International Journal of Botany Studies
ISSN: 2455-541X; Impact Factor: RJIF 5.12
Received: 13-04-2019; Accepted: 15-05-2019
www.botanyjournals.com
Volume 4; Issue 4; July 2019; Page No. 144-150

A comprehensive review on anti-cancer medicinal plants

Farah Abid[1], Muhammad Saleem[2], Sara Zahid[3], Shumaila Arshad[4], Saleha Yasir[5], Mehwish Qayyum[6], Kanwal Ashiq[7], Samreen Tanveer[8*], MayydaAsif Bajwa[9], Sana Ashiq[10]

[1-5] Faculty of Pharmacy, the University of Lahore, Lahore, Pakistan

[4] Riphah Institute of Pharmaceutical Sciences, Riphah international University, Islamabad, Pakistan

[6-9] Faculty of Pharmaceutical Sciences, Superior University 17-km Raiwind Road Lahore, Pa Comprehensive Review on Anti-Cancer Medicinal, Pakistan

[10] Sharif Medical and Dental College Lahore, Pakistan

Abstract
Cancer is a major health concern and one of the leading causes of death around the globe. Medicinal plants contain numerous phytochemicals and their usefulness for the treatment of cancer has been proven scientifically. The current review is aimed to provide a comprehensive knowledge about the herbal plants with established anti-cancer activity. For this study, different databases were used, including: PubMed, Google Scholar, Scopus and MEDLINE and literature search were done without any year limit. Studies have reported that numerous classes of phytochemicals have tumor inhibitory effect and these could be used for the cure of cancer. In this era, where the drug development process and its subsequent marketing and surveillance often take decades, the emerging evidence of the beneficial anti-cancer properties of plants have proved to be a mercy. There is need to explore more about the mechanism of action of phytochemicals having anti-cancer properties and further to ensure the medicinal plants safety and efficacy to justify their rational use for the treatment and management of the cancer.

Keywords: cancer, chemotherapy, medicinal plants, phytochemicals, tumor

1. Introduction

Cancer has been designated worldwide as a second leading cause of death. The prognosis of cancer, despite concerted efforts in innovating and improving current cancer therapies, remains dismal.In Asiatic countries, there is an ongoing increase in the progression of breast cancer and it has become one of the prominent causes of death. Annually, about 3 million new cancer cases are recorded and sofar more than 2 million deaths due to cancers have been reported only in Asia [1]. A limited or sporadic response has been associated with highly specific blockage of the single signaling pathway. Thus, a new paradigm for anticancer therapy that targets multiple signaling pathways has emerged by using targeted therapies [2]. Over the last decade, a significant change in the treatment of cancer has been viewed owning to the emergence of small molecule inhibitors and monoclonal antibodies, together which are termed as Targeted Therapies. These therapies have taken an integral place in the treatment of a wide array of common malignancies, including pancreatic, colorectal, lung and breast cancers. Despite the fact that targeted therapies are associated with several adverse effects including cardiac dysfunction, thrombosis and hypertension, they are well tolerated than cytotoxic chemotherapy which is the reason for paving the replacement of this hallmark of medical treatment of cancer with new targeted therapies [3]. Moreover chemotherapy used in treatment of breast cancer can lead to renal failure which is associated with variety of comorbid conditions [4]. In the past few years, an upward trend was seen in health burden due to prevalence of these comorbid conditions. This is in turn has adversely affected the quality of patient's life [5]. Two major factors that determine the success as well as the effectiveness of a targeted therapy is firstly the target's nature and secondly, the targeting characteristics of the agent developed to focus the identified target [6]. Nonetheless, to arrest the insidious nature of this dreadful disease one should not merely focus on targeted therapies as they too are embodied with severe side effects. Growing evidence has revealed that the use of folk medicine plant preparations provides a suitable alternative for rationalized allopathic drugs. In recent years, the anti-tumor actions of various phytochemicals have been thoroughly investigated and being increasingly used as therapeutic agents as they are capable to produce different pharmacological effects in living organisms [7]. Hoping for a better cure options, more and more patients together with medical health personnel are turning towards complementary and alternative traditional healthcare systems.

Cancer is a debilitating disease characterized by the formation of lumps and masses of tissues referred to as tumors which are formed due to uncontrollable division of damaged cells. The normal physiology of circulatory, nervous and digestive system is compromised and disrupted by the uncontrolled tumor growth. Benign tumors tend to demonstrate limited growth and characteristically stay located in one spot. On the other hand, the dangerous malignant tumors show invasion of distant tissues, by moving through blood and lymphatic systems from their primary genesis location and also promote angiogenesis. These metastasized tumors create dangerous circumstances with very narrow therapeutic options [8]. Among various causes of cancer, nanoparticles toxicity is one of the major causes of genetic mutations that can prove to be

carcinogenic as these nanoparticles are present in smoke, paints and even in air [9].

