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POTENTIAL OF MEDICINAL PLANTS FOR CANCER PREVENTION

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Abstract

Cancer, which is defined by the body's unregulated cell multiplication, is the second-largest cause of mortality worldwide. Medicinal plants have acquired a prominent position in the treatment of countless deadly illnesses, like cancer, due to their natural phytochemicals. Herbal medications are chosen over chemical-based medications because they are medicinally highly active and cause no or few negative impacts when employed to cure ailments. Multiple types of disastrous complications can arise with chemotherapy. Several plant compounds are now being utilized to cure cancer. A wide range of plant species have been demonstrated to be effective against cancer during in vitro experiments, yet their evaluation in humans is in need of an hour. The efficacy of these botanical compounds in managing human tumors needs more research. Multiple in vitro studies using plant-derived compounds have reported apoptotic and anti-proliferative activities against different cancers. This study will explore the anticancer potential of five different plants, along with their phytochemicals.

Keywords: *Medicinal plants; Cancer; Phytochemicals;Natural Products;Chemoprevention*

1. INTRODUCTION

Plants have been utilized as remedies since ancient times [1]. Currently, herbal remedies are the most widely utilized treatment for a wide range of illnesses, including cancer, both as a cure and a preventative. Non-communicable diseases (NCDs) constitute the leading cause of mortality worldwide, with cancer thought to emerge as the predominant cause of fatalities and a major barrier to increasing lifespans in the twenty-first century [2].Cancer accounts for one in every six fatalities. According to the World Health Organization (WHO), cancer is the second-largest cause of fatalities under the age of 70 in 91 out of 172 nations, and by 2040, there will be 29.4 million cancer cases worldwide[3]. Globally, there were 19.3 million newly diagnosed cancers and 10 million cancer deaths in 2020 [4].Surprisingly, Asia has a lower cancer prevalence rate than the West; the opposite is true for fatality rates [5].

The GLOBOCAN 2018 study reveals a dramatic increase in cancer diagnoses in India, with over 0.7 million fatalities and an estimated 0.8 million new cases per year. Roughly 2 million cancer diagnoses and 1 million fatalities are expected by 2040 [6]. Mizoram has the highest cancer incidence rate in India, followed by Delhi and Meghalaya [7]. Chemotherapy and radiotherapy are utilized as cancer therapies globally, but they are associated with risks [8]. Cancer cells grow rapidly due to a lack of essential regulatory mechanisms.Platinum-based medicines used in chemotherapy, such as cisplatin and carboplatin, are associated with resistance and adverse effects such as nephrotoxicity [9], ototoxicity [10], neurotoxicity [11], cardiotoxicity [12], and hepatotoxicity [13].

Moreover, cyclophosphamide, doxorubicin, fluorouracil, arsenic trioxide, etc. are not risk-free but are associated with major risks related to the heart, blood, kidney, pulmonary, and others [14]. The side effects of chemotherapeutic drugs create hurdles in combating cancer using modern medicine, disturbing the quality of life. In the present day, plant-based products have gained focus on treating cancer due to their low or no side effects. Plant products such as curcumin in

combination with cisplatin have shown improvements in ovarian and bladder cancer cells in vitro, leading to cancer cell death and lesser side effects [15,16]. Moreover, the combination of curcumin and docetaxel was shown to initiate programmed cell death in prostate cancer lineages [17]. Similarly, resveratrol, gemcitabine, uroslicacid, etc. are a few of the plant bioactive compounds with anticancer properties [18, 19]. This study is aimed at reviewing plants with potential anti-cancer effects and their phytochemicals, thus providing a platform for academic research on plant product benefits.

