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Herbs Used In Anti-Cancer Therapy

Pawar Sakshi Kiran kumar

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I. INTRODUCTION :

Cancer remains one of the leading causes of morbidity and mortality globally. Amongst the non-communicable diseases, cancer is the second leading cause of death, after cardiovascular disease. Cancer is responsible for one in eight deaths worldwide—more than AIDS, tuberculosis, and malaria together. Globally, the number of cancer deaths is projected to increase from 7.1 million in 2002 to 11.5 million in 2030.The Indian Council of Medical Research (ICMR) - National Centre for Disease Informatics and Research (NCDIR) - NCRP is a valuable data repository on cancer. According to a report by the Indian Council for Medical Research on the 'Burden of cancers in India', seven cancers accounted for more than 40% of the total disease burden: lung (10.6%), breast (10.5%), oesophagus (5.8%), mouth (5.7%), stomach (5.2%) liver (4.6%) and cervix uteri (4.3%).

Chemotherapy is routinely used for cancer treatment. Since cancer cells lose many of the regulatory functions present in normal cells, they continue to divide when normal cells do not. This feature makes cancer cells susceptible to chemotherapeutic drugs. Approximately five decades of systemic drug discovery and development have resulted in the establishment of a large collection of useful chemotherapeutic agents. However, chemotherapeutic treatments are not devoid of their own intrinsic problems. Various kinds of toxicities may occur as a result of chemotherapeutic treatments. [1].

The toxicity of chemotherapeutic drugs sometimes creates a significant problem in the treatment of cancer using allopathy or established medicine. Various therapies have been propounded for the treatment of cancer, many of which use plant-derived products. There are so many classes of plant-derived anticancer agents in the market today, the vinca alkaloids (vinblastine, vincristine and vindesine), the epipodophyllotoxins (etoposide and teniposide), the taxanes (paclitaxel irinotecan). Plants still have enormous potential to provide newer drugs and as such are a reservoir of natural chemicals that may provide chemoprotective potential against cancer. Recently, Taneja and Qazi, have suggested a number of compounds from medicinal plants with potential anti-cancer activities.

Plant compounds with anticancer properties

With successful clinical trials drugs being developed from plant origins are popular for clinical development. Their non-toxic effects on normal cells and their cytotoxic effects on cancer cells put them in high demand. A lot of the species investigated are selected from developing countries in Africa and Asia whereMedicinal plants have been used for thousands of years in folk medicines in Asian and African populations and many plants are consumed for their health benefits in developed nations. According to the World Health Organisation (WHO) some nations still reply of plant-based treatment as their main source of medicine and developing nations are utilising the benefits of naturally sourced compounds for therapeutic purposes [2]. Compounds which have been identified and extracted from terrestrial plants for their anticancer properties include polyphenols, brassinosteroids and taxols.

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a. Polyphenols

Polyphenolic compounds include flavonoids, tannins, curcumin, resveratrol and gallacatechins and are all considered to be anticancer compounds [3] Resveratrol can be found in foods including peanuts and grapes and red wine. Gallacatechins are present in green tea. It is thought including polyphenols in a person's diet can improve health and reduce risk of cancers by being natural antioxidants [3,4]The cytotoxicity of polyphenols on a range of cancer cells has been demonstrated and their antioxidant properties determined [3,5,6] Polyphenols are thought to have apoptosis including properties showing anticancer properties which can be utilized. The mechanism in which polyphenols are thought to carry out apoptosis initiation is through regulating the mobilization of copper ions which are bound to chromatin inducing DNA fragmentation. In the presence of Cu (II), resveratrol was seen to be capable of DNA degradation [3] Other properties plant polyphenols show is their ability to interfere with proteins which are present in cancer cells and promoting their growth. Cancer agents may be altered through the polyphenol regulating acetylation, methylation or phosphorylation by direct bonding. For example, curcumin treated cancer cells in various cells lines have shown suppression of the Tumour Necrosis Factor (TNF) expression through interaction with various stimuli [7].

b. Flavonoids

Flavonoids are from the polyphenolic compounds and constitute a large family of plant secondary metabolites with 10,000 known structures[8]. They are physiologically active agents in plants and becoming of high interest scientifically for their health benefits [9-10]

such as anthocyanins, flavones, flavonols, chalcones and many more which can be found in just one structure of the plant like its seed [11] identified and looked at the anticancer effects of flavonoids on human lung cancer cells (A456 cell line) from the fern species Dryopteris erythrosora. They found flavonoids to demonstrate cytotoxicity on cancer cells and to have high free radical scavenging activity [8] Purified flavonoids have also shown anticancer activities against other human cancers including; hepatoma (Hep-G2), cervical carcinoma (Hela) and breast cancer (MCF-7) [11] The flavonoids extracted from Erythrina suberosa stem bark (4'-Methoxy Licoflavanone (MLF) and Alpinumisoflavone (AIF)) were shown to have cytotoxic effects in HL-60 cells (human leukemia) [12] MLF and AIF induced apoptosis through intrinsic and extrinsic signaling pathways. The mitochondrial membrane potential is significantly reduced due to the induction of apoptotic proteins. With mitochondria damage to cells the cancer cells cannot survive [12] Other studies have looked at flavonoid extracts from fern species and found that even in low concentrations they still demonstrate high percentage of anticancer activity.

As previously mentioned, polyphenols can inhibit or alter the regulation of proteins and other agents which may be contributing to the survival of cancer cells. Signal Transducer and Activator of Transcription (STAT) proteins are anti-apoptotic and contribute to cancer cell growth. MLF and AIF inhibit members of this family of proteins by preventing their phosphorylation needed for the cancer cells survival [12]. Also, these flavonoids inhibit the expression of NF-κB which is needed for cancer cell survival and angiogenesis and proliferation.

c. Brassinosteroids

Brassinosteroids (BRs) are naturally occurring compounds found in plants which play roles in hormone signaling to regulate growth and differentiation of cells, elongation of stem and root cells and other roles such as resistance and tolerance against disease and stress. Also, BRs are used for regulation of plant senescence [13]. They are essential for plant growth and development. BRs are another naturally occurring compounds which have demonstrated therapeutic significance in the cause against cancer.

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-Table No. 1 : Plants drugs influenced in cancer treatment.

Sr. No.	Metabolities	Extracted Drug
1	Vinca	Vincristine
2	Vinca	Vinblastine
3	Vinca	Vindesine
4	Vinca	Vinorelbine
5	Taxan	Paclitaxel
6	Taxan	Docetaxel
7	Podophyllotoxin	Topotechan
8	Podophylotoxin	Irinotechan
9	Anthracyclines	Doxorubicin
10	Anthracyclines	Daunorobicin
11	Anthracyclines	Epirubicin
12	Anthracyclines	Idarubicin

Table2-Plant drugs influenced in cancer treatment.

SNO	Metabolites	Groups	Plant species	Type of cancer
1	Cucumin	Phenolic	Curcuma	Colorectal
2	Phenol	Phenolic	Ginger	Cancer
3	Resveraterol	Phytoalexin	Grapes	Breast
4	Genistein	Flavonoides		Leukaemia
5	Biocalein	Flavonoides	Shosiko	Hepatocellular
6	Hydroxystaurosporin	Alkaloid	Viscom album	Ovarian cancer
7	Lectine	Lectines		Cancer
8	Xanthorrhizol	Terpenoids	Curcuma	Cancer

Table 3: Extracted metabolites influence in different cancers.

1. CINNAMON [14]

Cinnamon is a spice obtained from the bark of an evergreen tree belonging to Lauraceae Family. Cinnamon is widely used in traditional Chinese medicine. Sevral studies have examined its antioxidant properties .

BIOLOGICAL SOURCE :

Cinnamomum zeylanicum, the source of cinnamon bark and leaf oils, is an indigenous tree of Sri Lanka, although most oil now comes from cultivated areas. C. zeylanicum is an important spice and aromatic crop having wide applications in flavoring, perfumery, beverages,and medicines.

