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ANTICANCER ACTIVITY OF MEDICINAL PLANTS *BERBERIS BALOCHISTANICA* AND *SOPHORA ALOPECUROIDES*: A BRIEF REVIEW

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Abstract

Cancer is characterized by spread of abnormal cell and unchecked growth. Cancer is the 2nd most significant leading cause of death. The human population worldwide is severely affected by cancer. This life-threatening disease is constantly being sought out for new therapies to treat and prevent. The attention of scientists is being drawn to compounds that come from nature as they consider less toxic as compared to other cancer treatments. Plants have been used for medicinal purpose by many ancient civilizations, and research has shown that plants derived compound can be helpful in treating cancer. The herbal medicine system throughout Pakistan utilizes numerous plants that are well known for their remedial potential. Balochistan is known for its abundance of medicinal plants. These therapeutic plants are used by native people to treat various disease. Berberis have been reported as medicinal pharmacopeias in folklore and have been used traditional medicines in Asia. Berberis balochistanica is a remedial herb. Isoquinoline alkaloids and berberine are present in berberis genus. It has been reported that they have anticancer activities and effects on the cardiovascular and immune system. Sophora.alopecuroides main key bioactive compounds is Quinolizidine alkaloids which includes Sophoridine, Oxysophocarpine, Sophocaepine, Oxymatrine and Matrine. S. alopecuroides alkaloids have significant biological activities and are used in medical trials which have pharmacological action of tumor suppression and anti-cancer. This review aims to summarize the current knowledge about the anticancer potential of Berberis balochistanica and Sophora alopecuroides and highlight their therapeutic prospects and naturally derived compounds from medicinal plants and their belongings that could potentially be used as target for anticancer treatments.

Keywords: *Anticancer activity, Berberis balochistanica, Medicinal plants, Sophora alopecuroides, Traditional medicine*

INTRODUCTION

Cancer is the major reason of death and a great barrier in the 21st era to the increase in life probability (1). Each year copious number of people is recognized with malignancy. Cancer can be treated using various agents and cytotoxicity is caused by these agents (2). Due to the high death rates associated with cancer and many complications of radiotherapy and Chemotherapy, several patients of cancer are seeking other opposite treatment methods. Eliminating tobacco use, effectively treating inflammatory conditions and taking dietary supplement are important methods to prevent cancer (3). Overall prevalence of cancer is increasing considerably (4).

Chemotherapy can cause severe adverse effects and can harm healthy cells. This concern has become point of interest for scientists worldwide. Research is being done to find alternative treatment options. In this regard, Herbs are still a significant contributor to the global cure of various disease, like cancer (5). World Health Organization (WHO) estimates that for major health requirements, approximately 80% people in the developing countries relies on traditional remedy (6). Herbal medicines are found to be

one of the most effective ways to treat and prevent cancer. The numerous active substances found in plants, which fight against many types of cancer through various mechanisms (7). There are many types of bioactive constituents such as allicin, vinblastine, silymarin, vincristine, berberine, Curcumin, campothecin which have shown promising effects in treating cancer and they are key active ingredients of plants (8).

Pakistan is an emerging country dealing with economic issues due to infectious illness like, AIDs, kidney, HIV and Cancer. Due to the absence of equipment's and new technology for screening, risk of identification and expensive cure are typically inaccessible for the poor individuals. On the other hand, healthcare can benefit from using medicinal plants that contain active substances (9). Balochistan is home to several medicinal plants. In Balochistan, various wild herbs were collected by local communities and sold in local markets. However, scientific evidence regarding herbs that may be grown and used for various purposes is very limited. It is important to realistically address the susceptibility of therapeutic herbs and spices to overexploitation and extinction. There are a variety of research activities that can address worries and issues related to the maintenance of these plants (10).

Berberis is a well-known genus in the berberidaceae family, and contains 650 species (11). This angiosperm is considered one of the greatest primitive and has excessive economic and therapeutic value due to presence of berberine as a major phytochemical (12). There have been 29 reports of Berberis species in Pakistan mountain ranges (13). With versatile ecological condition, area wise Pakistan's largest province is Balochistan. Due to its geographical, and climate, this province is home to a diverse array of flora and fauna. Against various disease local communities use this plant for treatment of Oedema, blood purification, hairs loss, high blood pressure, pimples, joints, and jaundice, snakebite, typhoid, and chest infections (14). The widespread specie of Balochistan is Berberis balochistanica. It is distributed in Hanna Urak, and Kalat. In Pashto, known as Zralga and in Brahui, known as Zarchin (15). Secondary metabolites can be found in this plant extracts, to treat cough, internal injuries and microbial infection in both humans and livestock, it is possible to use them as useful therapeutic agents. The antioxidant compounds present in this plant are reducing heart disease and cancer mortality (16).

BERBERINE

Pharmacological reports show that berberine are the main source of berberis species and also alkaloids such as palmatine, jatrorrhizine, isoteteandrine and berbamine. Palmatine was exposed to have anticholinesterase activity. Histamine or acetylcholine induced the function of isotetrandrine antagonizes contraction. Mice and animal sleep spoanteous activity provoked by pentobarbital and reduce by jatrorrhizine. It also influences sleep in mice given sub edge quantities of pentobarbital (17). Isoquinoline alkaloids are present in berberis genus. Berberis have huge kind of biological and pharmacological activity such as anti-inflammatory, anti-tumor and antimicrobial (18, 19).

In Fabaceae family, genus Sophora has around 70 species (20), with most of them being found in tropical and temperate areas (Fig. 1). *Sophora alopecuroides*, a plant that grows to a height of 1m has exceptional resistance to alkali and drought (21). It has a diversity of therapeutic properties with its roots and seeds. It can be referred to as bitter licorice grass, locust bitter bean grass, Hulan-Baoya (Mongolian) and in Uyghur in Buya language. It has become a part of the Chinese Pharmacopoeia "National Compilation of Chinese Herbal Medicine", middle Asia and western countries including northern India Japan, China, and Pakistan has a wide distribution of S. alopecuroides (22). *S. alopecuroides* is used for various disease including, eczema, dysentery, infectious disease, recurrent dermatitis and cancer. Antifungal and antitumor activities are present in this plant (23). Root system is highly developed and can tolerate drought, barren condition and high levels of salinity. Furthermore, it plays a vital role in sand fixation. The use of alkaloids of this plant show good biological activity against suppressing cancer, reducing and killing different microorganisms, and affecting the immune, cardiovascular, and nervous systems in significant ways (24).

