Journal of Traditional and Complementary Medicine 7 (2017) 195–204

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Review article

Role of traditional Islamic and Arabic plants in cancer therapy

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ARTICLE INFO

Article history:
Received 13 March 2016
Received in revised form
18 April 2016
Accepted 2 May 2016
Available online 21 May 2016

Keywords:
Cancer
Islamic and Arabic plants
TAI modalities
Ethno-pharmacological profile
Ethno-medicinal importance

ABSTRACT

Ethno pharmacological relevance: This review article underlines individual Traditional Islamic and Arabic plant (TAI) and their role in treating cancer. The aim of the study is to specifically evaluate the progress of herbs, Arabic and Islamic traditional herbs in particular, applied in cancer treatment, so far.
Materials and methods: Islamic and Arabic plants were selected and identified through different literature survey using "Google scholar", "Web of science", "Scopus" and "PubMed". Each plant, from identified Arabic and Islamic plants list, was search individually for the most cited articles in the aforementioned databases using the keywords, "Anticancer", "Uses in cancer treatment", "Ethno pharmacological importance in cancer" etc.
Results: The current review about Islamic and Arabic plants illuminates the importance of Islamic and Arabic plants and their impact in treating cancer. There is a long list of Islamic and Arabic plants used in cancer as mentioned in review with enormous amount of literature. Each plant has been investigated for its anticancer potential. The literature survey as mentioned in table shows; these plants are widely utilized in cancer as a whole, a part thereof or in the form of isolated chemical constituent.
Conclusions: This review strongly supports the fact; Arabic and Islamic traditional plants have emerged as a good source of complementary and alternative medicine in treating cancer. Traditional Arab-Islamic herbal-based medicines might be promising for new cancer therapeutics with low toxicity and minimal side effects. The plants used are mostly in crude form and still needs advance research for the isolation of phytochemicals and establishing its cellular and molecular role in treating cancer.

1. Introduction

The use of herbal medicine is leading modality, followed in Middle east, Europe, Israel and certain other advance countries, in order to treat cancer patients. According to latest WHO reports, even advanced countries have adapted traditional system of herbal treatment including; Belgium (31%), Australia (48%), France (49%), Canada (70%) and Germany (77%).[1] The 25% of the crude drugs used in last two decades are derived from plants, out of which only 5–15% have been investigated for bioactive compounds. Recent surveys reveal the use of such phytochemical for cancer treatment due to the fact; relatively low/nontoxic, antitumor property with minimal side effects, failure of the standard cancer therapy. A research finding on complementary and alternative medicines identified 143 articles from different Middle-Eastern countries. The report findings performed in Turkey, Israel and other advance countries showed, half of the patient diagnosed with cancer used CAM therapy even during chemotherapy.[2]

The history of cancer treatment reveals, the interest in cancer treatment goes back to the times of Islamic renaissance scholar.[3] As suggested by the famous scholar "Avicenna", "if it is the start of a cancer, it is possible to make it static and prevent it from growth and hence ulceration". Sometime it happens, that the starting

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

http://dx.doi.org/10.1016/j.jtcme.2016.05.002

cancer may be cured, but once it reaches to advance stages, verily it will not.[4] In order to reduce resistance to the existing mechanisms, modern medical research shifted its focus towards finding of new anticancer agents as an alternate. The most promising alternate which took place are herbs and other natural plant products. The easy availability, low in cost along with possessing minimal side effects, makes the herbs as mainstream for treating and playing a vital role in the prevention and treatment of cancer.[5] The wisdom of the past in the shape of folkloric and traditional uses served the better source for treatment of various human diseases including cancer. The most emerging role as observed for treatment or prevention in case of cancer was disclosed by Traditional Arab-Islamic (TAI) herbal-based medicines. The literature from ancient time as well as the use of Arabic and Islamic plants for cancer treatment by various Muslim and religious scholars, in contrast with standard use of these herbs in cancer now-a-days by different physicians and practitioners, is a self-comprehensible prove revealing the role of TAI herbs in cancer. The TAI herbs are promising for new cancer therapeutics due to low toxicity and minimal side effects also.[6–8]