CONSTITUENTS IN CINAMON :
Cinnamaldehyde
Eugenol
Terpinene
Carvacrol
Coumarin
Linalool
Safrole
Benzyl benzoate

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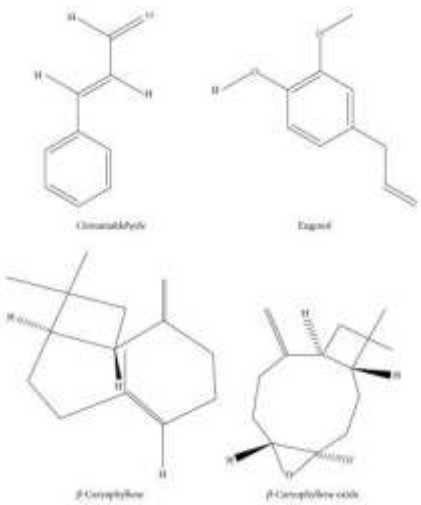


The ability of cinnamon extracts to suppress the in vitro growth of H. pylori, a recognized risk factor for gastric cancer, gastric mucosa-associated lymphoid tissue lymphoma, and possibly pancreatic cancer, has stirred considerable interest in the potential use of this spice to suppress human cancers (Farinha and Gascoyne 2005; Eslick 2006). The antibacterial effects of cinnamon extract may be due to cinnamaldehyde. The chemical components of cinnamon exert anti-tumor effects. Cinnamic acid derivatives can inhibit the growth of lung cancer cells (A549), breast cancer cells (MCF-7), a nd MCF-10A (Reddy et al., 2016).

2. Vinca rosea [15]

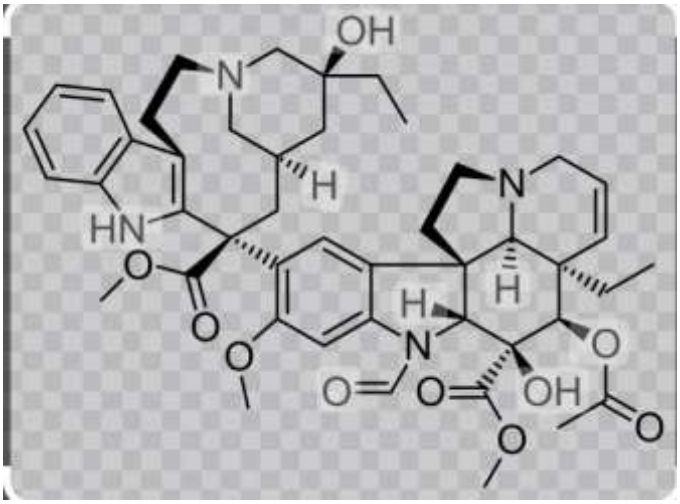
The leaves of vinca have been found as antibacterial properties and the crude leaf extract has anticancer properties. Vinca root is also used as anticancer. The other part of plant such as seeds, flower petals exhibit antioxidant properties. Due to the bitter and astringent leaves used as vomitive. The roots of vinca have been used as depurative, purgative, vermifuge, hemostatic and toothache remedy.

Drug

- Vindesine
- Vincristine
- Vinblastine
- Vinorelbine

Biological sources:

The botanical name is Vinca rosea. It belongs to family Apocynaceae. The biological source of vinca or sadafuli is the dried entire plant and aerial part of Catharanthus roseus Linn. It also known as catharanthus, Madagascar periwinkle.



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Chemical Constituents

Vinca contain indole alkaloid in large amount, mostly vinblastine and vincristine. Vinca also contain another alkaloid such as lochnerine, ajmalicine,serpentine as a chemical compound. When coupling of indole alkaloids such as catharanthine and vindoline occur, they produced vinca alkaloid

Morphological Features

- The colour of leaves is green.
- This plant is perennial.
- The colours of the flower are pinkish white or carmine red, violet.
- Roots are pale grey in colour.
- Odour- Vinca has characteristic odour.
- Taste- Vinka has bitter in taste.
- Leaves are oppositely arranged.
- Fruits of vinca are follicles with numerous black seed, fruits are divergent follicle.

Botanical Name

Catharanthus roseus, Pisum sativum, Brassica juncea, Allium cepa

Geographical source

India, Endemic to Madagascar.

Anti-cancer property- Vinca alkaloids are used in chemotherapy for cancer. They are a category of cell cycle specific cytotoxic drugs that work by inhibiting the ability of cancer cells to divide: Acting upon tubulin, they prevent it from forming into microtubules, a necessary component for cellular division. The vinca alkaloids thus prevent microtubule polymerization, as opposed to the mechanism of action of taxanes. Vinca alkaloids are produced synthetically and used as drugs in cancer therapy and as immunosuppressive drugs. These compounds include vinblastine, vincristine, vindesiine. According to researched vinca alkaloids include vincaminol, vineridine, and vinburnine. Throughout cell-division, vinca alkaloid molecules bind to the building blocks of a protein called tubulin, inhibiting its formation. The drugs work in the M-phase of cell reproduction. Tubulin protein generally works in cells to create “spindle fibers” (also called microtubules). These microtubules provide cells with both the structure and flexibility they need to divide and replicate. Without microtubules, cells cannot divide. The mechanism of vinca alkaloid’s is in a nutshell: by occupying tubulin’s building.

3.Viscum album [16]

Viscum album, also called Mistletoe, Muerdago, Visco, or white Visco belongs to theLoranthaceaeandViscaceae families, which are related to the Santalales order.TheViscaceaefamily has seven genera: Arceuthobium,, Ginalloa, Korthalsella, Notothixos, , Viscum, and various other genera worldwide.

Anti-cancer action : The VA plant can colonize a large number of host trees, such as fir (Abies), almond (Prunus dulcis), hawthorn (Crataegus), ash (Fraxinus), elm (Ulmus), willow (Salix alba), pine (Pinus), apple tree (Malus mali), poplar (Populus), or oak (Quercus), the last three being the main growth sites of VA Lectins are carbohydrate-binding proteins with various activities, such as anti-tumor and immunomodulatory effects increased phagocytic activities and the release of cytokines by granulocytes and monocytes. These substances are proposed as potentials, in biological and

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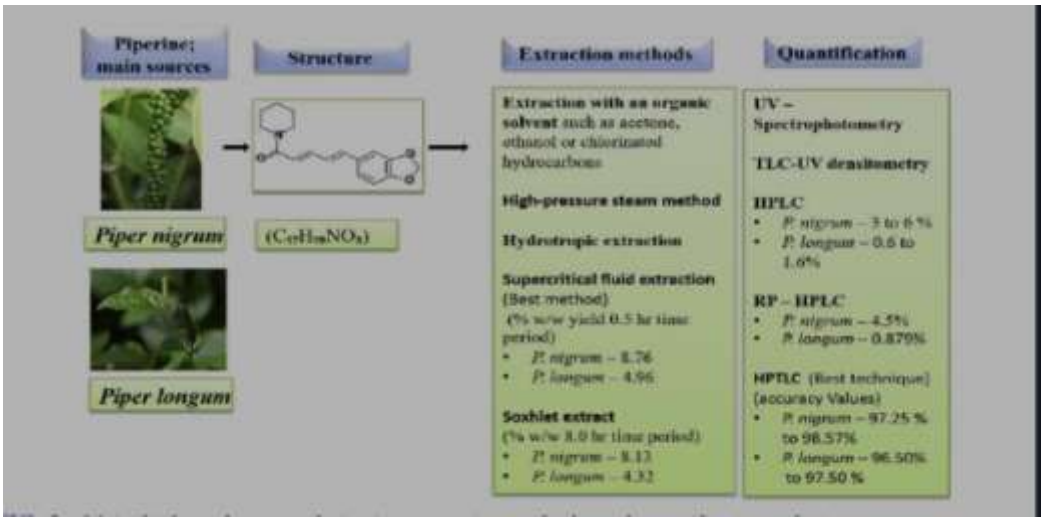
therapeutic research, due to their interactions with glycans bound to receptors on cell surfaces, responsible for primary cell signaling and biological response. In particular, lectins can induce the activation of several immune cells through the binding of Toll-like receptors (TLRs). They can also induce the secretion of cytokines (IL-10 and IL-12) through the activation of macrophages and dendritic cells by connection to TLR2 .

