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Potential applications of Herbal plants in cancer treatment

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ABSTRACT: Chronic and genetic level influenced diseases are now challenges for global medical sciences, especially different type of cancers like prostate, blood, breast, lung, rectum, cervix, liver are the major concern for human being now. Several novel approaches have existed for tumor cancer treatments that act on molecular and genomic levels but therapies like radiation, chemotherapies are leading to sever other harsh effects with the high cost too. So there is a strong need to find an alternative to these therapies at least in the early stages of tumor progression, reduce cytotoxicity and which can boost immunity or body defense mechanism. Because of cost efficiency and minimum severity, this era has brought herbal medicine therapeutics which can work on genomic and molecular levels of the tumor. So the present review discussed various herbal plant competencies in the management of cancer along with essential chemical constituents that are responsible for the tumor-inhibiting activity. Various plants like Ginger root, Cumin, Dill, Grapes, Turmeric, Caraway, Thyme, Fenugreek, Myrrh, Cinnamon, Ginseng, Coriander, Berberis, Garlic, Saffron, Aloevera, Astragalus, Milk Thistle, Bloodroot, Broccoli, Tulasi, Ashwagandha has been discussed here which might prevent or cure Different mechanism which imparts in cancer treatments are promoting the production of protective enzymes, cancer activating enzymes inhibition, antioxidant effect, DNA repair mechanism stimulation, enhancing and by inducing the activity of the immune cells. Using complex synergistic interaction of diverse constituents of anticancer herbal medicines, herbal formulations can be designed against cancerous cells without damaging normal cells of the body.

Keywords- Cancer, Herbal medicine, Tumor, Chemical constituents

I. INTRODUCTION

Cancer the deadliest disease that a living organism suffers is because the growth of abnormal cells in the body is uncontrollable (1). In this context, several plant species (around 3500 plant species) having anticancer activities have been examined by the National Cancer Institute (NCI) (2). Immune modulators stimulate your immune system to fight against cancer cells (3), while cytotoxic action kills the cancer cell; however, the conjointly kill healthy cells and may solely be used under the direction of a doctor or therapist. Anti-cancer may be a broad word that will be lessened into 3 elements i.e. Anti-tumor, Cytotoxic, Anti-cancer. Cancer occasionally takes several years to develop, thus bar is desirable to any treatment. Evade all known carcinogens such as processed food, excessive alcohol, tobacco, and exposure to chemicals. A plant-primarily based diet will facilitate to shield you from cancer as plants are made in inhibitor and anti-inflammatory compounds; each of these is powerful cancer fighters.

1.1 Cancer

Cancer is essentially a sickness of an uncontrolled organic process (cell division). Cells have many alternative mechanisms to limit the process of cell division, repair DNA injury, and stop the event of cancer. Because of this, it's thought that cancer develops in an exceedingly multi-step method, during which multiple mechanisms should fail before an essential mass is reached and cells become cancerous. These variations facilitate them to grow, divide, and kind tumors. For instance, cancer cells gain the power to migrate to different elements of the body, a method referred to as metastasis, and to push the growth of the latest blood vessels, a process called angiogenesis (which offers neoplasm cells a supply of Oxygen and nutrients). Cancerous cell fails to

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undergo apoptosis under conditions when normal cells would and this might be due to DNA damage (1, 4-8).

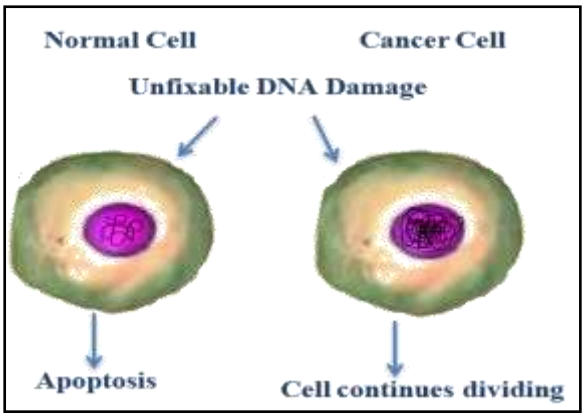

Figure 1: Responses of normal and cancer cells

Emerging research shows that cancer cells may undergo metabolic changes that support increased cell growth and division start superscript and end superscript different responses of normal and cancer cells to conditions that would typically trigger apoptosis.

- A normal cell due to unfixable DNA damaged undergoes apoptosis.
- A cancer cell with unfixable DNA damage undergoes continuous cell division (4)

1.2 Cancer development

Initial mutation inactivates a negative cell cycle regulator
↓
Next mutation over-activates a positive cell cycle regulator
↓
Third mutation inactivates genome stability
↓
Additional mutations accumulate rapidly
↓
Cancerous Cell

Figure 2: Process of development of cancerous cells

Cells have many various mechanisms to limit biological processes, repair DNA injury, and stop the event of cancer. As a result of cancer develops in an exceedingly multi-step method, during which multiple mechanisms should fail before an important mass is reached and cells become cancerous. Specifically, most cancers arise as a series of mutations acquired by cells via changes in DNA that made them divide quickly, and loss of internal and external controls over division with devoid of programmed necrobiosis.

