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Breast Cancer and Herbal Treatment

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ABSTRACT

All around the world about1.7 millions of females are resulted with breast cancer and arround 522,000 deaths. Which is more common in developed countries than the developing ones. Breast cancer mostly occurs in cells from the lining of milk ducts and the lobules that supply the ducts with milk. Symptoms of Breast cancer includes a lump in the breast, dimpling of skin, change in shape of breast, fluids coming from nipple. Risk factor for development of breast cancer includes age, sex, obesity, lack of physical exercise, alcohol consumption, hormone replacement therapy during menopause, exposure to ionizing radiation, early age at first menstruation, and family history. Breast cancer is the most serious health problem in developed countries, proper diet, exercise and healthy life style can reduces the risk of breast cancer. Surgery and chemotherapy are the treatment for breast cancer, as chemotherapy has many side effects 50% weakness occurs due to cancer and 50% weakness occurs due to chemotherapy, hence herbal drugs or herbal treatment is the best option for breast cancer. Number of herbal drugs are effective in breast cancer In this study detailed study of the herbal drug used in breast cancer is discussed in detail.

Key Words: Hormone,chemotherapy,dimpling,menopause,obesity.

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Introduction

Worldwide breast cancer is the most common invasive cancer in females. Which occurs mostly at the age of 40-75 yrs in females. All around the world breast cancer accounts for 16% of all female cancers and 22.9% of invasive cancers in women and 18.2% of all cancer deaths including both males and females [1]. Breast cancer mainly occurs due to starts off in the inner lining of milk ducts or the lobules which supply them with milk [2].2-3% risk of breast cancer has been increased annually in developed countries over the last several decade .It is the most serious health problem for women in developed and developing country. Herbal medicine most widely used for centuries to treat many diseases like hypertension,diabetes,depression,anxiety,cough,asthma,menstrual disorder,bowel syndrome,eczema,skin problem,feveretc. Herbal medicine cured the diseases as a natural way without producing any side effects .Most of the people used herbal medicine to treat different types of cancer. Some studies have shown that as many as 6 out of every 10 people with cancer (60%) use herbal remedies alongside conventional cancer treatments..Herbal medicine is the choice of treatment for cancer used by the people because of its no or less side effect, easily available and economically affordable as compared to allopathic treatment. Anticancer chemotherapeutic agent produce number of side effect, as 50% of weakness is due to cancer and 50% of weakness is due to chemotherapeutic agent hence herbal treatment is choice of cancer treatment which is life survivor. Breast cancer continues to be a major public health problem in developed as well as developing countries and continues to be the leading cause of cancer deaths among women worldwide, with approximately 375,000 deaths in the year 2000[3]. Herbal treatment improving quality of life, supporting to conventional cancer treatment, preventing recurrence of cancer and eventually to prolong survival amongst the breast cancer patients.

Immunological mechanisms of Anti-breast cancer agent and Herbal Drugs in breast cancer

From the study it has been shown that number of herbs rich in flavonoids may be protective against various types of cancer, from ovarian cancer to lung and pancreas cancers. About more than 5000 flavonoids were identified in fruits and vegetables. Flavonoids of genstein (principle isoflavonoid of soya) and quercetin present in many herbal plants also present at large amounts in the skins of apples and red onions have been shown to inhibit tumor cell growth. Though animal and cell culture studies indicate that tumor-preventive effects of electron donor flavonoids are due to their free radical scavenging properties [43,44], The spectrum of flavonoid effects spreads from inhibition of cyclin-dependent kinases (CDKs), which are critical for cell growth and division, to blocking angiogenesis and modulating MDR1 activity.

Taxol was found to be very effective in breast and ovarian cancer treatment, which is very effective in arresting cell cycle by blocking microtubules depolarization.

alkaloids vincrstine and vinblastine isolated from periwinkle Catharanthus roseus or Vinca rosea, were found as well be efficient in breast cancer treatment.