4. piperine

Piperine was first separated from the extracts of pepper by Hans Christian Orsted in 1819. . Black pepper, often termed as the "king of spices," has been exploited in Indian Systems of Medicine for the treatment of gastrointestinal and respiratory ailments (Gorgani et al., 2017). The characteristic pungency and biting taste of pepper is due high content of piperine in it. Piperine has been exploited for many therapeutic purposes in the past and is anticipated to remain so in the future. Piperine is an important dietary phytochemical due to its presence in spicy foods as well as its pharamacological activities (antiinflammatory, antimetastatic, anti-cancer, larvicidal, leishmanicidal, immunosuppressive, antimycobacterial, and antiparasitic activities) (Freire-de-Lima et al., 2008; Lu et al., 2012; Sahi et al., 2012; Rafiq et al., 2015; Rodgers et al., 2016; Samuel et al., 2016; Philipova et al., 2017; Soutar et al., 2017).

BIOLOGICAL SOURCE :

Piperine (1-Piperoylpiperidine, Figure Figure1)1) is the most important dietary alkaloid predominantly found in the fruits and roots of Piper nigrum L. (black pepper) and Piper longum L. (long pepper) species of Piperaceae family Zheng et al., 2016)



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Chemopreventive mechanisms of piperine

The importance of cancer chemoprevention was recognized early in human history with identification and development of raloxifene and tam Piperineoxifen for breast cancer prevention and a series of agents that can cure cutaneous preneoplastic lesions [17,18] The first translational study of a potential chemopreventive agent was conducted using 13-cis retinoic acid (a derivative of vitamin A) which showed a significant size reduction in premalignant lesions of oral leukoplakia and prevented primary head-and-neck tumors (Lippman and Hong,[19]. The main chemopreventive mechanisms of action of piperine include activation of apoptotic signaling cascades, inhibition of cell proliferation, cell cycle arrest, alterations in redox homeostasis, modulation of ER stress and autophagy, inhibition of angiogenesis, induction of detoxification enzymes, and sensitization of tumors to radiotherapy and chemotherapy[20]. The aforementioned mechanisms of action of piperine reveal that piperine can contribute significantly to cancer chemoprevention.

4. **Sanguinaria canadensis[31]**

Extracts of the plant Sanguinaria canadensis (Blood Root) and its related plant species are widely used under various commercial names, such as Xxterra™ (Larson Ltd., Fort Collins, CO), Blood Root Ointment and Newmarket Blood Root Ointment in the management of equine sarcoid (p. 195). For equine use, the material is conventionally combined with an escharotic zinc chloride (10–30%). Sanguinarine, the principal alkaloid found in extract of bloodroot (Sanguinaria canadensis and other plants of the same family) has escharotic properties107 and other properties that may be of value in cancer therapy including:

1.Inhibition of the nuclear transcription factor, NK-κB108
2.Induction of apoptosis in human epidermoid cancer cells109
3.Inhibition of mitogen-activated protein kinase phosphatase110
4.Inhibition of survivin, an inhibitor of apoptosis111
5.Antiproliferative, anti-angiogenic and anti-invasive effects in carcinoma.112,113

Studies on the positive cytostatic and cytotoxicity effects of sanguinarine have been reported on a variety of human cancer cells such as erythroleukemia, promyelocytic leukemia, human epidermoid carcinoma, bone cancer, prostate cancer, breast cancer, lung cancer, pancreatic cancer and colon cancer.

SYNERGISTIC INTERACTION OF SANGUINARINE WITH CHEMOTHERAPEUTIC AGENTS

Several plant SMs are capable of influencing effectively the multidrug resistance phenomenon in tumor cells and are able also to "chemo-sensitize" them[21-26] Some clinical studies have explored the possible advantage of combining natural products with classical chemotherapeutic regimens[27-29]. Phytotherapy, which employs plants extracts, is still used worldwide for the treatment of various human diseases. However, evidence has been proved that combinations of individual SM in an extract may exert synergistic effects. As an example, a recent study demonstrates that the combined use of non-toxic concentrations of sanguinarine and digitonin with doxorubicin, synergistically sensitizes Caco-2 (human colorectal adenocarcinoma) and CEM/ADR5000 adryamicin-resistant leukemia

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cells and increases the cytotoxicity of the chemotherapeutic agent doxorubicin[30]. In this regard, it is worth mentioning that the main advantage of combination therapies is represented by the possibility of reducing the doses and thus the toxicity of chemotherapy, while retaining its own efficacy. Thus, because of its potential synergistic interaction with chemotherapeutic agents, the therapeutic use of sanguinarine as an adjuvant, in association with chemotherapy, might be considered as a theoretical option in cancer therapy.

Curcuma longa:

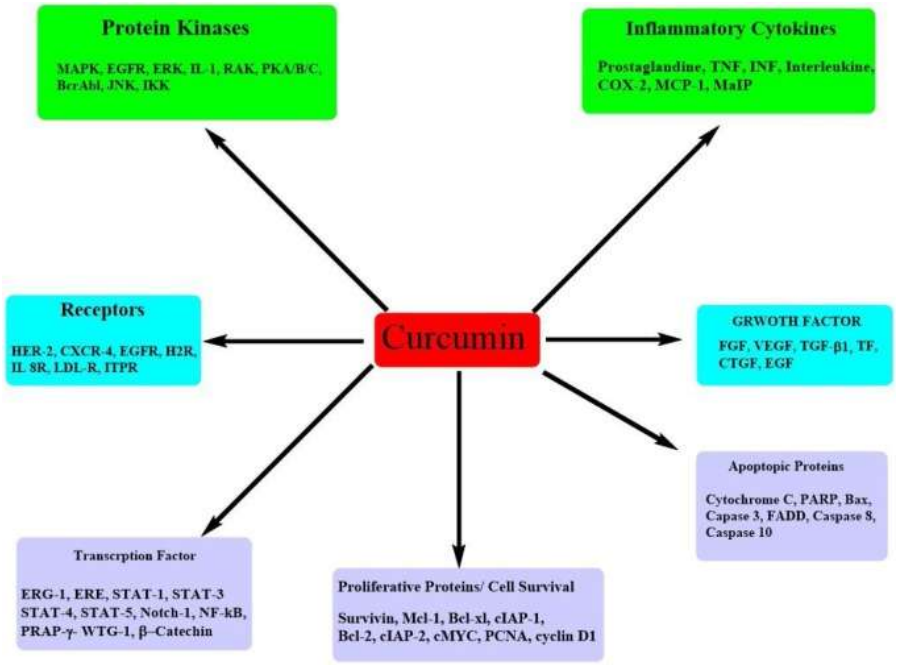
Curcuma longa phytoconstituent curcumin is one of these agents which have cancer chemopreventive characteristics. Among the three polyphenols present in the turmeric curcumin (bis-α,β-unsaturated β-diketone) is a potentand extensively investigated therapeutic agent [10].

BIOLOGICAL SOURCE :

Curcuma longa which is also known as turmeric and commonly known as Haldi, is present naturally in South Asia, Indonesia & India; grown largely in South India [33,34]]. Curcuma longa parts such as root and rhizome (underground stem) are boiled, dried and crushed into powdered turmeric and in this form it is used as a seasoning and a key ingredient in curry as well as preservative and coloring agent in food preparations worldwide.zka et al., (1910) [35].

CHEMICAL CONSTITUENTS :
Tumerone
Atlantone
desmethoxycurcumin
Zingiberone
bis-desmethoxycurcumin (BDMC).