Negative cell cycle regulation is inhibited by initial mutation. A replacement mutation takes place, creating a positive cell cycle regulator too active. In one of the descendants of this second cell, a 3rd mutation takes place, inactivating an ordering stability issue. Once the ordering stability issue is inactivated, further mutations accumulate apace within the cell's descendants (because mutations aren't any longer prevented or repaired as efficiently) (4). Once an important mass of mutations reaches, the cell acquires cancerous characteristics (uncontrolled division, evasion of cell death, capability for metastasis, etc.) and is claimed to be a neoplastic cell. Cancer is a leading disease that is the principal reason behind the mortality of humans being across the globe and numbers of cases are rising and predictable around 21 million by 2030 (9,10). The simple symbolic representation of mutation leading to cancer can be as below;

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Table.1. Overview of herbal medicinal plants specifications

S. N	Plant specifications	Plant image	S. N	Plant specifications	Plant image
11	✓ Name : GINGER ✓ Biological Name: Zingiber offcinale ✓ Family:Zingiberaceae		12	✓ Name : CUMIN ✓ Biological Name: Cuminum cyminum ✓ Family: Apiaceae	
2	✓ Name : DILL ✓ Biological Name: Anethum graveolens ✓ Family:Umbelliferae		13	✓ Name : GRAPES ✓ Biological Name: Vitis vinifera ✓ Family : Vitaceae	
3	✓ Name: TURMERIC ✓ Biological Name: Curcuma longa ✓ Family:Zingiberace		114	✓ Name : CARAWAY ✓ Biological Name: Carum carvi ✓ Family:Umbelliferae	
4	✓ Name : THYME ✓ Biological Name: Thymus vulgaris ✓ Family: Labiateae		15	✓ Name : FENUGREEK ✓ Biological Name : Trigonella foenumgraecum ✓ Family : Fabaceae	
555	✓ Name : MYRRH ✓ Biological Name: Commiphera myrrha ✓ Family: Burseraceae		16	✓ Name : CINNAMON ✓ Biological Name : Cinnamomum zeylanicum ✓ Family: Lauraceae	

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6	✓ Name : GINSENG ✓ Biological Name : Panax ginseng ✓ Family: Araliaceae		17	✓ Name : CORIANDER ✓ Biological Name : Coriandrum sativum ✓ Family: Umbelliferae	
7	✓ Name : BERBERIS ✓ Biological Name : Berberis vulgaris ✓ Family: Berberidaceae		18	✓ Name : GARLIC ✓ Biological Name : Allium sativum ✓ Family: Liliaceae	
8	✓ Name : SAFFRON ✓ Biological Name : Crocus sativus ✓ Family: Iridaceae		19	✓ Name : ALOE VERA ✓ Biological Name : Aloe barbadensis Miller ✓ Family: Asphodelaceae	
9	✓ Name: ASTRAGALUS ✓ Biological Name : Astragalus propinquus ✓ Family: Fabaceae		20	✓ Name : MILK THISTLE ✓ Biological Name : Silybum marianum ✓ Family: Asteraceae	
10	✓ Name: BLOODRO ✓ Biological Name : Sanguynaria canadensis ✓ Family:Papaveraceae		21	✓ Name : BROCCOLI ✓ Biological Name : Brassica oleracea ✓ Family: Brassicaceae	

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11	✓ Name : TULSI ✓ Biological Name : Ocimum sanctum ✓ Family: Lamiaceae		22	✓ Name : ASHWAGANDHA ✓ Biological Name : Withania sonifera ✓ Family: Solanaceae	

Figure 3: Herbal Drugs in Treatment of Cancer

II. DIFFERENT HERBAL PLANTS USED IN CANCER INCLUDING ITS ACTIVE CONSTITUENTS

2.1 Ginger (Zingiber Offcinale)

2.1.1 Chemical Constituents

Carbohydrates (50–70%) contribute a major part of ginger rhizome whereas lipid, terpenes (e.g. zingiberene, α-curcumene, α-farnesene, sesquiphellandrene and β-bisabolene) and penolic compounds (e.g. gingerol, paradols, and shogaol) complete the other contents of ginger. Gingerols and shogaol contribute major quantity of (23–25%) & (18–25%) respectively, apart from these, it contains essential elements like amino acids, raw fiber, ash, protein, phytosterols, vitamin A and minerals [11-13]. Some other minor compounds but reported in rhizome are 6-paradol, 1-dehydrogingerdione, 6- gingerdione, 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8-gingerdiol, 10-gingerdiol, and diarylheptanoids (14).

2.1.2 Anticancer Activity

Ginger components are effective against liver cancer. In a study, 6-shogaol has been reported to induce apoptotic cell death of Mahlavu hepatoma cells via an oxidative stress-mediated caspase-dependent mechanism. A decrease in Glutathione (GSH) level has been reported to be a major contributing factor in conciliating 6-shogaol-induced apoptosis of Mahlavu cells (14). Recently Jeena reported that blood concentrations of antioxidant enzymes superoxide dismutase (SOD), GSH, and glutathione reductase while liver concentrations of glutathione- S-transferase, glutathione peroxidase, and superoxide dismutase (SOD) enzymes increases after oral administration

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of ginger oil for one month to mice. Ginger oil conjointly created a vital reduction in acute inflammation created by carrageenan and dextran and formalin elicited chronic inflammation (15), suggesting its role in the hindrance of liver carcinogenesis.

2.2 Cumin (Cuminum Cyminum)

2.2.1 Chemical Constituents

The main chemical constituent of aroma compounds is cumin aldehyde and cuminic alcohol. Other significant aroma compounds of roasted cumin are the substituted pyrazines, 2-ethoxy-3-isopropylpyrazine, 2-methoxy-3-sec-butylpyrazine, and 2-methoxy-3-methylpyrazine. Other constituents present in cumin are γ-terpinene, safranal, p-cymene, and β-pinene (16).