Irrespective of its categories groups-herbs, shrubs or trees, the chemotherapeutic agents derived from natural botanical sources are attributed to being almost 60%. Recent research throws limelight over the fact that plants provide a paramount source of potential chemotherapeutic agents that are yet to be exploited. Significant therapeutic properties are possessed by numerous plants against common malignancies including colorectal, breast and lung cancers. Broadly, chemotherapeutic agents derived from plants are categorized into twelve major categories namely; alkaloids, phenylpropanoids, terpenoids, glycosides, aldehydes, lignans, lipids, unsaponified lipids, nucleic acids, polysaccharides, proteins and unidentified compounds. Since centuries, secondary metabolites isolated from plants have been used in folk medicine for the treatment of diseases including cancer. Some of the notable medicinal plants possessing anti-tumor activity are *Aloe vera, Helianthus annuus, Azadirachtaindica, Curcuma longa, Curcuma zedoaria,* and *Euphorbia tirucalli* [10].

Table 1: Active principles of Anti-Cancer Plants

Plant name	Botanical Origin	Family	Constituents	Properties
Aloe vera	*Aloe barbadensis*	Liliaceae	anthraquinonones	Strengthens the immune system and anti-tumor activity [11].
Sunflower	*Helianthus annus*	Asteraceae	Nevadensin	Anti-cancer agent [12]
Indian Lilac (Neem tree)	*Azadirachtaindica*	Meliaceae	Quercetin quercitrin	Potent Anti-Cancer activity [13].
Turmeric	*Curcuma longa*	Zingiberaceae	Curcumin	Anti-proliferative agent [14].
White turmeric	*Curcuma zedoaria*	Zingiberaceae	8,9-Dehydro-9-formyl-cycloisolongifolene, 6-ethenyl-4,5,6,7-tetrahydro-3,6-dimethyl-5-isopropenyl-trans-benzofuran, eucalyptol, and γ-elemene	Anti-cancer agents through the induction of apoptosis
Indian tree spurge	*euphorbia tirucalli*	Euphorbiaceae	Euphol	Cytotoxic effect on cancerous cell lines [15].
Hyptis fasciculata	*Hyptis fasciculata*	Labiatae	isoquercitin	Anti-tumorigenic action
Apple	*Malusdomestica*	Rosaceae	quercetin glycosides: hyperoside, isoquercitin, avicularin, rutin and a high concentration of quercitrin [16].	Chemopreventive & anti-cancer properties
Skullcap	*Scutellariabaicalensis*	Lamiaceae	Flavonoids [17, 18].	Tumor growth inhibition CDK1 Inhibitor
Bitter Orange	*Citrus aurantium L*	Rutaceae	phenethylamine alkaloids octopamine, synephrine, tyramine, hordenine and N-methyltyramine [19].	Chemopreventive& Anti-inflammatory actions
Pomelo	*Citrus maxima*	Rutaceae	Flavonoids (Naringin)	Tumor growth inhibition
Beet Root	*Beta Vulgaris*	Amaranthaceae	Betalains, phenolic compounds [20].	Anti-cancer & Anti-inflammatory
Kidney Breans	*Phaseolus vulgaris*	Fabaceae	polygalacturonic acid lectin [21].	Anti tumorigenesis& anti-inflammatory
Green tea	*Camellia sinensis*	Theaceae	Epigallocatechin [22].	Chemopreventive, anti-inflammatory& anti-tumorogenesis
Selfheal	*Prunella Vulgaris*	Lamiaceae	Phenolic compounds [23].	Anti- tumore proliferation & metastasis [24].

Citrus maxima

The habitat of *Citrus maxima* belonging to the family *Rutaceae*is Asian tropical areas. Neohesperidin and naringin are the two major flavanones isolated from the seeds of the citrus fruits and mediate anti-tumor and anti-inflammatory through its antioxidant activity by promoting free radical scavenging and reducing oxidative stress by counteracting reactive oxygen species in H_2O_2–treated HepG2 cells *in vitro*. On the contrary, flavonoids mediate a beneficial effect on signal transduction in cell proliferation and angiogenesis and thus, play a prophylactic role. As postulated by an experiment conducted by Kudusenand coworkers [25]. A decrease in tumor volume and an increase in the lifespan of nonviable tumor cell count is shown to be attributed to anintraperitoneal administration of 200 and 400 mg/kg BW of a methanolic extract of *Citrusmaxima* [26].*Citrus maxima contains an abundant concentration of naringin, a bioflavonoid, which has demonstrated significant anti-cancer potential through a dose& time dependent inhibitory effect on AGS cancerous cells [27]. Naringin is also actively* involved in the inhibition of FAK kinase activity, inhibition of FAK/mmps pathway, thus paving way for the suppression of cell invasion and apoptosis [28]. The mammalian enzyme activity is significantly influenced by flavonoids particularly protein kinase activity is modulated to a considerable extent. The interference of flavonoids with protein kinase activity is a major contributor to their anti-cancer potential [29]. The anti-tumorigenesis property of flavonoids is also linked to the biological activity of their active metabolites [30]. The methanolic extract of Citrus maxima leaves, in vitro, produces a twofold effect; a significant increase in life expectancy coupled with a leucocyte count decrease [25]. *Citrus aurantium* L.

