A REVIEW ON HERBS USED IN TREATMENT OF CANCER

A Project Report Submitted

In Partial Fulfilment of the Requirements

for the Degree of

BACHELOR OF PHARMACY

by

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May, 2022

CERTIFICATE

This is to certify that project work entitled **"A review on herbs used in treatment of cancer"** submitted to Department of Pharmacy, is a bonafide research work done by **Mr. Avinash Kumar** under the supervision and guidance of **Mr. Debashish Paramanick,** Assistant Professor, School of Medical and Allied Sciences, Greater Noida. The work is completed and ready for evaluation in partial fulfilment for the award of Bachelor of Pharmacy during the academic year 2021-2022. The project report has not formed the basis for the award of any Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Date:

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BONAFIDE CERTIFICATE

This to certify that the project work entitled **"A review on herbs used in treatment of cancer"** is the bonafide research work done by **Mr. Avinash Kumar**, who carried out the research work under my supervision and guidance for the award of Bachelor of Pharmacy under Galgotias University, Greater Noida during the academic year 2021-2022. To the best of my knowledge the work reported herein is not submitted for award of any other degree or diploma of any other Institute or University.

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DECLARATION

I hereby declare that the work embodied in this project report entitled **"A review on herbs used in treatment of cancer"** in Partial fulfillment of the requirements for the award of Bachelor of Pharmacy, is a record of original and independent research work done by me during the academic year 2021-22 under the supervision and guidance of **Mr. Debashish Paramanick,** Assistant Professor, School of Medical and Allied Sciences, Galgotias University, Greater Noida. I have not submitted this project for award of any other degree or diploma of any other Institute or University.

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Place: Name and Signature of candidate

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Avinash Kumar

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1. EMR: Evidence-based veterinary
2. USA: United States of America
3. FDA: Food and Drug Administration
4. LDH: Lactic dehydrogenase
5. XTT: XML Tunnelling Technology
6. HPV: Human papillomavirus
7. DNA: Deoxyribonucleic acid
8. AML: Acute myeloid leukaemia
9. CML: Chronic myelogenous leukaemia
10. ALL: Acute lymphocytic leukaemia
11. CLL: chronic lymphocytic leukaemia
12. AKT: Ak strain transforming
13. EGCG: Epigallocatechin-3-gallate
14. MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide

Abstract

Cancer is triggered by a breakdown in cell cycle control. Uncontrolled cell growth causes cancer. External (tobacco, chemicals, radiation, and infectious organisms) and internal (gene changes, hormone alteration, immunological conditions, and metabolic abnormalities) factors contribute to cancer. Cancer is a serious worldwide health concern due to a lack of widespread and complete detection techniques, poor prognosis of late-stage patients, and growing global incidence. Cancer is one of humanity's hardest problems.

Despite breakthroughs in anticancer therapy, cancer remains the second biggest cause of human death, behind cardiovascular disease. Most cancer treatments involve chemotherapy, but it's limited by resistant cancer cells. Safer and more targeted anticancer medicines are still needed. Steroid derivatives are interesting because to their hard mediated degradation skeleton, diversity of functionalization, capacity to interact with a wide range of biological targets and ways, broad spectrum of bioactivity, and ability to puncture cell membranes, etc. Cancer is the third leading cause of mortality, behind cardiovascular disease and accidents. Cancer is a public health concern in industrialised and underdeveloped countries. Anticancer compounds slow, halt, or reverse carcinogenic development. Plant-based chemotherapy is being studied as an alternative to man-made drugs. In vitro and in vivo methodologies have been used to examine the anti-cancer potential of natural compounds from medicinal plants. This research analyses 50 anti-cancer herbs from 35 Indian families. This comprises components, extracts, models, cancer cell lines, etc. These herbs treat sarcoma, lymphoma, carcinoma, and leukaemia. These plants have high in vitro anticancer action, making them prospective in vivo options.

1. INTRODUCTION

Cancer is term used to describe a group of illnesses that are caused by a breakdown of cell cycle regulation. Cancer is linked to uncontrolled, aberrant cell proliferation. External (tobacco, chemicals, radiation, and infectious organisms) and internal factors both contribute to the development of cancer [gene mutations, hormonal change, immune conditions, and mutations that occur from metabolism]. Cancer is major global health issue, owing shortage of broad & thorough detection tools, poor prognosis of people detected at late stages of the disease, and the disease's rising global occurrence. Cancer is, without a doubt, one of humanity's most difficult difficulties [1].

Despite major advances in anticancer treatment, cancer continues to be the second leading cause of mortality in humans, after only cardiovascular disease. Most cancer therapies today include chemotherapy, albeit it is restricted by the proliferation of cancer cells that are resistant to it. As a consequence, developing safer and more specific anticancer drugs is still a goal. Steroid derivatives have piqued interest due to their rigid mediated degradation skeleton with such a variety of functionalization, as well as their ability to connect with a broad variety of biological targets and methods, and also their broad spectrum of bioactivity, highly specialised ability to pierce cell membranes, and so on. Cancer is the third greatest cause of death after cardiovascular illnesses, accounting for one-sixth of all deaths worldwide [2], [3].

1.1. **Prevalence**

In 2016, 8.9 million people were anticipated to die from different types of cancer. Breast cancer is the most frequent cancer in the world, followed by colon, rectum, and prostate cancer [4]. While these cancer types are the most frequent in most countries, they are ordered differently throughout the globe. Cancer is anticipated to roughly treble in prevalence in the EMR by 2030, making it one of the top four major causes of death. Incidence rates of cancer are increasing over the globe and are expected to continue to rise in the future decades. The pace of increase in incidence and fatality differs by nation, with developing countries bearing the brunt of the load [5].

