



## **A Review on the Potential Application of Medicinal Species from Asteraceae Family in Cancer**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

Globally cancer is one of the most prevalent life-threatening diseases that have a significant impact on humans. The uncontrolled division of cells is a sign of the disease. Modern cancer therapies have several side effects on healthy cells. The problem of increasing tumour resistance to existing drug treatments is a serious concern. As a result, there is a critical need for more effective medicine to combat this condition. New ways to avoid this illness are in high need. Humans' pursuit of health is a never-ending drive for a healthier, longer life. Despite this, sickness and pain are still a part of his battle for survival. Natural products have a significant role in the battle against cancer and can be used to test novel therapeutic agents. Plants are natural remedies for a variety of illnesses. It is important to identify a variety of therapeutic plants which are useful for human being. Herbal therapies are a viable alternative to conventional cancer treatments. This article looks at plants from the Asteraceae family that have anticancer properties. Plants of the Asteraceae family play an important role in combating malignancies of the stomach, breast, colon, and lung, according to a thorough examination of research papers. The results of the study indicated a spectacular outcome in the prevention of cancer.

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**1. INTRODUCTION**

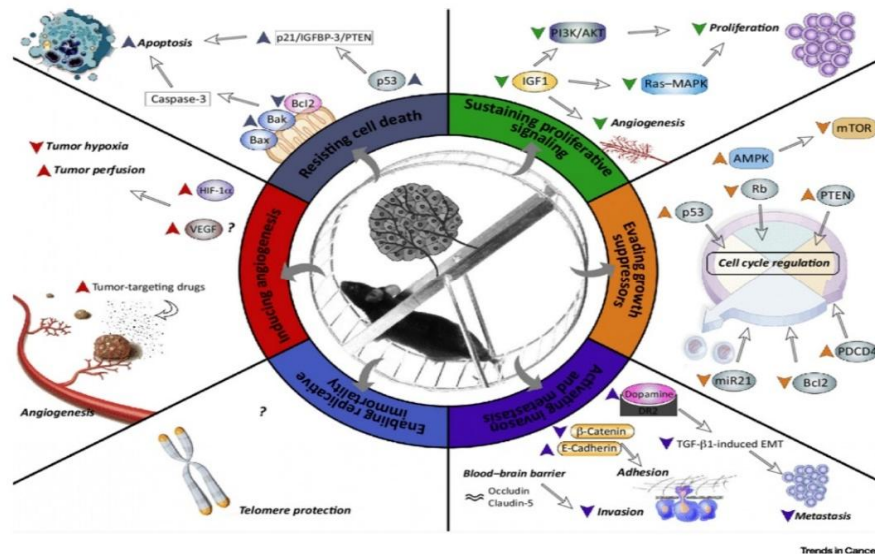
Cancer is a terminal illness. There are indeed several illnesses. One of the issues is this. Several beginnings cause, cofactors and promoters, and types of cellular harm done on the body's cells are all present. Cancer is caused by cells in the body that were once healthy. These altered cells continue to divide in an uncontrollable rate. They vary from the cells in the regular tissue from whence they develop just slightly at first. As a result, cancer cells's biochemistry and molecular regulatory systems are comparable to those of the body's cells.

In a bacterial infection, an invading Staphylococcus recognises itself as a foreign organism, whereas cancer does not. It is true that, the body may develop a partial immune response against cancer cells, but these immune systems responses become suppressed and ineffective as the disease develops. Lymphocytic leukaemia, Hodgkin's disease, Burkitt's lymphoma, bone cancer, kidney cancer, muscle tissue cancer, testicular cancer, specific ovarian cancer and oestrogenic sarcoma are

among the four forms of cancer. Every year, about one million people in India are diagnosed with cancer. Each year in India more than one million people are diagnosed with cancer. Each year, over 500,000 individuals succumb to cancer. The sickness will affect as many households as possible. Aside from the individual physical and mental toll, there is a significant financial toll on both the family and the country [1].

**2. CANCER BIOLOGY**

Cancer is caused by a multistep process in which cells accumulate genetic abnormalities, especially in oncogenes and tumour suppressor genes that lead to uncontrolled growth. These anomalies bring several development advantages. During the shift from normal cells to tumour cells, mutations in the cell genome are widespread. According to Harahan and Weinberg, six major alterations occur during the transition from a normal cell to a tumour cell, and these characteristics are referred to as cancer hallmarks [2].