Despite of advancement in treating diseases, the hallmark to cure cancer completely is not accomplished till to date. Although, endless efforts of researcher to eradicate cancer led to different molecular and cellular understanding i.e. signal transduction involved in angiogenesis, protein expression and apoptosis, the morbidity of this disease is so far rising. Research statistics showed that 20% of death in the world results from cancer, affecting more than one third of the world population.[9] Several treatment are available i.e. drugs from synthetic or semisynthetic origin, radiation therapy, chemotherapy etc. but these approaches are least effective and accompanied by severe side effects in most of the cases. The major effective alternate is herbal treatment, with less side effects and potentially safer in cancer. The CAM study conducted (2007) in the U.S. population reports; almost 4 out of 10 adults had used some form of CAM within the past year.[10] The American spent 33.0 billion U.S dollar (USD), accounting for 11.2% of total out-of-pocket health care expenditure, on Traditional products.[2] Even in the more developed countries the use of CAM and traditional medicine is comparably extensive.[11] According to WHO latest fact sheet; in India 70% of the population, in Ethiopia more than 90% of the population depends on traditional medicine for primary health care.[12] Proportionally, more than 70% population in Chile and 40% population in Colombia adopted the traditional medicine for their healthcare system.[13] The China (40%), too is in the list of countries using traditional medicine.[14] The advanced countries i.e. Belgium (31%), Australia (48%), France (49%), Canada (70%) and Germany (77%) showed a comparable data for the use of different CAM and traditional treatment modalities.

The importance of the traditional herbal medicine can be assumed from the fact that, the number of member state regulating the herbal medicine increased from 65 (1999) to 119 (2012) along with the upgradation of the research institute for herbal medicine from 19 (1999) to 73 (2012), respectively.[1]

The demand of traditional medicines and practitioners is raising on regular basis. The fact can be supported by the enormous data available i.e. an increase of 30% (1995–2005), when 750,000 visits were recorded in a two week period in Australia[15]; 907 million visits (2009) for the Traditional Chinese medicines, accounting for 18% of all medical visits[16]; a total of 18226 traditional health care services for 80% of population in Lao People's Democratic Republic[17] and the 560 U.S dollar/annum out-of-pocket expenditure for traditional medicines in Saudi Arabia.[18] Likewise, hundreds of literature data is available, which just shows the importance and utilization of herbal and traditional medicine for the treatment of diseases including cancer.

The study plans; to evaluate the claims i.e. TAI plants have folkloric uses in treatment of cancer. The main focus is on TAI alternative medicinal plants for establishing their role in prevention, treatment or procurement of cancer. This review is an eye-bird view on the ancient TAI plants used in cancer treatment along with herbal treatment research.

1.1. Cancer

Cancer, more appropriately described as, an uncontrolled growth or cell proliferation which invades other tissues as well. The mechanism behind tissue invading is through direct cell migration or blood and lymphatic system. The risk factors for cancer consist of chemicals, radiations, unhealthy diet, environmental factors, infection and tobacco smoke.[19]

There are hundred different types of cancer usually named by the tissue or organ or type of cell in which they begins. There severity can be benign (usually earlier stage) or malignant (end stage, mostly called cancer).[20] Cancer identified in earlier stages are cured most likely, as mentioned in their first time treatments of cancer, by Avicenna, Abulcasis and Rhazes in the earlier Islamic and Arabic era.[3,21]

1.2. Importance of plants

The advancement in drug discovery technology, diversification of the health sector and reduced funding for natural product-based drug discovery, couldn't kneel the herbs and herbal treatment systems. The natural products from plants and biological sources still remain an unlimited and uncondensed source of new phytochemicals and nutraceuticals. The World Health Organization[22] estimates; about 80% of the world population presently uses herbal-based medicines for some aspect of primary health care. The fact sheet also mentions the fact; herbal medicines are the most lucrative form of traditional medicine, generating billions of dollars in revenue.[22] The era of 1984–2003, witnessed numerous natural product-derived small molecules patent, despite of decrease in the industrial funding for natural product-based drug discovery, at the same time. A comprehensive review of human drugs introduced since 1981 suggests that, out of 847 small molecule-based drugs, 43 were natural products, 232 were derived from natural products (usually semi synthetically), and 572 were synthetic molecules. However, 262 of the 572 synthetic molecules had a natural product inspired pharmacophore or could be considered natural product analogs. Natural products continue to make the most dramatic impact in the area of cancer. From 155 anticancer drugs developed since the 1940s, only 27% could not be traced to natural products, with 47% being either a natural product or a direct derivation thereof. According to recent surveys, there are about 450 medicinal plants in the Eastern region of the Mediterranean and about 230 medicinal plants in the coastal Mediterranean region in Egypt. These plants are used by healers for the treatment and prevention of almost all types of human disease, such as cancer; skin, respiratory, digestive, and liver diseases; diabetes and others.[23]

1.3. Importance of Islamic and Arabic plants

Advanced tumors are treated usually by chemotherapy and although these drugs are effective, they are associated with severe adverse events and drug resistance.[24,25] Traditional Arab-Islamic herbal-based medicines might be promising candidates for new cancer therapeutics with low toxicity and minimal side effects.[5,6,8]