We present the number of new cancer cases and the truncated age standardised incidence rates (per 100,000) for all cancer sites combined for individuals 80 years or older the regional & global level in 2018, using GLOBOCAN estimates. The most common five malignancies

diagnosed by area & internationally in girls & men aged [65-79 years old] & 80 years old were also provided. Finally, using population estimates and 2018 incidence rates, we calculated the numbers of new cancer cases in 2050, the percentage of patients aged 80 years old and the proportionate rise between (2018 & 2050) by area. Among 2018, the estimated (2.3 million) new cancer cases [excluding non-melanoma skin cancers] were diagnosed in people aged 80 and above over the globe (13 percent of all cancer cases), with regional profiles varying greatly [6]. Breast, lung, and colon cancers were the most prevalent in the aged females, whereas lung, prostate & colon cancers are the most common in the aged men. Inyear 2050, [6.9] million new malignancies may be detected in persons were 80 and above over the globe (20.5 percent of all cancer cases) [7]. The predicted rise will test healthcare systems globally, having a significant economic & social effect on families & society, while the difficulty for cancer treatment in the elderly. It's past time for cancer control measures to take the elderly into account [8]. Cancer remains a high-priority intervention topic. Lung cancer is the second most common cancer in men and women, and it is the leading cause of cancer mortality in the USA [9].

1.1. Treatment:

Surgical removal, chemotherapy, and radiation are the three most prevalent cancer therapies. The illness may also be treated with targeted treatment, immunotherapy, lasers, hormone therapy, and other therapies. Below is an overview of the many cancer therapies, as well as an explanation of how each one works. For many kinds of cancer, surgery is a popular therapy option [10].

1.3. Approved drugs and its adverse effects

1.3.1. Abraxane [11]

- Used in lungs cancer

Adverse effect of Abraxane:

i. Hair loss.
ii. Numbness, tingling, pain, or weakness in the hands or feet.
iii. Tiredness.
iv. Changes in your liver function tests

1.3.2. Tamoxifen

- Used in breast cancer

Menopause-like symptoms include sweating at night, hot flashes, and dryness in the vaginal area. Gaining weight, which happens more often, or keeping water in your body, which happens less often (edema). Periods that don't match up or don't have enough of them [12].

1.3.3. Afinitor (Everolimus)

- Used in kidney cancer.

It may cause diarrhoea, elevated blood pressure, and soreness as adverse effects [13].

1.3.4. Apalutamide (Erleada)

- Used in Prostate cancer

By lowering testosterone levels, these medications slow the development of prostate cancer tumours [14].

1.3.5. bevacizumab

- Used for Colorectal cancer.

Long-term changes in bowel habits such as diarrhoea and constipation, or changes in the stool' texture. Rectal bleeding may be detected by bleeding from the genital region or by finding blood in the stool. gastrointestinal pain, cramps, gas, and bloating that occurs often. Having a feeling that your guts have not been totally emptied [15].

1.3.6. Atezolizumab [16]

- It is used for bladder cancer.

Adverse effect of Atezolizumab:

I. Bladder pain.
II. Chest tightness.

III. Difficulty in breathing.
IV. General feeling of tiredness and weakness.
V. Headache.
VI. Muscle aches.
VII. Nosebleed

1.3.7. Caprelsa (Vandetanib)

- It is used for Thyroid cancer.

Nausea, loss of appetite, taste changes, dry mouth, stomach discomfort, vomiting, diarrhoea, headache, or impaired vision are all possible side effects [17].

1.3.8. fluorouracil (5-FU)

- It is used for skin cancer.

At the application site, skin irritation, heating, redness, drying, discomfort, swelling, tenderness, and changes in skin colour may occur. Eye irritation (stinging, watering), insomnia, irritability, transient hair loss, and an odd taste in the mouth are all possible side effects [18].

1.4. Herbal drugs

Ayurveda, is a traditional Indian medical system based on plant medications, has proven effective in employing these natural remedies to prevent or inhibit malignant tumours using diverse lines of therapy since ancient times. Peoples of various ethnic group inhabiting different trainings in India have their own religious, culture, traditions, culinary habits, and wealth of traditional medicinal expertise [19]. They use herbal medicine to treat a wide range of ailments. For thousands of years, natural goods, particularly plants, have been utilised to cure a variety of ailments. From ancient times, traditional plants have already employed used medicines throughout [Egypt, India, China, and Greece] and a large numbers of contemporary pharmaceuticals had produced from their. Around 2600 BC, the Sumerians and Akkaidians wrote the earliest written documents on the medical benefits of plants [20]. The Institute Of Medicine has analysed roughly 114,000 extract for anticancer potential after collecting 35,000 plants from 20 nations. Over 3000 plant species having antitumor activities have been identified. Cancer is among the most common illnesses in humans, and

the ongoing identification of novel anticancer medicines using natural product sources is of great scientific and economic importance [21].

Chemoprevention is a well-known method of cancer control, and current research has concentrated on the development of new chemopreventive drugs. Natural materials, especially dietary components, have been crucial in the development of novel chemopreventive medicines. Differential cytotoxicity patterns have been linked to recognised classes of chemicals such as cardenolides, lignans, and quassinoids [22]. A concept based upon ethnobotanical & ethnopharmacological information may be more cost-effective & advantageous of finding possible anti-cancer compounds screening plant species in any cancer medication research effort. Natural products have long been thought to be key sources of potential chemotherapeutic drugs, and a number of anticancer treatments have originated from these sources. [23]

Over half of the medicines under clinical studies for anticancer characteristics, as per Cragg and Newman, were obtained from natural sources and are linked to them. Several plant-derived natural compounds have the potential to be used as chemotherapeutic medicines. Podophyllotoxin, taxol, vincristine, and camptothecin are some of the presently utilised anticancer drugs originating from plants. The use of medicinal plant products of drug discovery is most prevalent in the fields of cancer as well as infectious disorders. Natural-source anticancer and anti-infectious medications account for 60% and 75% of FDA-approved anticancer and anti-infectious pharmaceuticals, respectively [24]. Many in vitro and in vivo approaches to assess the effectiveness of natural anticancer drugs, whether they are pure chemicals or plant extracts. The most often used in vitro techniques for testing the anticancer properties of natural substances produced from medicinal plants include the Tryphan blue dye exclusion test, the LDH (Lactic dehydrogenase) test, the MTT assay, the XTT assay, and the Sulforhodamine B assay. MTT or Sulforhodamine B assays are the most widely used in vitro techniques for assessing anticancer activity [25].