**Fig. 1. Sustained proliferative signaling [3]**

Proliferation is a crucial aspect of cancer growth and progression. Cell cycle-related proteins' expression or activity are changed as a result of this. The stimulation of multiple signal transduction pathways on a continuous basis also promotes cell development. Early stages of tumor formation are linked to a fibro genic response and the establishment of a hypoxic environment that favours cancer stem cell survival and multiplication. Changes in cell metabolism may be part of cancer stem cells' survival strategy. Overproduction of relevant hormones, increasing angiogenesis, and undergoing epithelial to mesenchyme transition may encourage tumor development and spread once they occur. [4].

The TP53 gene produces the p53 tumour suppressor protein in humans. P53 suppresses abnormal growth in normal cells in part by interacting with the proapoptotic protein Bax, while mutations in the TP53 gene cause tumour suppression, loss of interaction with Bax, and apoptosis inhibition in cancer cells. Apoptosis, also known as programmed cell death, is a defensive process that prevents normal cells from being damaged or collecting mutations [4].

Telomerase activity is generally elevated in cancer cells. This allows them to become immortal, meaning they may divide eternally as long as their nutritional and oxygen needs are supplied. Proper cells divide for a finite number of replications and have normal telomere lengths [7].

To fuel their development, cancer cells need to consume more energy. Tumour cells primarily employ glycolysis rather than mitochondrial oxidative phosphorylation, therefore they must consume more glucose than normal cells. Furthermore, hypoxic circumstances and Ras expression upregulate glycolysis by increasing the expression of HIF1 and HIF2. HIF1 and HIF2 also stimulate the production of growth and angiogenic factors [9].

Changes in tumor-suppressing signalling proteins, such as p53, cause tumour cells to proliferate indefinitely. Another method that drives tumour cell proliferation is the escape from growth-suppressing signalling. In cancer cells, mutations in tumour suppressor genes are common: for example, p53 is often altered and affects the cell cycle in tumour cells [11].

## 2.1 Asteraceae Family

In the battle against illnesses, natural commodities play a crucial role. Even with recent advances in drug discovery methods like high-throughput screening, combinatorial chemistry, and rational drug design, these products were and continue to be a key source of early medicines. Natural materials are recognised as significant sources of lead compounds and new drug development potential since bench top chemical methods cannot achieve the molecular and structural variability of natural products. Sesquiterpene, found in the Asteraceae family, have a variety of biological effects, including cytotoxicity. [11] Plants in the Asteraceae family are considered good sources of chemo-preventive agents because they contain a wide range of antioxidant molecules [12].

With over 23,000 species found on every continent except Antarctica, Asteraceae is one of the largest plant families. The capitulum, or flower heads, is a highly compressed inflorescence branch system in which all the flowers are attached to a receptacle covered by involucre bracts and is the most distinctive feature of the Asteraceae family. As seen in Fig. 6 for gerbera and sunflower, the capitulum produces a pseudanthium, which resembles a single massive bloom. Two other characteristics that are diagnostic for the family are anthers united in a tube and inferior ovary placement. Pappus bristles are produced from the outer floral whorl [14]. Some of the interested medicinal plants having potential anticancer activity belongs to Asteraceae family are mentioned in Table 1.

## 2.2 Anticancer Plants

- *Achillea species*

*Achillea millefolium* has been used to treat haemorrhoids, cancer, vertigos, anaemia, anorexia, dyspepsia, gastralgia, haemorrhage, and *Achillea biebersteinii* has been collected from East Azerbaijan of Iran [15].and assayed on six cancerous cell lines, AGS human Caucasian gastric adenocarcinoma, SKLC6 human breast ductal carcinoma, SW741 human colorectal adenocarcinoma, SkLC6 human carcinoma, A375 human melanoma cancer cell and human liver hepatoma. In addition, complementary tests

were used to confirm the selectivity of herbal extracts. In comparison to their cytotoxicity effects on many carcinogenic cells, herbal extracts have a lower haemolytic capacity and antifungal test results, which might indicate that they have effects in producing cytotoxicity in human carcinogenic cells [16].