2.2.2 Anticancer Activity

Cumin seeds increase the levels of carcinogen/xenobiotic-metabolizing phase I enzymes, cytochrome P-450 (cyt P-450) and cytochrome b5 (cyt b5), the levels of cyt P-450 reductase and cyt b5 reductase, and the phase II enzymes, such as glutathione- S-transferase and DT-diaphorase. These obtained conclusions along with antioxidant effects, strongly recommend the cancer chemopreventive potential of cumin seed, which is attributed to its ability to modulate carcinogen metabolism. Cumin seeds also decrease remarkably the incidence of both B[a]P-induced neoplasia and 3'MeDAB induced hepatomas in Wistar rats (17,18).

2.3 Dill (Anethum Graveolens)

2.3.1 Chemical Constituents

The fruit yields about 3.5% of the essential oil, about 20% of fixed oil and protein. The essential oil is an aromatic liquid consisting of a mixture of paraffin hydrocarbon and 40 to 60% of d-carvone along with D-limonene and other terpenes. It also contains various saturated and unsaturated fatty acids such as lauric (1.29%), stearic acids (0.9-3.86%), capric (5.97%), myristic (0.08-0.25%), palmitic (2.31-4.66%), oleaic (36.38-53.87%), linolenic (0.26-0.4%), linoleic (5.8-45.13%), palmitoleic (0.2%), eicosenoic (0.04%) and arachidoic acids (0.1-1.32%). A number of phenolic acids like vanillic, caffeic, protocathechuic, p-coumaric, ferulic, chlorogenic, syringic, rosmarinic, o-coumaric and trans-cinnamic acid were found in ethanol extracts of dill (19).

2.3.2 Anticancer Activity

Methanol extracts of dill showed anti-proliferative activity against tumor cell lines MK-1, HeLa, and B16F10 (20). The aqueous extracts of dill weed and seed exhibited mutagenicity to Salmonella typhimurium. Mutagenic constituents like quercetin 3-sulfate and iso-rhamneticn 3-sulfate (persicarin), were observed in aqueous methanol extract when the diets of dill weed and seeds were administered to the inbred strain ACI rats (21). Detoxifying enzyme-like glutathione S-transferase is induced by dill weed oil when observed in target tissues of several mice (22).

2.4 Grapes (Vitis Vinifera)

2.4.1 Chemical Constituents

Different parts of grapes shown activities according to plant parts like leaves: 60-70% Polyphenolic derivatives: anthocyanins, leuco-anthocyanins**,** flavonoids (4-5%) (kaempferol-3-O-glucosides, quercetin3-O-glucosides, myricetin, rutin, quercitrin, isoquercitroside, kenferol, luteolol), gallic tannins and Catechins. Fruit contains carbohydrates (glucose) and organic acids (tartaric, malic, succinic, citric, and oxalic acids. And seed contains 15-20% unsaturated fatty acid (phenyl acrylic acid derivatives), procyanidins, or proanthocyanidins (mostly hexamers) (23).

2.4.2 Anticancer Activity

Resveratrol shows well-characterized anti-cancer and anti-neoplastic properties. Mitochondrial release of cytochrome-c, the formation of the apoptosome complex, and caspase activation is associated with Anticarcinogenic effects. The antiproliferative and pro-apoptotic effects of resveratrol in breast cancer cells are considered due to the accumulation of ceramide and the stilbenoids containing phenolic moiety, which is essential to induce ceramide associated growth inhibition (24). Human breast cancer cells have been inhibited by red wine polyphenolic which is demonstrated to be due to inhibition of cell proliferation by flavonoids, which could further be related to the inhibition of calcium calmodulin associated phosphodiesterase activity, indicating that flavonoids interfere with the function of the second messenger calcium (25).

2.5 Turmeric (Curcuma Longa)

2.5.1 Chemical Constituents

Turmeric has 5% of volatile oil, resin, abundant zingiberaceous starch grains, and curcuminoids. The principal component of curcuminoids is curcumin (50 - 60 %). Chemically

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the species of Curcuma consist of volatile oil, starch, and curcumin. Volatile oil ranges from 1 – 6.5% and is composed of mono & sesquiterpene such as α and β pinene, α-phellandrene, camphor, camphene, DL-ar-termerone zingiberene & α, β curcumenes (26).

2.5.2 Anticancer Activity

Curcumin has an anti-proliferative effect in multiple cancers and it inhibits transcription factor NF-κB and downstream gene products like including Cyclin D1, COX-2, NOS, c-myc, Bcl-2, interleukins, TNF-α, and MMP-9. It also affects a variety of growth factor receptors and cell adhesion molecules involved in tumor growth, angiogenesis, and metastasis (26).

2.6 Caraway (Carum Carvi)

2.6.1 Chemical Constituents

limonene, carvacrol, carvone, carvenone, γ-terpinene, α-pinene, linalool, and p-cymene are the major phyto-constituents reported in caraway seeds (27). Different plant parts of wild-growing caraway contain limonene, inflorescences limonene, and germacrene D with a quantitative proportion of 61-83%, 39-62%, 23-41% respectively. The oils from young fruits had a high proportion of limonene [61-83%], and those from inflorescences limonene [39-62%] and germacrene D [23-41%]. Contents of carvone have differed enormously in fruits, inflorescences, and leaves like leaves and stems, low in volatiles, were dominated by germacrene D and germacrene (28).