MATRINE

In current years *S. alopecuroides* main alkaloids is matrine and its anti-cancer effect have been extensively worried. Many scientists have exposed that matrine has a cytotoxic effect on cancerous cells due

to apoptosis inducing and preventing cells proliferation. Currently anticancer injection having matrine named "Compound Kushen Injection" has been medically useful in China. Experimental valuation of effectiveness and care on breast cancer also was applied. Currently, specific research studies showed that matrine have further valued assets that inform unaffected cancer cells to chemotherapeutic agents through suppressing medicine ABCB1 exporter and κB kinase β inhbitor, which is an NF-kappa B activator. There is currently no systematic study showing how to eliminate the impact of matrine on drug resistance (25). Study have suggest that OMA or Matrine has anti-cancer effects on tumor cells such as Breast cancer, liver, pancreatic, gastric and lungs cancer (26).

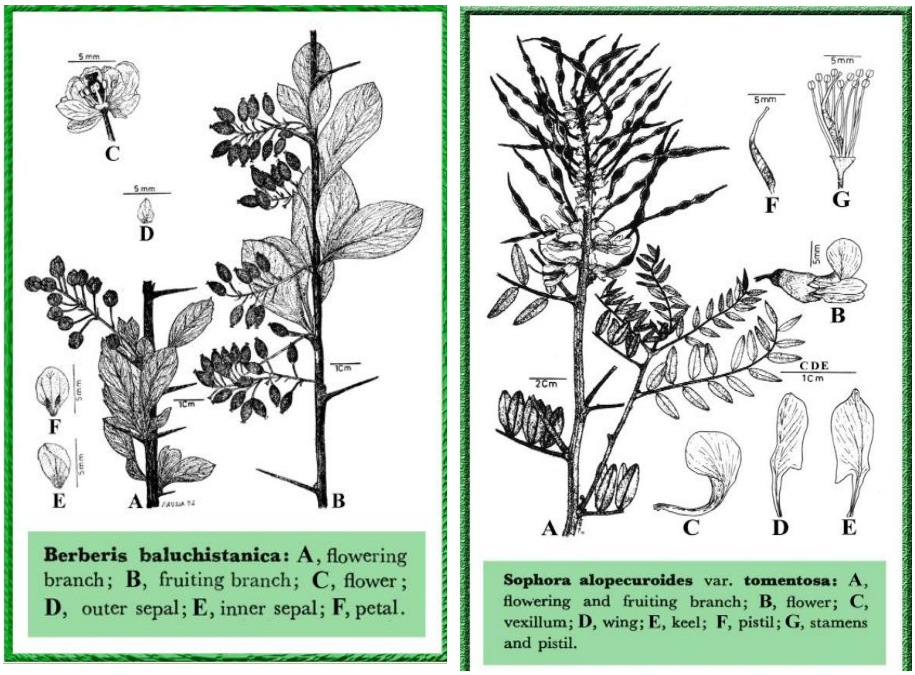


Fig 1. *Berberis balochistanica* and *Sophora alopecuroides* plants

MATERIALS AND METHODS

The compilation of this review article was accomplished using literature studies as data collection techniques. The method was used to search for literature such as primary data, official books, and international journals. Trustworthy websites like Elsevier, NCBI, Google scholar, Research gate, Science Direct and other journals were used as the main references in this review article.

CANCER

Cancer is characterized by spread of abnormal cell and unchecked growth. The spread of cancer cells which is known as metastasis can cause death if not controlled. Many external factors such as tobacco, radiation, chemicals, internal factor, genetic and random changes and hormones cause carcinoma. The sources of cancer are various and complex and only partially recognized. Environmental and dietary factors, obesity, less physical activity and certain infections can increase the threat of cancer (27). In ranking East Asia is in 1st number with highest number of cancer cases 31.1% (5.6 million) and death rate 36.2% (3.5 million). North America is the 2nd rank with most contemporary cases 2.4 million (13.2%) and death rate 698,000 (7.3). Eastern Europe 699.00 (7.3%) and South-Central Asia 12.2% (1.2 million) cancer cases (28).

CAUSES OF CANCER

Lobstein and Recamier thought that cancer is caused by replacing embryonic tissue and later after Cohnhein and Virchow declare that major cause of cancer is irritation. Afterward based on few experimental proof viruses were recognize the major cause of cancer. All these studies concluded that cancer is diversified disease with a difficult web of causes, and there is no single factor recognize for any type of cancer. Poor immune system, UV rays and air pollution, smoking high alcohol, unhealthy habits, gene mutations and for long period intake of non-steroidal and anti-inflammatory medicines are some factors that destroyed DNA and cause cancer (29) (Fig. 2).

CANCER TREATMENTS

Surgical procedures are common for cancer patients. Surgery used for diagnosing, treating or even preventing cancer in some cases. Chemotherapy consists of taking medications to treat cancer. In order to destroy or damage tumor cells, radiation therapy employs high energy particles or waves. Targeted therapy updated form of cancer treatment that utilizes drugs to treat cancer. Cancer cells can be recognized and attacked more precisely through targeted therapy or other substances, frequently, while causing minimal harm to usual cells. The immune system of body is used in immunotherapy to fight cancer (30).