• *Achyrocline bogotensis*

The family Asteraceae and the genus Gnaphalium are responsible for these plants [17]. These annuals or perennials reach a height of 1.5 metres and grow between 2000 and 3200 metres above sea level. They are readily mistaken with species belonging to different

genera because of their physical features. These genera are widely utilised for therapeutic purposes in many areas of the world [18]. As a result, several *Achyrocline* species are used in poultices to treat wounds, act as a haemostatic, combat infections, and reduce inflammation. It is suggested in the Andean areas for cancer treatment. He described the cytotoxic effects of two flavone isomers on human cancer cells from the breast (MCF7, SK-BR-3), colon (Caco-2, HCT116), and pancreatic (MCF7, SK-BR-3) (MIAPaCa, Pan28). The differentiation state and tumorigenic potential of these cells vary. These Asteraceae, namely the *Achyrocline* genus, are thought to have anticancer characteristics [19].

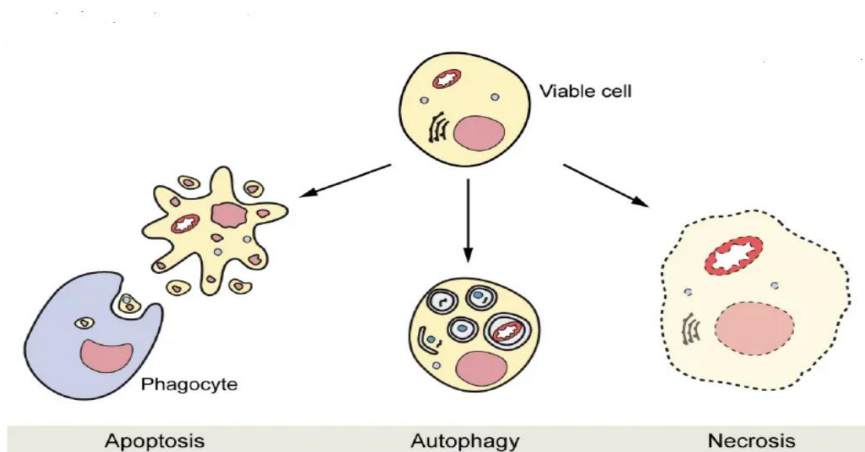


Fig. 2. Resisting cell death [5]

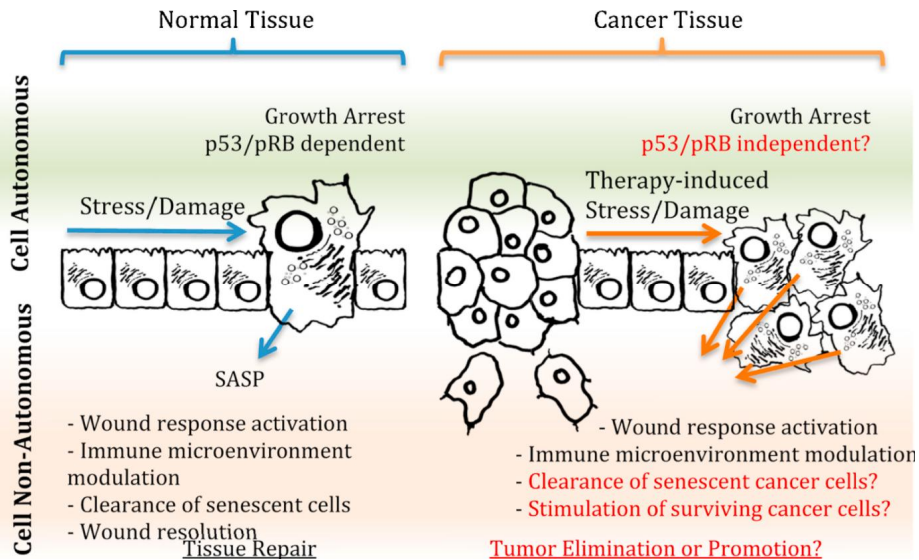


Fig. 3. Replicative immortality [6]