The *Citrus aurantium* L of the family *Rutaceae*,has a spectrum of biologically active constituents, most importantly, phenethylamine alkaloids octopamine, synephrine, tyramine, hordenine and N-methyltyramine. Consumption of this citrus fruit has been associated with a lowering in the incidence of cancer, as evidenced by the lower cancer prevalence amongst the mediterraneans where

a considerable portion of diet is composed of Citrus aurantium[19].Anti-inflammatory, antioxidant, and anti-tumorproperties have long since been attributed to the Korean *Citrus aurantium* L. The flavonoids isolated from the specie mediate, in a dose dependent manner, the inhibition of HepG2 cell proliferation. Various downstream targets of phosphoinositide-3-kinase/Akt pathway – P-4EBP1 and P-p70S6K and pAkt levels are shown to be reduced by flavonoids isolated from Korean *Citrusaurantium* L. In addition, an increase ratio in the expression of Bax/Bcl-xL coupled with a decrease in Bcl-2 and Bcl-xL and an increase in the expression of cleaved caspase 3, Bax and Bak is exhibited by cells that have been treated with flavonoids extracted.In flavonoid treated Hep-G2 cells, there has also been observed a loss in the motichondrial membrane potential [31].*The complex low molecular weight polysaccharide known as citrus pectin, abundantly found in the peel and pulp of a number of citrus fruits including citrus maxima, characteristically possesses sugar carbohydrate residues abundantly. The citrus pectin, has anti-tumorigenesis properties that specifically target cancerous cells of the gastrointestinal tract through a Bcl-xL-mediated process which results in a causing an apoptosis dampening in susceptible cells [32]. In addition, the galactomannans, isolated from Citrus aurantiumalso have the ability to scavenge free radicals and mediate anti-cancer activity at a very low concentration [33].*

Scutellariabaicalensis

Scutellariabaicalensis of the family Labiatae is a popular Chinese herbal medicine that has been used since ancient times for its anti-influenza, anti cancer properties as well as for its ability to effectively combat oxidative stress. Recently, a study was conducted byJi Et.al to elucidate various biologically active therapeutic constituents which were isolated through the use of various column chromatography techniques and semi-preparative HPLC. The successfully isolated constituents were then identified by the utilization of the process of HRE-SIMS and NMR spectroscopic analysis. The utilization of MTS assay to detect the cytotoxic effects of the isolated and identified constituents against HepG2, SW480, and MCF7 human cancer cells revealed that a majority of the free flavones exhibited such activity with a 61.2% inhibition rate at 10 μM.This discovery further highlights the fact that flavones being an important effective constituent of most anti cancer plants can be used as chemical markers in order to ensure quality control of pharmaceuticals or herbal medicines containing these biologically active components [34]. Baicalein, a flavone isolated from *Scutellariabaicalensis, demonstrates a potent anti-cancer activity in pancreatic cancer cells through the inhibition of erastin induced ferroptosis [35]. Inaddition to neuroprotective and anti-inflammatory effects, baicalein also mediates an analgesic effect in eliminating chronic bone pain induced by cancer. The effect is thought to be associated with an inhibition of inflammatory cytokines TNF-alpha and IL-6 expression [36]. Baicalein has also shown to possess crucial ability of being a CDK1 inhibitor. The only CDK1 involved and thought to have a major contribution in the process of cell proliferation is cyclin dependent kinase 1. Thus, the activity of baicalein against CDK1 is of tremendous importance and poses as a new anti-cancer agent to be exploited [18].*

Malus Domestica

One of the most popular and widely cultivated fruit trees in the world, *Malusdomestica*contains phenolic compounds and flavonoids which are attributed to have strong anti-oxidant properties. The apple leaves have shown to contain quercetin glycosides: hyperoside, isoquercitin, avicularin, rutin and a high concentration of quercitrin [16]. The best known and described property of phenolic compounds is their anti-oxidant property. The cellular dysfunction characteristic of cancer and various other diseases is a result of highly reactive oxidant molecules that mediate their degenerative effects through the capture of electrons leading to chemical structure modifications. The quercetin glycosides are powerful anti-oxidant molecules that act by scavenging free radicals or reactive oxygen species, thus, the chemopreventive properties of quercetin glycosides is attributed to their anti-oxidant and oxidative damage prevention effects.By using the technique of cancer cell viability assays for a comparison between quercetin, hyperoside, isoquercitin, and quercitrin reveals that due to glycosylation, isoquercitin is a promising candidate for chemotreatment because it confers more advantageous pharmacological changes its analogue quercetin. The effect of isoquercitin on pancreatic cancer progression was proliferation inhibition, promoted apoptosis and induced cell cycle arrest in those pancreatic cancer cells that were in G1 phase [37].

Hyptis Fasciculata

The *Hyptisfasciculata* of the family Lamiaceae, whose aerial parts serve as a valuable source of isoquercitin, is well known for its capacity to interrupt the glioblastoma cell growth. Though the exact mechanism through which isoquercitin reduces glioblastoma cell growth is not nonebut it is thought that it does by reducing cyclin D1 levels and increasing p27 levels [38].Artificially stressed cells when treated with *Hyptis fasciculate* extract exhibit the free radical scavenger properties of the plant. In addition to its scavenging properties, the extract has also shown to increase the tolerance of cells to H_2O_2 stress thus amplifying the anti-oxidant properties [39].