Among most extensively investigated flavonoids, flavopiridol, catechins, genistein and quercetin are known to prevent cancer and possess anti-tumour activities. alkaloid rohitukine [54]. Rohitukine was isolated for the first time from Amoora rohituka (family Meliaceae) in 19 [46,47] and later from Schumanniophyton magnificum [48], andDysoxylum binectariferum [49]. Rohitukine showed moderate cytotoxicity against human HL-60 promyelocytic leukemia and HCT-116 colon cancer cells [50]. After replacement of a methyl group by the chlorophenyl moiety at position 2 of rohitukine, additional pharmacological properties were acquired: [51,52] from inhibition of different CDKs, thus inducing apoptosis, to modulation of the immune response. In the breast carcinoma MCF-7 cell line, flavopiridol produced arrest of cell cycle in G1, and this action was not dependent on functional p53 [53]. It is to mention that flavopiridol was the first CDK inhibitor to be tested in clinical trials [54].

another example of a polyphenol which exerts both cell protecting and cancer cell killing effects is quercetin. This flavonoid present in high amounts in some fruits and plants is suggested to exert these opposing actions by playing a role of an antioxidant due to metal chelating and

Table1.List of Anti breast cancer agent

Sr.No.	Category	Phytoconstituents	Pharmacological activity
01	Flavonoids	Curcumin	Inhibit transcript of VEGFR and b-FGF
		Resveratrol	Interfering PI3K pathway
		Baicalin	Anti-breast cancer
		Scutellarin	Anti-breast cancer
02	Terpenoids	Parthenolide	Anti-breast, anti-cervical cancer
		Ursolic cid	Anti-breast cancer
03	Alkaloids	Berbamine	Anti-mammary cancer
		Camptothecin	Anti-mammary cancer
		Rescinnamine	Anti-mammary cancer
		Tomatidine	Anti-mammary cancer
		Vincristine	
		Ellipticine	Binding to DNA to produce antibreast cancer effect
04	Coumarins	Bergapten	Anti-breast cancer
		Cnidilin	Anti-breast cancer
		Dicoumarol	Anti-breast cancer
		Notoptol	Anti-breast cancer
		Psoralen	Estrogen-like activity
		Quercetin	Estrogen-like activity
05	Sulphar containing comp	Allilin,Allicin	
06	Quinone and other chemical classes	Plumbagin	Anti-breast cancer
		Artemisinin	Anti-breast cancer
		Artemisunate	Anti-breast cancer
07	Polyphenols	Catechin	Inhibit mutagen activated protein kinase

scavenging free radicals, and a role of pro-oxidant due to its ability to generate ROS. The latter species may a priori induce DNA damage [55]. Numerous effects of quercetin on breast cancer cell functions were reported, from inducing p21 (CDK inhibitor) and arrest of cell cycle in G_1 or G_2/M [56] to apoptosis which could be due to caspase activation, microtubules modification and an increase of stress proteins expression [55] Epidemiologic evidence of preventive and curative potential of tea (Camellia sinensis) is not consistent. This may be explained by large varieties of tea consumed in Western countries (predominantly black tea) and in Asian countries (green tea). Meanwhile, anticancer properties of green tea are known for many years, and they are presumably due to high content of water-extractable polyphenols which is 5–10 times lower in an oxidized green tea derivative obtained after fermentation (black tea) [57].

Catechin present in green causes arrest of cell cycle in G1, increase of apoptosis, antioxidant and anti-estrogenic actions. Green tea extracts were shown to have synergetic action with a conventional anti-estrogens drug, tamoxifen. When tested on estrogen receptor-positive MCF-7, ZR75, T47D human breast cancer cells combinations of tea extracts and the drug were found to be more effective in suppressing the cell proliferation than either agent given alone [58].Green tea containing flavonoid epigallocatechin gallate EGCG, inhibits P-glycoprotein, and the EGCG effects were found to exceed those of quercetin and verapamil [59].