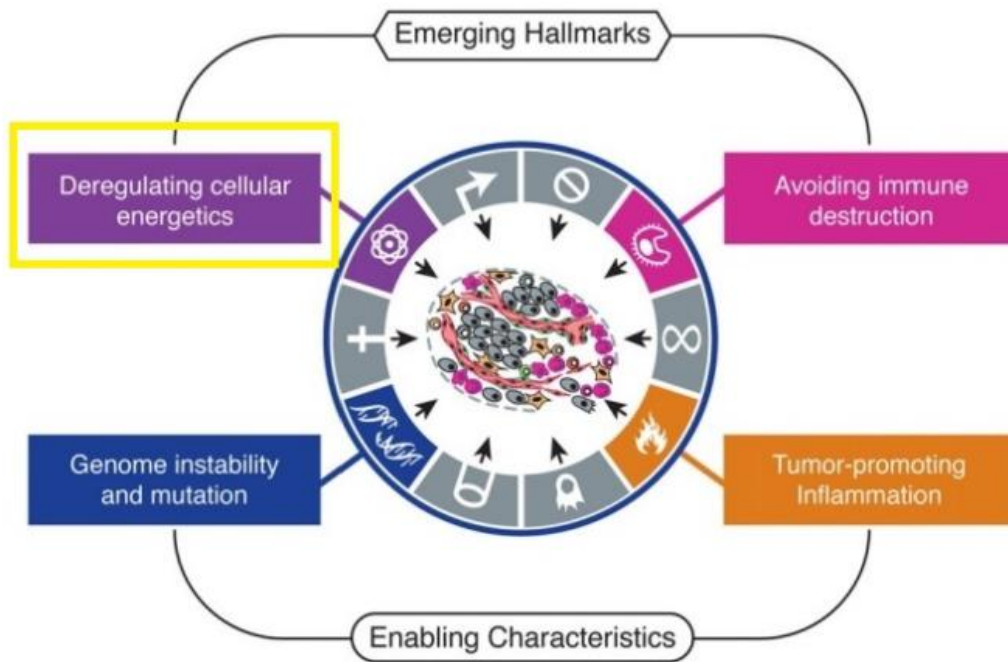


Fig. 4. Deregulating cellular energetics [8]

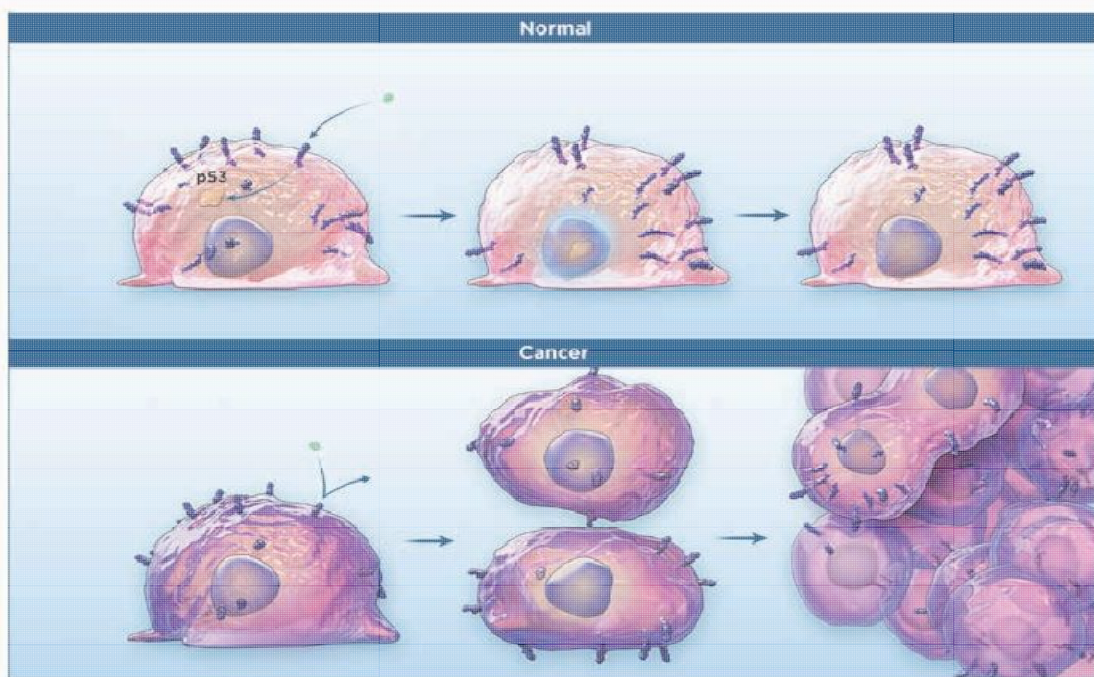


Fig. 5. Evading growth suppressors [10]