2.6.2 Anticancer Activity

DMH induced carcinogenic animal study has shown that long term feeding of caraway oil altered Wnt/βcatenin signaling pathway activation during colon cancer promotion and expression of colonic β-catenin which further leads to suppression of DMH induced premalignant lesions in rat colon (29).

2.7 Thyme (Thymus Vulgaris)

2.7.1 Chemical Constituents

Thyme contains 1.0-2.5% of volatile oil (mainly contains thymol (20-80%), carvacrol, terpineol, and linalool), flavonoids, caffeic acid, labiatic acid, ursolic acid, resins, and tannins. **Essential oil**: The dried herbal substance contains up to 2.5% essential oil; the main components are thymol, carvacrol, p-cymene, γ-terpinene, linalool, β-myrcene, terpinen-4-ol (30,31).

2.7.2 Anticancer Activity

Confirmatory literature not are not reported as an anticancer activity of thyme but as a cancer model, human colon cancer cells HCT-116 were selected as representative enough for interaction with dietary constituents (32,33)

2.8 Fenugreek (Trigonella Foenumgraecum)

2.8.1 Chemical Constituents

Oily embryo of fenugreek mainly contains disogenin which has glycosides with opened F ring precursor of disogenin which also reported as hederagin. Stem contains essentially trigocoumarin, nicotinic acid, trimethyl coumarin, and trigonelline which are alkaloids. Mucilage (28%) is a integral part of seeds which consist of proteins, alkaloids such as trigonelline and Choline, 5% of a stronger-smelling, bitter fixed oil, a volatile oil. Fenugreek is rich in iron which contains 58% carbohydrates, 23–26% protein and 6–7% fat which about 25% is dietary fiber (34).

2.8.2 Anticancer Activity

In vivo study of azoxymethane-induced colon cancer has revealed that fenugreek seed powder and its bioactive component disogenin extract inhibited the formation of aberrant crypt foci (ACF) which can be observed as a preneoplastic lesion. After getting a response from in vivo study, further in vitro study has performed on HT-29 human colon cancer cells in which disogenin inhibited proliferated cell along with the induction of apoptosis (apoptotic proteins was validated check factor). Diosgenin also detected anticancer activity in bone cancer through suppression of cell proliferation and bone cell development through inhibition of TNF (tumor necrosis factor) (35-39).

2.9 Myrrh (Commiphora Myrrha)

2.9.1 Chemical Constituents

The main chemical constituents isolated from frankincense are pentacyclic triterpenoids (1 – 25%), tetracyclic triterpenoids (26–37%), macrocyclic diterpenoids (38–51%), and a variety of essential oils (52–63%). Pentacyclic triterpenoids principal component in frankincense which divided according to its structure as: ursolidine (1–16%), oleanolic (17 –20%), and lupinane (21– 25%). Their representative compounds are β-boswellic acid (1%), acetyl-β-boswellic acid (2%), 11-keto-β- boswellic acid

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(KBA 3%), 3-acetyl-11-keto-β-boswellic acid (AKBA 4%), α- boswellic acid (17%), and acetyl-α-boswellic acid (18%), which have been considered to be the biomarkers of frankincense (40).

2.9.2 Anticancer Activity

Essential oil like macrocyclic diterpenes, and pentacyclotriterpenes of frankincense are mainly responsible for the anti-cancer activity. Apart from this bas in pentacyclo triterpenes are frequently reported anticancer effects. This essential oil has the peculiarity to identify the tumor cell, bladder cancerous cell, and normal cells which at certain concentrations, block the cancerous bladder cell line J82, inhibit the growth of the cell, and induces apoptosis (41). The essential oil of frankincense induces apoptosis of SMMC-7721 cells by regulating the expression ratio of bax/bcl-2 in mitochondria which is cell-dependent by this it inhibits proliferation of human hepatocellular carcinoma cell line SMMC-7721 (42). These essential oils also inhibit breast cancer growth by regulating AMPK/mTOR pathway along with the induction of apoptosis (43).

2.10 Cinnamon (Cinnamomum Zeylanicum)

2.10.1 Chemical Constituents

Cinnamon bark contains about 0.5 to 1.0% of volatile oil, 1.2 % of tannins mucilage, calcium oxalate, starch, and sweetner like mannitol. Only active constituent of the drug is volatile oil. Cinnamon oil contains 60-70% of cinnamaldehyde, terpenes like phellandrene, pinene, cymene, caryophyllene, 5-10% eugenol, benzaldehyde, cumin aldehydes (44).

2.10.2 Anticancer Activity

Basically Ceylon cinnamon (Cinnamomum zeylanicum) is tropical shrilankan indigenous tree widely founds in Madagascar or Indo china region. Some constituents of the oil that may interfere with ras transformation were indicated by the cytotoxic activity. Isoprenylation of proteins was inhibited by several monoterpenes from essential oils of Cinnamomum oil such as limonene and geraniol and 20-benzyloxycinnamaldehyde (46-50).

2.11 Ginseng (Panax Ginseng)

2.11.1 Chemical Constituents

Biologically active constituent of penax ginseg (other is american ginseg) is ginsenosides (dammarane-type) which further categorized as: 20 (S) protopanaxatriol and 20(S)protopanaxadiol. P. ginseng. P. ginseng, P. quinquefolius and P varieties have low level of Rb1, Rd and Re ginsenosides compared to American ginseg. Also dammarane-type ginsenosides has major constituents like vietnamensis, notoginseng (51).