The origins of Arab-Islamic medicine can be traced back to the time of the Prophet Mohammad, Peace Be upon Him (PBUH) as a significant number of Hadiths concerning medicine are attributed

to him. Several Sahaba were successfully treated of certain diseases by following the medical advice of the Prophet Mohammad (PBUH). Despite great progress in allopathic medicine, Arab-Islamic medicine has continued to be practiced within the Mediterranean as well as most Arab and Islamic countries. In addition, Arab-Islamic therapies are most often utilized by people who have faith in spiritual healers and herbalists. These people are the first to be consulted for problems such as infertility, impotence, diabetes, obesity, epilepsy, psychosomatic troubles, and many other diseases.[23]

1.4. Role of Islamic and Arab plants in cancer

The spreading of cancer is increasing over the world and the percentage of deaths caused by this fatal disease is rising, especially in the developing countries. Scientists and researchers are now giving more of their attention to the herbal medicine to provide treatment for more difficult diseases like cancer due to the fact that, the treatments of cancer patients with chemical therapy have serious side effects. Recently herbal medicines are coming to play a more vital role in the reduction and prevention of cancer. The rapid interest in traditional Arabic herbal medicine (TAHM) worldwide is stimulated by many factors; that herbal products are safe and economical, they exhibit an extensive spectrum of biological activities such as, stimulation of the immune system, antibacterial, antiviral, anti-hepatotoxic, antiulcer, anti-inflammatory, antioxidant, anti-mutagenic, and anti-cancer effects.[5,7,26–28]

A variety of grains, cereals, nuts, soy products, olives, beverages such as tea and coffee, and spices including turmeric, garlic, ginger, black pepper, cumin and caraway confer a protective effect against cancer.[26,27,29–31] Several studies have also documented the relationship between decreased cancer risk and high consumption of vegetables, including cabbage, cauliflower, broccoli, Brussels sprout, tomatoes, and fruits such as, apples and grapes.[5,28,30,32] In addition, a number of medicinal plants and herbs have also been reported to reduce the risk of cancer in multiple sites.[33,34]

Traditional herbal medicines provide a remarkable source for new drug development. Indeed, about 50% of the modern drugs are herbal based.[35] Since natural based products are inherently better tolerated in the body compared to synthetic chemicals and have higher chance to be approved as new drugs, searching for and purification of natural drug candidates is imperative. In the case of anticancer drugs, various drugs are derived from plant sources including but not limited to paclitaxel (Taxol), vinblastine, capsaicin, vincristine, the camptothecin derivatives, topotecan, irinotecan and etoposide.[28,36–38] Many commonly used anti-cancer herbs possess chemo preventive effects within their diverse pharmacological properties. Since cancer evolves over a long period of time, agents that inhibit or retard one or more of its stages could affect the overall course of the disease. Certain micronutrients (Oleuropein and Diallyl sulfide compounds found in olives and garlic respectively) possess potent cancer-preventive abilities.

2. Materials & methods

2.1. Searching facts

The databases used for literature search are; “PubMed”, “web of Science”, “Google scholar” and “Science direct”. The relevant research/review article, illuminating the use of Arabic and Islamic plants in cancer, was downloaded using the free access portal of University of Dammam, for specific libraries.

The keywords used mostly during the literature search were as follows;

1. Islamic and Arabic plants
2. Use of Islamic and Arabic plant in cancer
3. Anticancer activity
4. Cytotoxicity
5. Folkloric uses of plants
6. Ethno medicinal use in cancer
7. Ethno pharmacological use in cancer
8. Herbs in cancer

2.2. Selection and confirmation of Arabic & Islamic plants

The Islamic and Arabic plants used in the review were confirmed and referenced from the literature sources i.e.[4,39–48] The search for appropriate synonym of each plant, successively followed the step after confirmation.

2.3. Study of literature and reporting the most cited articles

The searching, confirmation and literature download step was repeated for each individual plant. This sequentially was followed by, a detail and extensive literature study for extracting out the material as mentioned in Table 1. The literature study showed an enormous contribution of these plants in cancer treatment. Table 1 shows the plants, synonym and their respective use in cancer as preventive or for treatment purposes.

3. Discussion

In recent years, traditional Arab-Islamic herbal medicine has been gaining interest in the scientific community, and more specifically, regarding cancer treatment. Herbal medicine is the leading modality used by patients with cancer in the Middle East (e.g., 35% of cancer patients using CAM in Jordan)[49] along with spiritual practices that are also prevalent (e.g., 75% of CAM users in Iranian study).[50] CAM use is also popular among patients with pediatric,[51] gynecological[52] and hematological[53] malignancies and among patients with an advanced disease.[54]

Several studies have been carried out for Arabic and Islamic plants. The Table 1 shows *in-vivo* and *in-vitro* studies for individual plants being applied in cancer and cancer related complications. Most of the research studies involve the application of these traditional plants against various human and animal cell lines. The same way, most of the plants, have been subjected to active isolation for the chemical entities responsible for cancer treatment.