Curcuma zedoaria

Curcuma zedoaria possesses a valuable essential oil with cytotoxic effects which are particularly efficient against non small lung carcinoma cells and mediates its therapeutic effect through the induction of apoptosis. The notable effects of the isolated essential oil are an increase in the population of sub-G1 cells along with an increased annexin-V binding levels, subsequent cleavage and caspase -3, -8, and -9 activation. In addition to these changes, an increase in the poly (ADP ribose) polymerase has also been observed [40].The principle physiologically active anti-tumor therapeutic agent of *Curcuma zedoaria* is α-Curcumene. However, the anti-tumor effect is proposed to be a synergistic effect of multiple anti-tumor agents and a reliance on a single agent effect has not been reported. An inhibition in growth of sarcoma 180 is mediated by protein-bound polysaccharides and single entity polysaccharides of this specie. In addition, it is evident from recent research that an anti-proliferative effect is brought about particularly on MCF-7, ovcar-3 cells as well as on HL-60 cells. Nonetheless, it is proposed that the principle anti-tumor

effect of *Curcuma zedoaria* is through the induction of apoptosis [41].

Intraperitonial administration of *Curcuma Zedoaria* crude extract produces direct cancer inhibiting actions including anti- angiogenesis effect and a suppressive effect on B16 melanoma cells in pulmonary metastasis. In experimental animals, curcumin isolated from *Curcuma Zedoaria* extract provides highly protective effects from chemically induced liver damage [42].

Aloe vera

The extract of *Aloe vera*follows a dose dependent and time manner to induce cytotoxicity against hepatocellular carcinoma cells. The induction of apoptosis is mediated through an increased expression of TP53 gene and a decrease in the expression of BCL-2 gene [43]. The hydroxy-anthraquinone of *Aloe vera*, Aloe Emodinpossesses a strong anti- neural ectodermal tumor activity both in-vitro and in-vivo. In mice models, this biologically active agent exhibits an inhibition of neuro-ectodermal tumor growth coupled witha combined and severe immunodeficiency without the mediation of any appreciable lethal effects. Moreover, the compound does not cause an inhibition inhemo-poieticprimogenitor cellproliferation nor does it mediates an inhibition in the proliferation of normal fibro-blasts [44].

Among other biologically active compounds isolated from Aloe-vera extracts are feruloyl, cinnamoyl, caffeoyl aloe-sin and p-coumaroyl. The ability of Caffeoyl aloe-sin toproduce a preventive effect on immune suppression induced by UV-B is shown through the utilization of contact-hypersensitivity reaction technique. In addition to thispreventive action, the enzymatic activities of tyrosine-hydroxylase and Dopa oxidase induced activities of monophenol mono-oxygenase is inhibited by aloe-sin in lysates of human melanocyte cells [45]. Another anthra-quinone isolated from aloe vera leaves is barbaloin which alone plays a major role in life span prolongation of animals that have undergone tumor transplantation procedure [46].

Helianthus annuus

Sunflower plants' multifaceted actions have gained it a tremendous popularity in traditional and western medicines alike. Phyto-esterol isan active principle which is rich in the seeds of Helianthus annuus and provides a strong preventive action against the development of breast cancer. In vivo, it has been demonstrated that the most abundant phyto-sterol, betasitosterol, not only causes a growth inhibition in tumor cells of specific types but also mediates a reduction in tumor size as well as extent of metastasis. Evidence from a recent study highlights the positive correlation between reduced risks of premenopausal breast cancer and associated high consumption of sunflower seeds. In skin tumor mouse models, helianthus annuus oil exhibits a chemo preventive potential by providing 40% protection against tumor development. In addition to chemo preventive characteristics, helianthus annuus also possesses significant anti inflammatory capacities [47]. Sunflower seeds are a source of a pharmacologically active bioflavonoid; nevadensin, which possesses an array of significant biological actions including tumor suppression and growth inhibition. The extract of striped sunflower seed cotyledons show a significant oxygen radicals scavenging capacity. Due to the strong antioxidant capacity of sunflower seeds they can mediate a significant preventive action against the development of cancer and other oxidative stress related diseases if consumed daily [12].

One of the most prominent aims of research efforts in the field of natural products is the search for anti-neoplastic agents which show a characteristically high affinity for the inhibition of signaling pathways in tumor cells without having a significant effect on the normal signaling pathways in non-cancerous cells. The polyphenols isolated from sunflower seed extract including chlorogenic and ferulic acid and caffeic acid demonstrate a strong antioxidant potential as well as a high anti-mutagenic actions. The observed characteristically high anti-mutagenic potential of sunflower polyphenols is due to their ability of mutagenic metabolic activation blockage and free radical scavenging and active screening. The trypsin inhibitor isolated from sunflower possesses a protein ring which acts differently in accordance with its form; when it is utilized in its natural form it acts by producing a chemo preventive action against breast cancer through the blockage of breast cancer specific enzymes; the utilization of the modified form, it acts by blocking enzymes involved in the genesis and proliferation of other types of cancer [48].