Anti-cancer drugs are classified into different subgroups on the basis of their mechanism of actions as anti-proliferative agents, carcinogen blocking agents or antioxidants. C. longa contains significant amount of curcumin which exhibited the characteristics of all three subgroups with various biochemical mechanisms of actions like apoptosis and the regulation of survival signals. Enzymes, receptors, growth factors, transcription factors and inflammatory cytokines (described in more detail in next section) are the major targets of curcumin from turmeric to manage the cancers [32] It was also reported that curcumin scavenges the reactive oxygen species (ROS), promoting proapoptotic & anti-inflammatory actions, and reduction in survival signal as combination of different mode of actions as anti-cancer agent (Fig. 2). It was reported that targeting of these signaling pathways in real setting is more complicated with curcumin and so currently different modes of curcumin'schemosensitizing, chemopreventive and radiosensitizing effects are more enthusiastically being studied now [36]



various main mechanism of actions/ molecular targets of curcumin from C. longa as anticancer agent.

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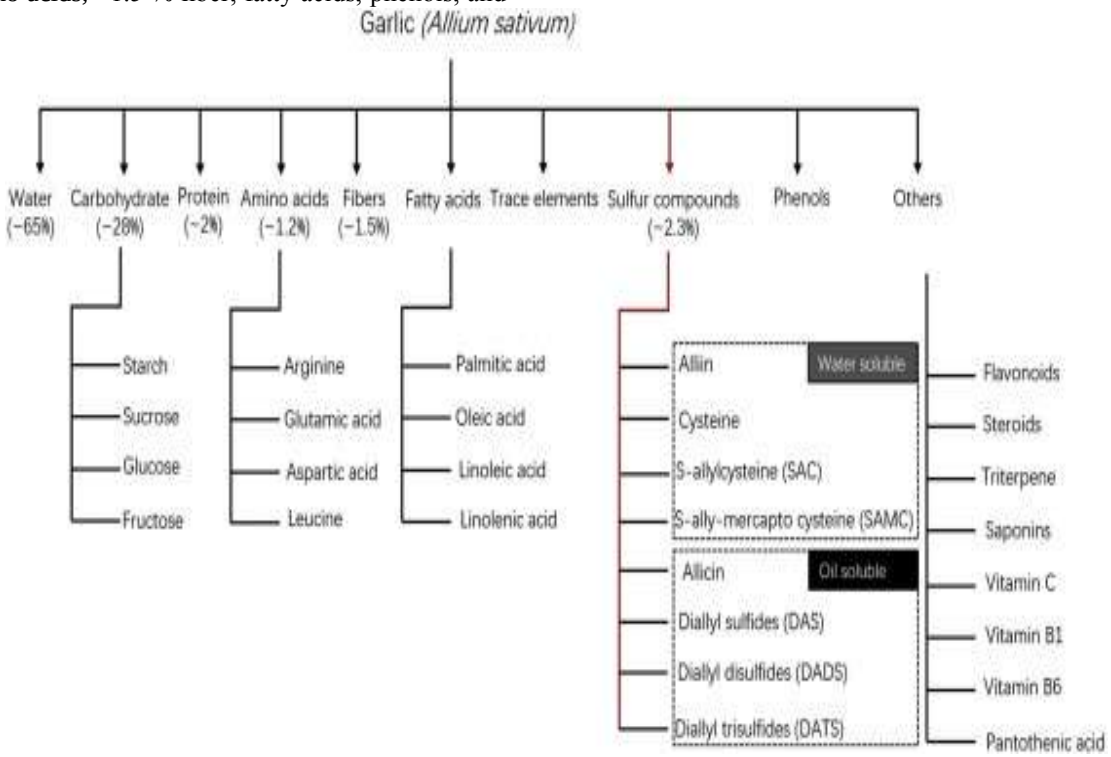
Allium sativum

Garlic (Allium sativum) is natively from central Asia and is now cultivated around the world. It is interesting to note that the medicinal potency of garlic has been widely known and used for over 5000 years.

CHEMISTRY OF ALLIUM SATIVUM:

Fresh raw garlic bulbs contain ~65 % water, ~ 28 % carbohydrate, ~2 % protein, ~1.2 % amino acids, ~1.5 % fiber, fatty acids, phenols, and trace elements, as well as more than 33 (~2.3 %) sulfur-containing compounds (Fig. 1) [36]. Garlic is well known for its pungent odor, which is from oil-soluble organosulfur compounds (OSCs), including allicin, alliin and ajoene. The main sulfur compound in both raw garlic and garlic powder is alliin. On average, garlic cloves contain 8 g/kg alliin. The transformed pathways and chemical structures of the widely studied organosulfur compounds are depicted in Fig. 2.



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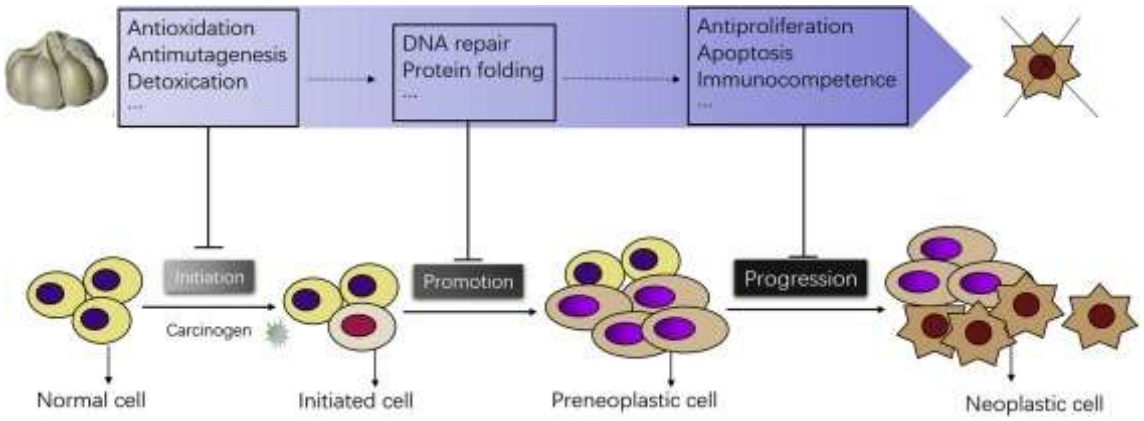
The anticancer actions of garlic have largely been attributed to the following categories : (1) suppressing mutagenesis, (2) scavenging free radicals, (3) regulating enzyme activities, (4) inhibiting protein folding in the endoplasmic reticulum, and (5) inhibiting cancer cellular behaviors, such as proliferation, apoptosis resistance, and evasion of immunosurveillance.



Anti-carcinogenic effect of garlic bioactive compounds in different stages of cancer progression.

In the initiation stage, blocking phytochemicals prevents the bioactivation of carcinogens through antioxidation, antimutagenesis and detoxication. In the promotion stage, suppressing phytochemicals inhibits the proliferation of clonal cells by modulating protein folding and DNA repair. In the progression stage, suppressing phytochemicals impedes the growth or metastasis of tumors by changing the cell behaviors, including antiproliferation, apoptosis and immunocompetence

Garlic has been demonstrated to exhibit anticancer activities via interfering with multiple stages of carcinogenesis. However, the nutritional or chemopreventive roles of garlic go far beyond the notion that garlic has therapeutic effects against cancers. More rationally designed experiments and trials are required to explore the novel properties of garlic. It should be noted that preparation processing and administration methods may depress the anticancer effects of garlic when the effective components of garlic are isolated and analyzed.

Crocus sativus L. (saffron)

Dried Stigma of saffron (Crocus sativus L.) is considered as the most expensive traditional spice by weight all over the world [37], [38], [39]. It has been estimated that Iran accounts for about 76% of the total world saffron production annually [40], [41]. Saffron has been used as a stomach pain soother, antispasmodic, digestion aid, renal colic pains reliever, antidepressant, and appetizer agent in Islamic- Persian traditional medicine [42], [43]. The stigma is the most used part of the saffron. The observed beneficial effects of the dried stigma are contributed to three main secondary metabolites including soluble crocin (mono-glycosyl or di-glycosyl polyenesters) which is responsible for saffron special color, picrocrocin (mono-terpene glycosideprecursorofsafranal) which is responsible for saffron bitter taste, and safranal which is responsible for its special odor. Saffron contains a considerable amount of lipophilic carotenoids and flavonoids, as well as trace amounts of B1 and B2 vitamins[44], [45], [46], [47][48], [49], [50], [51], [52][53]. Conducted researches have contributed beneficial effects of saffron to its antioxidant and anti-inflammatory properties, which may be related to saffron active constituents.