The Table 1, mentions all the research work and literature available in order to cover or evaluate the progress of plants in cancer treatment. This study sum up the research activities specifically in the area of cancer and will help the researchers in order to utilize the available knowledge under one heading, for the applied research.

The modalities applied for treatment consists of plants in different forms i.e. crude extract (aqueous, alcoholic, hydro-alcoholic, methanolic, ethanolic etc.), fractions, sub-fractions as well as isolated active compounds. Table 1 reveals the fact i.e. traditional plants in any form are efficacious in reducing the progression or treatment of cancer. *Allium cepa & Allium sativum* considered as common food herbs have shown considerable results in treatment of cancer. *Anethum graveolens, Apium graveolens, Artemisia absinthium, Acorus calamus, Beta vulgaris, Cucumis melo, Zingiber officinal, Triticum aestivum, Thymus vulgaris, Nigella sativa* and *Crocus sativus* as well as many other such plants have been utilized since long as plants for food, nutritious or common ailments treatments purposes. These plants have folkloric and traditional uses and their applications in cancer showed considerable

Table 1
Ethno-pharmacological profile of Islamic and Arabic Plants used in treatment of cancer.

Plant name	English name	Ethno pharmacological profile in cancer	References
Acacia seyal	Acacia	Demonstrated potential cytotoxic activities on the cancer cells HepG2 (hepatocellular carcinoma), MCF-7 (breast adeno carcinoma), A549 (lung carcinoma) and HCT-116 (colorectal carcinoma); It Prevents the development of cancer.	55–57
Acorus calamus	Sweet flag	Extract inhibits growth of several cell lines of mouse and human origin; Protected most of the changes in the rat brain induced by noise-stress; Studies have reported a wide range of pharmacological activities exhibited by *Acorus* rhizome and its constituents, particularly α.- and β.-asarone.	58–60
Agaricus campestris	Mushroom	Showed cytotoxic effects on human cancer cell line HO-8910 & 7721; Reduced glycemia levels in patients with colorectal cancer; Demonstrated cytotoxicity against cancer cell lines of larynx carcinoma (HEp-2) and breast carcinoma (MCF-7).	61–64
Allium ascalonicum	Leek	Showed anti-growth activity on the cancer cell lines Jurkat and K562; Anti-angiogenic activity of fractions and sub-fractions was examined on human umbilical vein endothelial cells (HUVECs) in collagen matrix and chicken chorioallantoic membrane (CAM) models; Anticancer activity of isoliquiritigenin (ISL) was reported in human uterine cervical carcinoma (HeLa cells).	65–67
Allium cepa	Onion	Low risk of colorectal, breast, and lung cancers was found in individuals using onion and garlic; Reduces the risk of esophageal and stomach cancer, distal colon cancer; Reduces the ratio of prostate cancer by 30–50%.	29,30,68–77
Allium sativum	Garlic	Death ratio (attributed to stomach cancer) was reduced by 10 fold with the use of garlic; Low risk of colorectal, breast and lung cancer due to onion & garlic use; Reduces the risk of esophageal and stomach cancer, distal colon cancer; Reduces the ratio of prostate cancer by 30–50%.	29,30,68–75,78
Aloe vera	Aloe	Aqueous cream was useful in reducing dry desquamation and pain related to radiation therapy; The use of mild soap and *Aloe vera* gel showed a protective effect towards skin reactions in patients undergoing radiation therapy; Studies reported presence of anticancer activity and extract of aloe vera demonstrated suppression of cell proliferation in human neuroblastoma cell lines (IMR-32, TGW, CHP-126 and NBL-S); Hydroxyanthraquinone compound Aloe emodin (AE) demonstrated antineoplastic activity in metastatic human melanoma cell lines and in primary stem-like cells (melanospheres).	79–84