2. TYPES OF CANCER

2.1. Carcinoma

The epithelial cell membrane that forms the lining of exterior parts of the body and the interior linings of organs inside the body gives rise to this kind of cancer.

Carcinomas, or cancers of epithelial tissue, accounting for 80 to 90% of all cancer occurrences because epithelial tissues are located throughout the body, from the skin to a covering as well as coating of organs including internal passages like the gastrointestinal system as shown in below figure (Figure 1) [26].

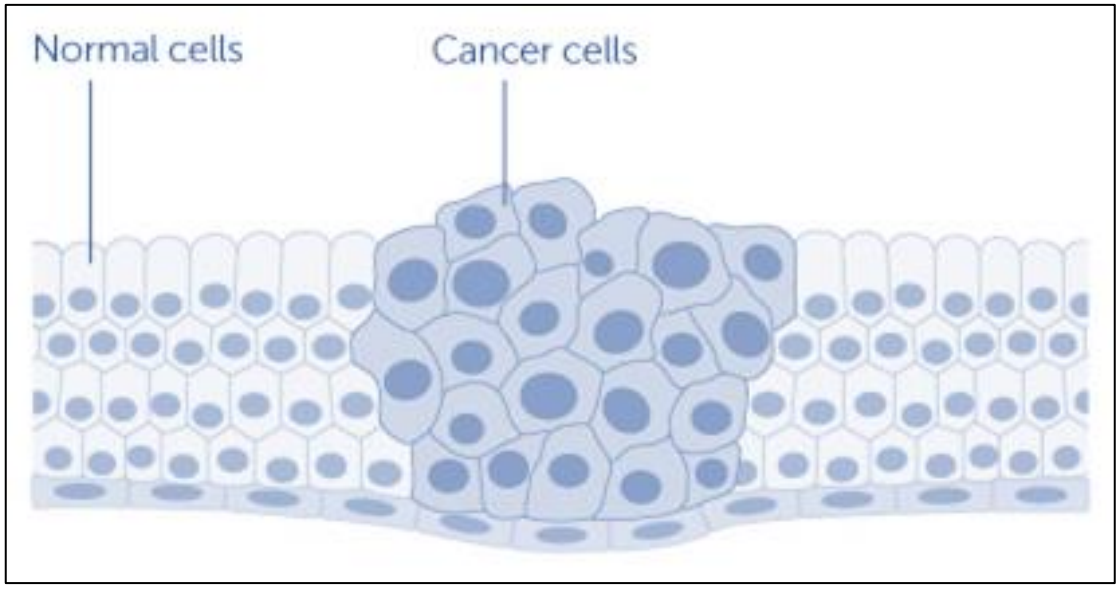

Figure 1: Diagrammatic representation of Carcinoma

Cancers most often occur in secreting organs or glands, such as the lungs, breast, bladder, colon, & prostate. Adenocarcinoma or squamous cell carcinoma are the two forms of carcinomas. Squamous cell carcinoma arises in the squamous epithelium and adenocarcinoma occurs in an organ or gland. Adenocarcinomas may damage the mucus membranes and appear as a thicker plaque-like white mucosa at first. These are malignancies that are fast spreading [27].

2.1.1. Pathophysiology

They're said to be the outcome of a number of things, including: Factors that run-in families. Asbestos, cigarette smoke, radiation, and industrial chemicals are all carcinogens. Viruses such include the human papillomavirus (HPV), hepatitis, and the Epstein-Barr virus [28].

2.2. Sarcoma

These cancers develop from tumours that grow in the body's connective and supporting tissues, such as muscles, bones, cartilage, and fat. Osteosarcoma is a kind of sarcoma that

appears in the skeletal system. Young people are the ones that suffer the most as a result of this. Sarcomas take on the appearance of the tissues from which they arise.

Chondrosarcoma (cartilage cancer), leiomyosarcoma (smooth muscle cancer), rhabdomyosarcoma (skeletal muscle cancer), Mesothelial sarcoma and mesothelioma (membranous wall of the body cavities), Fibrosarcoma (fibrous tissues), Angiosarcoma and hemangioendothelioma (blood vessel cancer), Glioma (mixed connective tissue types) [29]

.2.2.1. Pathophysiology

DNA mutations are frequent in soft tissue sarcomas. However, they are more often acquired throughout life than inherited before birth. Mutations may be acquired as a consequence of radiation or cancer-causing substances. The majority of sarcomas develop for no obvious cause [30].

2.3. Myeloma

These are made in the bone marrow's plasma cells. In response to infections, plasma cells may produce a variety of antibodies. Myeloma is a form of cancer that affects the blood [31].

2.3.1. Pathophysiology

Multiple myeloma is just a plasma cell cancer that causes osteolytic bone lesions to form frequently. The increase in activity of osteoclasts which occurs beside multiple myeloma cells and cause bone loss in multiple myeloma patients [32].

2.4. Leukemia

This is a comprehensive list of the many types of cancer that fall under the broad category of "blood cancers." The bone marrow, which produces new blood cells, is the primary target of many tumours. An overabundance of immature white blood cells is produced when cancer spreads to the bone marrow. These immature white blood cells are unable to carry out their usual functions, leaving the patient vulnerable to infection. [33].

2.4.1. Pathophysiology

A clone of malignant cells may emerge at any point in the evolution of leukemias, regardless of the leukemia's kind. DNA rearrangement seems to be involved in these situations even though the source of clonal proliferation is mostly unknown. [34].

