International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 2053-2065 www.ijprajournal.com ISSN: 2456-4494

Phytochemicals for Active Targeting In Cancer Treatment-A Review

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Submitted: 17-12-2022 Accepted: 31-12-2022

ABSTRACT-
In healthy people who use synthetic, natural, or biological agents to minimize the development of cancer, this is called chemoprophylaxis of cancer. Chemopreventive drugs suppress the development of cancer by blocking DNA damage that leads to malignant tumors, or by reversing or blocking the division of precancerous cells with DNA damage. Benefits This approach has been proven in clinical trials for breast, prostate, and colon cancer. The continued increase in cancer cases, the failure of conventional chemotherapy to control cancer, and the excessive toxicity of chemotherapy clearly require a different approach. The first attempt to demonstrate the benefits of chemoprophylaxis was tamoxifen, which showed a significant reduction in invasive breast cancer. Strategies that usechemopreventive agents to protect high-risk populations from cancer are healthy and promising. Dietary ingredients such as capsaicin, cucurbitacin B, isoflavones, catechins, lycopene, benzyl isothiocyanate, phenethyl isothiocyanate, and piperonal gum have been suggested to suppress cancer cells and act as chemopreventive agents. This review explored the mechanisms of chemoprophylaxis and anticancer effects. Some natural substances. Chemoprophylaxis is a relatively safe and inexpensive approach because it can prevent cancer. By changing your diet. This approach gained momentum after tamoxifen raloxifene was approved by the US Food and Drug Administration to reduce the risk of breast cancer.
KEYWORDS-Cancer, Phytoconstituent, Chemotherapy, chemoprophylaxis.

I. INTRODUCTION-

Cancer is a serious health problem that continues to be one of the leading causes of death worldwide. Advanced knowledge of the underlying molecular mechanisms of cancer progression has resulted inthe development of a large number of anti-cancer drugs. However, the use of chemicalsSynthetic drugs have not significantly improved overall survival in recent yearsmany decades. Therefore, new chemopreventive strategies and agents are needed to complement existing cancer therapies to enhance their effectiveness [1].

Natural Compounds from plants known as phytochemicals, serve as important resources for new drugs and also a source of cancer therapy. Some good examples include taxolanalogs, periwinkle alkaloids such asanalogs of vincristine, vinblastine, and podophyllotoxin. These phytochemicals usually work throughregulating molecular pathways involved in cancer development and progression. theSpecific mechanisms include increased antioxidant status, carcinogenic inactivation, inhibition of proliferation, induction of cell cycle arrest and apoptosis; and regulation of the immune system [2].

The main goal of this review is to describe what we know so far about compounds in natural products, as well as their pharmacological and molecular activities, or exact target. Recent trends and gaps in phytochemical-based cancer drug discovery were also discovered. The authors wish to expand the field of phytochemical research not only to their scientific robustness but also to their medicinal potential. Therefore, the emphasis is onInformation on anticancer phytochemicals is being evaluated at the preclinical and clinical levels [3].

The use of synthetic, natural, or biological agents to reduce the occurrence of cancer in healthy individuals is defined as cancer prevention. Cancer-preventing agents inhibit cancer growth by blocking DNA damage, which leads to malignancy, or by reversing or preventingthe division of damaged precancerouscells'DNA. The benefits of this approach have been demonstrated in clinical trials for breast, prostate, and colon cancer. The continued increase in cancer cases, the failure of conventional chemotherapeutic agents to control cancer, and the excessive toxicity of chemotherapeutic therapiesrequire an approach. to replace. The first trial showing the benefit of chemotherapy was performed in breast cancer patients with the use of tamoxifen, which

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 2053-2065 www.ijprajournal.com ISSN: 2456-4494

demonstrated a significant reduction in invasive breast cancer [4].

The success of The use of chemopreventive agents to protect high-risk populations from cancer suggestsA reasonable and promising strategy. Food ingredients such as capsaicin, cucurbitacin B, isoflavones, catechins, lycopene, benzyl isothiocyanate, phenethyl isothiocyanate, and piperlongumine have shown inhibitory effects on cancer cells, suggesting that they may act as agents. chemical prevention. In this review, we have addressed the mechanism of action of chemopreventive and anticancer effects. of a natural agent [5].