	Target cells	Intervention	Results
	Lung tumor cells, normal lung fibroblasts and transformed fibroblasts	Saffron alcoholic extract	Saffron inhibited the growth of malignant cells by blocking the synthesis of RNA and DNA

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	Human embryonic epithelial cells of the cervix (Hela) and liver carcinoma cells (Hep G2)	Saffron alcoholic extract, and crocetin like substances	Saffron and crocetin like substances inhibited the growth of tumor cells by apoptotic and non-apoptotic mechanisms
	Hepatocellular carcinoma epithelial-like cells (Hep G2) and human cervical carcinoma cells	Saffron alcoholic extract	Saffron had selective cytotoxicity against tumor cells
	Human alveolar carcinoma cells (cells A549)	Saffron aqueous extract	Apoptotic malignant cells percentage increased dose dependently in the presence of saffron
	HeLa cells and human malignant cell layer	Isolated substance from saffron	ID50 against Hela cells was 9µgr/ml, and 7 to 22 µgr/ml against malignant cells
	HeLa cervical carcinoma cells	Crocin, crocetin, picrocrocin, and safranal	All the constituents inhibited cancer cells growth. The effect of crocin was more considerable.
	Human cells infected with adenovirus	Crocin and di glucosyl crocetin	Crocin and di glucosyl crocetin had inhibitory effects on primary expression of tumor antigen at adenovirus infected cells
	HT-29 cells and DHD/k12 (adenocarcinoma cells in rat and human colon carcinoma cells)	Crocin	Crocin exhibited strong selective cytotoxicity against HT-29 and DHD/k12 cells
	Hep G2 cells	Crocin	Crocin exhibited selective cytotoxicity against cancer cells
	Three layers of colorectal cancer cells (HCT-116, SW-480 and HT-29)	Crocin	Crocin significantly inhibited these three cells layers with a dose dependent manner
	PC12 Cells	Crocin	Crocin had neuro protective effect on acrylamide induced cytotoxicity in PC12 cells with a dose dependent manner
	HeLa cells, lung cancer cells modified fetal lung fibroblast	Crocetin	Crocetin inhibited cancer cells growth through dose dependent inhibition of protein and nucleic acid synthesis
	Human rhabdomyosarcoma cells	Crocetin	Crocetin had selective cytotoxicity against human rhabdomyosarcoma compared with cisplatin
	MDA-MB-231 and MCF-7 breast cancer	Crocetin and its analogs	Crocetin and its analogs dose dependently inhibited breast

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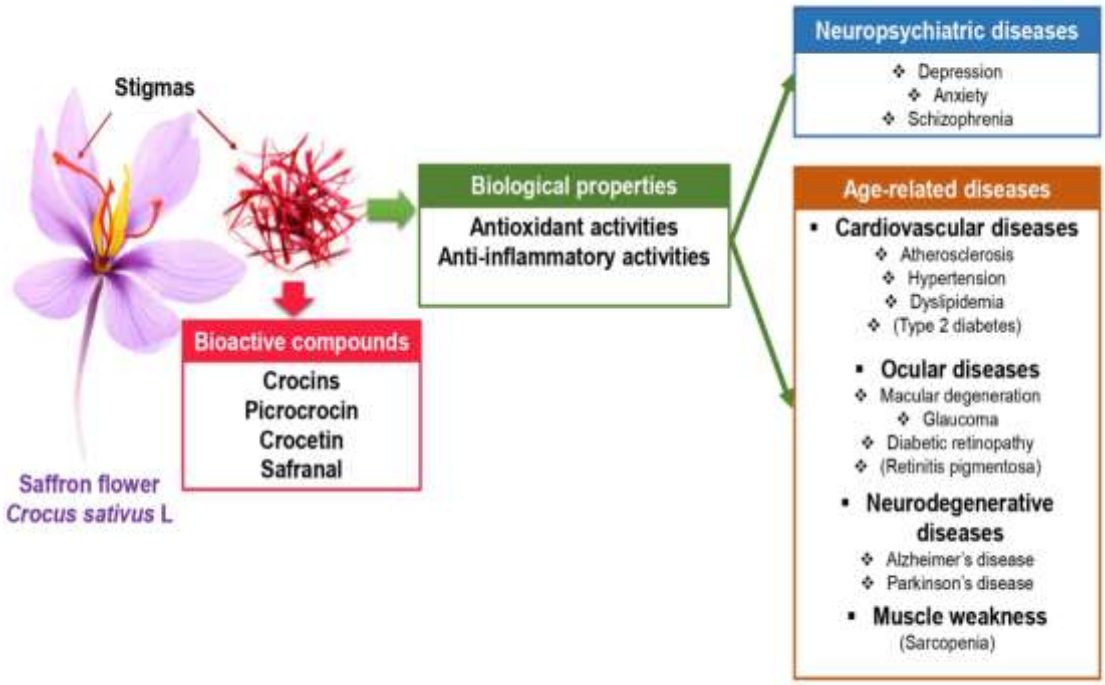
	cells		cancer cells growth
	MCF-7 cells	Crocetin	Crocetin had a pro-apoptotic effect on cancer cells
	Promyelocytic leukemia cells (HL60) and human myelogenous leukemia cells (K562)	Crocetin	Crocetin had cytotoxic effects against leukemia cells
	Fibroblast cells C3H10T1/2	Crocetin	Pretreatment with crocetin significantly inhibited aflatoxin induced cytotoxicity in fibroblast cells
	A549 (lung carcinoma) and VA13 (SV-40 transformed fetal lung fibroblasts) Cells	Crocetin	Crocetin had inhibitory effects on nucleic acid synthesis and lung cancer cells colony formation
	MIA-PaCa-2, BxPC3, Capan1 and Ascpc1 pancreatic cancer cells	Crocetin	Crocetin had anti-tumorigenic effects on pancreatic cancer cells

Saffron toxicity against cancer cells at in vitro.



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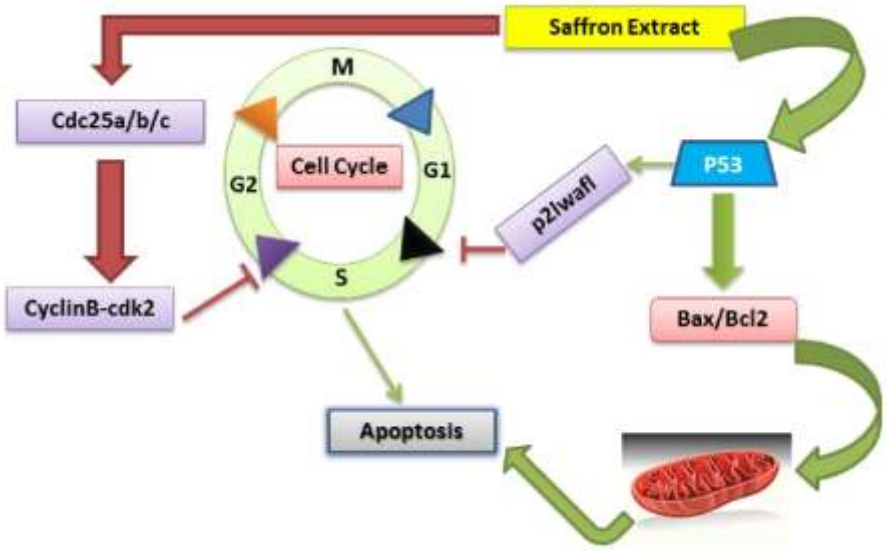

Emblica [54]

Emblica officinalisGaertn. belonging to family Euphorbiaceae is commonly known as Indian gooseberry or "Amla" in India. It is used as a 'rejuvenating herb' in traditional system of Indian medicine. It has been shown to possess antioxidant, anti-inflammatory and anti-apoptotic effects.