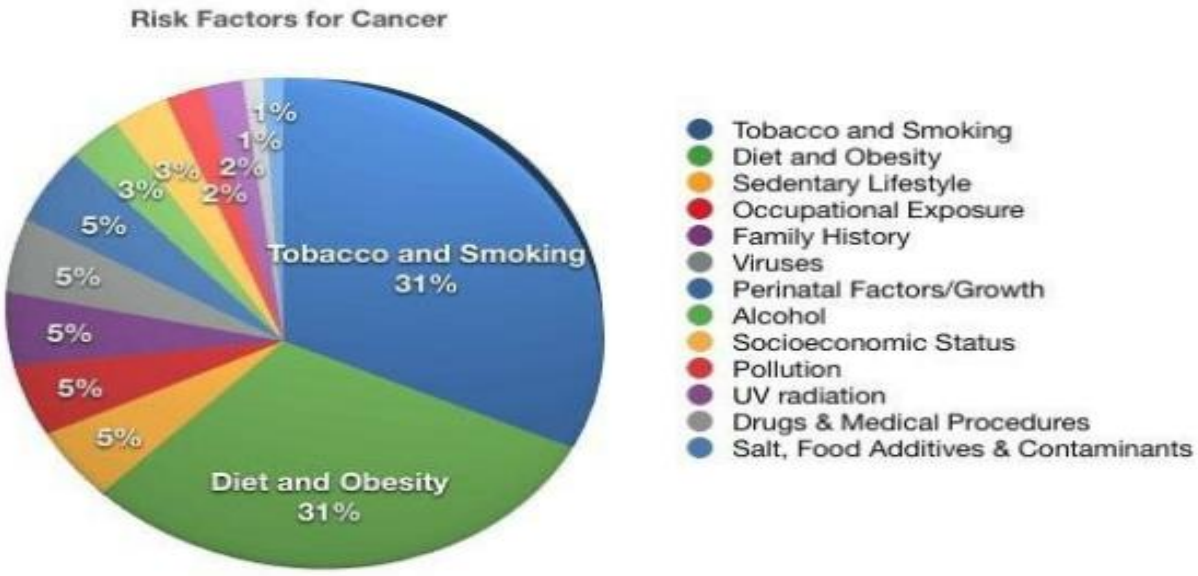


Fig. 2. Main factors causing cancer worldwide (Food, Nutrition, Physical activity, and the prevention of cancer: A global perspective., 2007)

DISADVANTAGES OF CANCER TREATMENTS

In the current year the treatments of cancer particularly radiation, surgery and chemotherapy have side effects and are linked with post-therapy recurrence rate (31). However, chemotherapy is the major treatment for various types of cancer. The monoclonal antibody Bevacizumab which inhibits angiogenesis when it combines with cisplatin can expand life for 3.7 months in cancer victims. The drawback of these therapies is that they are expensive and they can harm healthy cells. However, drug resistance to cancer cells is evaluated as a common failure of oncological therapy (32). Consequently, in health problems numerous people select herbal plants as an alternative treatment. Some studies recommended that herbal plants contain secondary metabolites which inhibit the spread and growth of tumor cells (33). Up to that time more than three thousand plants have been found which has possibilities as anticancer properties (34).

Plants produce abundance of chemical compounds that do not play a straight part in their development. Tannins, pigments like molecules, alkaloids, terpenoids, flavonoids these are chemicals which are known as secondary metabolites. These chemicals show biological outcomes on hematopoietic cells (35) and lipids (36) also anti-inflammatory, and anticancer properties. The treatment of cancer has been greatly developed by the recognition of secondary metabolites in medicinal herbs. Enzymes which promote cancer cells discourage by plants secondary metabolites, plants speed up DNA repair and motivate the antitumor enzymes in cells, improve immunity and provide antioxidant effects to fighting cancer. It is necessary to find plants with cytotoxic properties that can replace chemotherapy and other cancer treatment (37).

MEDICINAL PLANTS

The health benefits of therapeutic plants are substantial for both individuals and society (38). Therapeutic plants are used for the cure of various diseases. Plant crude extract contains different kinds of bioactive compounds and these bioactive compounds have major antimicrobial, chemo-preventative, antioxidant and cytotoxic possibilities. Herbal therapy accommodates secondary metabolites of plants

(phytochemical constituents) are used as allopathic and synthetic medicines and are less harmful to person and the environment (39). Utilization of these herbal drugs contributes to the few main phytochemical components and correlated with necessary and non-necessary trace elements (40). These plants have positive impact on human`s health and trace element have substantial roles in healing a diversity of human disease (Fig. 3). Due to the successful various treatment of diseases it is necessary to identify the absorption of these trace elements in all fragments of plants laterally with pharmacological effects (41).

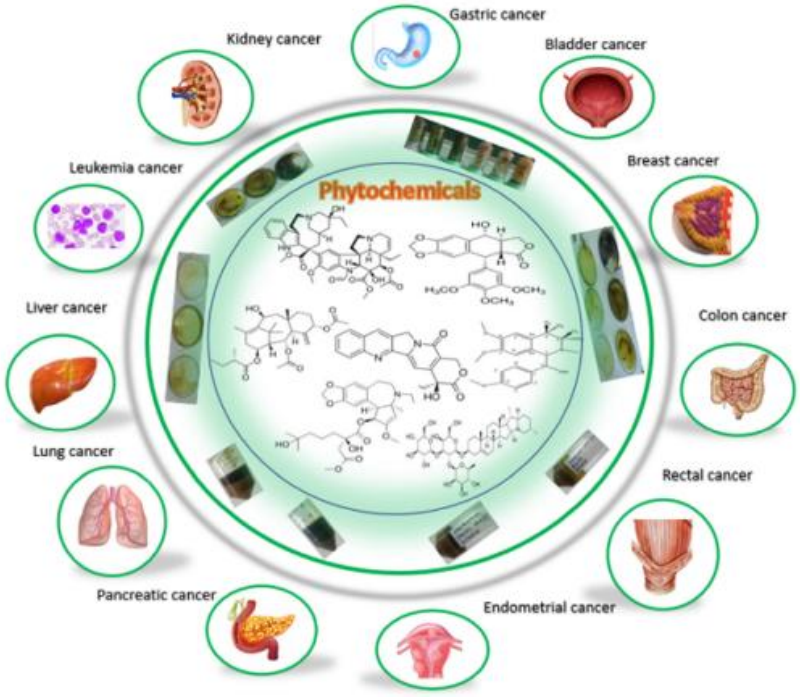


Fig. 3. Illustration activity of plants against several types of cancers (Figure adapted from Regassa *et al.*, 2022)