Examples of leukaemia types:

• Acute myelocytic leukaemia (AML) is a juvenile leukaemia that affects both myeloid or granulocytic white blood cell types.

• Chronic myelocytic leukaemia (CML) is a kind of leukaemia that develops in adults.

• Acute lymphoblastic, lymphocytic, or lymphoblastic leukaemia (ALL) – Acute lymphoblastic, lymphocytic, or lymphoblastic leukaemia (ALL) is a cancer of a lymphoid and lymphocytic blood cell types that affects children and young adults.

• CLL (chronic lymphocytic, lymphocytic, or lymphoblastic leukaemia) is a kind of leukaemia that affects the elderly.

• Polycythemia vera, also known as erythremia, is a malignancy that affects a variety of blood cell components, with a focus on red blood cells [34].

2.5. Lymphoma

Lymphocytic malignancies refer to tumours of the lymphatic system. Lymphomas, on the other hand, are "solid malignancies," while leukemias are "liquid tumours" that affect the blood. These may have an impact on lymph nodes in specific locations such the stomach, brain, and intestines. Extranodal lymphomas are a kind of lymphoma that arises outside of the lymph nodes. [35].

2.5.1. Pathophysiology

The majority of lymphomas are nodal, with bone marrow or peripheral blood involvement varying. In up to 50% of children and roughly 20% of adults with certain kinds of non-Hodgkin lymphoma, a leukemia-like appearance with peripheral lymphocytosis including bone marrow involvement may be seen [36].

2.6. Mixed types

There are two or more cancer components in these. Mixed mesodermal tumour, carcinosarcoma, Aden squamous carcinoma, and teratocarcinoma are only a few examples. Another form that incorporates embryonic tissues is blastomas.

Mixed malignancies arise when two distinct kinds of cells by one or more groups coexist. Myeloma: This kind starts from plasma cells which circulate in the blood and is often seen in the bone marrow [37].

3. TREATMENT

3.1. Biomarker testing

It is possible to identify cancer-related genes, proteins, and other substances by conducting a biomarker test (also known as biomarkers or tumour markers). Biomarker testing may be able to assist you and your doctor in determining the most successful course of treatment for your particular kind of cancer. [38]

3.2. Chemotherapy

Chemotherapy is a type of cancer treatment in which chemicals are used to destroy cancerous cells. It's important to learn about chemotherapy's role in cancer treatment and how it interacts with other cancer therapies. [39]

Drug used in chemotherapy:

- Altretamine
- Busulfan
- Carmustine
- Clofarabine

3.3. Treatment with hormones

Breast and prostate cancers, which rely on hormones to grow, may be treated with hormone therapy, which slows or stops their progression. Learn about the many types of hormone therapy and the potential side effects that they may have. [40]

Drug used in hormone therapy:

- Anastrozole (Arimidex)
- Exemestane (Aromasin)
- Fulvestrant (Faslodex)
- Goserelin (Zoladex)

3.4. Hyperthermia

Hyperthermia is a treatment approach that kills or eliminates cancer cells while causing little or no harm to healthy tissue. This is performed by heating the biological tissues of the patient to temperatures of up to 113 degrees Fahrenheit. Learn more about the many forms of malignancies which hyperthermia has been found to effectively cure, including precancers, how the therapy is administered, and the pros and cons of using it. [41]

Drug used: Dantrolene (Dantrium, Revonto, Ryanodex)

3.5. Immunotherapy in cancer

In order to help our body's immune system fight cancer, immunotherapy is a therapeutic option. This page discusses immunotherapy's many forms, their uses in cancer treatment, and what to anticipate at each step of the process. [42]

Drug used

- Ipilimumab [Yervoy]
- Pembrolizumab [Keytruda]
- Nivolumab [Opdivo]
- Atezolizumab [Tecentriq]

3.6. Photodynamic therapy in cancer

A medicine that is activated by light is used in photodynamic therapy, which is used to eradicate cancer cells as well as other abnormal cell types. Gain an understanding of photodynamic therapy, including its mechanism of action, the types of tumours and precancers that it may cure, as well as the pros and downsides associated with this treatment. [43]

Drug used

- Porfimer sodium (Photofrin)
- Aminolevulinic acid

3.7. Radiation therapy

The administration of high doses of radiation to cancer cells as part of a cancer treatment is known as radiation therapy. The goal of radiation therapy is to kill cancer cells and shrink tumours. Discover the many types of radiation, the reasons why they occur, the possible adverse effects you may encounter, and other relevant information. [44].

Drug used

- Cetuximab
- Trastuzumab
- panitumumab

3.8. Stemcell transplants

Stem cell transplants are procedures that replace stem cells that have the potential to grow into blood cells. These transplants are performed on patients whose stem cells have been destroyed as a result of high doses of chemo and radiotherapy treatment. [45]

Drug used

- Cisplatin
- Filgrastim
- Fluconazole
- Ganciclovir

3.9. Surgery in cancer

Surgery is a method of treating cancer in which the cancerous tissue is removed from your body by a medical professional. Acquaint yourself with the many approaches that surgery may take in the cancer therapy, as well as the processes that you can anticipate experiencing before, during, and after the procedure. [46]

Drug used

- Neulasta.
- Ibrance.
- Opdivo.
- Zytiga

3.10. Targeted therapy

A treatment for cancer known as targeted therapy zeroes down on the alterations that are responsible for the growth, division, and dissemination of cancer cells. Find out how targeted therapy for cancer works and how to prevent the side effects that occur most often. [47]

Drug used

- Alemtuzumab
- Trastuzumab
- cetuximab

4. SIDE EFFECTS OF CANCER TREATMENT

It’s possible that cancer treatments and the disease itself might have unforeseen repercussions. A negative influence that a treatment has on normally functioning organs or tissues is what medical professionals call a side effect. Do not be afraid to voice any concerns or complaints that you may be experiencing. It is possible that you may get treatment from your medical team, and/or they may talk to you about ways to decrease such side effects so that you can feel better