Molecules from Phyllanthus emblica fruit extract having proven anticancer properties.

Phenolic compounds from Phyllanthus emblica extract identified by HPLC having anticancer properties	**Cancer model utilized to identify antiproliferative and antitumor properties**
Ellagic acid (tannin)	Colon, prostate cell lines, and breast and prostate xenografts
Corilagin (tannin)	Ovarian cancer cells, liver cancer cells, and hepatocarcinoma

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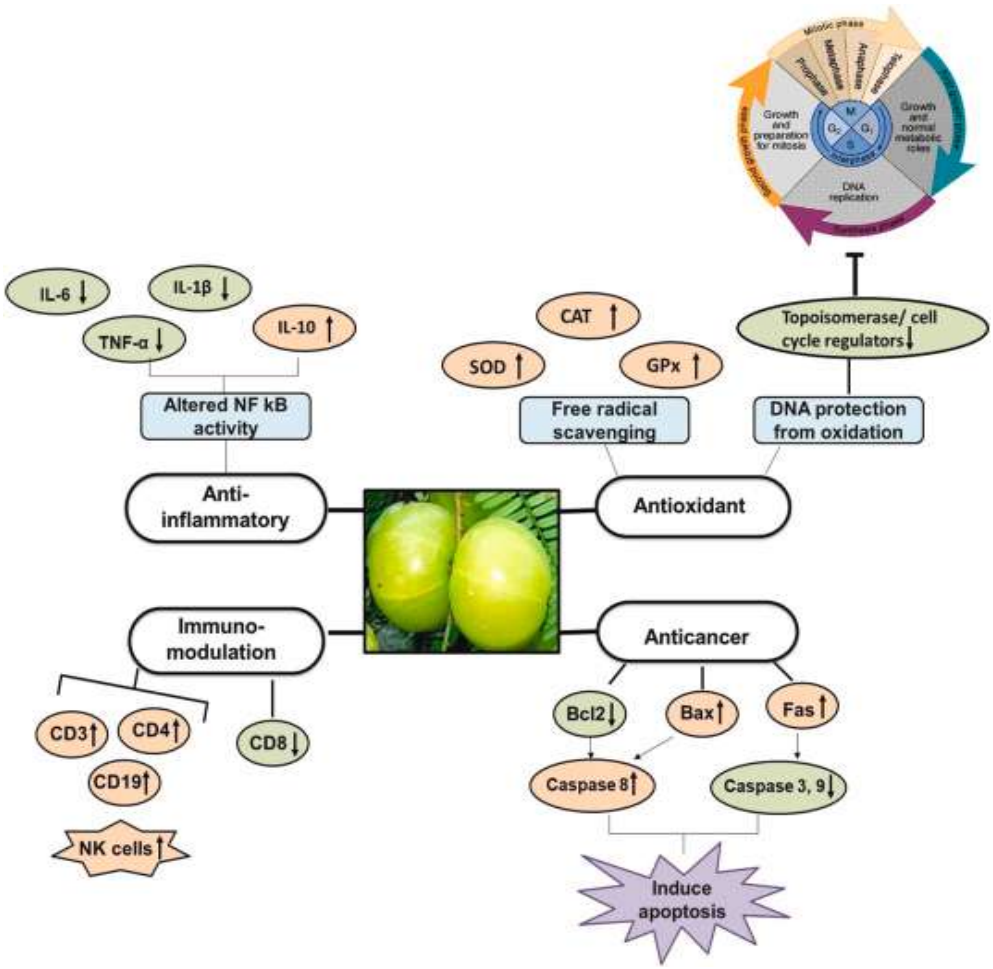
	xenografts
Pyrogallol (tannin)	Lung cancer cells, gastric cancer cells, and lung adenocarcinoma xenografts
Chebulagic acid (tannin)	Retinoblastoma colon cancer, breast cancer, prostate cancer, and leukemia cancer cell lines
Gallic acid (tannin)	Breast and lung cancer cell lines, some activity against lung cancer xenograft
Quercetin (flavonoid)	Numerous cancer cell lines from multiple tissue types, transgenic murine model of breast cancer, leukemia xenograft, and phase I clinical trial



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Some Anti-cancer Natural Products : [55]

Name	Biological source	Geographical source	Chemical constituents	uses
Aconite	Dried root of aconitum napellus, Ranunculacece	Hungary, germany, spain Switzerland	Aconitine, hypaconitine, neopelline, napelline, neoline	Treatment of rheumatism, inflammation
Allium Sativum (Garlic)	Bulb of the plant know as allium sativum, lilaceae	Central asia, southern Europe, USA and India	Carbohydrate, protein (albumin), fat, mucilage	Carminative, aphrodisiac, expectorant, stimulant, disinfectant
Artemisia	Unexpanded flower heads of Artemisia cina, Artemisia buvifolia wall, Artemisia maritime, compositae	Pakistan, turkey, from Kashmir to kumaon in Himalayas	Essential oil, santonin, artemisin	Anthelmintic
Camellia sinensis	Prepared leaves and leaf buds of Thea sinensis, Theaceae	India, Shri lanka., china, Indonesia, japan	Caffeine, theobromine, theophylline, gallatonic	CNS stimulant, diuretic
Comptothecaaccuminata	Dried stem wood of comptotheca acuminate, nyssaceae	China, Tibet, southern china	Quinoline alkaloid, camtothecin, 10 hydroxy camptothecin, 10 meth camptothec	DNA topoisomerase Iinhibitors, antitumour, antileukemiA
Catharanthus roseus	Dried whole plant of catharanthus roseus, apocunaceae	South africa, india, USA, Europe, australia	Vincristine, vinblastine, ajmalicine	Antineoplastic, acute leukemia, hodgkin's disease
Curcuma longa	Dried as well as fresh rhizome of the plant known as curcuma longa, zingiberaceae	Tamil Nadu, Andhra Pradesh, kerala	Curcuminoids, curcumin, volatile oil, starch	Anti inflammatory, anti arthritic, cervical cancer
Glycyrrhiza glabra	Dried peeled or unpeeled root and stolon of glycyrrhiza glabra, leguminosae	Spain, sicily, England	Glycurrhizin, glycyrrhizinic acid which on hydrolysis yield glycyrrhetinic acid	Expectorant, demulcent, antigastric effect
Panax ginseng	Dried root of panax ginseng, Araliaceae	Korea, china, Russia, Canada, USA	Ginsenoisides, panaxosides, chikusetsusaponin	Immunomodulatory drugs
Podophyllum peltatum	Dries rhizomes and root of podophyllum peltatum, barberidaceae	From Kashmir to Sikkim and parts of U.P	Podophyllin, podophyllotoxin, alpha and beta pelta Major tins	Cytotoxic action, treatment of veneral, purgative
Taxus brevifoli	Dried leaves, bark and root of various species of taxus, taxaceae	India, Canada, America	Taxane, cephalomannine, 10- deacetyl	Lung carcinoma, gastric and cervical cancers and also carcinomas of head,

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			baccatin, taxol	neck, prostate and colo
Viola odorata	Dried aerial parts obtained from viola odorata, violaceae	India (Kashmir, himachal Pradesh, kumaon hills)	Essential oil, alkaloid, saponins, glycoside of methyl salicylate.	Expectorant, diaphoretic, antipyretic, antibacterial
Zingiber	Rhizomes of zingiber officinale roscoe, zingiberacea	South asia, Africa, Australia, Mauritius, jamaica, Taiwan, india.	Volatile oil, starch, fat, fibre, inorganic material, residual moisture, acrid resinous matter.	Stomachic, aromatic, carminative, stimulant, flavouring agent

Marketed Prepration :