HISTORY OF THE USE OF MEDICINAL HERBS

The word phytotherapy is obtained from the Greek word pyton, which signifies plant and the term therapy refers to healing with plants. Plants are the first choice of medicine for humans. There are approximately 250,000 higher plant species on earth. It is believed that between 35,000 to 70,000 species have been utilized in certain culture for medicinal purpose. Herbs have been essential in the healing process throughout history and have been used by people worldwide to improve their health (42). The literature on medicinal plants is almost 5,000 years old in India, Egypt and China, Greece and Central Asia. People have been seeking to cure their own sickness with the use of nature. Consequently the lack of knowledge about the disease's causes and useful plants for treating it everything was empirical when it came to using them for such a purpose. The empirical framework was gradually rejected and the use of medicinal plants it was restricted to the facts. Nearly 5000 years ago, Nagpur Sumerian clay slab was the first written documentation of the use of therapeutic plants has been discovered for the preparation of drugs (43). In the opinion of some inscription Chines and Egyptians who used plants as drug in the last twenty seven centuries BC were amongst the most primitive human beings who did so (44). Greek persons from ancient time are known about some therapeutic plants and their medicinal properties. The initiator of Greek medicines Hippocrates and student of Hippocrates Aristotle used herbal plants for the treatment of disease. After that a Greek scientist Theophrastus established the Medicinal plants school. A surgeon and physician Pedanius Diaoscroides he lived in 1st century A.D year 75-45 BC, inscribed an encyclopedia, called De Materia Medica to report six hundred therapeutic plants in the form of scientific work (45).

PAKISTAN AND BALOCHISTAN VALUE IN MEDICINAL PLANTS

Due to unique plant biodiversity variety of climate ecological condition, geographical location, and important medicinal plant diversity Pakistan is one of the richest country. Nine hotspots for medicinal plant

biodiversity exist in Pakistan. Well-known flowering species from 6000 top plants in which 500 to 700 plants are recognized and used as ethno medicinal therapies for centuries (46). A part from this 203 prevalent species of about 4% of the flora was announced. In northern and western area and high mountain of Kashmir and Pakistan area more than 80% flowering plants are found. Balochistan consider medicinal plant biodiversity having three important hotspots. The people of Balochistan have great concern with the use of therapeutic plants from decade. Now a day's high economical also financial trade both national and international level of herbal plants is in progress in the province. The nourishment of Balochistan people depend on original resources. From these original resources plant medicines are used by people as in expensive, approachable treatment for different kind of health problems. From the start different parts of Plants roots, powder form, seeds, and even whole plant are used for herbal preparation (47).

PLANTS USED FOR CANCER TREATMENT

From ancient time plants extract is considered for their anticancer activities. Plants are used in the treatments of several types of cancer .Plants are the main source of natural products that are effectively used in drugs. Populations, who consume a high level of natural herbal products, generally have a declined occurrence of cancer. Anticancer activities of medicinal herbs may be due to combination of complexes and single compound. Polyphenols, brassinosteroids, resveratrol's and flavonoids (48). In peanuts, red wine and grapes Resveratrol is present. In green tea Gallacatechins are present. Natural antioxidant properties are present in polyphenols that lower the risk of cancers and boost human health (49-51).

Polyphenols through apoptosis kill cancer cells. They can attain apoptosis by the mobilization of cu ions which are certain to chromatin induce fragmentation of DNA. DNA degradation is caused by Resveratrol in the existence of Cu ions II. In cancer cell polyphenols interfere with protein and destroy cancer cells (52).

Flavanoids are from the Polyphenolic compounds and contain a huge family of plants secondary metabolites with 10 thousand recognized structures (53). Anticancer activity and high flavonoides content have been explored. Chalcones seed of specific plants flavones, anthocyanins, flavonols are high ammount of flavonoids compound. Plant extracts show anticancer avtivity for example Alpinumi soflavone (ALF) and 4'-Methoxy licoflavanone (MLF) are flavonoids extracted from Erythrina suberosa stem bark show cytotoxic effects in human cells HL-60 (leukaemia cells). Plant extract which is high in flavonoids also indicates anticancer activity against different malignancy cell line such as cervical carcinoma (Hela), Hepatoma (Hep-G2) and breast cancer (MCF-7) (54).

Brassinosteroids have hormones regulation progression that can control development, elongation of roots, differentiation of cells, tolerance and resistance against stress and disease. 24-epibrassinolide (24epiBL) and 28-homocastasterone (28-homoCS) are naturally brassinosteroids which shown anticancer effects (55).

BERBERIS BALOCHISTANICA

In 1753, Linnaeus first described the genus berberis in the species plantarum. Quattrocchi (1947) states that Berberis is derived from the Arabic name 'Berberys' which is used for fruit. Similarly in 1789 A. L. De Jussieu established the Berberidaceae family for the first time under the name of (Berberide) which he regarded as one of the most primitive dicotyledonous angiosperms. The major dicotyledonous genus is Berberis which belongs to Berberidaceae family; mostly perennial shrubs or minor trees with wood and yellow flowers, spiny and deciduous. Diverse numbers of species have been reported from this genus. Previous reports specify 17 genera and 650 species of Berberidaceae (56). Aitchison (1879) was the first person to describe Pakistan's Berberis. In 1975 Jafri published the first account of genus Berberis (Berberidaceae) from Pakistan (57). In Pakistan berberis species are mostly present in mountain area above the sea 1400m-3500m and are the basic part of the modern and traditional medicine (58). *B. balochistanica* is important valued for its roots and bark and considerd as less harmful and eaten up in raw form either decoction or powder. This plant is used for the treatment of various diseases like, wound healing, cough, eye disease, and infections of human, internal injury fever, rheumatism and kidney stone removal (59).

B.balochistanica is contain secondary metabolites like berberine, oleanolic acid, berberisinol , phenols, palmatine, 8-oxoberberine gallic acid, carotenoids and vitamins were isolated and found with extraordinary anti-diabetic, antifungal antibacterial, antioxidant, antileishmanial, potential (60). *B.balochistanica* plant species are listed and detailed (local and botanical name, family, part used and therapeutic used) below in Table I.