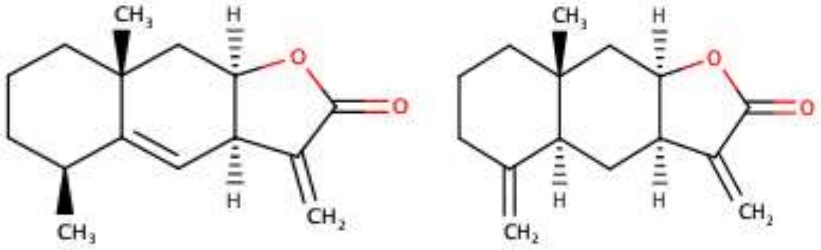
2. PLANT PRODUCTS AND CANCER TREATMENTS

Plants have long been explored for their anti-cancer properties.In the 1960s, the National Cancer Institute tested around 114,000 extracts from 35,000 plants against various cancers, primarily mouse leukemias.Combretastatin A-4, isolated from Combretumcaffrum, has demonstrated potential effectiveness for colon cancer cell lines. Similarly, other plant products like vinblastine, vincristine, etoposide, and teniposide have also shown potential anti-cancer activity [20].Plants like Annonasquamosa, Buchananialanzan, Cocculuspendulus, Flemingiachapper, Zizyphusrugosa, etc. were actively confirmed for anticancer activity. Moreover, tannins contributed to anticancer activity in Cleistanthuscolinus, Coloneastermarginatus, Flemingiachapper, and Zizyphusrugosa [21]. Plants are being researched for their anticancer potential, and several plants that have shown anticancer promise are discussed below.

2.1 Inularoyleana

Inularoyleana is commonly called Gugiphool in Kashmir. It is a threatened (Kashmir) medicinal herbaceous perennial plant of the asteraceae family. It occurs primarily in northern Pakistan and the western Himalayas, at elevations extending from 3400 to 3500 meters above sea level. The plant is small and unbranched, with bright yellow flower heads. Inularoyleana's isolated alantolactone and isoalantolactone exhibit antifungal and antibacterial properties, while its alkaloidal root extract has been found to treat neuromuscular disorders [22, 23, 24]. Furthermore, it hampered the growth of various cancer cell lines, including melanoma, prostate, colon, ovary, lung, and leukemia [25, 26]. In vivo investigations on mice indicated that alantolactone and isoalantolactone did not cause severe hepatotoxicity or nephrotoxicity; hence, if explored further, they might emerge as leading agents against cancer [27].

Alantolactone alone has shown anti-inflammatory activity and is a good substitute for insulin in diabetes [28]. The active component of Inularoyleana, alantolactone, effectively inhibited glioblastoma cell growth and migration, promoting apoptosis through caspase activity [29]. Moreover, sesquiterpene lactones represent a significant and diversified collection of biologically active inula chemicals with anticancer behaviour, requiring further exploration in both in vitro and in vivo studies [30, 31]. The plant exhibits antiproliferative activity against various lung cancer cell lines due to the presence of diterpene alkaloids, alantolactone, and sesquiterpene lactone [32]. I.royleanais also used to heal wounds and hoof irritations in cattle [33]. Recent studies have shown that sesquiterpene lactones, a diverse group of plant specialised metabolites from the asteraceae family, exhibit anticancer activity, inhibiting the expansion of various cancer cells, including squamous cell lung cancer, gastric,colorectal, breast, and pancreaticcancers, through cell cycle arrest and apoptosis [34, 35]. Fig. 1 represents the structure of alantolactone and isoalantolactone. From a bird's-eye view, there is a study gap in the scenario of I.royleana, which needs to be investigated further due to its anticancer potential.



Alantolactone Isoalantolactone

Figure 1. Structure of alantolactone and isoalantolactone

2.2 Boswelliaserrata

For hundreds of years, plants have been used as medicines with natural compounds or derivatives comprising around 50% of anticancer substances.Boswelliaserrata, a species of Burseraceae, is known by white guggal, loban, and Indian olibanum, or shallaki in Sanskrit.It is a medium-sized tree that is widely seen in Africa and India. Frankincense, a product of B.serrata, was approved in Europe as a remedy for inflammation. In the beginning of its research, B.serrata was used to treat inflammatory illnesses in traditional Ayurvedic medicine in India,including arthritis, ulcerative colitis,Crohn disease, ulcers, diabetes, diarrhoea, rheumatoid arthritis, and osteoarthritis[36, 37,38].