Major side effects of cancer treatment:

- May cause Anemia
- Bleeding and Bruising (Thrombocytopenia) from body
- May cause Appetite Loss
- May suffer from Fatigue
- May causes Constipation
- May suffer from Diarrhea

- May cause Edema (Swelling)
- May cause Fertility Issues in Girls and Women
- May cause Fertility Issues in Boys and Men
- May show Flu-Like Symptoms
- May cause Hair Loss (Alopecia)
- May cause Memory or Concentration Problems
- May cause Mouth and Throat Problems
- May suffer from Nausea and Vomiting
- My cause Immunotherapy and Organ-Related Inflammation
- Suffer from Pain
- May cause Sexual Health Issues in Men
- May cause Sexual Health Issues in Women
- May cause Skin and Nail Change
- May suffer fromUrinary and Bladder Problems

Note: Remember that each person's experience with side effects will be unique, even if they are all undergoing the same sort of cancer therapy. [48]

5. HERBAL DRUGS

When treating cancer using allopathy or traditional medicine, the toxicity of chemotherapeutic drugs may be a significant problem that has to be addressed. Numerous therapies have been developed for the treatment of cancer, the majority of which make use of chemicals that are derived from plants. Four different kinds of plant-derived anticancer drugs are currently available on the market. These include vinca alkaloids (including vinblastine, vincristine, and vindesine), epipodophyllotoxins (including etoposide and teniposide), taxanes (including paclitaxel and docetaxel), and camptothecin derivatives (camptotecin and irinotecan). Despite this, plants hold a great deal of promise as a source of novel therapies since they are a reservoir of naturally occurring substances that have the potential to be chemopreventive against cancer. Taneja and Qazi have presented a number of different compounds that are produced from medicinal plants and that may have qualities that are anti-cancer. [39]

Figure 2: Herbs used in cancer treatment

In this article, we will discuss a few of the plant components that have lately been the subject of research and which show promise as possible cancer treatments. Some of them are shown in figure 2. Investigation is being conducted on the modes of action of such plant chemicals. [49]

5.1. Benefits of Herbal Medicine

For thousands of years, both traditional and alternative medicine have relied on herbal remedies. Modern medicine is built on the basis of herbal treatment. This drug also has a low incidence of natural side effects. Although herbal medications have several health benefits, they are generally disregarded in favour of standard pharmaceutical therapy, which is a shame. These days, herbal therapy is most often used to treat very serious and long-lasting conditions. [50].

- More affordable than conventional medicine
- Easier to obtain than prescription medicine
- Stabilizes hormones and metabolism
- Natural healing
- Strength in immune system
- Fewer side effects
- cost effective

Table 1: List of Indian medicinal plants used in cancer treatment and application

Sr. No.	Scientific name [family, vernacular name]	Parts used	Reported &Traditional reported uses	Reference No.
1	*Abrus precatorius* L. (Chanothi, Fabaceae)	Stem	Leucoderma, a condition of the skin, is the most common ailment.	[51], [52]
2	*Allium sativum* L. (Lasan, Liliaceae)	Peel	Anti-asthmatic, anticholesterolemic, antiseptic, antithrombotic, cancer, cholagogue, diaphoretic, and diuretic qualities	[53], [54]
3	*Alstonia scholaris* L. (Saptaparna, Apocynaceae)	stem	Antioxidant, diarrhoea, dysentery and treat malaria	[55], [56]
4	*Andrographis paniculata* Burn.f. (Kariyatu, Acanthaceae)	Aerial parts	Hepatoprotective, antifertility Antifertility, antihepatotoxic, antiplatelet, aggregation, antihyperglycaemic, antioxidant anti-inflammatory, and antimalarial are names used to describe medications with these effects.	[57]
5	*Annona reticulate* L.	leaves	Antioxidant, antidysentric	[58], [59]

	(Ramfal, Annonaceae)			
6	*Asparagus racemosus* Willd. (Shatavari, Liliaceae)	Root	Ulcers of the stomach, dyspepsia, inflammation, and illnesses of the liver, as well as antioxidant	[60], [61]
7	*Azadirachta indica* Juss. (Neem, Meliaceae)	Leaves	Anti-inflammatory, anti-ulcer, anti-malarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic, and anticarcinogenic activities	[62], [63]
8	*Bacopa monniera* L.(Brahmi, Scrophulariaceae)	Whole plant	Mental disorders, tumors, ascites, antioxidant and inflammation	[64]
9	*Bauhinia variegate* L. (Kanchhanar, Caesalpiniaceae)	Stem	Antibacterial, antifungal, and antioxidant properties are used to treat bronchitis, leprosy, tumours, and ulcers.	[65]
10	*Berberisvulgaris* L. (Barberry, Berberidaceae)	Rootbark	Diseases of the urinary system, gastrointestinal tract, gallbladder, liver and leishmaniasis	[66]
11	*Beta vulgaris* L. (Beet, Chenopodiaceae)	Juice	Leukemia, antioxidants, and cancers of the breast, oesophagus, glands, head, intestines, and leg	[67], [68]

12	*Bidens pilosa* L. (Shemaro, Asteraceae)	Whole plant	Urinary tract infections (UTI), hepatitis, and wounds may all benefit from antioxidants	[69], [70]
13	*Calycopteris floribunda* Lam. (Bukshi, Kokaranj Combretaceae)	leaves	Colic, antihelminthic, astringent laxative, diarrhoea and malaria	[71]
14	*Catharanthus roseus* L. (Sadabahar, barmachi Apocynaceae)	Root,Leaves	Anti cancer, menorrhagia and antioxidant	[72]
15	*Cedrus deodara* G. Don (Devdaar, Pinaceae)	Wood	Astringent, antioxidant, antidiarrhoeal febrifuge, and antiseptic.	[73]
16	*Citrullus colocynthis* L. [Indrayan, Cucurbitaceae]	Leaves	Beneficial benefits on the body's cells and organs as well as its cardiovascular and hepatic systems, antioxidants, and blood sugar levels	[74]
17	*Crocus sativus* L. [Kesar, Iridaceae]	Stigmas	Antioxidant properties	[75]
18	*Curculigo orchioides* Gaertn. (Kalimusli, Amaryllidaceae)	Root	Antioxidant, diarrhoea, jaundice, asthma, and itch and skin disease poultice	[76]
19	*Curcuma longa* L. (Haldi, Zingiberaceae)	Rhizomes	Antimutagenic, anticarcino- genic	[77]