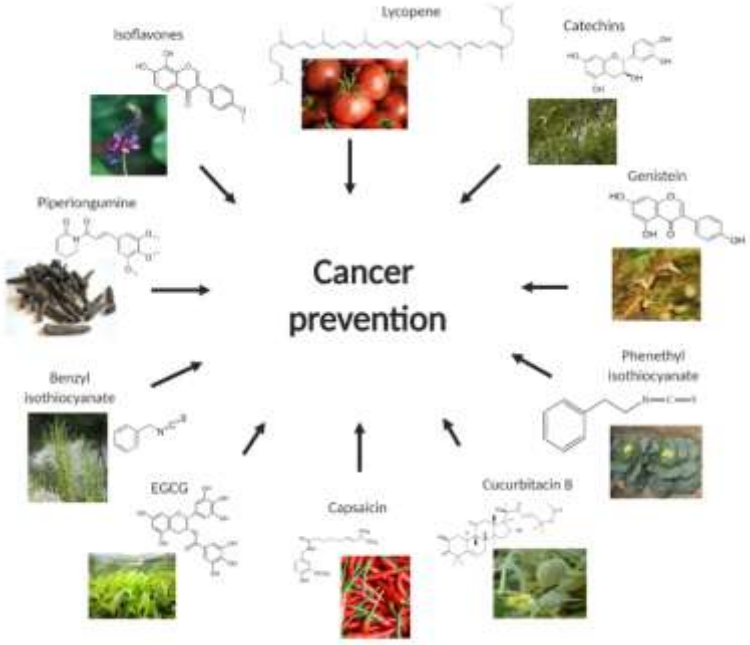

Figure 1. Phytochemicals used in chemotherapy.

CONVENTIONAL MEDICINE AND TREATMENT OFCANCER-

Variations in response to suggested treatment Intrinsic or acquired resistance to therapy persists for a subset of cancer patients. This often leads to treatment failure, disease progression, and often mortality rate. Cancer can be treated invasively and non-invasive treatment modalities such as surgery, chemotherapy, radiation therapy, as well as Other treatment modalities include gene therapy, immunotherapy, hormone therapy, photodynamics therapy, targeted therapy, palliative care, and a combination of these (eg, radiosurgery) [6].

WhenChemotherapy and radiotherapy are still the main standard care for cancer patients, as it helps reducetumor size and kill cancer cells at major sites or metastasis site, response to treatment is very different between different types of cancer, or even in patients with the same type of cancer. Among the common procedures, radiation therapyTherapy or radiation therapy is one of the most common cancer treatments [7]. Traditional radiotherapy use high-energy electromagnetic waves (eg:X-ray) to destroy and destroytumor cells by damaging their DNA. In addition, studies of radiation therapy in rodent models of cancer using radioactively labeled derivatives of J591 with an α. emitterproduces minimal anti-proliferative potential damage to surrounding normal cells [8].

An ideal cancer drug would selectively kill tumor cells but not normal cells. Most conventional anticancer drugs, however, arenon-specific, causing many toxic side effects and patient discomfort. In fact, given the ineffectiveness of 4044 current drugs, previous studies 4044 provide a model in which understanding the underlying tumor-host 4044 interaction mechanism could lead to discoveringnew drugs to overcome drug resistance [9].

In addition to purechemotherapy, a specific chemical agent (radiation sensitizer) can generally improve cell viability in response to

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Volume 7, Issue 6 Nov-Dec 2022, pp: 2053-2065 www.ijprajournal.com ISSN: 2456-4494

ionizing radiation and promote direct effects and radiation exposure. Tumor represents an exciting new area and is a major focus of Modern Cancer Research [10].

SHORTCOMINGS OF CONVENTIONAL THERAPY-

Although effective, Chemotherapy often has many side effects. For example, Easy Xoererensititive reactions were seen in Patients receiving platinum-based treatments Alkali agents, topoisomerases, and mitotic inhibitors; Pigments are widely available with alkaline agentsUses such as Ifosfamide, Cyclophosphamide and Thiipepa.Disseminated LiposomalSyndrome Doxorubicin, Daunorubicin, and 5`Fluorouracil. The development of biopharmaceuticals such as alternative hybrid therapy is also pushing the limits. Biologics are complex anti-cancer occupational macromolecules such as single-sugar antibodies, antibody fragments, and Anticorn complexes [11].

These therapies have been clinically proven to have low efficacy and low probability of penetrating solid tumors. Other therapies such as 4044 drug delivery systems (DDS) are engineered with active drug molecules that typically bind to 4044 biological carriers such as liposomes, nanoparticles or 4044 biodegradable polymers. Molecularly targeted therapies such as DDS have been reported to be associated with 4044 ophthalmic toxicity, ranging from 4044 unclear vision to conjunctivitis, keratitis, and optic neuritis. One of the main disadvantages of relapse therapy is that all cancer stem cells are eliminated from the body [12].

In addition, 4044 The development of multidrug resistance (MDR) is an important clinical challenge 4044. In addition, in many countries, the economic and social costs of 4044 incurred as a result of treatment costs remain one of the many obstacles to a cure for 4044 in order to reduce the overall incidence of 4044 cancers and the incidence of 4044 cancers [13]. death rate. So there is an urgent need Identify new methods and therapies Offer relatively expensive reporting programs with fewer unwanted side effects. Many of Complementary and Alternative TherapiesChemotherapy or Chemotherapy are mainly Inspired by Nature, especially the phytochemicals of Plants [14].