Product Name :	**Activity**
Ashwagandha Capsules	**It possesses natural rejunvating properties to the Body.**
Guggul Capsules	**It has blood purifying property**
TIG- 10	**Used in mouth cancer treatment**
GILOY [Extract Capsules]	
Stocol	**Used in stomach cancer treatment, carcinoid tumors**
Curcumin Capsules	**Fight against infection and toxin to reduce carcinogenic effect**
ChanderprabhaVati	**Calming the effect of entire body**
Kanchnaar Guggul	**Helps to maintain cells and tissue healthy**
Punarnava capsules	**Reduces growth of cancer cells, tumor, inflammation and Swelling on the affected area**
Guduchi Capsules	**Deals with the sign and symptoms related to cancer, anti-oxidant**
Graviola capsules	**Used in treatment -breast cancer, liver cancer, pancreatic cancer, colon cancer**
Swarna Bhasma Tablet	**Anti-microbial, anti-cancer property**
Green Essential Capsules	**Inhibits all stages of tumor growth, used to treat breast, colon, skin, prostate, Lung Cancer**
Moringa Capsules	**Anti-inflammatory, immunomodulatory properties, Routine use of these capsules stop the growth of benign and malignant cancer**
Palakya	**Reduce risk of developing cancers**

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Medihope-D	**Useful in treatment of blood**
Wheatgrass	**Used in cancer, Diabetes, leukemia, obesity**
Karavella	**Anti-cancer property**
Ufb-10	**Used in treatment of cervical cancer**
Medihope	**Decrease side effects of chemotherapy and radiation therapy**
SJ 29 Ointment	**In breast cancer treatment in kerala**
Cancertame	**Helps to fight cancer at every step i.e., genesis, growth and spread of cancer**
Kaya Cure Churna	**Useful in curing various kinds of cancers like blood, breast, colon and rectal, lung, thyoride cancer**
KarsiGO	**Prevent abnormal growth of cells and tissues**
CARCINEX [Liquid]	**Helpful in malignant tumors and cancer. Especially cancer in throat, breast, stomach and intestine.**
Onco Blaze Churna	**Helpful in breast cancer, helpful in cyst and tumors related problems**
Shuddhi Powder	**Used in lung cancer**
Arkeshwara Rasa	**Pancreatic Cancer**

II. CONCLUSION

Medicinal plants have contributed a rich health tohuman beings. Plant extracts and their bioactive compounds present in them which are responsible for anticancer activity have to be screened for their valuable information. This review had given some of the plants possessing anticancer activity for various types of cancer. This review can help others to explore herbs to further extent and its use in various other disease and toxicity studies along with clinical trials.

REFERANCE

[1]. Fraiser LH, Kanekal S, Kehrer JP. Drugs. 1991;42(5):781–795. [PubMed] [Google Scholar]

[2]. Rajeswara Rao BR, Singh K, Sastry KP, Singh CP, Kothari SK, Rajput DK, Bhattacharya AK. Cultivation Technology for Economicaly Important Medicinal Plants. In: Reddy KJ, Bahadur B, Bhadraiah B, Rao MLN, editors. Advances in Medicinal Plants. University Press; Hyderabad: 2007. pp. 112–122. [Google Scholar]

[3]. Azmi AS, Bhat SH, Hanif S, Hadi SM. Plant polyphenols mobilize endogenous copper in human peripheral lymphocytes leading to oxidative DNA breakage: A putative mechanism for anticancer Properties. FEBS Letters. 2006;580:533–538. [PubMed] [Google Scholar]

[4]. Apostolou A, Stagos D, Galitsiou E, Spyrou A, Haroutounian S, Portesis N, Trizoglou I, Hayes AW, Tsatsakis AM, Kouretas D. Assessment of polyphenolic content, antioxidant activity, protection against ROS-induced DNA damage and anticancer activity of Viti vinifera stem extracts. Food and Chemical Toxicology. 2013;61:60–68. [PubMed] [Google Scholar]

[5]. Siriwantanmetanon N, Fiebich BL, Efferth T, Prieto JM, Heinrich M. Traditionally used Thai medicinal plants: In vitro anti-inflammatory, anticancer and antioxidant activities. Journal of Ethnopharmacology. 2010;130:197–207. [PubMed] [Google Scholar]

[6]. Heo BG, Park YJ, Park YS, Bae JH, Cho JY, Park K, Jastrzebski Z, Gorinstein S. Industrial Crops and Products. 2014;56:9–16. [Google Scholar]

[7]. Gupta SC, Tyagi AK, Deshmukh-Taskar P, Hinojosa M, Prasad S, Aggarwal BB. Downregulation of tumor necrosis factor and other proinflammatory biomarkers by polyphenols. Archives of Biochemistry and Biophysics. 2014;559:91–99. [PubMed] [Google Scholar]

[8]. Cao J, Xia X, Chen X, Xiao J, Wang Q. Characterization of flavonoids from Dryopteris erythrosora and evaluation of their antioxidant, anticancer and

acetylcholinesterase inhibition activities. Food and Chemical Toxicology. 2013;51:242–250. [PubMed] [Google Scholar]

[9]. Agati G, Azzarello E, Pollastri S, Tattini M. Flavonoids as antioxidants in plants: Location and functional significance. Plant Science. 2012;196:67–76. [PubMed] [Google Scholar]Huntely AL. The health benefits of berry flavonoids for menopausal women: Cardiovascular disease, cancer and cognition. Maturitas. 2009;63:297–301. [PubMed] [Google Scholar]

[10]. 11Wen L, Wu D, Jiang Y, Prasad KN, Lin S, Jiang G, He J, Zhao M, Luo W, Yang B. Identification of flavonoids in litchi (Litchi chinensis Soon.) leaf and evaluation of anticancer activities. Journal of Functional Foods. 2014;6:555–563. [Google Scholar]

[11]. Kumar S, Pathania AS, Saxena AK, Vishwakarma RA, Ali A, Bhunshan S. The anticancer potential of flavonoids isolated from the stem bark of Erythrina suberosa through induction of apoptosis and inhibition of STAT signalling pathway in human leukaemia HL-60 cells. Chemico-Biological Interactions. 2013;205:128–137. [PubMed] [Google Scholar]

[12]. Bishop GJ, Koncz C. Brassionsteroids and Plant Steroid Hormone Signaling. The Plant Cell. 2002;(supplement 2002):97–110. [PMC free article] [PubMed] [Google Scholar]

[13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896244/#!po=7.00000

[14]. INTERNATIONAL JOURNAL OF TREND INSCIENTIFIC RESEARCH AND DEVELOPMENT (IJTSRD)UNIQUE CODE IJTSRD30720

[15]. I INTERNATIONAL JOURNAL TRENDS OF SCI AND RESERCH [IJSR] ISSN2319-7064 SJIF [2019]7.583

[16]. Kelloff G. J., Crowell J. A., Steele V. E., Lubet R. A., Boone C. W., Malone W. A., et al. (1999). Progress in cancer chemoprevention. Ann. N. Y. Acad. Sci. U.S.A. 889, 1–13. 10.1111/j.1749-6632.1999.tb08718.x [PubMed] [CrossRef] [Google Scholar] [Ref list]

[17]. Wu X., Patterson S., Hawk E. (2011). Chemoprevention–history and general principles. Best Pract. Res. Clin. Gastroenterol. 25, 445–459. 10.1016/j.bpg.2011.10.012 [PubMed] [CrossRef] [Google Scholar] [Ref list]

[18]. Lippman S. M., Hong W. K. (1992). 13-cis-retinoic acid and cancer chemoprevention. J. Natl. Cancer Inst. Monogr. 13, 111–115. [PubMed] [Google Scholar] [Ref list]

[19]. Manayi A., Nabavi S. M., Setzer W. N., Jafari S. (2017). Piperine as a potential anti-cancer agent: a review on preclinical studies. Curr. Med. Chem. [Epub ahead of print]. 10.2174/0929867324666170523120656 [PubMed] [CrossRef] [Google Scholar] [Ref list]