20	*Cymbopogon flexuosus (*Steud.) Wats. (Lemon grass, Poaceae)	Grass	Stress-related disorders, antifungal and antimicrobial properties	[78]
21	*Emblica officinalis* Gaertn. (Amla, Euphorbiaceae)	Dry Fruits	Antimutagenic, antioxidant, and anticarcinogenic capabilities protect the liver.	[79]
22	*Ephedra sinica* Stapf (Ephedra, Ephedraceae*)*	Aerial Parts	Asthma, Colds, headaches, fever, flu,wheezing, and nasal congestion are all common ailments.	[80]
23	*Indigofera aspalathoides* (Vahl, Papilionaceae)	Stem	Antioxidant, various skin disorders and cancer	[81]
24	*Ipomoea aquatica* Forskal. (Kalmisag, Convolvulaceae)	Leaves	Antioxidant properties	[82]
25	*Ipomoea squamosa* (Cairo Morning Glory, Convolvulaceae)	Leaves	hypertension, dysentery, constipation, fatigue, arthritis	[83]
26	*Jatropha curcas* L. (Ratanjota, Huphorbiaceae)	Stem	Skin diseases, antioxidant, ulcers, tumours	[84]
27	*Lantana camara* L.	Dry fruits,Leaves, Root,Stem	Antitumoral,antioxidant ,	[85]

	(Ghaneri, Verbenaceae)		antibacterial and antihypertensive	
28	*Mangifera indica* L. (Keri, Anacardiaceae)	Flower,Bark,Leaves	Antitumour, antioxidant, antiviral, antibacterial, analgesic, antiinflammatory, antidiarrhoeal, antiamoebic, spasmolytic, immunostimulant and immunomodulatory properties	[86]
29	*Melia azedarach* L. (White Cedar, Meliaceae)	Leaves	Antiparasitic activity, anthelmintic activity	[87]
30	*Morinda citrifolia* L. (Noni, Rubiaceae)	Root, Flower	Antidiabetic, antiviral, antibacterial, anticancer and antioxidant	[88]
31	*Moringa oleifera* L. (Saragavo, Moringacae)	Stem	Antioxidant, antimicrobial, antigenotoxic and antiinflammatory activities	[89]
32	*Nigella sativa* L. (Black seeds, Ranunculaceae)	Stem	Antioxidant, antidiabetic, antihistaminic, antiepileptic, antiinfective, antitumor, and antiperoxidative properties	[90]
33	*Ocimum gratissimum* L.	Stem,Leaves	Chemoprevention, anticarcinogenicity,	[91]

	(Damro, Lamiaceae)		radioprotection, and a variety of additional pharmaceutical applications	
34	*Ocimum sanctum* L. (Tulsi, Lamiaceae)	Leaves	Properties such as anti-stress, antioxidant, hepatoprotective, anti-inflammatory, antibacterial, and radioprotective	[92]
35	*Phellinus rimosus* (Berk, (Hymenochetaceae)	sporocarps	Antioxidant	[93]
37	*Polyalthia longifolia* Benth. & Hook. f. (Annonaceae)	Leaves	Antibacterial and antifungal activities	[94]
38	*Psidium guajava L.* (Jamphal, Myrtaceae)	Leaves	Antioxidant	[95]
39	*Punica granatum* L. (Dadam, Lythraceae)	Juice,Peel	Antioxidant and antiinflammatory	[96]
40	*Tragia involucrata* Linn. (Euphorbiaceae)	Aerial parts	Antimicrobial, antiinflammatory, antifertility activity	[97]
41	*Rubia cordifolia* L. (Manjistha, Rubiaceae)	Root	Antitumor, antioxidant, anti-inflammatory, urinary problems, anti-stress, anti-microbial, hepatoprotective, and	[98]

			radioprotective properties	
42	*Semecarpus anacardium* L. (Bhallika, Anacardiaceae)	Dry fruits	Antioxidant, immunostimulant, antiinflammatory, analgesic, antipyretic, and ulcerogenic properties	[99]
43	*Tephrosia purpurea* Pers. (Sarapunkha, Fabaceae)	Root	Various inflammatory, liver, spleen, and renal problems, as well as antioxidant deficiencies	[100]
44	*Terminalia chebula* Retz. (Karakkaya, Combretaceae)	Flower	Diabetes, colic pain, chronic cough, sore throat, asthma, antioxidant, and antiinflammatory	[101]
45	*Tiliacora racemosa* Coleb. (Tiliacoru, Menispermaceae)	Root	anticancer activities against human cancer cell.	[102]
46	*Tinospora cordifolia [*Willd.] Hook. f. & Thom. [Guduchi, Menispermaceae]	Stem	Antioxidant, antiinflammatory, antiarthritic, antiallergic, antimalarial, antidiabetic, and aphrodisiac activities.	[103]
47	*Viscum album* L. (Vando, Viscaceae)	Leavs	Nervine, hypotensive, myocardial depressant, antioxidant, vasodilator, relaxant, diuretic, and	[104]

			stimulant are all examples of drugs.	
48	*Withania somnifera* L. (Ashwagandha, Solanaceae)	Root	Radiosensitizer, anti-oxidant, anti-stressor, immunomodulatory, anti-inflammatory, and anti-bacterial	[105]
49	*Woodfordia fruticosa* Salisb. (Dhavdi, Lythraceae)	Flower	Fever, inflammation, liver protection, and antibacterial characteristics are all active.	[106]
50	*Zingiber officinale* Rosc. (Adu, Zingiberaceae)	Rhizomes	Carminative, antispasmodic, diuretic, expectorant, astringent, increases appetite, reduces inflammation, diuretic, and digestive.	[107]