**Fig. 6. Flower heads in Gerbera hybrid and Helianthus annu [13]**

- *Ageratum conyzoides*

The family Asteraceae includes *Ageratum* species. It's common in Central America, the Caribbean, the United States, and Southeast Asia, including India [20,21]. It's known as "ufu opioko" [22]. It has anticancer properties and is used to treat colds, rheumatism, headaches, and wounds [23,24]. Plant-based natural products might also be a good place to look for anticancer and antioxidant compounds. The sulphorhodamine B (SRB) assay was used to test the in vitro activity of ethanol and petroleum ether extracts of *Ageratum conyzoides* in cancer cell lines. Human non-small cell lung carcinoma (A-549), human colon adenocarcinoma (HT-29), human gastric carcinoma (U-251), human breast cancer (MDA-MB-231), and human prostate carcinoma are some of the cell lines that have been studied (DU-145) [25].

- *Ambrosia peruviana*

Although the genus *Plagiochila* contains hundreds of species there have been no previous pharmacological or phytochemical findings on this species to our knowledge. *Ambrosia peruviana* is a South American plant whose extract is the subject of two patents, one of which refers to its application

in the treatment of skin and phaneres. The other concerning its potential as a source of anticancer or anti-inflammatory medicines [26]. Pharmacological screening of the ethanol extracts and fractions of two Peruvian medicinal plants, *Plagiochila disticha* and *Ambrosia peruviana*, resulted in the isolation and characterization of three ent-2,3-secoaromadendrane-type sesquiterpenoid, plagiochiline, as well as two pseudoguaianolides, damsine(4) and confertin(5), which exhibited significant cytotoxic activity against [27].

- *Artemisia macrocephala*

*sieversiana* var. *pygmaea* is a kind of *A. sieversiana*. The synonym is kryl. Khovs, Mong-Dag g, and Alsh are the most common locations. Large and small rivers are used to grow it. It's a grey-coloured annual herb. The stems are solitary and branching from the base, measuring 6 to 25 cm tall. Oblong ovate to broadly ovate leaf blades. Long: 15-4 cm the bitter taste is utilised to treat throat, lung, and fever infections, as well as malignancies [28]. Mohammad Shoaib uses a gravity column chromatography method to isolate a physiologically rich chloroform fraction to explore the antioxidant and anticancer effects of *Artemisia macrocephala*. DPPH and ABTS free radical

scavenging activities were used to evaluate the antioxidant activity of the isolated STLs. MTT test was used to evaluate anticancer activity in 3T3, HeLa, and MCF-7 cells [29].

- *Artemisia herba-alba*

*Artemisia inculca Del* is a synonym. Desert wormwood is a common name for a perennial plant that grows in the Irano-Turanian steppes of Spain, North Africa, and the Middle East [30]. It is primarily used to treat colds, coughs, and digestive problems, as well as an anti-diabetic. Anthelmintic, antimycotic, and antispasmodic are some of the other popular applications of the plant extract. This species is especially beneficial for neurological problems. In human colon cancer HCT116 cells, Giulio Lupidi looked into the antioxidant and anticancer activities of aqueous and ethanol extracts of AHE. Cell viability tests, cell cycle progression by flow cytometry, and DNA fragmentation analyses were used to determine antitumor effects, as well as the expression of essential cell cycle and apoptotic proteins [31].

- *Artemisia sieversiana*

- In Asia, Europe, and North America, *Artemisia sieversiana* (Asteraceae) is used to treat infections, colds, diarrhoea, jaundice, fever, and hysteria [32]. The genus of bioactive chemicals and their historic ethnomedicinal uses. Flavonoids, sterols, coumarins, and terpenoid substances have all been found in the plant's different parts. *A. sieversiana* has been shown to have a variety of biological activities. The plant's anticancer and anti-inflammatory properties were first discovered in early research [33]. The antioxidant activity of the alcoholic extract of *A. sieversiana* was found to be equivalent to that of ascorbic acid. The aerial portions of *A. sieversiana* were extracted in ethanol and tested against three colorectal cancer cell lines: HT-29, HCT-15, and COLO 205. COLO 205's development was slowed by apoptosis, DNA damage, and a decrease of mitochondrial membrane potential [34].

