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Review Article

Review on anti-cancer herbal drugs

Shital Tiware[1,*], Komal Khond Warghane[2], Prasad Makde[1], Harshal Yeskar[1]

[1]*Dept. of Pharmaceutical Chemistry, Kamla Nehru College of Pharmacy, Nagpur, Maharashtra, India*
[2]*Dept. of Prosthodontics, VYWS Dental College and Hospital, Amravati, Maharashtra, India*

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ABSTRACT

One of the most important health issues facing humanity, cancer is a scary disease that demands a proactive approach to treatment. Plants, a source of novel chemical entities and a promising topic for cancer research. Despite its success, chemotherapy has so far had some unfavourable side effects. However, the use of plants and products generated from them is revolutionising the field as a simple, secure, cost-effective, time-saving, environmentally friendly, and less hazardous alternative to traditional treatment procedures. Phytochemicals have selective activities that are targeted towards tumour cells. The complex process known as carcinogenesis involves a number of signalling cascades. Phytochemicals are thought to be attractive prospects for the development of new therapeutics because of their pleiotropic effects on the target event in a number of ways."

Researchers are looking at which of these phytochemicals might be possibilities for inhibiting or reducing the growth of cancer cells without causing any unfavourable side effects. There are a lot of phytochemicals and the analogues they were made from that have been identified as potential anticancer therapeutic possibilities. An effort has been made to highlight the most recent developments and noteworthy accomplishments in phytomolecule-based cancer therapies that target nuclear and cellular components through this succinct overview.

1. Introduction

Uncontrolled cellular proliferation within the body is cancer. It can be debatable whether or not common plants, herbs, and foods can act as anticancer agents. About 35000 plant species have been examined by the National Cancer Institute (NCI) for their powerful anticancer properties.[1] One will only believe in the benefits of chemotherapy for every person who thinks that plants and herbs can weaken or even destroy cancer cells. Here is a list of herbs and medicinal plants that have been the subject of scientific research and have shown promise in the fight against cancer, even though there is still more to be done in this field.[2]

2. Cancer

Essentially, uncontrolled cell division is what causes cancer. Numerous mechanisms exist in cells to regulate cell division, repair DNA damage, and prevent the spread of cancer. It is believed that cancer develops in a multistep process because several processes must fail before a critical mass is reached and cells become malignant. These changes promote their multiplication, proliferation, and tumour development. For instance, cancer cells can induce the growth of new blood arteries (angiogenesis), which provides oxygen and nutrition to tumour cells, and spread throughout the body through a process called metastasis. Additionally, cancer cells do not undergo apoptosis, or programmed cell death, when normal cells would (for example, because of

* *Corresponding author*.
E-mail address: tiwareshital@gmail.com (S. Tiware).

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DNA damage)

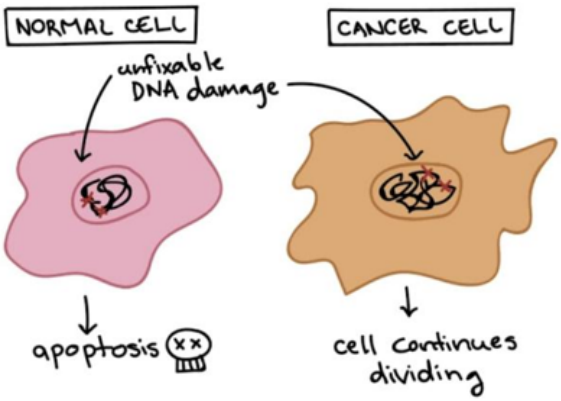

Fig. 1: Diagram shows different responses of normal and cancer cells to conditions that would typically trigger apoptosis.

Additionally, new research indicates that cancer cells may experience metabolic alterations that encourage enhanced cell growth and division (see Figure 1 for details), which contrasts how normal and cancer cells react to conditions that would ordinarily cause apoptosis:

1. A normal cell that has DNA damage that cannot be repaired and will die.
2. A cancer cell that has irreparable DNA damage won't go through apoptosis; it will keep dividing. [1]

