |
|---|---|
| PC3 and DU145 prostate cancer cell lines. | Cell proliferation inhibition, provokes S cell cycle arrest and reduction of G0–G1 phase [13]. |
| Prostate cancer cell line, PC3. SW480 colon and T47D breast cancer. | A methanolic extract obtained potently inhibited the viability of PC-3 cells. The viability of SW480 colon and T47D breast cancer cells was also significantly decreased. Flow cytometry suggested that the reduction of cell viability was due to induction of apoptosis [14]. |
| H322 and A549 lung cell lines. | TP plant extract inhibits cell proliferation and deregulates cell cycle progression. It causes a dramatic cell death in both cell lines in comparison with untreated cells [15]. |
| Glioblastoma multiform REYF-1. | The result shows the cytotoxic activity of extracts on cells [16]. |
| A549, BT20, MCF7, and PC12. | Ethanol extract of *T. polium* suppressed the growth of all tested cell lines effectively and also inhibited formation of colonies in agarose efficiently [17]. |
| Skmel-3, Saos-2, SW480, MCF-7, KB, EJ and A431 cell lines. | The vincristine/Me-TP, vinblastine/Me-TP and doxorubicin/Me-TP combinations showed a strong synergistic effect in the cell growth inhibition (0.13<CI<0.36). Similar results were observed by colony formation assay. The combinations of vincristine/Me-TP and vinblastine/Me-TP resulted in a massive apoptosis (>80%) compared to effect of individual drugs (0-3%). Me-TP reduced marginally to significantly the cytotoxic effects of vincristine and vinblastine toward the human fibroblasts ($p<0.05$ to 0.001) [18]. |

**Table 2:** *Portulaca Oleracea* from Portulacaceae family with local name of Khorfeh.

| Cell line | Result |
|---|---|
| A549 cell, Hela cells, Hep-2 cell and RD cell. | It has selective cytotoxicity to the tumor cells [19]. |
| KATO III (human gastric carcinoma cell line), COLO 320 HSR cells (human colon adenoma cell line), L929 (murine lung connective tissue) and W138 (human lung diploid cell) cells. | *P. oleracea* showed a tumoricidal activity against KATO III, and COLO 320 HSR cells in a dose-dependent and time-dependent manner, but not against the non-tumorous cell lines, L929 and W138 cells. Subcutaneous injection of six week old CD1 nude mice with COLO 320 HSR cells and subsequently *Portulaca oleracea* extract showed a clear inhibition of tumor growth as compared to the control nude mice which received only COLO 320 HSR cells [20]. |

**Plantago Major from Plantaginaceae family with local name of Kalghooreh.**

| Cell lines | Result |
|---|---|
| Balb/C Mouse with Ehrlich Ascites Tumor. | It has an inhibitory effect on EAT in a dose dependent manner [21]. |
| Ehrlich ascites carcinoma in mice. | *P. Major* extract had an inhibitory effect against Ehrlich ascites carcinoma. Therefore, results show that *P. Major* could be proposed as an effective agent for cancer prevention [22]. |

**Table 3:** *Pistacia Atlanta Desf* from Anacardiacea family with local name of Baneh, Pesteh Koohi.

| Cell lines | Result |
|---|---|
| Human breast cancer T47D cells. | Baneh extract contains phytochemicals, which act as an inhibitor of cell proliferation and inducer of apoptosis in human breast cancer T47D cells [23]. |
| Human colon carcinoma HT29 cells. | Methanolic extract of the Baneh has significant cytotoxic effects against human colon carcinoma HT29 cells [24]. |
| T47D human breast cancer cells. | Baneh extract induced G0/G1 cell cycle arrest in conjunction with a marked decrease in expression of cyclin D1 and cdk4 that was strongly dependent on time of exposure. In parallel, Dox-treated T47D cells in early time points were accumulated on S phase, but after 48 h cell cycle progression was inhibited on G2/M. Dox promoted striking accumulation of cyclin B1 rapidly and enhanced cyclin A abundance [25]. |

**Table 4:** *Perovskia Abrotanoides* from Lamiaceae family with a local name of Hoosh.

| Cell lines | Result |
|---|---|
| P388 murine leukemia cells. | The concentrations giving 50% inhibition of the cell growth ($IC_{50}$) were recorded [26]. |

**Table 5:** *Peganum Harmala* from Nitrariaceae family with local name of Ispand**.**

| Cell lines | Result |
|---|---|
| Hep-2 cancer cell line. | The results revealed dose dependent significant differences, And the results showed that was increasing on apoptotic process after treated with methanol extract of *P. harmala* to repairing the damage of the cell and induction of cell death compared with control [27]. |
| Human bladder carcinoma RT112, human laryngeal carcinoma Hep2 and human myelogenous leukemia K562. | Did not show a good anticancer activity against these cell lines [28]. |
| Reticuloum-cell sarcoma **(LI)** of mice | It was shown that the growth of Transplantable tumors in mice was inhibited by this alkaloid [29]. |
| Three tumoral cell-lines, UCP-Med, Med-mek carcinoma and UCP-Med Ž.sarcoma. | Proliferation was significantly reduced at all tested concentrations 20-120 µg ml during the first 24 h of contact. A cell lysis effect occurred after 24 h and increased thereafter to complete cell death within 48-72 h, depending on tested concentration [30]. |