Boswellic acids from B.serrata were discovered to possess antiproliferative and proapoptotic properties, potentially providing antineoploastic activity in various human cancers like melanoma cells, colon cancer cells, prostate cancer cells, and leukemia HL-60 cells, thereby promoting apoptosis through caspase-3 and bcl-2 family activation [39, 40, 41, 42].An in vivo study demonstrated that B.serrataextract effectively combats doxorubicin-induced liver toxicity, resulting in substantial enhancements in liver function [43].Boswellic acids, a key component of B.serrata gum resin, have shown good anticancer activity in prostate cancer treatment through nanoparticle formulations causing apoptosis and DNA fragmentation[44].

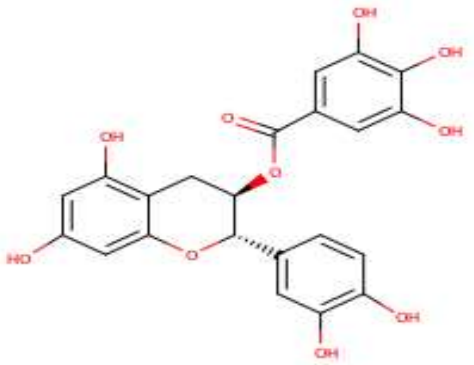
Drug resistance hinders modern treatments, necessitating new treatments. Frankincense's chemical constituents may offer promising compounds for anti-inflammatory and cancer drug development. Boswelliaserrata'soleogum resin demonstrated effective potential against prostate cancer, glioblastoma, and colo-rectal responses in vitro and in vivo by reducing growth, arresting the cell cycle, and inducing apoptosis [45, 46, 47]. Moreover, 3-O-acetyl-β-boswellic acid inhibited breast cancer in vitro through increased apoptosis, decreased proliferation, cell survival, and metastasis [48]. Further research on the clinical potential of B.serratacompounds and their modes of action is needed for cancer, as they have shown promise as effective anticancer agents in both in vitro and in vivo studies with lower toxicity.

2.3 Bergenia ciliata

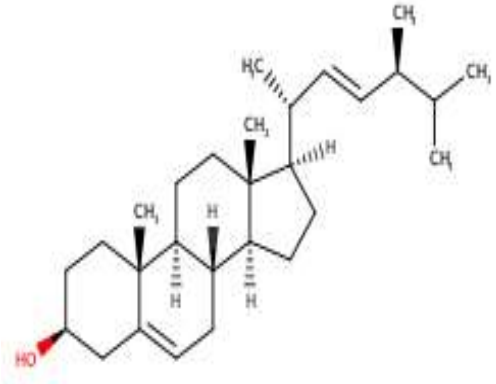
Plants have been utilized in medicine since antiquity and have been discovered to be a substantial source of anticancer medicines due to vinca alkaloids, podophyllotoxins, taxols, and camptothecin. Bergeniaceliata, a member of the Saxifragaceae family, is known by various names, including Zakhm-e-hayat, hairy Bergenia, and Pashanbheda (meaning to dissolve kidney stones). This small perennial herb is prevalent in India, Pakistan, Nepal, and other nations [49].Traditional Ayurvedic medicine utilizes B.celiata for treating various diseases such as fever, cough, diarrhea, pulmonary infections, and epithelioma. In Kashmir, it is used as a local remedy for asthama, boils, and fever, while in Sikkim, its rhizome is used for cough [50, 51, 52]. B. ciliata, a medicinal plant with antioxidant phytochemicals, has been linked to various therapeutic benefits, including anti-inflammatory, anti-diabetic, antipyretic, antibacterial, Parkinson's disease, and antimalarial activities [53, 54, 55].

The plant has also demonstrated positive effects on hepatorenal toxicity and cancerous growth [56]. B. ciliata is an herb with various compounds, primarily found in its rhizomes and leaves, with bergenin, a glycoside, and paashanolactone as its main constituents [57, 58]. A recent study found that B. ciliata compounds such as stigmasterol, β-sitosterol, paashaanolactone, and afzelechin are helpful against breast cancer [59]. Bergenin from B. ciliata exhibits significant anticancer properties against human cervical cancer cells, primarily cell cycle arrest and apoptosis [60]. The extracts of catechin 3-gallate, sitosterol, and rhizome significantly reduced cell viability in hepatocellular cancer, both in vitro and in vivo [61, 62]. The first preparation of zinc oxide nanoparticles from B. ciliata rhizome extracts revealed crucial cytotoxicity against colon cancer and human cervical cell lines [63]. Fig. 2 depicts the structure of bergenin, catechin 3-gallate, stigmasterol and beta-sitosterol. Additional study is required to validate the potential of various compounds from B. ciliata, including stigmasterol, β-sitosterol, catechin 3-gallate, bergeninpaashaanolactone, afzelechin, and leucocianidol, as potential cancer treatment agents.