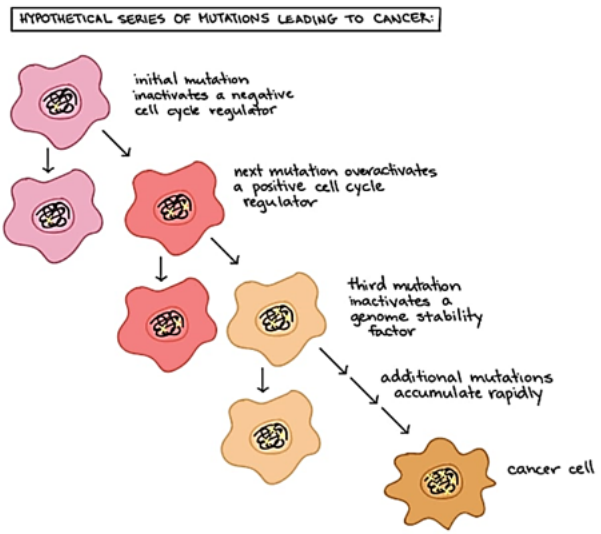

Fig. 2: Mutations leading to Cancer

An unfavourable cell cycle regulator is rendered inactive by an early mutation. A new mutation results in an overactive positive cell cycle regulator. One of the offspring of this second cell experiences a third mutation that renders a part of the genome stability inactive. Once the genome stability factor is off, more mutations quickly build up in the cell's offspring. [1] When a sufficient number of mutations affecting essential processes are present, the cell with the mutations develops malignant characteristics and is referred to be a cancer cell. By 2030, there will likely be 21 million new cases of cancer worldwide, making it one of the main causes of death. [3,4]

3. Pharmacologically Active Anti-Cancer Herbal Plants

With mounting scientific evidence from biological research and clinical trials, herbal medicines are being embraced more widely as complementary and alternative therapies for the treatment of cancer. The history of anti-cancer medications derived from herbal remedies is extensive, and some of them have been applied in clinical settings in place of traditional anti-cancer medications. Actually, the development of anti-cancer drugs has been aided by the study of herbal remedies. In order to produce novel anti-cancer therapies in single pure molecules, research has recently continually focused on cues from the traditional use of herbal remedies.

4. WHO Guidelines

The WHO established guidelines for standardizing herbal drugs and focused on present and future trends of methods used for analysis of herbal drugs for such as:

1. Quality control of raw drug materials, plant preparations and finished products.
2. Evaluation of stability and shelf life
3. Safety assessment and documentation based on toxicological studies or experience
4. Evaluating biological activity and ethno medical data to determine effectiveness. The chromatographic fingerprints and active principal or major compounds should be used to standardize bioactive extract.

About 35,000 plant species have received approval from the National Cancer Institute [NCI] for possible anticancer properties. One person will solely believe in the benefits of chemotherapy, while another will think that herbs and plants can actually delay or even kill cancer cells. Here is a list of herbs and medicinal plants that have been the subject of scientific research and have shown promise in the fight against cancer, even though there is still more to be done in this field. [5]

Table 1:

Sr. No.	Name of the Plant [1,2,6]	Common Name
1.	Allium sativum	Garlic
2.	Aloe barbadensis Miller	Aloe Vera
3.	Beta vulgaris	Beet
4.	Digitalis purpurea	Digitalis
5.	Glycyrrhiza glabra	Liquorice
6.	Hydrastis canadensis	Orangeroot, Goldenseal root
7.	Trifolium pratense	Red Clover
8.	Inonotus obliquus	Chaga Mushroom
9.	Lycopersicum esculentum	Cherry Tomato
10.	Curcuma longa	Turmeric
11.	Crocus sativus Linn	Saffron
12.	Camptotheca acuminate	Chinese Happy Tree
13.	Cardus marianus	Dudhpatra
14.	Berberis vulgaris	Barberry
15.	Vitis vinifera	Grapes

Fig. 3: Garlic

Synonyms	:	Allium sativum , alliaceous plant
Biological Source	:	The leaves and cloves having medicinal importance are obtained from A. sativum.
Family	:	Liliaceae
Chemical Constituents	:	Garlic contains diverse bioactive compounds, such as allicin, allin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and S-allyl-cysteine. [7]
Uses	:	Garlic seems to detoxify chemical carcinogens and prevent carcinogenesis and can also directly inhibit the growth of cancer cells. [7]

Fig. 4: Aloe vera

Synonyms	:	Kumari , Korphad
Biological Source	:	Aloe is the fresh latex of leaves of Aloe barbadenis Miller.
Family	:	Liliaceae (Asphodelaceae)
Chemical Constituents	:	Aloe contains a mixture of crystalline glycosides known as aloin 4-5% in cape Aloe 18-25% in Curacao Aloe, Resin (16-37%), emodin and volatile oil. It also possess the anthraquinonei glycoside like barbaloin (aloe-emodin anthrone C-10 glucoside), Chrysophanic acid, B-barbaloin and Iso-barbaloin. [8]
Uses	:	Acne treatments, burns, or skin irritations, anthraquinone death amount human bladder cancer cells, hepatocellular carcinoma, etc. [9]