SOPHORA ALOPECUROIDES

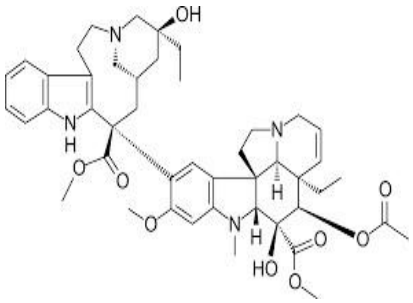
S. alopecuroides from the sophora genus also well-known as (Ku dou zi or ku gan cao) are found in Central and Western Asia. It is a one-meter-tall everlasting herb with good capability to stand alkali and drought. *S. alopecuroides* can be divided into two considerable sub species on the bases of different feature leaflets. One is *S. alopecuroides* unusual variant with appressed leaflets and 2nd is tomentose with densely patulous. All parts of plant roots, seeds, leaves have been taken as therapeutic herbs. *S.alopecuroides* is used in the cure of various disease like eczema, dysentery, furuncle, recurrent dermatitis, infectious disease and cancer (61). *S.alopecuroides* is an everlasting herb and modest halophyte which is dispersed in the Steppe desert, west and north China. In the previous year less precipitation merging with high evaporation has decreased and expanded soil salinization. In the ecological conservation and vegetation formation soil formation caused limitation (62). As a consequence, in those regions certain salt-tolerant species are expanding and salt intolerant species are decreasing (63). *S. alopecuroides* play a significant role for ecological ecosystem and modest salt resistance due to its well-developed roots. This plant contains biological compounds such as flavonoids, stilbenes, antioxidant and harmless alkaloids which have making biological and pharmaceutical insecticides (64). *S. alopecuroides* plant species are listed and detailed (local and botanical name, family, part used and therapeutic used) below (Table I). Alkaloids present in *S. alopecuroides* have good biological activity and utilize in clinical trials which have pharmacological activity of anticancer, killing and inhibition of microorganism, cancer suppression and have pharmacological effect on nervous, cardiovascular and immune system. Studies have shown that Total alkaloids of *S. alopecuroides* (TASA) has a broad-spectrum anti-bacterial activity and can inhibit apoptosis of SMMC-7721(hepatoma cells) (24).

Table I. *B. balochistanica* and *S. alopecuroides* description and medicinal uses

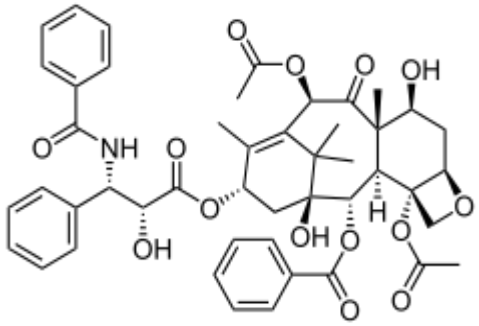
Botanical name	Family	Local name	Distribution	Life form	Part used	Therapeutic used	Reference
Berberis balochistanica	Berberidaceae	Zarlag	Ziarat, Muslim Bagh, Quetta	Shrub	Leave, Stem	Fracture, wounds	(47)
Sophora alopecuroides	Fabaceae	Busunduk	Quetta, Loralai	Herb	Root, seeds, leaves	Eczema, dysentery, furuncle, recurrent dermatitis, infectious disease and cancer	Flora of Pakistan (61)

ANTICANCER NATURAL PRODUCTS

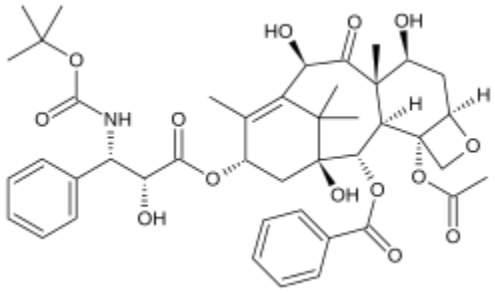
Natural products of anticancer are obtained from plants which have been successfully determined by clinical trials. These medicines are conducted as portion of the patient's nutritional consumption (65). Vinca alkaloids such as vinblastine, Docetaxal, Vincreistine, vindesine, vinorelbine and vinflunine are instances of natural stuffs which are obtained from plants and used as anti-cancer medicine. Fig. 4 shows some isolated natural product with anticancer activity. Microtubules formation of cancer cells is discouraged by these drugs and binding by β-tubulin. Paclitaxel and its correspondent docetaxel belong to taxanes class, and these drug functions as microtubules inhibitor of cancer cells. Paclitaxel stops the cancer cell replication and polymerizes and stabilizes the microtubules in the cells. Combination of medicine may have synergistic result that increases the activity of anticancer and boost their potency as natural anticancer agents (66).



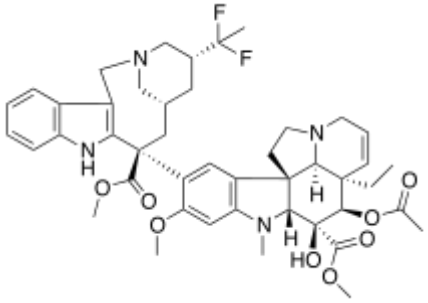
Vinblastine



Paclitaxel



Docetaxel



Vinflunine

Fig. 4. Structures of some anticancer natural products

ANTI-CANCER PLANT DERIVED DRUGS

Anticancer treatment is favored by natural and easily accessible medicines naturally derived from plants compounds. The patient's nutritional supply can be easily administered with ease (67). They are like lectins, liganans, some taxanes and cyanogenetic glycosides (68). Research proves that herbal medicine is less toxic comparison with normal cell line and has cytotoxicity in cancer cell lines and it should consider in clinical trials. Medicinal products of vegetable origin may belong to four categories of medicinal products having these activities include methytransferase, preventive drugs against DNA damage and inhibitors of histone deacetylases (HDAC) disruptive mitotic effects (69).