Anethum graveolens	Dill	Anethofuran a potential cancer chemopreventive has been isolated.	39,85
Apium graveolens	Celery	Bioassay guided isolation resulted different compounds, out of which, 3-n-butyl phthalide and sedanolide were both active in tumor inhibition; Topoisomerase-I and II enzymes inhibitory compounds, Senkyunolide-N, Senkyunolide-J & 3-hydroxymethyl-6-methoxy-2, 3-dihydro-1H-indol-2-ol have been isolated from the seeds; The seed extract of celery demonstrated antiproliferative activity and apoptosis on human stomach cancer cell line BGC-823.	86–89
Artemisia absinthium	Wormwood	*Artemisia absinthium* induced anti-proliferative effects on human breast cancer cells trigger apoptosis in both cell lines through the modulation of Bcl-2 family proteins and the MEK/ERK pathway; Wormwood (*Artemisia absinthium*) suppresses tumor necrosis factor alpha;*A. absinthium* and *A. vulgaris* demonstrated cytotoxic activity in breast cancer cell line (MCF7) and human embryonic kidney normal cell line (HEK293).	4,90–92
Arum palaestinum	Palestine Arum	Treatment of different human cancer cell lines with the ethyl acetate fraction led to dose-dependent suppression in the proliferation of both breast carcinoma cells (MCF-7) & lymphoblastic leukemia cells (1301); A novel alkylated piperazine was isolated which showed a significant cytotoxicity against cultured tumor cell lines *In vitro*; Study showed inhibition of prostate cancer spheroids and reduce growth rate of prostate tumors in mice.	77,93–96
Astoma seselifolium	Astoma	Used in cancer prevention and treatment.	4
Beta vulgaris	Beet-Root	An *In-vivo* anti-tumor promoting activity evaluation against the mice skin and lung bioassays revealed a significant tumor inhibitory effect; The cytotoxic effect of the red beetroot extract in the androgen-independent human prostate cancer cells (PC-3) and in the well-established estrogen receptor-positive human breast cancer cells (MCF-7) suggested a potent anticancer activity; Betanin/isobetanin extract demonstrated anticancer activity in MCF-7 treated cells.	97–100
Boswellia carterii	Olibanum	Acetyl-11-keto-β-boswellic acid, a compound isolated from *Boswellia carterii*, caused G1-phase cell cycle arrest with an induction of p21 and a reduction of cyclin D1 as well in prostate cancer cells; Frankincense oil derived from *Boswellia carterii* induces tumor cell specific cytotoxicity; Extracts of the plant demonstrated cytotoxicity in HepG2 and HCT 116 cell lines.	101–104
Brassica nigra	Mustard	Mustard acts as a potent antagonist of the adverse biological effects of the ultimate metabolites of Benzo[a]pyrene mutagenicity; Tumoricidal activity was demonstrated on *In vivo* Drosophila melanogaster (SMART) and the *In vitro* HL60 (human promyelocytic leukemia cell line) systems; Mustard essential oil, allyl isothiocyanate (AITC) exhibited antineoplastic activity on bladder cancer cell lines carrying a wild type (wt; RT4) or mutated (T24) TP53 gene.	105–108
Brassica oleracea	Wild Cabbage	Inhibit the growth of estrogen receptor (ER)-positive (ER+; MCF-7 and BT474) and ER-negative (ER−; MDA-MB-231 and BT20) human breast cancer cell lines; Widely regarded as potentially cancer preventative.	4,77,109,110
Bryonia syriaca	Syrian Bryony	Used in treatment of cancer.	4,77
Capparis spinosa	Caper	Protein are isolated from caper, which inhibited proliferation of hepatoma HepG2 cells, colon cancer HT29 cells and breast cancer MCF-7 cells; Essential oil and aqueous infusion showed high inhibitory effect on HT-29 cell proliferation and on nuclear factor κB (NF-κB) activity; Study reported *C. spinosa.* extract mediated apoptosis through mitochondrial pathway in SGC-7901 cells.	111–114
Cassia senna	Senna	Senna aqueous extract avoid H_2O_2-induced mutagenesis and toxicity in *Escherichia coli* IC203 (uvrA oxyR) and IC205 (uvrA mutM) strains;	115–117