Fig. 5: Beetroot

Synonyms	:	Beta vulgaris, Common Beet
Biological Source	:	It consists of fresh roots of Beta vulgaris.
Family	:	Amaranthaceae
Chemical Constituents	:	It consists of multiple biologically active phytochemicals including betalains (e.g., betacyanins and betaxanthins), flavonoids, polyphenols, Saponins and inorganic Nitrate; is also rich source of diverse minerals such as potassium, sodium, phosphorous, calcium, magnesium, copper, zinc and manganese. [10]
Uses	:	In recent study, betavulgarin, isolated from beetroot was found to suppress the growth, migration, colony formation, and mammospherei formation in breast cancer. [11]

Fig. 6: Digitalis

Synonyms	:	Digitalis purpurea , Foxglove-Flower
Biological Source	:	It is obtained from the herbaceous plant of Digitalis purpurea.
Family	:	Scrophulariaceae
Chemical Constituents	:	Contains three important primary glycosides namely Purpurea glycoside A, Purpurea glycoside B, and Purpurea glycoside C, which upon hydrolysis gives rise to digitoxini, gitoxin, and gitalin, respectively. Gitoxigenin and gitaligenin, tannins, gallic, formic, acetic, succinic and benzoic acids, fatty acids and enzyme digipuridase solely responsible for hydrolysis of purpurea glycosides. [11]
User	:	Strong antitumor possibilities. A study performed in Spain in 2003 look at the cytotoxic activity from the leaves of the strain purpurea against human cancer cells. [11]

Fig. 7: Liquorice

Synonyms	:	Glycyrrhiza glabra , sweet wood
Biological	:	Liquorice consists of peeled and unpeeled roots, stem of Glycyrrhiza glabra Linn.
Family	:	Fabaceae [Leguminosae]
Chemical Constituents	:	Glycyrrhizine (6-8%) [Sweet Instant 50 times more than sugar]. Liquiritin and isoliquiritin are responsible for yellow colour. Glucose, sucrose, asparagin, gum, protein, fats, resins, traces of tanins. Glycyrrhizinic acid are produces glycyrrithilnic acid and glycyrrhitic on hydrolysis. [12]
Uses	:	Liquorice and its derivatives may protect against carcinogen-induced DNA damage and may be suppressive agents as well. [12]

Fig. 8: Goldenseal root

Synonyms	:	Eyebalm, Ground Raspberry, Orangeroot , Yellowroot, Yellow puccoon, Indian Dye, Jaundice root
Biological Source	:	It obtained from perennial herb in buttercup (Hydrastis Canadensis)
Family	:	Rannuculacae
Chemical Constituents	:	The active ingredient of goldenseal include isoquinoline alkaloids, such as berberin 0.5-6 % , canadine, hydrastine 1.5-4% , berberastine 2-3%
Uses	:	Improve gut and gastrointestinal tract(GI) health, relief from sinus conditions, healing of skin ailments, protection for the liver, reduce the risk of cancer, effective against urinary tract infections (UTI). [6]

Fig. 9: Red clover

Synonyms	:	Purple Clover, Trifolium Pratense
Biological source	:	It is a herbaceous species of flowering plant of Trifolium Pratense
Family	:	Fabaceae
Chemical Constituents	:	Calcium, Chromium ,Magnesium, Manganese, Iron, Niacin, Phosphorus, Potassium, Protein, Riboflavin, Selenium, Silica, Thiamine, Vitamin A, Vitamin C, Zinc, Coumarins, Saponins, Isoflavones.
Uses	:	The University of Maryland Medical Center found that Red clover help to prevent breast cancer, other use as Bowel Regulatory, Immune System. [13]

Fig. 10: Chaga mushroom

Synonyms	:	Inonotus obliquus
Biological Source	:	It grows on Birch trees throughout the northern hemisphere. It often resembles a dark clump of dirt but has bright orange tissue beneath its exterior.
Family	:	Hymenochaetaceae
Chemical Constituents	:	It consists of Inotodiol, Betulin, Betulinic acid, Trametenolic acid, Melanin, Flavan, Beta-glucan, Lanosterol.
Uses	:	Inotodiol from Chaga exerted antitumor effects against cervical cancer cells. In some studies, chaga demonstrated selective apoptosis in tumor cells with no effects on healthy cells. (14)