6. **Herbal medications with anticancer properties have been used in clinical trials.**

6.1. For breast cancer

- Coumarins: Inhibition of cancer cell growth
- Vitamin A (Fenretinide): In premenopausal women,(200mg/day)dramatically decreases locally advanced breast cancer returning after treatment.
- Vitamin E: In cancer patients, it causes malabsorption or maldigestion; a balanced and nutritious diet is recommended.
- Isoflavone: Reduce risk of breast cancer
- Genistein and daidzein are isoflavones that have weak estrogenic effects.
- Alkaloids : Cancer cell growth inhibition

- Flavonoids and polyphenols: Antiproliferation
- Quinone:Inhibiting AKT/rapamycin in breast cancer cells induces G2-M arrest and autophagy..
- Artemisunate: Reduce breast cancer cell growth. [108].

6.2 Prostate cancer

- Prevents metabolic diseases by maintaining homeostasis - Vitamins A, D & retinoid
- Vitamin E: - Reduce fatal and advanced prostate cancer risk compared to nonusers
- EGCG: - Stop prostate cancer cells in G0-G1 phase
- Soy isoflavones: - Chemopreventive and 6α-reductase inhibiting
- Scutellaria baicalensis (baicalin): - Inhibit eicosanoids' enzymatic production.
- Baicalein: - Inhibit androgen-independent PC-3 and DU146 prostate cancer cell development. [109].

6.3 For lung cancer

- Platycodon grandiflorum (Campanulaceae): Used for anticancer treatment
- Morus alba (Moraceae): Anticancer impact in people with lung cancer
- Prunus armeniaca (Rosaceae): Used for anticancer treatment
- Rhus verniciflua (Anacardiaceae): Used for anticancer treatment
- Perilla frutescens (Labiatae): Used for anticancer treatment
- Stemona japonica (Stemonaceae): Used for anticancer treatment
- Tussilago farfara (Compositae): Used for anticancer treatment [110]

6.4 For the treatment of liver cancer and fibrosis

- Inchin-ko-to (TJ-136): Efficacy in preventing liver fibrosis
- Curcumin has an anti-fibrotic and anti-carcinogenic action on the liver.
- Hepatic fibrogenesis is inhibited by compound 861. [111]

6.6 For the treatment of cancer of the pancreas

- GDC-0449, IPI-926: SMO antagonists; deregulation of sonic hedgehog homology (SHH)

• Cyclopamine inhibits SHH signalling by attaching to the SMO protein's 7-helix bundle; it stops pancreatic tumour development. Reduces cancer cell BMPC recruitment formation of tumor vasculature [112]

7. Difficulties in Using Herbal Medicine in Cancer Treatment

In Europe and North America a growing number of people are turning to traditional medicinal plants, phytomedicines, therapeutic foods, & complementary and alternative therapies.

Over the last decade, they do not appear to have piqued mainstream medicine practitioners' interest or been accepted by western countries, particularly for standard cancer. Many biomedical experts are concerned about the lack of evidence or information and recommendations to the regular & regulated use as well as herbal remedies "pharmaceuticals" for public health. Six major issues prevent the use of phytomedicines: a lack of stable and accurate real medicinal plant sources, with regard to species identification and authentication, cultivation following good agricultural practises standards, and standardized/normalized methodologies and procedures for plant filtration preparation are all included., an inability to concepts as well as routine time to prepare of the physiochemical ingredients [113]. We won't be able to handle the difficulties of modernising herbal medicines until we solve all of the aforementioned concerns. Despite the fact that researchers examined a broad range of research lab, pre - clinical, & case reports on the possible applications of natural supplements for cancer patients' care, the majority of these studies failed to meet its strict requirements and guidelines required for creating western style drugs and medicative food. As a consequence, our research community's researchers must engage in systematic and coordinated operations [114].

According to a core principle in modern western medicine, a drug should be made up of extremely well active compounds or a single pure molecule which selectively interact with the recognised & particular molecular target in the system of the body. It has been shown in many commercial medications {e.g. doxorubicin ,aspirin,} can bind & function in multiple molecular targets and thus in search of single molecules which may affect single or highly specific critical variables in disease process has become increasingly difficult and sometimes incorrect. A range of cell types, targeted substances, and/or signalling pathways are thought to be responsible for a number of illnesses. Herbal extracts/mixtures used in

traditional herbal remedies represent combinatorial chemistry, and are "thus claimed" to contain a wide range of chemical entities capable of conferring the complex and embedded effect on spectrum of the molecular characteristics & elements, results in profound and medication balance [116].

According to current FDA & NIH cancer clinical research rules of the United States, like "claims" sometimes to violate existing guidelines or directions. As a result, the shortage of defined molecular targets is a major drawback in integrating herbal drugs into conventional western medicine. An increasing number of omics studies have shown that the "typical" therapeutic agent has a multi-mode of action and multi-pharmacological activity. This is in response to this worry [116]. As a result, as per we previously discovered in tumour cell study, there should may be many less distinctions between single chemical treatments and complex medicinal plant extracts in terms of the quantity of molecular targets addressed than previously thought. As a result, we may conclude the "multi-target" approach and activity offered for varieties of herbal treatments is "rational and acceptable," and so should be considered and created in the creation of botanical drugs. The use of a meta-analysis approach to combine data from several trials might be a useful tool for evaluating the results for a series of studies that aren't conclusive [117].