Euphorbia tirucalli

The succulent shrub of *Euphorbia tirucalli*, African continent native small tree, is cultivated throughout the world due to its immense popularity owing to its vast use in traditional remedies and herbal medicines. Recent identification of bioactive principles, isolated from the plant latex, has led to the identification of their therapeutic properties including anti-tumorigenic properties. An array of bi- and tri-terpenoids and gallic acid are amongst the bioactive principles isolated from the plant latex. Potent anti-oxidant abilities and oxidative stress combating capacity is observed with the extract of leaf and stems of *Euphorbia tirucalli*. A paradox surroundinganti-cancer biological activity of the specie is; interaction with anti-oxidant enzymatic activities through anti-oxidant enzyme geneup regulationis observed with aqueous extracts of the whole plant thus; highlighting the need for the practice of caution during dose calibrations and administration which should be limited to latex extracts till further evidence is demonstrated by prospective studies [49]. The speculated mechanism of action of latex active bio principles in mediating tumor growth inhibition is through granulocyte and macrophage production regulation and functional action expression regulation. The suppressed action of plant latex is mediated on CD4+ and CD8+ T lymphocytes; an inhibition is also induced upon interleukin II and also on the production of interferon-gama and the associated subsequent immunomodulation [50]. Euphol isolated from latex extract is biologically a triterpenealcohol belonging to euphane group, bears a striking structural similarity to cholesterol, possesses a spectrum of therapeutic activities such as, anti-tumorigenic and inflammation combating properties [51]. A characteristic property of euphol is that it specifically targets CS-12 human gastric cancer cells with a greater affinity and exhibits negligible effects on non-cancerous cells [52].

Curcuma longa

Curcuma longa or turmeric, is a rich source of diferuloyl-methane (curcumin), a polyphenol, which has since centuries been extensively utilized in Traditional medicines

particularly Ayurvedic medicines due to its vast spectrum of therapeutic properties such as anti-flammatory and oxidative stress scavenging. Recent studies have revealed additional potential of curcumin including anti-cancer actions through the induction of a variety of pathways. The mutagenesis biological pathways targeted by curcumin are expression of oncogenes, regulation of cell cycle, induction of apoptosis, tumor genesis and inhibits matastasis. A number of receptors of growth factors and molecules pertaining to cell adhesion involved in cancerous cell growth are affected by curcumin. In addition, anti-proliferative effect on a variety of cancer types is mediated by curcumin [53]. A disturbing issue associated with thyroid cancer is metastasis. The natural polyphenoliccompound, curcumin, demonstrates an inhibition in proliferation and mediates an induction of apoptosis [54]. In animal models, curcumin demonstrates an inhibition in tumor development [55].

Beta Vulgaris

The extract of beet root, *in vitro & in vivo*, demonstrates an inhibitory effect on tumor cells. The consumption of beet root mediates a chemo preventive effect [56]. The plant pigments isolated from beet root, betalains, are water soluble and in addition to characteristic properties such as anti-inflammatory, hepatoprotection, radical scavenging, also possess anti-cancer actions. The antioxidant potential is positively correlated with concomitant presence of total phenolic compounds and betalains. The association is thought to be the presence of a synergistic effect of phenolic compounds on the activity of betalains [20].

Phaseolus vulgaris

Phaseolus vulgari, also known as kidney beans, is an annual herbaceous specie, demonstrates a specifically high toxicity human liver carcinoma cells coupled with a negligible activity against normal liver cells. The activity is associated with the presence of a polygalacturonic acid lectin isolated from the specie. In addition to anti-tumor genesis effects, the lectinis also involved in the mediating dose dependent increase in the synthesis of mRNAs coding for the production of pro inflammatory cytokines [21].

Camellia sinensis (Green tea)

Green tea is scientifically referred to as *Camellia sinensis*. The anti cancer potential of *Camellia sinensis*, is attributed to the presence of a moderate concentration of polyphenolic compounds. The specie contains a small amount of Epigallocatechin, a polyphenol attributed to mediating a protective effect on DNA by scavenging harmful oxygen radicals. Green tea, in addition to its chemoproventive effect, also produces an anti tumor genesis and inhibits mutagenic activities. Catechins isolated form green tea; demonstrate an inhibitory effect on angiogenesis and metastatic events. Furthermore, green tea is associated with decreasing the overall risk of development of cancer of stomach and colon [22]. The components of green tea mediate an overall positive effect on the health of an individual, not only through the reduction cancer risk, but also a protective effect against the development of diabetes and hepatitis [57]. The beneficial effects of gallic acid esterified catechins are exerted through a modulation of mitochondrial activity byan impact on the biogenesis of mitochondria, control of bioenergetism, cell cycle alterations and apoptosis regulation [58]. A strong anti proliferative and metastatic properties is demonstrated against human breast carcinoma cells [59]. The inflammatory responses mediated through the MAPK pathways are also inhibited by green tea water [34]. The gallic acid esterified catechins modulate a number of functions of susceptible cells by binding to cell specific protein sites [60].

Prunella Vulgaris

The herbaceous plant, *Prunella Vulgaris*, is associated with producing an anti-cancer effect through an array of targets and pathways. The mechanisms that are possibly involved are calcium ion regulation to maintain a steady state concentration, regulation of cell cycle, and producing an inhibitory effect on proliferation of tumor cells and metastasis [24].