**Table 6:** *Origanum Vulgare* L from Lamiaceae family with local name of Marjan Joush.

| Cell lines | Result |
|---|---|
| Human colon cancer $Caco_2$ cells. | It leads to growth arrest and cell death in a dose and time dependent manner. Both extrinsic and intrinsic apoptotic pathways appear to be activated by spice extract. Moreover, whole extract, instead of a specific component, can be responsible for the observed cytotoxic effects [31]. |
| MCF-7 breast cancer cell. | Luteolin-7-O-glucuronide, Luteolin-7-O-xyloside and Rosmarinic acid have shown moderate antitumoral activity [32]. |
| HCT-116 and MDA-MB-231 cell line. | Cell growth is significantly lower in extract treated cells compared to untreated control. The effect of inhibition of cell growth was higher in the treatment of HCT-116 cell line than in MDA-MB-231. Based on the results it is determined that *O. vulgare* is a significant source of biologically active substances that have cytotoxic and antiproliferative activity in vitro [33]. |

**Table 7:** *Myrtus Communis* L from Myrtaceae family with local name of Mord, Mort.

| Cell lines | Result |
|---|---|
| Human breast cancer cell lines (MCF 7 and MDA-MB-231). | The results showed significant cytotoxic potential of examining extracts, with IC50 values ranging from 7 to 138 µg/ml for *M. communis* [34]. |

**Table 8:** *Medicago Sativa* L from Fabaceae family with local name of Yongeh**.**

| Cell lines | Result |
|---|---|
| AMN3, **(GB)** Glioblastoma and normal cell line **(MEF)** Mouse Embryo Fibroblast cell line. | Aqueous extracts from alfalfa have significant effects P value ≤ 0.05 on the growth of AMN3 cell lines and GB malignant cell line in culture in a dose and time- dependant manner, The results also indicated that GB cell lines were more sensitive to the Alfalfa aqueous extracts as compared with the growth of AMN3 cell lines [35]. |

**Table 9:** *Malva Sylvestris* L from Malvaceae family with local name of Panirak, Tooleh, Mamapir.

| Cell lines | Result |
|---|---|
| Four human cancer cell lines: breast cancer MCF-7, prostate cancer LNCaP, amelanotic melanoma C32 and renal adenocarcinoma ACHN. | Showed *in vitro* anti-proliferative properties against those cancer cell lines below established limits [36]. |

**Table 10:** *Juglans Regia* from Juglandaceae family with local name of Gouz.

| Cell lines | Result |
|---|---|
| Human renal cancer cell lines A-498, 769-P and the colon cancer cell line Caco-2. | All extracts showed concentration- dependent growth inhibition toward human kidney and colon cancer cells. Concerning A-498 renal cancer cells, all extracts exhibited similar growth inhibition activity (IC50 values between 0.226 and 0.291 mg/mL), while for both 769-P renal and Caco-2 colon cancer cells, walnut leaf extract showed a higher antiproliferative efficiency ($IC_{50}$ values of 0.352 and 0.229 mg/mL, respectively) than green husk or seed extracts. The results obtained herein strongly indicate that walnut tree constitute an excellent source of effective natural antioxidants and chemo preventive agents [37]. |
| MDA-MB-231 human breast cancer cells. | Suppressed proliferation and induced apoptosis in a dose and time dependent manner by modulating expression of key genes. This involved characteristic changes in cytoplasmic and nuclear morphology, DNA fragmentation (TUNEL assay), levels of mRNA and expression of corresponding proteins. Real Time PCR and western blot analysis revealed that the expression of of Bax, caspases, tp53, and TNF-α was markedly increased in MBA-MB-231 cells treated with the RBJR extract. In contrast Bcl-2 and mdm-2 expression was down regulated after exposure. In summary, our data suggest the presence of bioactive compound(s) in WNRB capable of killing breast carcinoma cells through induction of apoptosis, and therefore a candidate source of anticancer drugs [38]. |

**Table 11:** *Cichorium Intybus* from Asteraceae family with local name of Kasni.

| Cell lines | Result |
|---|---|
| Prostate, breast and colorectal cells. | Plant extracts exhibited a modest inhibition of cell proliferation for all three cell lines [39]. |

**Table 12:** *Capparis Spinosa* L from Capparidaceae family with local name of Kalir.

| Cell lines | Result |
|---|---|
| HT-29 human colon carcinoma cell line. | Caper essential oil and aqueous infusion showed time- and dose-dependent high inhibitory effect on HT-29 cell proliferation. In addition, they induced the inhibition on nuclear factor jB (NF-jB) activity in a dose-dependent manner, while they did not show any effect on apoptosis in HT-29 cells. Flow cytometric analysis indicated that treatment with caper essential oil and aqueous infusion resulted in G2/M cell cycle arrest in a dose-dependent man- ner. Presented results suggest that caper contains volatile and non-volatile compounds which potentially can play an important role in colon cancer prevention [40]. |
| Human larynx carcinoma (Hep-2) and Human cervix adenocarcinoma (HeLa). | Polyphenolic extract showed a cytotoxicity concentration 50% (CC50%) 6400 and 6800 µg/ml on Hep-2 tumor cell line after 24 and 48 hrs. Metabolites extracts of mature fruit of *C.Spinoza* caused less inhibition activity on the growth of Hep-2 and HeLa tumor cell lines [41]. |
| H22 bearing mice. | The anti-tumor activities of CSPS were dose-dependent [42]. |


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