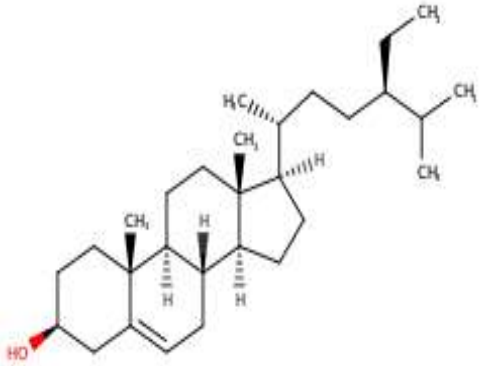
Bergenin



Catechin 3-gallate



Stigmasterol



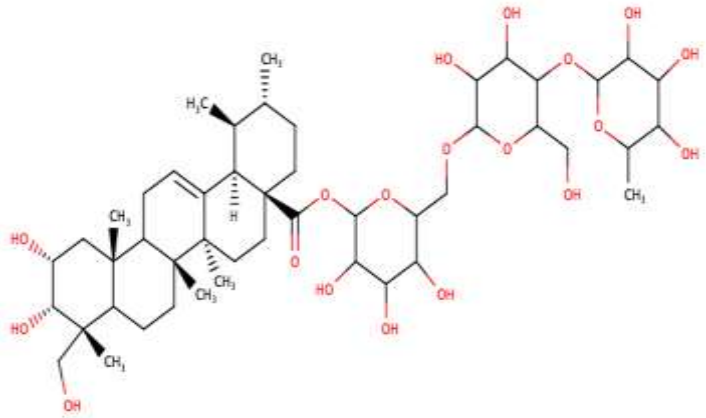
β-sitosterol

Figure 2. Structure of bergenin, catechin 3-gallate, stigmasterol and β-sitosterol.

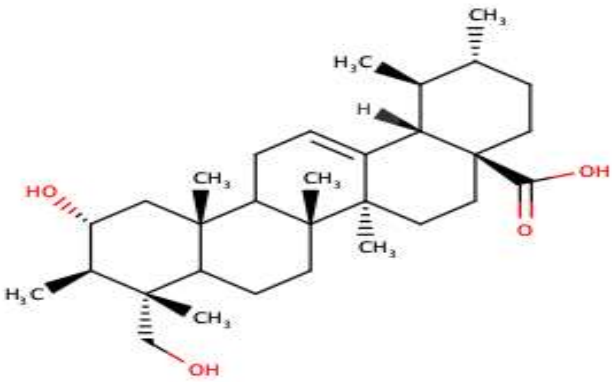
2.4 Centellaasiatica

Centellaasiatica belongs to Apiaceae family commonly called Gotukola, Brain Food, Indian Pennywort, and Tiger Herb. It is a perennial herbaceous perennial plant indigenous to South Africa, India, and China and is used as a dietary supplement and medicine [64, 65]. The plant contains various biochemicals, including triterpenoids, alkaloids, glycosides, and flavonoids, with triterpenes, primarily madecassoside, asiaticoside,asiatic acid, and madecassic acid, being the primary medicinal constituents [66, 67,68].It has been determined to have multiple pharmaceutical benefits, such as anti-inflammatory, immunomodulatory, anticancer, cardioprotective, anti-bacterial, anti-oxidant, neuroprotective, and wound healing abilities [69, 70,66].C.asiatica is a