The imprecise or poorly defined composition of herbal remedies also poses safety issues, since evidence shows that some extracts may interact dangerously with prescription pharmaceuticals. Optimizing CMC (chemistry, manufacturing, and controlling) parameters of each herbal preparation would have to considered as a vital technology to verifying & standardising the parts of certain medicinal herbs and how they work to address the upcoming challenge. A sequence approach (fingerprint analysis) is a good strategy for evaluating the integrated and comprehensive characteristics of test herbal medicines because it allows us to compare the resemblances and differences as well as co-relation of results from analysis of the entire production steps, including the preparation of raw materials, intermediate goods, finished goods and distribution of finished products. [118] [116].

Even if individualised treatment becomes increasingly widespread, "new drugs" may be administered to the majority of patients with the same condition. It is common for traditional herbal remedies to use plant extracts that contain a wide range of phytocompounds, which

are considered to have a variety of medical effects [119]. In order for herbal medications to be used in cancer treatment, the assessment of "real" active ingredients and its targets for so many different reasons is a big roadblock. Aside from their apparent differences in pharmacological underpinnings, traditional herbal remedies and contemporary chemical drugs may have certain underlying pharmacological foundations. Several kinds of herbal medicine have a structural substructure in common, which might explain their effectiveness in similar target populations. The most important indicator for medicinal chemist in categorising & looking for new pharmacological actions, as well as refining herbal drugs, will be these structures and their activity information. [120], [121].

8. CONCLUSION

In both industrialised and developing nations, cancer is a serious public health issue. Compounds' ability to delay, stop, or reverse carcinogenic growth is known as their "anticancer activity." Plant-derived chemotherapy therapies are being investigated as a possible alternative to man-made medications for treating the sickness. As a result, a study of several in vitro & in vivo approaches to assessing the anti-cancer capabilities of natural chemicals produced from medicinal herbs has been undertaken. An in-depth analysis of 60 India anti-cancer medicinal herbs origin from 36 families is presented in this study. This includes information on the component (s), extract (s), model (s), cancer cell lines studied, and so on. Sarcoma, lymphoma, carcinoma, and leukaemia are just a few of the cancers for which these herbs are still used. There is strong anticancer activity in vitro for each of these plants, which makes them potential candidates for in vivo investigation.

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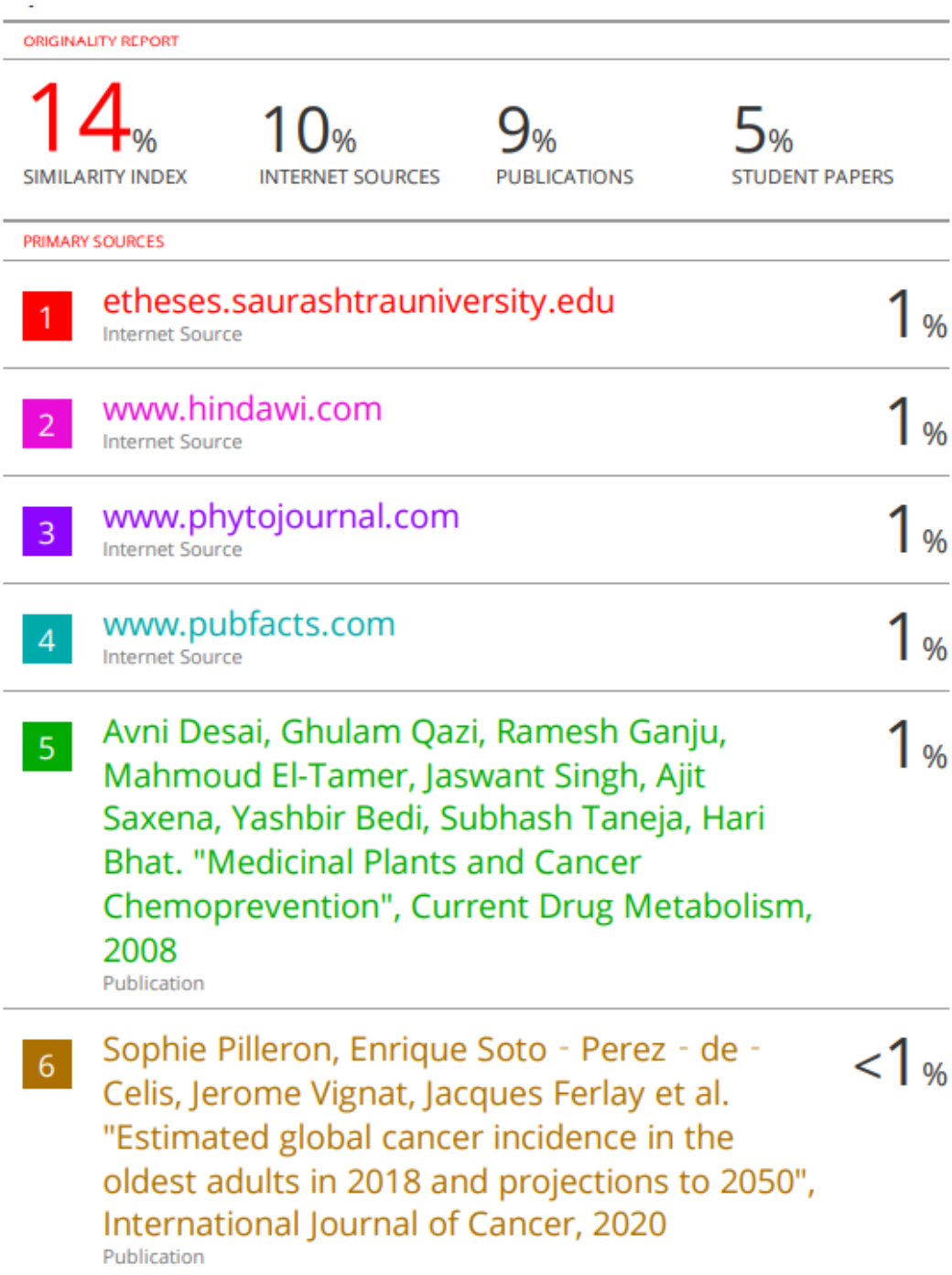

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