- *Artemisia vulgaris*

*Artemisia* is a vast genus of tiny plants and shrubs that grows in northern temperate climates. *Artemisia* is one of 1,000 genera and 20,000 species in the Composite family.

In Chinese traditional medicine, *Artemisia vulgaris* species is frequently used as a medicinal plant. Antiseptic, antispasmodic, gastrointestinal, anticancer, and nervous system illnesses are just some of the actions described for this plant in studies [35,36]. The methanolic extract was tested for anticancer efficacy against the human colon cell line HCT-15 [37].

- *Bellis perennis*

It is a medicinal plant species belonging to the Asteraceae family that has long been used as a wound-healing herb in Europe [38]. Rheumatism, the common cold, and headaches have all been treated using the aerial portions of *B. Perennis* [39]. In traditional medicine, they are used for expectorant, sedative, and anti-inflammatory properties [40]. Traditional applications of *B. perennis* include wound healing and sedative effects [38]. Controlled experimental animal investigations back it up. *B. perennis* aerial portions have also been utilised as herbal tea to treat breast and uterine cancer [41]. There were 19 distinct extracts used, and two fractions were extracted from wild-grown flowers and foliage using different extraction methods. Bioassays were used to evaluate the biological activity of various extractions and fractions. The greatest cytotoxic activity was found in leaves extracts produced in vitro against chosen cell lines [42].

- *Bidens pilosa*

These plants may be found in India's south. Glandular sclerosis, wounds, the common cold and flu, acute and chronic hepatitis, and urinary tract infections have all been treated with it in the past. The in-vitro comet assay for anticancer was used to screen several extracts and fractions from the plant *Bidens pilosa*. Hexane, chloroform, and methanol extracts were used to obtain the extract of the entire plant. The extracts were fractionated with ethyl acetate, acetone, and water using a column chromatography technique. The antitumor efficacy of all extracts and fractions was investigated. It demonstrates outstanding anticancer properties [43].

- *Blumea balsamifera*

It's a wild terrestrial plant that may reach altitudes of 2200-3500 metres in wet to dry

climates. It goes by a variety of names in different nations, including Ainaxiang and Dafeng China. Local names in Indonesia include sembung gantung, Langu (Java), Kamadhin (Madura), Capo (Sumatra), and Madikapu (Madikapu) (Eastern Indonesia) [44]. Because of its high essential oil concentration, it is often used as incense. In Thailand, the dried leaves of this plant may be used as a cigarette to treat sinusitis, colic pain, and cough, and can also be combined with other plants as a bath component for new mothers [45]. People in the Philippines are more familiar with the term Sembung, a traditional medication used to treat kidney stones, the common cold, and as a diuretic [46]. Sembung is also used as an Ayurvedic medicine in other Asian nations, such as Malaysia and India [47].

- *Blumea lacera*

India, China, Malaya, and tropical Africa are the most common locations of this plant [48]. Kukusunga is the native name for an herbaceous weed. The herb has been used as an anthelmintic, astringent, diuretic, and antibacterial for thousands of years [49]. It is said to be effective in the treatment of bronchitis and blood disorders. The antileukemic activity of a hot extract of *B. lacera* against anti-K562, L1210, and U937 leukaemia cells has been observed [50]. Raushanara Aktar described the isolation and characterization of a novel steroidal glycoalkaloid as well as the identification, characterization, and cytotoxic action of this plant. Its cytotoxic activity, apoptotic potential, and cell cycle impact are all being assessed [51].

- *Blumea eriantha*

It's a tiny annual plant that grows up to 1 m in height and has a camphor-like odour. It's often found in tropical areas, and the juice is used as a carminative. Antibacterial,

antifungal, and insecticidal activities are found in the essential oil taken from the leaves and stem [52]. Traditionally, this herb has been used as a diuretic and to cure Cholera [53]. MTT assays on HeLa and B16F10 cell lines were used to assess the cytotoxic and antiproliferative properties of *B. eriantha* methanolic extract of leaves in vitro [54].