traditional medicine used in north India for treating cancer [71].Recently, studies have demonstrated thatC.asiatica inhibits cell proliferation in human liver cancer cells, brain cells, mouse fibrosarcoma cells,human gastric adenocarcinoma cells, blood cancer cells, murine melanoma cells, skin cancer cells, and keratinocytes. In an in vivo model, it inhibited cell growth and promoted apoptosis in colon and intestinal cancers [72, 73, 74,75, 76, 77].Asiatic acid extracted from C.asiatica suppressed the growth of many cancer cells, like colon cancer, ovarian cancer, and hepatoma, through apoptosis [78].The silver nanoparticles derived from C.asiatica leaves were found to enhance caspase activity, thereby causing apoptosis in MCF-7 breast cancer cells [79]. Another study reported that triterpenoids like madecassic acid, asiatic acid, and asiaticoside reduced lung cancer cell invasion and migration and promoted apoptosis in leukemia cancer cells [69]. Fig. 3 displays the structure of asiaticoside and asiatic acid.C. asiatica, despite its anti-cancer properties, requires further research on its inhibitory mechanisms.



Asiaticoside



Asiatic acid

Figure 3. Structure of asiaticoside and asiatic acid

2.5 Arnebia benthamii

Arnebia benthamii, a monocarpic, erect, herbaceous perennial plant from the Boraginaceae family, is native to the Himalayan region, also known as Kahzaban in Kashmir [80]. The species grows in the alpine and subalpine Himalayan Mountains of India, Pakistan, and Nepal, at elevations ranging from 3000 to 3900 meters [81]. A. benthamii, a traditional anti-diabetic medicine, is used for anti-fungal, wound healing, inflammatory, cardiac disorders, antihelminthic, and antipyretic purposes, and its flowering shoots are used to prepare syrup for throat and tongue diseases [82, 83,84].In China, it is being utilised as conventional medicine to treat diseases of the

liver and kidney [81]. The plant has been found to possess antioxidant properties, which protect DNA from oxidative damage [82,85].Furthermore, it is a potent antioxidant and cytotoxic agent in various cancers, including lung, leukemia, colon, pancreatic, and prostate [84].Arnebia species contain various compounds such as alkaloids, phenols, benzoquinones, steroids, triterpenoids, flavonoids, β-hydroxy-sovalerylshikonin, deoxyshikonin, β-hydroxy-sovalerylshikonin, napthoquinones, acetyleshikonin, arnebinone, arnebin-7, and stigmasterol [86, 87].The species has been found to possess anticancer activity through the isolated compounds arnebin-1 and arnebin-3 [88]. Rather et al.,isolated new compounds from A.benthamii, such as β-sitosterol,β-D-glucoside, rhamnocitrin, and aromadendrin [89]. Recent research indicates that shikonin, a phytochemical known to have anti-cervical cancer properties, is also present in Arnebia [90].

3. Conclusion

Plants have been used for millennia as natural bioactive ingredients in treating various fatal illnesses, with around half of current pharmaceuticals derived from these natural sources. The present article gives a detailed examination of the various pharmacological applications of plants, focusing on their potential for anti-cancer properties.Plants have been shown in several studies to be effective in slowing the growth oftumors, encouraging apoptosis, and inhibiting the expansion of cancer cells.Phytochemicals, including flavonoids, alkaloids, and terpenoids, possess antioxidant, anti-inflammatory, and anti-proliferative properties, which are crucial in preventing cancer initiation and progression.Moreover, plants in this review have shown good anti-cancer activity due to the presence of a variety of phytochemicals. Medicinal plants offer advantages in cancer prevention and treatment, including fewer side effects, cost-effectiveness, and rich biodiversity.

They are safer, more accessible, and provide potential candidates for further exploration and discovery of novel anti-cancer agents, making them a valuable alternative for patients in resource-limited settings. Further research is needed to understand the mechanisms of action, optimize the use of medicinal plants in chemoprevention, and evaluate their long-term safety and efficacy.In conclusion, medicinal plants offer enormous potential as natural and sustainable alternatives to chemoprevention. Their rich phytochemical makeup and various biological actions make them promising candidates for the development of new anti-cancer medicines. Exploring the potential of medicinal plants can lead to more effective and specific cancer prevention techniques.

4. Conflicts of interest

The authors declare no conflicts of interest to disclose.

5. Acknowledgements

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