2.11.2 Anticancer Activity

The chronic intake of Panax ginseng C. A. Meyer decreases the incidence of cancers such as lung, gastric, liver, and colorectal tumors. Ginsenoside Rh2 has been shown to suppress proliferation in several human cancer cells including breast, prostate, hepatic and intestinal cancer, but also in animal cell lines (52-55). Various mechanisms are being hypothesized or proved for anticancer activity of ginseng among which in vivo and in vitro model helped to observed the suppression of human epithelial cells (e.g. MCF-10A) and marked suppression of TPA-induced cyclooxygenase-2 (COX- 2) expression has been reported by Surah and his colleagues. Along with this, they observed the same suppressive effect on NF-κB in mouse skin and extracellular regulated protein kinases (ERK) activation in TPA stimulated MCF-10A cells (56).

Consistent with the results of Surh, Keum reported that topical application of ginseng extract prior to each topical dose of the tumor promoter TPA markedly lowered the papilloma formation in mouse skin and caused a substantial reduction in epidermal ornithine decarboxylase (ODC) activity and suppressed the expression of its mRNA. All of the above-mentioned enzymes and factors are, in part, involved in tumorigenesis. COX-2 was upregulated in transformed cells and in various forms of cancer. Its overexpression inhibited apoptosis and increased the invasiveness of tumor cells. ODC is a rate-limiting enzyme in the biosynthesis of polyamines that play a pivotal role in cell proliferation and tumor promotion. Mitogen-activated protein kinase (MAPK) cascade is responsible, in part, for the upregulation of COX-2 as specific inhibitors of the corresponding MAPK abolish the induction of COX-2 and result in the production of prostaglandin E2. NF-κB is a ubiquitous eukaryotic transcription factor implicated in cellular proliferation and malignant transformation (57).

2.12 Coriander (Coriandrum Sativum)

2.12.1 Chemical Constituents

The major chemical constituents in seeds are up to 1.8% volatile oil according to origin. The

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coriander oil BP (distilled oil) contains 65 to 70% of (+) -linalool (coriandrol), depending on the source. The minor chemical constituents includes Monoterpene hydrocarbons (viz. α and - β pinene, limonene, γ-terpinene, αand γ-terpinene, ρ-lymene, borneol, citronellol, geraniol and geranyl acetate), Heterocyclic compounds (viz – pyrazine, pyridine, thiazole, furan, tetrahydrofuran derivatives; Isocoumarins viz coriandrin, dihyrocoriandrin, coriandrones A-E, flavonoids), Phthalides (viz - neochidilide, Z- digustilide; Phenolic acids and sterols, flavonoids) (58).

2.12.2 Anticancer Activity

In coriander seed essential oil, such as linalool, its main component, has been shown to have anti-cancer effects. Indeed, this natural compound moderately inhibited cell proliferation and hence could improve the therapeutic index of anthracyclines in the management of breast cancer, especially in multidrug-resistant tumors (59). Various experiments proved cancer preventive and inhibitory effects in coriander leaf and seeds extract e.g. in vitro antitumor and immunomodulating activities on the breast cancer cell line (60, 61). Moreover, the anti-tumorigenic properties of coriander have been recognized to its protective role against the deleterious effects in lipid metabolism associated with this malignancy in experimental colon cancer (62). Thus, coriander would be useful as supplements used in combination with conventional drugs to enhance the treatment of diseases such as cancer.

2.13 Berberis (Berberis Vulgaris)

2.13.1 Chemical Constituents

The plant B. aristata contains berberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine, and taxilamine. Berberis aristata contains protoberberine and bis isoquinoline type of alkaloid (63). Roots of plant B. aristata contains alkaloids such as berbamine, Berberine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorrhizine, karachine dihyrokarachine, taximaline, oxyberberine, aromoline and columbamine (64-68). Four alkaloids, pakistanine, 1-O-methyl pakistanine, pseudopalmatine chloride and pseudoberberine chloride were alsoisolated from Berberis aristata. A secobisbenzlisoquinoline or simple isoquinoline alkaloid was derived from B. aristata. The major alkaloid found in Berberis aristata is Berberine having a yield of 2.23% followed by palmatine (69-70). The chemical components are isolated from the plants belonging to the genus Berberis during the last two decades. Alkaloids are the main chemical constituents of Berberis species reported by different researchers. The major alkaloids reported from various Berberis species are berberine, berbamine, palmatine, columbamine, jatrorrhizine, oxyacanthine (71-72). The most biologically active compounds, berberine, and berbamine are widely distributed in almost all Berberis species (73).

2.13.2 Anticancer Activity

Therapeutic activity of methanolic extract obtained from stem of Berberis aristata was screened for anticancer effect against cancerous cell line of human colon and found to be effective along with this, it also indicated for concentration-dependent HT29 cells inhibition by extract. Dose-dependent study of cancer induced by 20-methylcholanthrene or nitrosodiethylamine performed in small animals shows that berberine alkaloid obtained from B. Arista inhibits carcinogenesis (74).

2.14 Garlic (Allium Sativum)

2.14.1 Chemical Constituents

Garlic bulb contains more than 200 chemical compounds, which are the volatile oils with sulfur-containing compounds like Ajoene, Alliin, and Allicin, enzymes like allinase, peroxidase, and myrosinase, other vital compounds like linalool, α- phellandrene, β-phellandrene, citral, and geraniol (75)

2.14.2 Anticancer Activity

Higher ingestion of allium vegetables is specially scallions and garlic is supposed to decrease prostate cancer risk around 50% and the same concepts are applied to pancreatic cancer also, however, the confirmatory study needs to be reported. Allicin is the most important predecessor of bioactive compounds of Garlic, is producing sulfur compounds. Some animal models have shown the efficiency of allium vegetables in boosting defense mechanisms against cancer through organosulfur compounds (OSC). The anticancer mechanism of garlic worked through influencing cancer cells by promoting the early mitotic arrest followed by apoptotic cell death devoid of disturbing healthy cells (75).