Conclusion

The emergence of modern innovative society is plagued with increased incidence of debilitating diseases which not only cripple the economic backbone of a country but also deplete scarce medicinal resources. In such a scenario, the need for focusing attention and increasing reliancetowards plants as a source of therapeutic principles has been heightened. In such an era, where the drug development process and its subsequent marketing and surveillance often take decades, the emergent evidence of the beneficial anti-tumor genesis properties of plants have proved to be a mercy.

Acknowledgement

Authors would like to acknowledge Department of Pharmacy, University of Lahore, Pakistan for their kind support and encouragement.

References

1. Arshad S, Rehman M, Abid F, Yasir S, Qayyum M, Ashiq K, Tanveer S, Bajwa M, Ashiq S. Current situation of breast cancer in Pakistan with the available interventions. *Int J Biosci*, 2019; 11(6): 232-240.
2. Khan M, Maryam A, Qazi JI, Ma T. Targeting apoptosis and multiple signaling pathways with icariside II in cancer cells. Int J Biol Sci, 2015; 11(9): 1100-1112.
3. Gerber DE. Targeted therapies: a new generation of cancer treatments. Am Fam Physician, 2008; 77(3):313-319.
4. Tanveer S, Ashfaq M, Parveen R, Ashiq K, Qayyum M, Bajwa M, Ashiq S, Arshad A. Assessment of the risk factors and various patient related attributes influencing hemodialysis. Int J Biosci, 2019; 14(4): 238-247.
5. Kanwal A, Abida L, Sana A, Ahlam S. A systematic review on the prevalence, pathophysiology, diagnosis, management and treatment of gout (2007-2018). GCS Biol Pharm Sci, 2018; 5(1): 50-55.
6. Offermann M. The Era of Targeted Therapies. *Am Fam Physician*, 2008; 77(3): 294-296.
7. Tanveer S, Latif A, Ashiq K, Qayyum M, Bajwa MA. A comprehensive review on pharmacological and phytochemical potential of Cassia Fistula Linn: A Magical Herb. Int J Biol Pharm Allied Sci, 2019; 8(6):1134-1157.
8. Sharma H, Parihar L, Parihar P. Review on cancer and anticancerous properties of some medicinal plants. J Med Plants Res. 2011; 5(10):1818-1835.