ADVANTAGES OF HERBAL DRUGS OVER CONVENTIONAL DRUGS

There are some common reasons to use herbal drugs such as:

1. Health issue
2. Prevention of disease
3. Increasing price of conventional cancer treatment
4. Deficiency of effective medicine to heal firm tumors encouraged
5. Herbal medicine has fewer side effects as compared to conventional medicine.
6. Impoverished outcomes
7. Restricted treatment options for a severe disease.
8. Fatigue of conventional remedy
9. Discontentment or unsuccessful conventional treatment.
10. Risk linked with conventional medicine and deadly side effects
11. Speculation that herbal products are safer and good
12. Preference for individual participation in decision making procedure.
13. Societal or spiritual partiality (70)

DEMANDS OF MEDICINAL PLANTS

With effective clinical trials drugs being originate from plants are admired for medical expansion. In Africa and Asia, a lot of the species examined and selected where herbal treatments are accomplished and

therapeutic plants are dependent for primary treatment. In 2007 WHO estimate that the plant-based medicine marketing cost US$100 billion and in 2050 trade likely to reach US$ 5 trillion (71). The safety of therapeutic plants is an issue because of rapid population growth, increasing urbanization and deforestation (72). Maintenance of these plants is necessary. When uncultivated therapeutic plants are collected only particular plant fragments are used in therapy like bulbs, tubers from tuberous plants and bark of tree. Taking out only part of plant may harm and induce its survival. In established and developing countries to increase sustainability of therapeutic plants all parts of plants are utilize such as leaf, bark, stem and root and must be included in treatment. Germplasm conservation, preserving biological material in tissue culture, liquid nitrogen, cryopreservation, and storing viable seeds are the methods of conservation in these methods plants are grow in sterile conditions and manufacture mature colonies of plants rapidly of rare species. In developed countries these methods of preservation are allowed for industrial utilization (73).

CONCLUSION

Since ancient time, plants resources have been the source of human needs. Approximately 80% of the citizens particularly those in rural areas, in emerging countries depends on herbal remedies to fulfil their requirements of health (WHO report 2001). It can be concluded from this review that herbal medicinal plants and their extract have anti-cancer properties. In developing countries Rural and underprivileged communities can benefit greatly from the herbal treatment. Current methods have their limitation because of the toxic effects they have on non-targeted tissues, which further increase problems of human health. As a result there is a demand for alternative treatment that utilize anticancer agents that are naturally derived, and plants are the preferred option. The study of plants secondary metabolites like brassinosteroids, polyphenols and flavonoids has shown that they could be used as anticancer agents. The increase in demand for plant derived medicines is affecting high value medicinal plants and posing a risk to their biodiversity. The effectiveness of plant-derived anticancer agents in inhibiting cancer cell making them in highly sought after.

References:

1. Omara T, Odero MP, Obakiro SB. Medicinal plants used for treating cancer in Kenya: an ethnopharmacological overview. Bulletin of the National Research Centre. 2022;46(1):148.
2. Kadali VN, Pola SR, Sandeep B. Anti cancer properties of plants present in west Godavari district of Andhra Pradesh, India-a mini review. Indian J Tradit Knowl. 2010;3:(2)11-7.
3. Madhuri S, Pandey G. Some dietary agricultural plants with anticancer properties. Plant Arch. 2008;8(1):13-6.
4. Thakor AS, Gambhir SS. Nanooncology: the future of cancer diagnosis and therapy. CA: a cancer journal for clinicians. 2013;63(6):395-418.
5. Kaur R, Singh J, Singh G, Kaur H. Anticancer plants: a review. J Nat Prod Plant Resour. 2011;1(4):131-6.
6. Omara T, Kiprop AK, Kosgei VJ. Intraspecific variation of phytochemicals, antioxidant, and antibacterial activities of different solvent extracts of Albizia coriaria leaves from some agroecological zones of Uganda. Evidence-Based Complementary and Alternative Medicine. 2021;1(23) 35-45.
7. Hassan B. Plants and cancer treatment. Med Plants Use Prev Treat Dis. 2019:1-11.
8. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environmental health perspectives. 2001;109:69-75.
9. Khan A, Ali S, Murad W, Hayat K, Siraj S, Jawad M. Phytochemical and pharmacological uses of medicinal plants to treat cancer: A case study from Khyber Pakhtunkhwa, North Pakistan. Journal of Ethnopharmacology. 2021;1:(11)44-37.
10. Khan AM, Aslam M. Medicinal plants of Balochistan. Project on Introduction of Medicinal Herbs and Species as Crop Ministry of Food, Agriculture and Livestock, Qarshi Industries (Pvt) Ltd. 2004:3-44.
11. Belwal T, Bisht A, Devkota HP, Ullah H, Khan H, Pandey A. Phytopharmacology and clinical updates of Berberis species against diabetes and other metabolic diseases. Frontiers in pharmacology. 2020;11:41.
12. Nazir N, Rahman A, Uddin F, Khan Khalil AA, Zahoor M, Nisar M. Quantitative ethnomedicinal status and phytochemical analysis of Berberis lyceum royle. Agronomy. 2021;11(1):130.