EGCG (also known as epigallocatechin gallate, epigallocatechin-3-monogallate, L-epigallocatechin gallate, epi-gallocatechin 3-O-gallate or epi-gallocatechin gal EGCG (also known as epigallocatechin gallate, epigallocatechin-3-monogallate, L-epigallocatechin gallate, epi-gallocatechin 3-O-gallate or epi-gallocatechin gallate) is the main green tea polyphenol.Direct pro-apoptotic effects of green tea extracts and tea catechins on tumor cells in vitro and in vivo were also demonstrated. When tested on different breast cancer cell lines, EGCG revealed a modest pro-apoptotic activity. However, treatment of 4T1 cells with EGCG in combination with taxol led to a dramatic increase in cell apoptosis compared to treatment with taxol alone [60]. The chemical structure of EGCG provides its ability to be a metal chelating agent, and to possess, depending on its concentration, either pro- or antioxidant activity. Different actions of EGCG were summarized in a review [61]. Other studies also indicate that green tea inhibits angiogenesis. It was demonstrated that crude green tea extracts and EGCG, the main green tea polyphenol, decreased in a dose-dependent manner transcription of vascular endothelial growth factor (VEGF) and inhibited MDA-MB231 breast cancer cell and human umbilical vein endothelial cell (HUVEC) proliferation. In mouse tumor models, green tea extracts suppress angiogenesis which was manifested by decreased necrosis areas and lower blood vessel density in the treated xenografts [58].

Herbal Drugs used in breast cancer-Most commonly used herbs to treat breast cancer includes echinacea, St John's wort, green tea and ginger,curcuma, the herbs such as Vinca rosea, Taxus species, Allium sativum, Aloe vera, Astragals membranaceus, Glycine max, Glycyrrhiza glabra, Hordeum vulgare, Hydrocotyle asiatica, Medicago sativa, Morinda citrifolia, Panax pseudoginseng, Saussurea lappa, Taxus wallichiana, Tinospora cordifolia, Viscum album, Withania somnifera, Zingiber officinale etc. Flavonoids,flavanol,sulphur containing agents, terpenoids,alkaloids, quinol related compound, polyphenols, coumarin etc are the Phytoconstituents which are present in herbal drugs effective against breast cancer listed in table 1.

All this mentioned drugs are naturally occurring substances used for centuries to treat the disease and to promote health, and all the time medicine relies mostly on plants, plant extracts, and other plant products. Day by day the research for new anticancer agents of natural and synthetic origin rests a very active field of scientific activity, due to acquired single- and multidrug resistance of tumor cells, a relatively new phenomenon appeared due to intense use of anticancer compounds.

Conclusion-Risk of breast cancer has been increased day by day due to busy schedule, lack of exercise, improper diet, lack of breast feeding, obesity, life style, alcohol consumption, genetics, hormonal contraceptive. Surgery and chemotherapy are the treatment for breast cancer, as per study chemotherapy produces number of side

Table 2.Herbal Drug used in breast cancer

Sr. No.	Name of antibreast cancer drug	Biological source	Phytoconstituents	Pharmacological effect	References
01	Green Tea	Camellia sinensis Family-Theaceae	epicatechin ,epicatechin-3-gallate, epigallocatechin (EGC),epigallocatechin-3-gallate,catechin, and gallocatechin	Antiangiogenic,antimutagenic, to scavenge reactive oxygen species as antioxidant	4
02	Cinnamon	Cinnamomum zeylanicum nees Family-Lauraceae	Cinnamon aldehyde	induction of apoptosis by methanolic extract of Cinnamomum zeylanicum bark in human hepatoma cancer cells indicates its anticancer activity	15,16,17
03	Glycerrhiza	Glycerrhiza glabra Family-Leguminosae	Glycyrrhizin, glycyrrhetinic acid	supplement the movement of natural killer cells and modulate the growth response of lymphocytes through augmentation of IL-2 production	5,6,7
04	Garlic	Allium sativum Family-Liliaceae	alliin, alliinase, allicin etc. Ajoene, another sulphur holding compound, present in garlic oil,	to augment action of the immune system by activating lymphocytes and macrophages to kill cancer cells. It is also identified to interrupt the metabolism of tumor cells	8,9,10
05	Turmeric	Curcuma longa Family-Zingiberaceae		slows down the development of cancer by averting the production of toxic eicosanoid such as PGE-2, curcumin hampers the initiation of cancer as well as encourages its	11,12,13,14