[20]. Möller M, Weiss J, Wink M. Reduction of cytotoxicity of the alkaloid emetine through P-glycoprotein (MDR1/ABCB1) in human Caco-2 cells and leukemia cell lines. Planta Med. 2006;**72**:1121–1126. [PubMed] [Google Scholar]

[21]. 86. Ma Y, Wink M. Lobeline, a piperidine alkaloid from Lobelia can reverse P-gp dependent multidrug resistance in tumor cells. Phytomedicine. 2008;**15**:754–758. [PubMed] [Google Scholar]

[22]. 87. El-Readi MZ, Hamdan D, Farrag N, El-Shazly A, Wink M. Inhibition of P-glycoprotein activity by limonin and other secondary metabolites from Citrus species in human colon and leukaemia cell lines. Eur J Pharmacol. 2010;**626**:139–145. [PubMed] [Google Scholar]

[23]. 88. Li S, Lei Y, Jia Y, Li N, Wink M, Ma Y. Piperine, a piperidine alkaloid from Piper nigrum re-sensitizes P-gp, MRP1 and BCRP dependent multidrug resistant cancer cells. Phytomedicine. 2011;**19**:83–87. [PubMed] [Google Scholar]

[24]. Wink M, Ashour ML, El-Readi MZ. Secondary Metabolites from Plants Inhibiting ABC Transporters and Reversing Resistance of Cancer Cells and Microbes to Cytotoxic and Antimicrobial Agents. Front Microbiol. 2012;**3**:130. [PMC free article] [PubMed] [Google Scholar]

[25]. Li JH. [A study on treatment of lung cancer by combined therapy of traditional Chinese medicine and chemotherapy] Zhongguo Zhong Xi Yi Jie He Za Zhi.

1996;**16**:136–138. [PubMed] [Google Scholar]

[26]. Li JH. [A study on treatment of lung cancer by combined therapy of traditional Chinese medicine and chemotherapy] Zhongguo Zhong Xi Yi Jie He Za Zhi. 1996;**16**:136–138. [PubMed] [Google Scholar]

[27]. Cai HB, Dai FG, Min QF, Shi M, Miao JX, Luo RC. [Clinical study of the effects of radiotherapy in combination with traditional Chinese medicine on non-small cell lung cancer] Di Yi Jun Yi Da XueXue Bao. 2002;**22**:1112–1113. [PubMed] [Google Scholar]

[28]. Efferth T, Davey M, Olbrich A, Rücker G, Gebhart E, Davey R. Activity of drugs from traditional Chinese medicine toward sensitive and MDR1- or MRP1-overexpressing multidrug-resistant human CCRF-CEM leukemia cells. Blood Cells Mol Dis. 2002;**28**:160–168. [PubMed] [Google Scholar]

[29]. Eid SY, El-Readi MZ, Wink M. Synergism of three-drug combinations of sanguinarine and other plant secondary metabolites with digitonin and doxorubicin in multi-drug resistant cancer cells. Phytomedicine. 2012;**19**:1288–1297. [PubMed] [Google Scholar]

[30]. World J Gastrointest Oncol. 2016 Jan 15; 8(1): 30–39.Published online 2016 Jan 15. doi: 10.4251/wjgo.v8.i1.30

[31]. W. Park, A.R. Amin, Z.G. Chen, D.M. Shin**New perspectives of curcumin in cancer prevention**Cancer Prevention Research, 6 (5) (2013), pp. 387-400Google Scholar

[32]. J.S. Jurenka**Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research**Alternative medicine review, 14 (2) (2009)Google Scholar

[33]. R. Wilken, M.S. Veena, M.B. Wang, E.S. Srivatsan**Curcumin: A review of anti-cancer properties and therapeutic activity in head and neck squamous cell carcinoma**Molecular cancer, 10 (1) (2011), p. 12 View PDFThis article is free to access.View Record in ScopusGoogle Scholar

[34]. J. Miłobędzka, S. Kostanecki, V. Lampe**Notes on Curcumins**BerDeut Chem Ges, 43 (1910), pp. 2163-2170 View PDFCrossRefGoogle Scholar

[35]. M.S. Butt, M.T. Sultan, M.S. Butt, J. Iqbal**Garlic: nature's protection against physiological threats**Crit. Rev. Food Sci. Nutr., 49 (6) (2009), pp. 538-551 View PDFCrossRefView Record in ScopusGoogle Scholar

[36]. S.K. Sandur, A. Deorukhkar, M.K. Pandey, A.M. Pabón, S. Shentu, S. Guha, B.B. Aggarwal, S. Krishna**Curcumin modulates the radiosensitivity of colorectal cancer cells by suppressing constitutive and inducible NF-κBactivity**International Journal of Radiation Oncology* Biology* Physics, 75 (2) (2009), pp. 534-542ArticleDownload PDFView Record in ScopusGoogle Scholar

[37]. A. Jemal, R. Siegel, J. Xu, E. Ward**Cancer statistics, 2010**CA a cancer J. Clin., 60 (5) (2010), pp. 277-300 View PDFThis article is free to access.CrossRefView Record in ScopusGoogle Scholar

[38]. R. Doll, R. Peto**The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today**J. Natl. Cancer Inst., 66 (6) (1981), pp. 1192-1308 View PDFCrossRefGoogle Scholar

[39]. J. Peto**Cancer epidemiology in the last century and the next decade**Nature, 411 (6835) (2001), pp. 390-395View Record in ScopusGoogle Scholar

[40]. P. Anand, A.B. Kunnumakara, C. Sundaram, K.B. Harikumar, S.T. Tharakan, O.S. Lai, et al.**Cancer is a preventabledisease that requires major lifestyle changes**Pharm. Res., 25 (9) (2008), pp. 2097-2116 View PDFThis article is free to access.CrossRefView Record in ScopusGoogle Scholar

[41]. W.C. Evans**Trease and Evans' Pharmacognosy**Elsevier Health Sciences (2009)Google Scholar

[42]. T. Fleming**PDR for Herbal Medicines**Medical Economics Company (1998)Google Scholar

[43]. K.C. Huang**The Pharmacology of Chinese Herbs**CRC press (1998)Google Scholar

[44]. J.A. Duke **Handbook of Medicinalherbs**CRC press (2010)Google Scholar
[45]. S. Sweetman, I. Martindale**The Complete Drug Reference**Pharmaceutical Press, London, UK (2002)Google Scholar
[46]. K. Abe, H. Saito**Effects of saffron extract and its constituent crocin on learning behaviour and long-term potentiation**Phytotherapy Res., 14 (3) (2000), pp. 149-152View Record in ScopusGoogle Scholar
[47]. F.S. D'AmelioSr**Botanicals: a Phytocosmetic Desk Reference**CRC Press (1998)Google Scholar
[48]. A.R. Gohari, S. Saeidnia, M.K. Mahmoodabadi**An overview on saffron, phytochemicals, and medicinal properties**Pharmacogn. Rev., 7 (13) (2013), p. 61 View PDFCrossRefView Record in ScopusGoogle Scholar
[49]. M. Kamalipour, S. Akhondzadeh**Cardiovascular effects of saffron: An evidence-based review**J. Tehran Heart Cent., 6 (2) (2011), p. 59View Record in ScopusGoogle Scholar
[50]. M. Schmidt, G. Betti, A. Hensel**Saffron in phytotherapy: pharmacology and clinical uses**Wien. Med. Wochenschr., 157 (13–14) (2007), pp. 315-319View Record in ScopusGoogle Scholar
[51]. F. Abdullaev BIOLOGICAL **effects of saffron**BioFactorsOxf. Engl., 4 (2) (1993), pp. 83-86View Record in ScopusGoogle Scholar
[52]. F.I. Abdullaev**Cancerchemopreventive and tumoricidal properties of saffron (Crocus sativus L.)**Exp. Biol. Med., 227 (1) (2002), pp. 20-25 View PDFCrossRefView Record in ScopusGoogle Scholar
[53]. Oxidative medicine and cellularlongevity (www.researchgate.net)
[54]. Nidhi Agrawal et al\int.d.Pharmatech Res.2012,4(3)