13. Khan T, Khan IA, Rehman A. Evaluation and detailing of taxonomic and historical perspectives on genus Berberis from Pakistan. J Bio & Env Sci. 2015;6:(3)61-7.
14. Baloch N, Nabi S, Yasser M, Kahraman A. In vitro Antileishmanial, Cytotoxic, Antioxidant activities and Their Phytochemical Analysis on Methanolic Extract and it is Fractions of Perotis hordeiformis leaves. International journal of Pharmacy. 2013;10;(4):165-70.
15. Kakar SA, Tareen RB, Kakar MA, Jabeen H, Kakar S, Al-Kahraman Y. Screening of antibacterial activity of four medicinal plants of Balochistan-Pakistan. Pak J Bot. 2012;44(2010):245-50.
16. Pervez S, Saeed M, Khan H, Shahid M, Ullah I. Nephroprotective effect of Berberis baluchistanica against gentamicin-induced nephrotoxicity in rabbit. Bangladesh Journal of Pharmacology. 2018;13(3):222-30.
17. Hoessel R, Leclerc S, Endicott JA, Nobel ME, Lawrie A, Tunnah P. Indirubin, the active constituent of a Chinese antileukaemia medicine, inhibits cyclin-dependent kinases. Nature cell biology. 1999;1(1):60-7.
18. Ivanovska N, Philipov S. Study on the anti-inflammatory action of Berberis vulgaris root extract, alkaloid fractions and pure alkaloids. International journal of immunopharmacology. 1996;18(10):553-61.
19. Akhter M, Sabir M, Bhide N. Anti-inflammatory effect of berberine in rats injected locally with cholera toxin. 1977.
20. Aly SH, Elissawy AM, Eldahshan OA, Elshanawany MA, Efferth T, Singab ANB. The pharmacology of the genus Sophora (Fabaceae): An updated review. Phytomedicine. 2019;64:(15)30-70.
21. Zhou H, Li J, Sun F, Wang F, Li M, Dong Y. A review on recent advances in aloperine research: pharmacological activities and underlying biological mechanisms. Frontiers in Pharmacology. 2020;11:538137.
22. Wang R, Deng X, Gao Q, Wu X, Han L, Gao X, . Sophora alopecuroides L.: An ethnopharmacological, phytochemical, and pharmacological review. Journal of Ethnopharmacology. 2020;248:(11)21-72.
23. Li T, Yin X, Liu D, Ma X, Lv H, Sun S. Isolation and characterization of a novel lectin with antifungal and antiproliferative activities from Sophora alopecuroides seeds. Acta Biochim Biophys Sin. 2012;44(7):606-13.
24. Chang A, Cai Z, Wang Z, Sun S. Extraction and isolation of alkaloids of Sophora alopecuroides and their anti-tumor effects in H22 tumor-bearing mice. African Journal of Traditional, Complementary and Alternative Medicines. 2014;11(2):245-8.
25. Chen Z, Nishimura N, Okamoto T, Wada K, Naora K. Molecular Mechanism of Matrine from Sophora alopecuroides in the Reversing Effect of Multi-Anticancer Drug Resistance in K562/ADR Cells. BioMed Research International. 2019(1):1269532.
26. Ling Q, Xu X, Wei X, Wang W, Zhou B, Wang B. Oxymatrine induces human pancreatic cancer PANC-1 cells apoptosis via regulating expression of Bcl-2 and IAP families, and releasing of cytochrome c. Journal of Experimental & Clinical Cancer Research. 2011;30:1-6.
27. Anand P, Kunnumakara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS. Cancer is a preventable disease that requires major lifestyle changes. Pharmaceutical research. 2008;25(9):2097-116.
28. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. International journal of cancer. 2019;144(8):1941-53.
29. Khanam S, Prakash A. An overview of medicinal plants as anticancer agents. IP International Journal of Comprehensive and Advanced Pharmacology. 2021;6(2):53-62.
30. Singh G, Sharma R, Sharma S, Singh A, Kour H, Singh M. Challenges and Future of Cancer Pharmacogenetics. Handbook of Oncobiology: From Basic to Clinical Sciences: Springer; 2023;1-9.
31. Adhvaryu MR, Reddy N, Parabia MH. Anti-tumor activity of four Ayurvedic herbs in Dalton lymphoma ascites bearing mice and their short-term in vitro cytotoxicity on DLA-cell-line. African Journal of Traditional, Complementary and Alternative Medicines. 2008;5(4):409-18.
32. Król SK, Kiełbus M, Rivero-Müller A, Stepulak A. Comprehensive review on betulin as a potent anticancer agent. BioMed research international. 2015;(1):41-89.
33. Imran M, Rauf A, Abu-Izneid T, Nadeem M, Shariati MA, Khan IA. Luteolin, a flavonoid, as an anticancer agent: A review. Biomedicine & Pharmacotherapy. 2019;11(2):108-612.
34. Tascilar M, de Jong FA, Verweij J, Mathijssen RH. Complementary and alternative medicine during cancer treatment: beyond innocence. The oncologist. 2006;11(7):732-41.