2.15 Saffron (Crocus Sativus)

2.15.1 Chemical Constituents

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The Crocus sativus L. contains major compounds like crocin, crocetin, picrocrocin and safranal.

The hydrophilic carotenoids of saffron which includes crocins constitute about 6-16% of saffron's dry matter. The other minor chemical constituents includes β-crocetin (mono) and γ-crocetin (dimethyl), esters of crocetin and mangi-crocin, an unusual xanthone-carotenoid glycosidic conjugate (76).

2.15.2 Anticancer Activity

Saffron has shown some positive results against cancer disease, chemo-preventive effects, and tumoricidal as well. Saffron has shown tumor-inhibiting in different malignant cells in some animal models e.g. recent studies have shown the tumor inhibitory activities of two natural components of C. sativus viz. crocin, safranal and some newly designed components derived from chemical modifications of safranal on the human monoamine oxidases (hMAO-A and hMAO-B-those are the major enzymes for targeting treatment of neuropsychiatric and neurodegenerative diseases). Their results confirmed crocin as a relatively weak inhibitor of hMAO. The described chemical derivatives of safranal, however, displayed much improved inhibitory activities against both hMAO enzymes (76).

2.16 Aloe Vera (Aloe Barbadensis Miller)

2.16.1 Chemical Constituents

High water content is the peculiarity of Aloe vera plant which ranging from 99% to 99.5%, while the remaining 0.5–1.0% solid contains more than 200 different potentially active compounds like simple and complex polysaccharides, organic acids, phenolic compounds, enzymes, vitamins, minerals (77). In the structural component study of Aloe vera plant leaf, it was observed that ring (dry weight basis) composed of the rind and pulp contain 2.7% and 4.2% lipids, and 6.3% and 7.3% proteins, respectively (78). Glucose as soluble sugars contents around 11.2% and 16.5% and in calcium contents of ash shows 13.5% and 15.4%. Non-starch polysaccharides and lignin show the bulk of each leaf fraction and were found to be 62.3% dry weight of the rind and 57.6% of the pulp, respectively (79).

2.16.2 Anticancer Activity

Aloe vera is one of the plants being studied extensively for its diverse health benefits, including cancer prevention. The cytotoxic potential of Aloe barbadensis crude extract (ACE) alone or together with cisplatin in human breast cancer cells (Factor-MCF-7) and cervical (Factor-HeLa) cancer cells was studied by cell activity assay, nuclear morphological study, and cell cycle analysis. Effects were correlated with modulation of expression of genes involved in cell cycle regulation, apoptosis and drug metabolism by RT-PCR. Exposure of cells to ACE resulted in considerable loss of cell viability in a dose- and time-dependent fashion, which was found to be mediated by the apoptotic pathway as evidenced by changes in the nuclear morphology and the distribution of cells in the different phases of the cell cycle. The effects were correlated with the downregulation of cyclin D1, CYP 1A1, CYP 1A2 and increased expression of bax and p21 in MCF-7 and HeLa cells. Additionally, a low dose combination of ACE and cisplatin shows a mixed index < 1, indicating synergistic growth inhibition compared to the agents applied one by one. In conclusion, these results signify that Aloe vera may be an effective anti-neoplastic agent to inhibit cancer cell growth and increase the therapeutic efficacy of conventional drugs like cisplatin. Thus promoting the event of plant-derived therapeutic agents seems secure for novel cancer treatment methods (80).

2.17 Astragalus (Astragalus Propinquus)

2.17.1 Chemical Constituents

Astragalus root mainly consist of components like polysaccharide mainly cycloartane glycosides fractions which include astragalosides-1, astragalosides-4 and trigonosides-1, trigonosides-3, foremost isoflavonoids like formononetin, ononin, calycosin, and its glycoside, saponins. Along with said constituents; it contains several minor isoflavonoids with some biogenic amines. It also contains structurally similar steroid hormone precursor e.g. triterpenoids. Triterpenoids and saponins (81).

2.17.2 Anticancer Activity

Gastric cancer induced by N-methyl-N'-nitro-N-nitrosoguanidine in vivo study performed on rat revealed that when AS IV considerably lowers the ratio of LC3-II/LC3-I along with the expression levels of proteins like ATG12, p62, Beclin-1, Ambra-1, ATG5 etc as compared to a comparative group of animals. Which finally concluded about the prevention of gastric mucosal injury? Recent studies have observed enhanced effects of apatinib when given with APS, also

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combined inhibited cell proliferation, migration, and invasion in pancreatic cells by a different mechanism of various down-regulating factors like MMP- 9, p-AKT etc.

In gastric cancerous AGS cells, conjointly apatinib and APS partially inhibits ATK signaling which further shows antitumor effects. Another cervical cancer HeLa cells study revealed that disease sensitivity could be enhanced by APS to cisplastin by enhancing HeLa cells autophagic activity through the mechanism of probably up-regulating Beclin-1, and down-streaming changes of proteins (82).