Table1 - The effects of numerous phytochemicals and their corresponding molecular targets on tumor growth, differentiation, proliferation, invasion, and metastasis, as well as treatment resistance, immune surveillance, inflammation, and tumor cell metastasis via diverse pathways.

Sr. No	Source	Active Constituent	Activity	Reference
1	Broccoli	-Indole-3-Carbinol (I3C)	I3C inhibits activation of transcription factors including nuclear factor-kappa B, SP1, estrogen receptor, androgen receptor, and nuclear factor-E2-related factor 2 (Nrf2). I3C has a broad spectrum of activities, combined with low toxicity. I3C up-regulated the tumor suppressor protein p23 and down-regulated cell cycle checks protein pRb and survival indicatorSurvivinI3C induces apoptosis, antiangiogenic activities and growth inhibition in multiples cancer cell lines and tumors.I3C induces G1 cell cycle arrest. I3C inhibitsAkt.	[15]
2	Grape skin and seeds	Resveratrol (RE)	Apoptosis is triggered when RE inhibits AKT activation. RE promotes acetylation of p53 and apoptosis. RE causes G1 arrest. RE downregulates	[16]

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			survivin expression and causes apoptosis through TRAIL sensitization. Resveratrol inhibitsproliferation, migration, and invasion via the Wnt/-catenin signalling pathway mediated by NEAT1.	
3	Stamens of Saffron	Crocin (Cr)	DMBA-induced skin cancer is inhibited by saffron. Apoptosis is the process by which saffron kills cells. Saffron and its primary compounds, such as crocusatin H, crocin-1, and crocin-3, have anticancer and anti-tumor properties, according to animal and in vitro research.	[17]
4	Spirulina	Phycocyanin (P)	Due to the MAPK, Akt/mTOR/p70S6K, and NF-B pathways, P suppresses cell growth and promotes apoptosis. P inhibits MDR1 via mechanisms involving reactive oxygen species and cyclooxygenase-2. Anti-inflammatory, anti-cancer, and potent dietary phyto-antioxidant.	[18]
5	Tea	Epigallo-Catechin Gallate (ECG)	Hsp70 and Hsp90 functions are inhibited by ECG. Hypoxia and serum-induced HIF-1 alpha protein buildup and VEGF expression are inhibited by ECG. ECG has been found in tests to increase the responses elicited by curcumin on breast cancer cells.	[19]

VARIOUS PLANTS USED IN VARIOUS TYPE OF CANCER-

It induces DNA fragmentation in

Dihydroartemisinin (DHA):

DHA is a derivative of artemisinin, a compound extracted from the mugwort plant Artemisia annua, a speciesin the chrysanthemum family and used by ancient Chinese herbalists to treat fever. It is has been shown to kill many types of cancer cells by inducing cell death. It is cytotoxic to epithelial cell-expressingpapilloma virus in vitro and in vivo and induces apoptosis by activating the mitochondrial caspase pathway in a p53 -independent method. It regulates the expression of VEGF in RPMI18226 multiple myeloma cells. and more Inhibits proliferation, migration and tube formation Oh HUVE. It has cytotoxic effects on C6 [20].

glioma cells and inhibitedhypoxia-induciblefactor1αactivation. DHA was shown to synergistically with temozolomide for cytotoxicity in mouse C6 glioma cells. It has been shown to bind humans to fortivirus; (antiapoptotic molecule overexpressed in many cancers) increases its prevalence and Depression [21].

fortivirus-dependent U205 cells. The data indicate that fortivirus is a molecular target of DHA. Developed as an antimalarial drug, it has undergone in vivo animal and human trials. He gave Human ovarian cancer cell sensitization to carboplatin therapy. demonstrated that a cohort of ovarian cancer cells responded to treatment with dihydroartemisinin alone; cancer cell lines 510 times more sensitive than normal ovarian cell lines. It induces cell cycle arrest G2,reducing the anti-apoptotic proteins BclxL, Bcl2, increasing pro-apoptotic proteins Bax and Bad [22].

Procyanidin-

Cocoa, berries, apples, and grapes all have a high quantity of procyanidin. Procyanidin is a powerful inhibitor of P-gp (a multidrug-resistant gene) and stimulates mRNA expression of the tumor suppressor genes IGF-2R and PTEN. It is recommended as an adjunct to traditional therapy. Procyanidin's chemopreventive potential in lung and breast cancer has recently been confirmed through research [23].

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Lycopene-

Tomatoes have a high percentage of lycopene, a pigment derived from vegetables and fruits. Lycopene decreases intercellular reactive oxygen species (ROS) via increasing antioxidants including glutathione-S-transferase-omega-1 (GSTO-1) and superoxide dismutase-1 (SOD-1) and ERO-1. Lycopene has been shown to slow the growth of ovarian tumours, lessen the risk of breast and prostate cancer, and prevent the cellular growth of colorectal and lung cancers.