Fig. 11: Cherry tomato

Synonyms	:	Lycopersicum esculentum , Love Apple
Biological Source	:	Cytotoxicity effect is effect is found in leaves of Lycopersicum esculentum.
Family	:	Solanaceae
Chemical Constituents	:	It is a good source of phenolic compounds (phenolic acids and flavonoids), carotenoids (lycopene, α, and β carotene), Vitamins (ascorbic acid and vitamin A) and glycoalkaloids (Tomatine)
Uses	:	Methanolic extract of leaves of Lycopersicum esculentum shows cytotoxicity effects on cancer cells to address potential therapeutics in MCF-7 breast cancer cell line and toxicity towards Vero cells. [14]

Fig. 12: Turmeric

Synonyms	:	Curcuma longa, Haldi, Haridrai
Biological Source	:	It is a dried root obtained from the perennial plant of Curcuma longa
Family	:	Zingiberaceae
Chemical Constituents	:	Turmeric are three gold-colored alkaloid Curcuminoids: Curcumin, Dimethoxy-curcumin, and Bisdemethoxy-curcumin. 95% Curcuminoids, raw state (Turmeric is only 3-5% Curcuminoids). The Rhizome is 70% carbohydrates, 7% protein, 4% minerals, and at least 4% essential oils. It also has vitamins, other alkaloids, and is about 1% resins. (16)(17)
Uses	:	There are at least 20 molecules that are antibiotic. 14 molecules are known for cancer preventives. 12 molecules are anti-tumor. 12 molecules are anti-inflammatory.

Fig. 13: Saffron

Synonyms	:	Crocus, Spanish saffron, French saffron.
Biological Source	:	Saffron is dried stigma and styletops of Crocus sativus Linn.
Family	:	Iridaceae
Chemical Constituents	:	It contains number of carotenoids colored compounds such as ester of crocin (color glycosides), picrocrocin (colorless bitter glycoside), crocetin, gentibiose, α and β carotenes, crocin-II, lycopenea and zeaxanthin and safranal. It contains volatile oil, fixed oil and wax, etc.
Uses	:	Saffron contain a carotenoid compound called crocetin. The results of studies done, both in vivo and in vitro, show that this compound has the potential to be a strong anti-tumor agent. Saffron was found in another study to inhibit skin cancer in mice. [14,15]

Fig. 14: Chinese happy tree

Synonyms	:	Camptotheca acuminate, Camptothecin tree
Biological Source	:	Camptothecin [CPT] is an alkaloid extracted from the bark portion of the Chinese happy tree, Camptotheca acuminate.
Family	:	Nyssaceae
Chemical Constituents	:	The bark and stem contains alkaloid camptothecin. Derivatives of camptothecin including irinotecan, topotecan, rubitecan. It also contains trifolin and hyperoside
Uses	:	It is a quinolone alkaloid, used as chemotherapeutic agent in the treatment of leukemia.[16]

Fig. 15: Dudhpatra

Synonyms	:	Milk-Thistle-Flower, Marian Thistle, Mary Thistle, Cardus marianus.
Biological Source	:	It is obtained from the plant of Silybum marianum.
Family	:	Asteraceae
Chemical Constituents	:	Approximately 4-6 % silymarin (flavonolignan complex) 20-30% fatty acids silymarin is a complex mixture of polyphenolic molecule, including 7 closely related flavonolignans (silybin A , silybin B, isosilybin A, isosilybin B , silychristin, Isosilychristine , silydianin) and one flavonoid (taxifolin)[17]
Uses	:	Cirrhosis, jaundice, hepatitis, gallbladder disorders, other potential health benefits including protecting heart health by lowering cholesterol level and helping people manage Type 2 diabetes. The extract of seed coating of milk thistle has anti-cancer effect.[18]

Fig. 16: Barberry

Synonyms	:	European Barberry, Jaundice Berry, Oregon Grape
Biological Source	:	It is a fresh fruit obtained from plant of berberies vulgaries
Family	:	Berberidaceae
Chemical Constituents	:	The chief constituent of barberry bark is berberin, a yellow crystalline, bitter alkaloid, other constituents of berberies are oxyacanthine, berbamine, berberrubine, bervulcine, columbaminea, isotetrandine, jatorrhizine, palmitine, vulcracine, carbohydrates, organic acids , some vitamins, polyphenolic compounds, pectins, tannins, and mineral elements. The berries contain citric (vitamin C) and malic acids and possess astringent and antiscorbutic properties.
Uses	:	Adrenergic activity, anti-amoebic activity, anti-hypertensive activity, anti-inflammatory activity, anti-microbial activity and anti-neoplastic activity. (22)