Table 1 (*continued*)

Plant name	English name	Ethno pharmacological profile in cancer	References
		Rhein (0.1 and 1 μg/ml) significantly reduced cell proliferation as well as mitogen-activated protein (MAP) kinase activation.	
Ceterach officinarum	Yellow pincushion	The chemical 3,4-dihydroxybenzaldehyde present in *Officinarum* acts as an inhibitor of growth of human cancer cells; Plasmid DNA after treatment with UV and H_2O_2, supercoiled DNA was successfully protected in the presence of 20 mg/ml or above concentrations of aqueous extract.	4,39,118,119
Chrysanthemum coronarium	Crown Daisy	Sesquiterpene lactones is isolated, which showed weak activities against human cancer cell lines such as A549, PC-3, HCT-15; Dihydrochrysanolide derivatives isolated were also examined for their cytotoxic activity against such human cell lines as A549, PC-3 and HCT-15; Essential oil of *Chrysanthemum coronarium* demonstrated antiproliferative effect in human colon cancer cell lines.	4,39,120–122
Cichorium intybus	Chicory	Chicory showed tumor-inhibitory effect against Ehrlich ascites carcinoma in mice; Protected DNA against oxidative damage to its deoxyribose moiety; Demonstrated notable growth inhibition in leukemia cell lines.	77,123–125
Cinnamomum camphora	Camphor	Camphorin isolated, which showed inhibition to the human hepatocarcinoma cell-line 7721 and solid melanoma in the skin of the nude mouse; Subamone a novel *Cinnamomum* monoterpenoid, was evaluated against A549 (human lung cancer cell), and DU-145 and LNCaP (human prostate cancer cell lines).	126–128
Citrullus colocynthis	Colocynth	Cucurbitacin glucosides exhibit pleiotropic effects on cells, causing both cell cycle arrest and apoptosis; Cucurbitacins-type triterpene glucoside had potent inhibitory activity on HepG2.	129–131
Commiphora molmol	Myrrh	*C. molmol* offered protection against mucosal damage caused by indomethacin and its combination with ethanol; Emulsion used protected against PbAc-induced hepatic oxidative damage and immunotoxicity; Hybrids from the compound Myrrhanone-C demonstrated significant anticancer activity in human lung A-549, cervical (Hela), breast (MCF-7), renal (ACHN), colon (Colo-205) and mouse melanoma (B-16) cell lines; Gulgulipid extract from the plant exhibited anticancer activity in human prostate cancer cell line LNCaP (androgen-dependent) and its androgen-independent variant (C81).	132–136
Crataegus azarolus	Azarole Hawthorn	Hexanoic extract showed cytotoxic effect against larynx HEp-2 cells; *Crataegus azarolus* ethyl acetate extract showed antiproliferative activity and apoptosis in human metastatic colorectal cancer cell lines HCT-116 and HT-29; It also demonstrated growth inhibition in mice B16F10 melanoma cells and inhibited melanin synthesis.	4,39,136–138
Crocus sativus	Saffron	Crocin from *Crocus Sativus* possesses significant Anti-Proliferation effects on human colorectal cancer cells; human lung adenocarcinoma cell lines A549 and SPC-A1 and mice MCF-7 cell lines Isolated carotenoid ingredients of saffron demonstrated cytotoxic activity against in vitro tumor cells.	139–143
Cucumis melo	Cucumber	Cucurbitane-type triterpenoids showed significant cytotoxic activity against the proliferation of A549/ATCC and BEL7402 cells in vitro; Reduces risk of cancer and other chronic diseases; Cucurbitacin-E (CuE) isolated from the plant may have antitumor activity in glioma therapy.	144–147
Matricaria aurea	Chamomile	Exhibited cytotoxic effect on PC-3, A-549 and MCF-7 cancer cells; Showed positive effects in Anti-genotoxicity studies. Apigenin glucosides are present which inhibited cancer cell growth; Bisabolol and α-Bisabolol-Rich Oils showed anticancer properties.	4,39,148–151
Narcissus tazetta	Bunchflower daffodil	Extracts strongly decreased the survival rate of cell lines: HL-60, K562, KT1/A3, and A3R; Pseudolycorine alkaloid showed remarkable antileukemic activity; Fractions of narcissus bulbs has been demonstrated against Ehrlich ascites tumor and # 6C3HED solid lymphosarcoma cells in mice; Cytotoxic effect was studied for different part of the plant.	4,39,152–154
Nigella sativa	Black seed	Seeds ethanol extract possess antitumor activity in mice tumor primary cells; Thymoquinone, main active compound inhibited cell proliferation of many types of cancer cell lines i.e. breast, ovarian and human pancreatic adenocarcinoma, colorectal cancer, uterine sarcoma, human osteosarcoma, neoplastic keratinocytes and fibrosarcoma, lung carcinoma and suppression of, anti-apoptotic genes expression (e.g., IAP1, IAP2, XIAP Bcl-2, Bcl-xL), NF-kappa B activation pathway and thus enhances apoptosis induction	155–164
Olea europaea	Olive	Hydroxytyrosol was found to induce apoptosis and arrest cell cycle progression at the G1 phase; Incidence of breast cancer was 70% less in rats group fed with olive oil; The oil extract was shown to reduce DNA damage (initiation), increase barrier function (promotion), and reduce cell invasion of surrounding tissue (metastasis); Oleuropein and hydroxytyrosol, major phenolic compound of olive oil, decreased cell viability, inhibited cell proliferation, induced cell apoptosis in MCF-7 breast cancer cells and may possibly be used to prevent cardiotoxicity induced by doxorubicin; Phenolic extract obtained from virgin olive oil was effective as antiproliferative and apoptosis-inducer in HL60 cells.	165–172
Peganum harmala	Harmala, Africa Rue	Harmane alkaloids present causes DNA topoisomerase inhibition; Harmine alkaloids present showed cytotoxicity against HL60 and K562 cell lines; Showed minor anticancer activity against several cell lines (human bladder carcinoma RT112, human laryngeal carcinoma Hep2 and human myelogenous leukemia K562); β-carboline compounds are inhibitors of cyclin dependent kinases; Alkaloids isolated from the plant exhibited antiproliferative activity in human gastric cancer cells MCG-803.	4,39,173–177
Pistacia Lentiscus	Mastic Tree	Anthocyanins extracted induces apoptosis in haepatocellular carcinoma; *P. lentiscus* inhibit proliferation and induce death of HCT116 human colon cancer cells *in vitro*; Increase cell membrane integrity in cultured PC12 and HepG2 cells; Fixed oil and phenolic extract of the plant demonstrated antiproliferative activity in BHK21 cancer cell lines.	4,39,178–181
Punica granatum	Pomegranate	Fruit extract decreases proliferation and induced apoptosis of DU-145 prostate cancer cells and suppressed invasive potential of PC-3 cells; Showed significant inhibition of tumor growth in prostate tumor model mice; It is effective in inhibition of lung tumorigenesis in mice; Pomegranate inhibits inflammatory cell signaling in colon cancer; Peel and seeds oil have been shown to be effective against tumor cell proliferation, cell cycle, invasion and angiogenesis;	182–192