				deterioration	
06	Burdock	Arctium lappa Family-Asteraceae	Arctigenin, tannin andother active polyphenol and phenolic comp.	that averts mutations in the oncogenes. ability to eradicate nutrient-deprived cancer cells, It induces macrophage responses, inhibits tumor growth and possesses immuno-modulatory properties It has been used in the management of breast cancer, ovary, bladder, malignant melanoma, lymphoma and cancers of the pancreas.	18,19,20
07	Ginseng	Panax ginseng Family-Araliaceae		inhibit the production of tumor necrosis factor in mouse skin, inhibit the growth and proliferation of cancer cells in animal models, inhibit cell proliferation, induce differentiation, and stimulate interferon levels. Other tumor cell processes may also be interfered with by ginseng constituents	21,22,23
08	Flaxseed	Linum usitatissimum Family-Linaceae.	Lignans	lignan metabolites hold a structural resemblance to estrogens and can attach to estrogen receptors to hinder the development of estrogen-stimulated breast cancer.	24,25,26,27,28
09	Cat`s claw	Uncaria guianesis and U. tomentosa are two species of	glycosides, tannins, flavonoids, sterol fractions	inhibits the activation of nuclear factor-kappa beta, an inflammatory that is associated with cancer and other deadly diseases, Extracts and fractions	29,30,31

		cat's claw family-Rubiaceae		of cat's claw have been reported to stimulate T cells, macrophages, and other components of the immune system have antimutagenic and antiinflammatory properties	
10	Ochrosia elliptica	Ochrosia elliptica Family-Apocynaceae	Ellipticine	Lipophilic derivatives of ellipticine operates by binding to the DNA	32
11	American coneflower	Echinacea purpurea Family-Asteraceae	Phenols, alkylamides or alkamides, polysaccharides, glycoproteins, and caffeic acid derivatives.	increases the amount of natural killer cells in the experimental, act as an immune-stimulant, by promoting the activity of lymphocytes, increasing phagocytosis by macrophages and the activity of natural killer cells and inducing interferon production	33,34,35
12	Ginger	Zingiber officinale roscoe Family-Zingiberaceae		appeared to positively modulate a large number of molecular anti-cancer mechanisms, including induction of programmed cell death (apoptosis), up-regulation of the apoptosis gene Bax, down-regulation of numerous ancer-associated genes and proteins, increased expression of cancer-fighting proteins and inhibition of cancer-associated enzymes.	36
13	Black cohosh	Actaea racemosa L.	triterpene glycosides deoxyactein,	decrease in the development of breast cancer cells in culture	37,38

		Family-Ranunculaceae	acetein, and cimifugoside, resins and caffeic, isoferulic and fukinolic acid		
14	Dandelion	Taraxacum officinale Family-Asteraceae		decreased the growth of (Michigan cancer foundation) MCF-7/AZ breast cancer cells	39
15	Vinca	Cathranthus roseus Family-Apocynaceae	Vincristine,vinblastine, alstonine, ajmalicine and reserpine	they halt the division of cells and cause cell death. During cell division, vinca alkaloid molecules bind to the building blocks of a protein called tubulin, inhibiting its formation	40
16	Bitter melon	Momordica charantia L. Family-Cucurbitaceae	momordin, vitamin C, carotenoids, flavanoids and polyphenols.	bitter melon extract modulates several signal transduction pathways, which induces breast cancer cell death	41,42
17	Harin-hara	Amoora rohituka Family-Meliaceae	diterpene,alcohol, aphanamixol and ß-sitosterol. Seeds yield a limonoid, rohitukin, polystachin.	Rohitukine showed moderate cytotoxicity against human HL-60 promyelocytic leukemia and HCT-116 colon cancer cells	50

effects and responsible for weakness in patient. Number of herbal drugs are available which are effective against breast cancer. Herbal treatment is the best option for breast cancer because they have not any side effect and survive the life of breast cancer patient. Proper diet, exercise and herbal treatment are effective to control breast cancer

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