35. Mansouri E, Kooti W, Bazvand M, Boroon MG, Amirzargar A, Afrisham R. The effect of hydro-alcoholic extract of Foeniculum vulgare Mill on leukocytes and hematological tests in male rats. Jundishapur Journal of Natural Pharmaceutical Products. 2015;10(1):83-96.
36. Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpoor A, Abadi A, Afrisham R. The effects of hydro-alcoholic extract of celery on lipid profile of rats fed a high fat diet. Adv Environ Biol. 2014;8(9):325-30.
37. Khalighi-Sigaroodi F, Jeddi-Tehrani M, Ahvazi M, Shahnazi S, Bayat A, Mohajer N. Cytotoxicity evaluation of Taverniera spartea on human cancer cell lines. 2014.
38. Akbar A, Ali I, Samiullah NU, Khan SA, Rehman Z, Rehman S. Functional, antioxidant, antimicrobial potential and food safety applications of curcuma longa and cuminum cyminum. Pakistan Journal of Botany. 2019;51(3):1129-35.
39. Javed S, Shahid AA, Haider MS, Umeera A, Ahmad R, Mushtaq S. Nutritional, phytochemical potential and pharmacological evaluation of Nigella Sativa (Kalonji) and Trachyspermum Ammi (Ajwain). Journal of Medicinal Plants Research. 2012;6(5):768-75.
40. Regassa H, Sourirajan A, Kumar V, Pandey S, Kumar D, Dev K. A review of medicinal plants of the himalayas with anti-proliferative activity for the treatment of various cancers. Cancers. 2022;14(16):3898.
41. Anal JMH, Majeed R, Bez G, Syiem D, Hamid A, Saxena AK. In vitro cytotoxicity of the polar extracts of Potentilla fulgens L. against human cancer cell lines: Detection and isolation of bioactive phenolics. J Chem Pharm Res. 2014;6(9):89-95.
42. Jütte R, Heinrich M, Helmstädter A, Langhorst J, Meng G, Niebling W. Herbal medicinal products–Evidence and tradition from a historical perspective. Journal of ethnopharmacology. 2017;20(7):220-5.
43. Qiu J. Traditional medicine: a culture in the balance. Nature. 2007;448(7150):126-9.
44. Schippmann U, Leaman D, Cunningham A. A comparison of cultivation and wild collection of medicinal and aromatic plants under sustainability aspects. Medicinal and aromatic plants: Springer; 2006;75-95.
45. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: Past history and future perspective. Journal of herbmed pharmacology. 2017;7(1):1-7.
46. Ali S. Significance of flora with special reference to Pakistan. Pak J Bot. 2008;40(3):967-71.
47. Rehman KU, Rehman SU, Ahmad M, Shinwari ZK, Zafar M, Majeed S. An ethnomedicinal survey of indigenous knowledge on medicinal plants and their current marketing in the kakar region of balochistan pakistan. Pak J Bot. 2023;55(3):1117-30.
48. Azmi AS, Bhat SH, Hanif S, Hadi S. Plant polyphenols mobilize endogenous copper in human peripheral lymphocytes leading to oxidative DNA breakage: a putative mechanism for anticancer properties. FEBS letters. 2006;580(2):533-8.
49. Apostolou A, Stagos D, Galitsiou E, Spyrou A, Haroutounian S, Portesis N. Assessment of polyphenolic content, antioxidant activity, protection against ROS-induced DNA damage and anticancer activity of Vitis vinifera stem extracts. Food and chemical toxicology. 2013;61:60-8.
50. Siriwatanametanon N, Fiebich BL, Efferth T, Prieto JM, Heinrich M. Traditionally used Thai medicinal plants: in vitro anti-inflammatory, anticancer and antioxidant activities. Journal of ethnopharmacology. 2010;130(2):196-207.
51. Heo B-G, Park Y-J, Park Y-S, Bae J-H, Cho J-Y, Park K. Anticancer and antioxidant effects of extracts from different parts of indigo plant. Industrial Crops and Products. 2014;56:9-16.
52. Cao J, Xia X, Chen X, Xiao J, Wang Q. Characterization of flavonoids from Dryopteris erythrosora and evaluation of their antioxidant, anticancer and acetylcholinesterase inhibition activities. Food and Chemical Toxicology. 2013;51(2)42-50.
53. Agati G, Azzarello E, Pollastri S, Tattini M. Flavonoids as antioxidants in plants: location and functional significance. Plant science. 2012;19(6):67-76.
54. Wen L, Wu D, Jiang Y, Prasad KN, Lin S, Jiang G. Identification of flavonoids in litchi (Litchi chinensis Sonn.) leaf and evaluation of anticancer activities. Journal of functional foods. 2014;6:(5)55-63.
55. Steigerová J, Oklešťková J, Levková M, Rárová L, Kolář Z, Strnad M. Brassinosteroids cause cell cycle arrest and apoptosis of human breast cancer cells. Chemico-biological interactions. 2010;188(3):487-96.
56. Khan T, Khan IA, Rehman A. A review on Berberis species reported from Gilgit-Baltistan and Central Karakoram National Park, Pakistan. J Med Plants. 2014;2(6):16-20.
57. Perveen A, Qaiser M. Pollen flora of Pakistan–LXV. berberidaceae. 2010.
58. Shinwari Z, Watanabe T, Rehman M, Youshikawa T. A pictorial guide to Medicinal Plants of Pakistan. KUST Kohat, Pakistan. 2006.

59. Baloch N, Nabi S, Yasser M, Kahraman A. In vitro antileishmanial, cytotoxic, anti-oxidant activities and phytochemical analysis of Berberis baluchistanica roots extracts and its fractions. J Phytopharmacol. 2013;4(2)82-87.
60. Pervez S, Saeed M, Ali MS, Fatima I, Khan H, Ullah I. Antimicrobial and antioxidant potential of berberisinol, a new flavone from Berberis baluchistanica. Chemistry of Natural Compounds. 2019;55(2)47-51.
61. Gao H-y, Li G-y, Wang J-h. Studies on the dynamic accumulations of Sophora alopecuroides L. alkaloids in different harvest times and the appropriate harvest time. Journal of Chromatography B. 2011;879(15-16):1121-5.
62. Cao S, Tian T, Chen L, Dong X, Yu X, Wang G. Damage caused to the environment by reforestation policies in arid and semi-arid areas of China. Ambio. 2010;(39:2)79-83.
63. Wang H, Guo S, Qian D, Qian Y, Duan J-a. Comparative analysis of quinolizidine alkaloids from different parts of Sophora alopecuroides seeds by UPLC–MS/MS. Journal of pharmaceutical and biomedical analysis. 2012;67:16-21.
64. Lin T, Zhao L, Yang Y, Guan Q, Gong M. Potential of endophytic bacteria isolated from'Sophora alopecuroides' nodule inbiological control against Verticillium wilt disease. Australian Journal of Crop Science. 2013;7(1):139-46.
65. Cornblatt BS, Ye L, Dinkova-Kostova AT, Erb M, Fahey JW, Singh NK. Preclinical and clinical evaluation of sulforaphane for chemoprevention in the breast. Carcinogenesis. 2007;28(7):1485-90.
66. Amos LA, Löwe J. How Taxol® stabilises microtubule structure. Chemistry & biology. 1999;6(3):R65-R9.
67. Amin A, Gali-Muhtasib H, Ocker M, Schneider-Stock R. Overview of major classes of plant-derived anticancer drugs. International journal of biomedical science: IJBS. 2009;5(1):1.
68. Steigerová J, Rárová L, Oklešťková J, Křížová K, Levková M, Šváchová M. Mechanisms of natural brassinosteroid-induced apoptosis of prostate cancer cells. Food and chemical toxicology. 2012;50(11):4068-76.
69. Perveen A, Qaiser M. Pollen flora of Pakistan-IV. Boraginaceae. Pakistan Journal of Botany. 1995;27(3)27-60.
70. Saddam,Suman,Shashi Alok. Anti-Cancer activity of medicinal plants.International journal of Pharmaceutical Science and Research 2023;14(5)2236-2252
71. Rajeswara Rao B, Singh K, Sastry K, Singh C, Kothari S, Rajput D. Cultivation technology for economically important medicinal plants. Advances in Medicinal Plants, 1st ed; Reddy, KJ, Bahadur, B, Bhadraiah, B, Rao, MLN, Eds. 2007.
72. Parveen S, Jan U, Kamili A. Importance of Himalayan medicinal plants and their conservation strategies. Australian Journal of Herbal Medicine. 2013;25(2):63-7.
73. Zschocke S, Rabe T, Taylor JL, Jäger AK, Van Staden J. Plant part substitution–a way to conserve endangered medicinal plants? Journal of ethnopharmacology. 2000;71(1-2):281-92.