9. Tanveer S, Farrukh MA, Ali S, Khaleeq-ur-Rahman M, Imtiaz A. In vitro Toxicological Study of Metal Oxides Nanoparticles on Oxidation of Succinate in Krebs cycle and Their Resultant Effect in Metabolic Pathways. *J Chin Chem Soc*, 2014; 61(5): 525-532.
10. Das G, Gouda S, Mohanta YK, Patra JK. Mangrove plants: A potential source for anticancer drugs. Indian J GeomarineSci, 2015; 44(5): 1-8.
11. Surjushe A, Vasani R, Saple DG. Aloe vera: a short review, *Indian J Dermatol*, 2008; 53(4): 163-166.
12. Dwivedi A, Sharma GN. A review on Heliotropism plant: *Helianthus annuus* L. *J Pharmacol, 2014; 23(2): 149-155.*
13. Krishnamoorthy M, Balakrishnan R. Docking studies for screening anticancer compounds of Azadirachtaindica using Saccharomyces cerevisiae as model system. J Nat Sci Biol Med, 2014; 5(1): 108-111.
14. Awasthi PK, Dixit SC. Chemical composition of *Curcuma Longa* leaves and rhizome oil from the plains of Northern India. J Young Pharm, 2009; 1(4): 312-316.
15. Reis RM, Silva VA, Rosa MN, Tansini A, Lima JP, Jones C, Pianowski LF. Cytotoxic effect of euphol from *Euphorbia tirucalli* on a large panel of human cancer cell lines. J Clin Oncol, 2013.
16. Liaudanskas M, Viškelis P, Raudonis R, Kviklys D, Uselis N, Janulis V. Phenolic composition and antioxidant activity of Malusdomestica leaves. Sci World J, 2014, 1-11.
17. Scheck AC, Perry K, Hank NC, Clark WD. Anticancer activity of extracts derived from the mature roots of *Scutellaria baicalensis* on human malignant brain tumor cells. BMC Complement Altern Med. 2006; 6(1):27-27.
18. Guo HM, Sun YM, Zhang SX, Ju XL, Xie AY, Li J, Zou L, Sun XD, Li HL, Zheng Y. Metabolism and pharmacokinetics of 8-hydroxypiperidinylmethyl-baicalein (BA-j) as a novel selective CDK1 inhibitor in monkey. Fitoterapia. 2015; 107:36-43.
19. Suryawanshi JA. An overview of Citrus aurantium used in treatment of various diseases. Afr J Plant Sci. 2011; 5(7):390-395.
20. Georgiev VG, Weber J, Kneschke EM, Denev PN, Bley T, Pavlov AI. Antioxidant activity and phenolic content of betalain extracts from intact plants and hairy root cultures of the red beetroot Beta vulgaris cv. Detroit dark red. Plant Foods Hum Nutr. 2010; 65(2):105-111.
21. Fang EF, Pan WL, Wong JH, Chan YS, Ye XJ, Ng TB. A new Phaseolus vulgaris lectin induces selective toxicity on human liver carcinoma Hep G2 cells. Arch Toxicol. 2011; 85(12):1551-1563.
22. Shareef M, Ashraf MA, Sarfraz M. Natural cures for breast cancer treatment. Saudi Pharm J. 2016; 24(3):233-240.
23. Hwang YJ, Lee EJ, Kim HR, Hwang KA. *In vitro* antioxidant and anticancer effects of solvent fractions from Prunella vulgaris var. lilacina. BMC Complement Altern Med. 2013; 13(1):310.
24. Wang P, Li Z, Fu L, Zhu J, Wu X, Wang Z, Zhang L. Effects of extracts of *Prunella Vulgaris* L. on proteome of human lung adenocarcinoma cell line A549. Zhonghua yi xue za zhi. 2014; 94(28):2216-2221.
25. KunduSen S, Gupta M, Mazumder UK, Haldar PK, Saha P, Bala A. Antitumor activity of Citrus maxima (Burm.) Merr. leaves in ehrlich's ascites carcinoma cell-treated mice. ISRN Pharmacol. 2011, 2011:1-4.
26. Merina N, Chandra KJ, Jibon K. Medicinal Plants with Potential Anticancer Activities: A Review. Int J Pharm. 2012; 3(6):26-30.
27. Raha S, Yumnam S, Hong GE, Lee HJ, Saralamma VV, Park HS, Heo JD, Lee SJ, Kim EH, Kim JA, Kim GS. Naringin induces autophagy-mediated growth inhibition by downregulating the PI3K/Akt/mTOR cascade via activation of MAPK pathways in AGS cancer cells. Int J Oncol. 2015; 47(3):1061-1069.
28. Li J, Dong Y, Hao G, Wang B, Wang J, Liang Y, Liu Y, Zhen E, Feng D, Liang G. Naringin suppresses the development of glioblastoma by inhibiting FAK activity. J Drug Target. 2017; 25(1):41-48.
29. Kanadaswami C, Lee L, Lee PH, Hwang J, Ke F, Huang Y, Lee M. The antitumor activities of flavonoids. *in vivo.* 2005; 19(5):895-909.
30. Manthey JA, Guthrie N, Grohmann K. Biological properties of citrus flavonoids pertaining to cancer and inflammation. Curr Med Chem. 2001; 8(2):135-53.
31. Lee SH, Yumnam S, Hong GE, Raha S, Venkatarame Gowda Saralamma V, Lee HJ, *et al*. Flavonoids of Korean Citrus aurantium L. induce apoptosis via intrinsic pathway in human hepatoblastoma HepG2 cells. Phytother Res. 2015; 29(12):1940-1949.
32. Wang S, Li P, Lu SM, Ling ZQ. Chemoprevention of low-molecular-weight citrus pectin (LCP) in gastrointestinal cancer cells. Int J Biol Sci. 2016; 12(6):746-756.
33. Stegmayr J, Lepur A, Kahl-Knutson B, Aguilar-Moncayo M, Klyosov AA, et al. Low or no inhibitory potency of the canonical galectin carbohydrate-binding site by pectins and galactomannans. J Biol Chem. 2016; 291(25):13318-13334.
34. Ji S, Li R, Wang Q, Miao WJ, Li ZW, Si LL, Qiao X, Yu SW, Zhou DM, Ye M. Anti-H1N1 virus, cytotoxic and Nrf2 activation activities of chemical constituents from Scutellariabaicalensis. J Ethnopharmacol. 2015; 176:475-484.
35. Xie Y, Song X, Sun X, Huang J, Zhong M, Lotze MT. Identification of baicalein as a ferroptosis inhibitor by natural product library screening. *Biochem Biophys Res Commun*. 2016; 473(4):775-780.
36. Hu S, Chen Y, Wang ZF, Mao-Ying QL, Mi WL, Jiang JW, Wu GC, Wang YQ. The analgesic and antineuroinflammatory effect of baicalein in cancer-induced bone pain. Evid Based Complement Alternat Med, 2015, 1-8.
37. di Camillo Orfali G, Duarte AC, Bonadio V, Martinez NP, De Araújo ME, Priviero FB, et al. Review of anticancer mechanisms of isoquercitin. World J Clin Oncol. 2016; 7(2):189-199.
38. Amado NG, Cerqueira DM, Menezes FS, da Silva JF, Neto VM, Abreu JG. Isoquercitrin isolated from Hyptisfasciculata reduces glioblastoma cell proliferation and changes β-catenin cellular localization. Anti-cancer drugs. 2009; 20(7):543-552.
39. Silva CG, Raulino RJ, Cerqueira DM, Mannarino SC, Pereira MD, *et al*. *In vitro* and in vivo determination of antioxidant activity and mode of action of isoquercitrin and Hyptis fasciculata. *Phytomedicine.* 2009; 16(8):761-767.
40. Chen CC, Chen Y, Hsi YT, Chang CS, Huang LF, Ho