Fig. 17: Grapes

Synonyms	:	Vitis vinifera, Angoor, Berry, Vine fruit
Biological Sources	:	It is fresh fruit obtained from the Vitis vinifera.
Family	:	Vitaceae
Chemical Constituents	:	Proanthrocyanidins (GSPs) fruits contains abundant carbohydrates (glucose) and organic acids (tartaric malic succinic, citric and oxalic acids). Seed contains 15-20% unsaturated fatty acids (phenylacrylic acid derivatives)
Uses	:	The fruits are vitaminics, tonics, anti-cancer, and hepatoprotective, promote hair growth and prevent ischemic processes. The seed oil: hypolipidermic, prevent the increase of vascular permeability.[19]

5. Conclusion

Around the world, cancer is the primary cause of mortality, expected to account for around 10 million deaths in 2020, or almost one in every six. The most prevalent malignancies are those of the breast, lung, colon, reticulum, and prostate. A third of cancer-related fatalities are attributed to factors including smoking, having a high BMI, drinking, eating few fruits and vegetables, and not exercising enough. About 30% of cancer cases in low- and lower-middle-income nations are caused by cancer-causing diseases such the human papillomavirus (HPV) and hepatitis.[16] If identified early and treated appropriately, many tumors are curable.

As a result, there is a huge need for a cancer treatment and prevention. Drugs made from chemicals have been created, and there are already certain cancer therapies available. Humans today enjoy a higher level of health, thanks to medicinal plants. The bioactive chemicals found in plant extracts that are responsible for their anticancer action must be evaluated for their useful information.[21,22] Some of the plants with anticancer properties for various cancer kinds were listed in this review. This review can

Table 2: List of some important medicinal plants and their phytochemicals against specific type of Cancer:

Sr. No.	Plant Name	Part Used	Phytochemical	Specific Cancer
1.	*Allium sativum*	Whole plant	Allin, Allylmercaptocysteine, Allicin	Carcinoma of human (mammary) gland, Lymphoma, Cervix Cancer.[7]
2.	*Aloe barbadensis Miller*	Whole plant	Aloesin, Emodin, Alexin B	Anti-angiogenic activity, Leukemia, stomach cancer,[8,9]
3.	*Beta vulgaris*	Roots	Betavulgarin	Breast cancer[10]
4.	*Digitalis purpurea*	Leaves	Cardenolide glycosides	HL-60 Leukemia[11]
5.	*Glycyrrhiza glabra*	Roots	Licochalcone-A, Licoagrochalcone	Prostate, breast, lung, stomach and kidney cancer[12]
6.	*Hydrastis canadensis*	Roots and leaves	Berberin	Prostate and Breast cancer[6]
7.	*Trifolium pratense*	Flowers	Isoflavones	Prostate and endometrial cancer[13]
8.	*Inonotus obliquus*	Whole body	Inotodiol	Cervical cancer[15]
9.	*Lycopersicum esculentum*	Leaves	Lycopene	Mammary cancer cell lines[14]
10.	*Curcuma longa*	Rhizome, Roots	Curcumin, Ascorbic Acid	Breast, Lung, Prostate, Oesophagus, Liver, Skin Cancer, Leukemia, Glioblastoma and colon adenocarcinoma[16,20]
11.	*Crocus sativus Linn*	Dry Stigmas	Crocetin	Hippocampal cell death and lung cancer[17,21]
12.	*Camptotheca acuminata*	Bark , Seeds	Camptothecin	Leukemia, Endocrine-resistant breast cancer[18])
13.	*Cardus marianus*	Seed	Silibinin, Silymarin	Prostate, Lung, Colon, Skin and Acute lymphoblastic leukemia[22]
14.	*Berberis vulgaris*	Root, Stem, Bark	Berberin, Cannabisin	Breast, Liver, Prostate, Colon cancer[23]
15.	*Vitis vinifera*	Seed, Fruit	Cyanidin, Procyanidins	Human colon cancer[19]

aid others in their future exploration of herbs and their application in toxicity and illness investigations in addition to clinical trials. Utilizing raw byproducts in industries and mass cultivating therapeutic plant species might both aid in conservation.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Shital Tiware, Assistant Professor

Komal Khond Warghane, Assistant Professor

Prasad Makde, Student

Harshal Yeskar, Student

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