(*continued on next page*)

Table 1 (*continued*)

Plant name	English name	Ethno pharmacological profile in cancer	References
		Methanolic extract of peel and seeds exhibited antitumor activity in A549 (lung non small cell carcinoma), MCF-7 (breast adenocarcinoma), SKOV3 (ovarian cancer cells), and PC-3 (prostate adenocarcinoma) cells; Polypenolic-rich extracts of the non-edible parts of *P. granatum* induced apoptosis in human U266 multiple myeloma cells.	
Quercus calliprinos	Palestine Oak	Fruit and bark decoction used for cancer treatment as Arab medicine	4,5,7,39
Thymus vulgaris	Thyme	Exhibited cytotoxic effect against PC-3, A-549 and MCF-7 cancer cells; Demonstrated notable growth inhibition in leukemia cell lines.	125,148,193
Triticum aestivum	Wheat	Wheat bread can prevent colon tumorigenesis; Lignans (in wheat) are also thought to be involved in cancer prevention in mice probably by apoptotic mechanisms; Bioactive components i.e. vitamins, lignans, isoflavones, and phenolic acids act as antioxidants or via mechanisms related to inhibition of tumor progression; Demonstated antiproliferative activity in HCT 116 and A549 cancer cell lines; A phenolic compound in the plant Triticumoside demonstrated apoptosis in human lung cancer cells.	194–199
Zingiber officinal	Ginger	Exhibited cytotoxic effect against PC-3, A-549 and MCF-7 cancer cells; Studies reported the benefits of ginger supplementation in reducing risk of liver cancer and breast neoplasms.	148,200–202
Urtica pilulifera	Stinging Nettle	Flavonoid glycosides were isolated showing high intracellular killing activity; The root extract are used in treatment of benign prostate hyperplasia; Leaves aqueous extract showed inhibition of adenosine deaminase activity in prostate cancer; Studies reported cytotoxic activity.	4,39,203–206
Viscum cruciatum	Red-berry mistletoe	Hirsutanone isolated showed cytotoxicity against melanoma, renal and breast cells; Hexanoic extract showed cytotoxic effect against larynx HEp-2 cells; Mistletoe also showed anticancer activity against BJAB cells, with IC50 value of 14.21 μg/ml.	4,39,137,207,208
Vitis vinifera	Grapes	Exhibited cytotoxic effect against PC-3, A-549 and MCF-7 cancer cells; Extracts isolated from the plant seeds and stems demonstrated antitumor activity in human breast cancer cell lines MCF-7 and MDA-MB-23), colon (HT29), renal (786-0 and Caki-1), thyroid (K1), hepatocellular carcinoma cell lines, oral squamous cell carcinoma and normal human fibroblasts.	148,209–213

results in treating or reducing the cancer progression. Most of the aforementioned (Table 1) plants have been studied in-depth for immunomodulatory and cancer treatment purposes i.e. *N. sativa, Acacia seyal, A. sativum, Olea europaea, Vitis vinifera*, resulting in isolation of lead compound with promising results in treating cancer. Resveratrol is a leading example isolated from *V. vinifera* applied effectively in treating cancer. Likewise Thymoquinone from *N. sativa* is proved an immunomodulatory for treatment in cancer therapy along with alliin and alliicin from *A. sativum* and *Oleuropein*/omega-3 fatty acids from *Oleae europeae* showed antioxidant and anticancer effects.

The aforementioned examples are an indication for the folkloric TAI plants implicated in the form of crude extract, fractions or subfraction in treating cancer, to be studied further in order to isolate active drug for cancer treatment. This review article provides data regarding TAI plants having folkloric uses and utilized in TAI system for treating cancer. The purpose of this study is to highlight these plants in order to be studied more for their biological, therapeutic and toxicological properties. Advancement in science and analytical techniques provides opportunities to study these plants for reducing any toxicological effects related to the use of these plants in cancer. These plants, as showed considerable results in treating cancer, even in the form of crude extract can be converted to nanoparticles or nanoemulsions in order to enhance its bioavailability and targeted therapy in the affected areas of cancer. These plants have a wide scope to be utilized for covering the deficient areas and hurdles of treating cancer as they having reports for folkloric uses with well-established research literature mentioned in Table 1 for individual plants.