CT, Way TD, Kao JY. Chemical constituents and anticancer activity of Curcuma zedoaria roscoe essential oil against non-small cell lung carcinoma cells in vitro and *In vivo*. J Agric Food Chem. 2013; 61(47):11418-11427.
41. Shin Y, Lee Y. Cytotoxic activity from Curcuma zedoaria through mitochondrial activation on ovarian cancer cells. Toxicol Res. 2013; 29(4):257-261.
42. Carvalho FR, Vassão RC, Nicoletti MA, Maria DA. Effect of Curcuma zedoaria crude extract against tumor progression and immunomodulation. J Venom Anim Toxins incl Trop Dis. 2010; 16(2):324-341.
43. Shalabi M, Khilo K, Zakaria MM, Elsebaei MG, Abdo W, Awadin W. Anticancer activity of Aloe vera and Calligonum comosum extracts separetely on hepatocellular carcinoma cells. Asian Pac J Trop Biomed. 2015; 5(5):375-381.
44. Pecere T, Gazzola MV, Mucignat C, Parolin C, DallaVecchia F, Cavaggioni A, *et al*. Aloe-emodin is a new type of anticancer agent with selective activity against neuroectodermal tumors. Cancer Res. 2000; 60(11):2800-2804.
45. Yagi A, Takeo S. Anti-inflammatory constituents, aloesin and aloemannan in Aloe species and effects of tanshinon VI in Salvia miltiorrhiza on heart. Yakugaku Zasshi. 2003; 123(7):517-532.
46. El-Shemy HA, Aboul-Soud MA, Nassr-Allah AA, Aboul-Enein KM, Kabash A, Yagi A. Antitumor properties and modulation of antioxidant enzymes' activity by Aloe vera leaf active principles isolated via supercritical carbon dioxide extraction. Curr Med Chem. 2010; 17(2):129-38.
47. Nandha R, Singh H, Garg K, Rani S. Therapeutic potential of sunflower seeds: An overview. Int J Res Dev Pharm L Sci. 2014; 3(3):967-972.
48. Al-Jumaily RM, Al-Shamma NM, Al-Halbosiy MM, Al-Shamma LM. Anticancer Activity of Sunflower (*Helianthus annuns* L.) Seeds oil against cell lines. Iraqi j sci. 2013; 54(5):1003-1009.
49. Munro B, Vuong Q, Chalmers A, Goldsmith C, Bowyer M, Scarlett C. Phytochemical, antioxidant and anti-cancer properties of *Euphorbia tirucalli* methanolic and aqueous extracts. Antioxidants. 2015; 4(4):647-661.
50. Aljabarin KL, Farraj M, Jabarin B, Feng ZJ. Antimicrobial susceptibility of Euphorbia tirucalli extracts and the effect of latex on growth and viability of mouse breast cancer cells EMT-6. IOSR J Dental Med Sci. 2014; 13(3):59-63.
51. Chen CL, Chen YP, Lin MW, Huang YB, Chang FR, *et al*. Euphol from euphorbia tirucalli negatively modulates TGF-β responsiveness via TGF-β receptor segregation inside membrane rafts. PloS one. 2015; 10(10):e0140249.
52. Lin MW, Lin AS, Wu DC, Wang SS, Chang FR, Wu YC, Huang YB. Euphol from Euphorbia tirucalli selectively inhibits human gastric cancer cell growth through the induction of ERK1/2-mediated apoptosis. Food Chem Toxicol. 2012; 50(12):4333-4339.
53. Wilken R, Veena MS, Wang MB, Srivatsan ES. Curcumin: A review of anti-cancer properties and therapeutic activity in head and neck squamous cell carcinoma. Mol Cancer. 2011; 10(1):12.
54. Zhang L, Cheng X, Gao Y, Zhang C, Bao J, Guan H, Yu H, Lu R, Xu Q, Sun Y. Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-β/Smad2/3 signaling pathway. Exp Cell Res. 2016; 341(2):157-165.
55. Kuttan R, Bhanumathy P, Nirmala K, George MC. Potential anticancer activity of turmeric (*Curcuma longa*). Cancer Lett. 1985; 29(2): 197-202.
56. Kapadia GJ, Tokuda H, Konoshima T, Nishino H. Chemoprevention of lung and skin cancer by Beta vulgaris (beet) root extract. Cancer Lett. 1996; 100(1-2):211-214.
57. Hayakawa S, Saito K, Miyoshi N, Ohishi T, Oishi Y, Miyoshi M, Nakamura Y. Anti-cancer effects of green tea by either anti-or pro-oxidative mechanisms. Asian Pac J Cancer Prev. 2016; 17(4):1649-1654.
58. de Oliveira MR, Nabavi SF, Daglia M, Rastrelli L, Nabavi SM. Epigallocatechin gallate and mitochondria—a story of life and death. Pharmacol Res. 2016; 104:70-85.
59. Luo KW, Yue GG, Ko CH, Gao S, Lee JK, Li G, Fung KP, Leung PC, Lau CB. The combined use of Camellia sinensis and metronomic zoledronate in 4T1 mouse carcinoma against tumor growth and metastasis. Oncol Rep. 2015; 34(1):477-487.
60. Zhou H, Chen JX, Yang CS, Yang MQ, Deng Y, Wang H. Gene regulation mediated by microRNAs in response to green tea polyphenol EGCG in mouse lung cancer. BMC Genomics. 2014; 15(11):S3.