- *Calendula officinalis*

It's sold throughout Central and Southern Europe, Western Asia, and the United States of America [55]. Pot marigold is the English name, while Zergul is the Hindi name [56, 57]. It's a biennial or annually flowering plant. The flowers and leaves are the main therapeutic components of the plant. Flowers were also utilized medicinally for their essential oil, which grew to be 30-60 cm tall. 10-20 cm long, lower spatulate leaves Flower heads yellow to orange, corolla oblong spatulate, and stem angular, hairy, and solid. Saponins and triterpenes, for example, were among the chemical components. Antibacterial, antifungal, anthelmintic, antiviral, antioxidant, and hepatoprotective are some of the therapeutic benefits [58].

- *Tagetes erecta*

It is a beautiful plant that is frequently used to treat bronchitis, rheumatoid arthritis, colds, and respiratory illness, as well as a stimulant and muscle relaxant. In the Amazonia area, the essential oil of *T. erecta* leaves has schistosomicidal effects and is used as an anthelmintic. The essential oils of *Tagetes erecta* were tested for their cytotoxicity action. It was tested on tumour cell lines such as human colon carcinoma (HT29), human breast adenocarcinoma (MCF-7), human cervical adenocarcinoma (HeLa), and human hepatocellular liver cancer (HepG2). The cytotoxic activity was evaluated using the XTT assay [59].

**Table 1. List of In-Vitro Anticancer Activities of Different Plant**

Sr. No	Plant Name	Part of the plant Used	Specific Cancer cell line suppressed	Reference
1	<i>Achillea millefolium</i>	Leaves, Stem	MCF7,SW742, SKLC6,A375	[16].



2	<i>Achyrocline bogotensis</i>	Leaves	MCF7, Caco-2, HCT116, MIA PaCa	[19].
3	<i>Ageratum conyzoides</i>	Leaves	A-549, HT-29, SGC-7901, DU145, BEL-7402.	[25].
4	<i>Ambrosia peruviana</i>	Aerial parts	MCF-7, M-14, HT-29, DU145, H460.	[27].
5	<i>Artemisia macrocephala</i>	Aerial parts	HeLa, MCF-7	[29].
6	<i>Artemisia herba-alba</i>	Whole plant	HCT116	[31].
7	<i>Artemisia sieversiana</i>	Leaves and flower	HT-29, HCT-15, COLO 205.	[75].
8	<i>Artemisia vulgaris</i>	Aerial Parts	HCT-15	[37].
9	<i>Bellis perennis</i>	Aerial parts	A-549, DLD-1	[42].
10	<i>Bidens pilosa</i>	Whole plant	HeLa	[43].
11	<i>Blumea balsamifera</i>	Leaves	HepG2	[76].
12	<i>Blumea lacera</i>	Leaves	MCF-7	[51].
13	<i>Blumea eriantha</i>	Leaves	HeLa, B16F10	[54].
14	<i>Calendula officinalis</i>	Flowers and Leaves	HepG2	[58].
15	<i>Tagetes erecta</i>	Flowers and Leaves	B16F10, HT29, MCF-7, HeLa, HepG2.	[59].



*Achillea millefolium*



*Achyrocline bogotensis*



*Ageratum conyzoides*



*Ambrosia peruviana*



*Artemisia macrocephala*



*Artemisia herba-alba*



*Artemisia sieversiana*



*Artemisia vulgaris*



*Bellis perennis*



*Bidens pilosa*



*Blumea balsamifera*



*Blumea lacera*



*Calendula officinalis*



*Tagetes erecta*



*Blumea eriantha*

**Plate 1. Anticancer Plants [60-74]**

**3. CONCLUSION**

Cancer is a major issue in both developing and wealthy nations. Various synthetic medicines have been employed to treat cancer, but their effectiveness is limited due to their toxicity to healthy cells. As a result, there is a desire for alternative medicine for cancer therapy. The medicinal plant has made a significant contribution to human health, and it includes a variety of secondary metabolites with disease-fighting capabilities. Most of the herbal plant from Asteraceae family shows anticancer activity. Due to their immune-modulatory and antioxidant characteristics, medicinal plants from the

Asteraceae family have been shown to have a high anticancer potential.

**CONSENT**

It is not applicable.

**ETHICAL APPROVAL**

It is not applicable.

**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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