The Table 1, helps to provide a list of plants used in cancer as well as available literature in order to accomplish the purpose of study i.e. TAI plants needs more research exploration. Despite the fact; some plants have been studied in the form of crude extract as well as isolation of therapeutic ingredient, via bioassay guided isolation, still most of the plants having lack of studies with respect to toxicity and mechanism involved during cancer treatment and hence needs further research profiling. Similarly most of the isolated active drugs showed greater toxicity as compared to crude extract. Table 1 gathers all these plants and the literature study regarding use in cancer providing sufficient information to use these plants in crude form as well as combination of these plants in raw or crude extract form for the treatment of cancer.

As mentioned in table, different types of cancer and tumors have been treated with these TAI plants which includes; hepatocellular carcinoma, breast adeno carcinoma, lung carcinoma, colorectal carcinoma, colorectal, breast, and lung cancers, esophageal and stomach cancer, prostate cancer, solid melanoma in the skin and benign prostate hyperplasia. The TAI plants showed cytotoxicity against different cell lines i.e.; larynx HEp-2 cells, BJAB cells, PC-3, A-549 and MCF-7 cancer cells, PC12 and HepG2 cells, HCT116 human colon cancer cells, human bladder carcinoma RT112, human laryngeal carcinoma Hep2 and human myelogenous leukemia K562, HL60 and K562 cell lines, 6C3HED solid lymphosarcoma cells, A549 (human lung cancer cell), and DU-145 and LNCaP (human prostate cancer cell lines), (ER)-positive (ER+; MCF-7 and BT474) and ER-negative (ER−; MDA-MB-231 and BT20) human breast cancer cell lines and HO-8910 & 7721 cell lines showing effective cancer treatment by these plants.

Different mechanism i.e.; chemo preventive, antioxidants, Topoisomerase-I and II enzymes inhibitory, suppresses tumor necrosis factor alpha, G1-phase cell cycle arrest with an induction of p21 and a reduction of cyclin D1, inhibitory effect on nuclear factor κB (NF-κB) activity, mitogen-activated protein (MAP) kinase activation, protected DNA against oxidative damage to its deoxyribose moiety and inhibition of adenosine deaminase activity in prostate cancer were evaluated for these TAI showing promising result.

The literature cited in current review article highlights the lead compounds isolated which may be a target and source of new drug development for researchers in order to modify, carry out SAR and study new pathways in order to find a complete cure for cancer. The lead compounds isolated and discussed are; Hirsutanone, Flavonoid glycosides, Lignans, isoflavones, and phenolic acids, Anthocyanins, Harmane and Harmine alkaloids, Oleuropein and hydroxytyrosol, Hydroxytyrosol, Thymoquinone, Pseudolycorine alkaloid, Cucurbitane-type triterpenoids, Crocin and carotenoid ingredients of saffron, Cucurbitacins-type triterpene glucoside, Subamone a novel *Cinnamomum* monoterpenoid and Camphorin,

Sesquiterpene lactones and Dihydrochrysanolide derivatives, Acetyl-11-keto-β-boswellic acid, 3-n-butyl phthalide and sedanolide and Senkyunolide-N, Senkyunolide-J & 3-hydroxymethyl-6-methoxy-2, 3-dihydro-1H-indol-2-ol and Anethofuran. The nature and structures as well as classes of aforementioned compounds are source of knowledge for finding effective class of drugs to be utilized in cancer treatment.

The table also includes herbs which are used as food or nutraceuticals. These Arabic and Islamic plants, used in any of the modality as aforementioned, showed the better alternative source for the treatment of cancer and malignancies. The extracted material from literature survey of these Arabic and Islamic traditional medicinal plants as mentioned in Table 1 justifies the fact; Arabic and Islamic traditional plant as medicine, are well documented in literature. The next major outcome of the study proved significant is; the active use of these folkloric used traditional plants by most of the practitioners, even today. These plants are the major source for research too and numerous pharmacological, toxicological, biological and cytotoxicity studies have been carried out for these herbs as shown by the unlimited literature available for each plant.

4. Conclusion

The wisdom of the past led to the discovery of chemopreventive drugs. The Arabic and Islamic plants studied in this review article are more important as alternate for cancer research and treatment. These traditional plants and their folkloric/traditional pharmacological profile need to be preserved. The main area of emphasis; isolation of the active chemical having potency to treat cancer with minimal side effects and ensuring the safe use of these medicinal plants, should be strived more. These plants need effective utilization in order to make a hallmark through complete cancer cure and cheap regimen to be available for ordinary population.

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