2.18 Milk Thistle (Silybum Marianum)

2.18.1 Chemical Constituents

Silymarin, a flavonoid complex that can be extracted from the seeds of the milk thistle, is composed of three isomers. (83). A standard milk thistle extract contains 70% silymarin, a mixture of the flavonolignans (silydianin, silychristin), and silibinin, which is the most biologically active constituent according to in vitro assays. Other constituents, including dehydrosilybin, desoxy-silydianin, and silybinomer have also been isolated (84).

2.18.2 Anticancer Activity

University of Texas Cancer Center has anticipated that Silymarin acts in inflammation and carcinogenesis via regulation of genes regulated by suppression of nuclear transcription factor. In human leukocytes, hydrogen peroxide damaged DNA protected by the Silymarin and in some in vivo UVB and chemically induced carcinogenesis mouse topical model has shown noticeably antioxidant properties (85).

2.19 Bloodroot (Sanguynaria Canadensis)

2.19.1 Chemical Constituents

Herbal plant of bloodroot mainly contains of eight isoquinoline alkaloids which includes six benzophenanthridine alkaloids (QBAs) e.g. Sanguilutine, chelerythrine, sanguirubine, sanguinarine, chelilutine, chelirubini and protopine alkaloids like allocryptopine. Some research highlighted anticancer effects of these biogenic constituents especially sanguinarine and chelerythrine (86).

2.19.2 Anticancer Activity

When Sanguinarine is compared with daunorubicin and doxorubicin, it is shown to interact with DNA via cell death mechanism through impairment of DNA polymerase inducing DNA strand breaks, additionally, cell cycle terminated via binding to G-Quadruplex oncogenes c-Myc, KRAS, and C-kit. Sanguinarine responsible for the death induced by inhibition of cell proliferation resulted from targeting the cellular cytoskeleton and inducing irreversible microtubule depolymerization. The study showed that Sanguinarine responsible for the impairment of H-DNA by binding it which is responsible for poorer results in colorectal cancer. It also responsible for altering chromatin structure and gene expression through a combination of B-DNA and Z-DNA (87-92).

2.20 Broccoli (Brassica Oleracea Var. Italica)

2.20.1 Chemical Constituents

The chief constituents of Broccoli are glucosinolates, flavonoids, hydroxycinnamic acids. Bioactive compounds like isothiocyanates, nitriles, thiocyanates, epithicyanates, epithionitriles, and oxazolidines are the resulted from the hydrolysis of Glucosinolates through β-thioglucosidase enzyme (myrosinase), apart from these lot more glucosinolates are identified e.g. gluconapin, sinigrin, glucocheirolin, glucoraphanin, glucoiberverin, 4 methoxyglucobrassicin, hydroxyglucobrassicin, glucoerucin etc (93).

2.20.2 Anticancer Activity

Some animal studies shown that after intake of broccoli, it digested and broken down in bioactive compounds like isothiocyanates, thiocyanates, nitriles, isothiocyanates etc, helps in multiple organ's cancer inhibition. Several pathways of cancer prevention have been helped by these bioactive compounds in animal or in vitro cell lines which are identified by National Cancer Institute (NCI) e.g. helping in various mechanisms like protecting cell from DNA damage, cell death induction (apoptosis), inhibition of tumor blood vessel formation and migration of tumor cells etc. Routine diet consumption of broccoli leads to reduced risk of some cancer (94-95).

2.21 Tulasi (Ocimum Sanctum)

2.21.1 Chemical Constituents

Ocimum sanctum is extremely refined plant containing several biologically active compounds and nutrients. Different parts of Ocimum sanctum includes different active compounds like leaf contain volatile oil methyl carvacrol, urosolic acid, caryophyllene, eugenol, euginal (eugenic acid), carvacrol, limatrol, linalool

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etc. Seed mucilage made up of some sort of sugars (polysaccharides) and anthromycin but only seed contains Sitosterol with some volatile oils. Saponins, flavonoids, triterpenoids, and tannins like bioactive compounds are the part of stem and leaves of Ocimum sanctum. It also includes antioxidant and anti-inflammatory activity showing active compounds like apigenin, cirsimaritin, rosmarinic acid, isothyrnonin, isothymusin etc (96).

2.21.2 Anticancer Activity

The dose of Ocimum sanctum L. leaves on biologically processed mice containing 600 mg diet for 10 weeks, effectively reduce the 3,4-benzopyrene [B (a) P] and 3'-methyl-4-dimethyl amino azobenzene (S'MeDAB) show squamous cell carcinoma and the occurrence of a hematoma. In the second case, fresh leaves juice was applied on the skin of experimental rats three times a week for 20 min along with tumor promoter agents (dimethylbenzanthracene as initiator and croton oil as a promoter of cancer). No occurrence of the tumor was found in 20 weeks follow up periods in Ocimum sanctum L. treated groups. The ethanolic extract of Ocimum sanctum L. leaves at a dose of 400 and 800 mg kg_1, b.wt., has been found to modulate the carcinogen metabolizing enzymes such as cytochrome P450, cytochrome-b5, and aryl hydrocarbon hydroxylase of mice liver (97).

2.22 Ashwagandha (Withania Somnifera)

2.22.1 Chemical Constituents

The water-insoluble extract obtained from the Root of Ashwagandha has shown presence of active constituents like α + β glucose, β-sitosterol glucoside, β- Sitosterol, stigmasterol, stigmasterol glucoside, viscosa lactone B etc. The chief constituents present in withanolides, steroidal lactones, cuscohygrine, withaferin A, tropine, alkaloids. Withanolides are structurally similar with ginsenosides of Panax ginseng, leading to a common name for W. somnifera, "Indian ginseng" (98).

2.22.2 Anticancer Activity

Urethane-induced adenomas in male albino mice when given orally Withania somnifera (200 mg/kg), have reduced tumor incidence. Study shown protection of the lung of animals by W. somnifera as compared to the control drug animal group. W. sominfera has increased the life span of animals might be by the evocation of cancer when intraperitoneal administration of the root extract (20 mg/dose/animal, IP) was given (98).

III. SUMMARY OF THE ROLE OF DIFFERENT HERBAL PLANTS PARTS IN VARIOUS DISEASES AND AVAILABLE MARKETED preparations

S. N	Drug	Part of drug used	Type of Cancer Cured	Key Ingredients	Marketed preparations
1	Ginger root	Rhizome	Colon, ovarian prostate cancer	Terpenes, oleoresin	1) Focalgin-B 2) B-Nexa
2	Cumin	Seeds	Colorectal, breast ovarian, myeloblastic and prostate cancer	Contain large amounts of iron	1) N-cumin 2) Zovika Black Cumin oil
3	Dill	Seeds, leaves , flowers	Cancer	Anethofuran, carvone	1) Bloatonil 2) Biofinest Dill Weed
4	Grapes	Leaves, fruits , seeds	Lung, prostate, colon and breast cancer	Proanthocyanidins	1) Swanson Grape seed 2) Livestamin Grape seed extract
5	Turmeric	Rhizome	Colon and cervical cancer	Curcumin	1) Mothertree Curcumin turmeric extract 2) Healthy Way turmeric cucumin
6	Caraway	Fruit	Colon cancer	Nutrients, vitamins, minerals, dietary fibers	1) Hawaii pharm caraway 2) Pure Caraway essential oil
7	Thyme	Stem	Liver, colon, breast lung and prostate cancer	Chamomile	1) Balkan Herb Thyme Tincture 2) Folha Dagua

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8	Fenugreek	Leaves , seeds	Breast, prostate and bone cancer	Dietary fiber, B vitamin, iron and dietary minerals	1) Hemani Fenugreek oil 2) Healthy Hey Fenugreek extract
9	Myrrh	Stem	All kinds of cancer	Volatile oil, resin, gum	1) Eden Garden Myrrh Oil 2) Gya Labs Myrrh oil
10	Cinnamon	Leaves, Bark	Cervical, stomach colon, lung, breast cancer	Proanthocyanidins and cinnamaldehydes	1) Bangota cinnamon oil 2) Gaia Herbs cinnamon bark
11	Ginseng	Root	Breast cancer	Ginsenosides and polysaccharides	1) Ginseng RHs Capsule 2) Genmax
12	Coriander	Dried Fruit, Seeds	Breast and liver cancer	Coriandrol	1) Kazima Coriander Oil 2) Revive Coriander essential oil
13	Berberis	Root, Rhizome, Stem	Ovarian cancer, prostate cancer	Alkaloids	1) Magisol Berberis tablets 2) EZYABSORB Berberin
14	Garlic	Bulb	Brain and colon cancers	Phytonutrients, minerals, vitamin	1) HealthDiva PhycoMax 2) Ranbaxy's Garlic pearls
15	Saffron	Dry Stigma	Skin, liver, lung stomach, pancreatic, colon and breast Cancer	Carotenoids and crocetin	1) Docufer –XT 2) NanoMax.ca
16	Aloe vera	Leaves	Prostate and lung cancer	Vitamins, minerals, tannins and some elements	1) Nature's swachh aloe vera 2) Sriram herbals TIG-10
17	Astragalus	Root	All types of cancers	Astragloside, triterpeneglycosides, polysaccharides	1) MEDI HERB Astragalus Complex M 1123 2)SOLGAR Astragalus root
18	Milk thistle	Herb	Liver cancer	Silymarin	1) Panaseeda milk thistle oil 2) Parker Naturals liver support
19	Bloodroot	Rhizomes	Breast and skin cancer	Sanguinarine, alkaloids	1) Baxter Endoxan 2) Herb Era bloodroot
20	Broccoli	Flowers	Colo-rectal and bladder cancer	Lutein and zeaxanthin	1) Prostaphane 2) Vitalica The Original sulforaphane glycosinolate
21	Holy basil	Leaves	Breast, lung, liver, oral skin cancers	Oleanolic aid, ursolic acid,	1) Living herbs Ocimum basilicum

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	(Tulasi)			rosmarinic acid, eugenol, carvacrol, linalool, β caryophyllene, germacrene	Essential Oil 2)Swarna Kapila Tulsi Arka
22	Ashwagandha	Whole Plant	Slows down growth of cancer cells	Iron, glycowithanolides, tannins, glucose, potassiumnitrate, alkaloids, fatty acids and some other substances	1) Sudhanta herbal products Ashwagandha capsules 2)MEDLIFE Essentials ashwagandha

IV. CONCLUSION

Because of the severity of cancerous tumor progression and global prevalence of this disease along with successful but mild treatment like chemotherapy and radiation, has proved the most toxic, lethal side effects of these treatments. So there is a need for the alternative and least toxic with minimum side effective therapy since the cancerous condition has already been diminished the physical state of patients. Recent era exploring the use of herbal plant medicines like ayurvedic or unani preparations in different disease conditions but confirmatory herbal medicines not been explored much especially for cancer treatment. As far as future perspective concerns, confirmatory in vivo studies can give more reliable results for herbal treatments in different types of cancer.

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