Importantly, lycopene can also alleviatesradiation-induced esophagitis andscisplatin-induced nephropathy [24].

Isoflavones-

Isoflavones are naturalbioflavonoidsfound in plants of the legume family. Isoflavones are widely present in soybeans, lentils, beans, and chickpeas and are of effective importance as phytoestrogens in mammals. Soybeans are a rich source of isoflavones, such as genistein, glycation, and daidzein vary in concentrations between 560 and 3810 mg per kg soybean. Isoflavones are inactive as glycosides in plants and are activated to become biologically active [25]. aglycones by hydrolysis to beta-glucosidase in the intestine. Aglycones are conjugated to the liver glucuronide and excreted in the urine.

Interestingly, the active form of isoflavones has an absorption rate than the inactive form. A clinical trial using purified isoflavones started in 2009 (NCT01036321) and ended in 2018. The primary objective of this trial was to compare safety, efficacy, and mechanism of action Pure isoflavones in African-American and Caucasian Mentopatients with prostate cancer [26].

Change Percentage of Ki67 evaluated in tumor tissues of the prostate after 3 to 6 weeks of intervention with isoflavones (40 mg daily) compared with placebo. Based on the results of this clinical trial, isoflavones maybe developed as a potential chemotherapeutic and chemopreventive agent [26].

Phenethyl Isothiocyanate-

Phenethyl isothiocyanate (PEITC) is another isothiocyanate found mainly in cruciferous plants. PEITC is one of the active ingredients present in cruciferous vegetables which has been extensively studied for Its anti-tumor effects in glioblastoma, prostate cancer, breast cancer and leukaemiarequirement. Several studies have shown that consumption of cruciferous vegetables such as broccoli, watercress, and watercress has resulted in the detection of phytochemicals. in different rodent models. The study demonstrated the reactivation of RASSF1A by PEITC, which is known to function as a tumor suppressor by promoting G2/M cell cycle arrest and apoptosis in cancer cells. prostate letter [27].

Our study identifies the anti-breast cancer potential of PEITC for the first time in a breast cancer model. Our results showed that oral administration of 10 mol of PEITC for 10 days inhibited the metastasis of mammary glandtumor cells in the brain. Our other study showed that HER2 is a potential target of PEITC in breast carcinoma [28]. PEITC showed a synergistic effect in combination with doxorubicin and was associated with the downregulation of HER2 and STAT3. PEITC has also been shown to induce ROS in p53-deficient chronic lymphocytic leukemia (CLL) cells and thus may be effective in treating,CLL patients with p53 mutations. Interestingly, the combination of PEITC and paclitaxel increased the antiproliferative effects of paclitaxel on breast cancer cells. by inducing apoptosis and cell cycle arrest. PEITC in combination with adriamycin or etoposidehas been reported to induce activation of caspases 3 and 8 by regulating PKC and telomerase and thereby sensitizing cervical cancer cells.

One study recently showed chemopreventive effects of PEITC and an association of curcumin in prostate cancer xenografts. Our laboratory demonstrated immunomodulation by PEITC in mice bearing mammary tumorxenografts. We observed that PEITC treatment significantly reduced the growth of breast tumors by reducing myeloidtumorsuppressor cells (MDSCs) and upregulating T white blood cells [29].

Table2- List of phytochemicals currently in the clinical trial on various cancers

Sr. NO	Chemical Constituents	Type Of Cancer	Work	References
1	Berberine (alkaloid)	Colorectal cancer	Prevention of recurrence	[30]
2	Curcumin	Advanced	Quality of life, safety	[31]

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	(polyphenol)	andmetastatic breast cancer	incombination, progression-free survival, time to diseaseprogression, and time to treatment failure	
3	Epigallocatechin (flavonoids)	Colorectal cancer	Change in methylation pattern compare to baseline	[32]
4	Lycopene (carotenoids)	Metastatic colorectal cancer	Effectiveness in reducing skin toxicity alone or in combination with panitumumab.Pharmacokinetics.	[33]
5	Quercetin (carotenoids)	Prostate cancer	EGCG, ECG, quercetin, and their methylated metabolites in prostate tissue andplasma. Enzyme activity expression of COMT, DNMT1, and MRP1. Inter-individualvariation in genotype of COMT	[34]
6	Sulforaphane (isothiocyanate)	Former smokers with a high risk of developing lung cancer	Bronchial dysplasia index, cell proliferation marker Ki-67, apoptosis markersincluding caspase-3 and TUNEL	[35]

CHEMICAL STRUCTURES OF SOME ANTICANCER PHYTOCHEMICALS IN CLINICAL TRIALS.

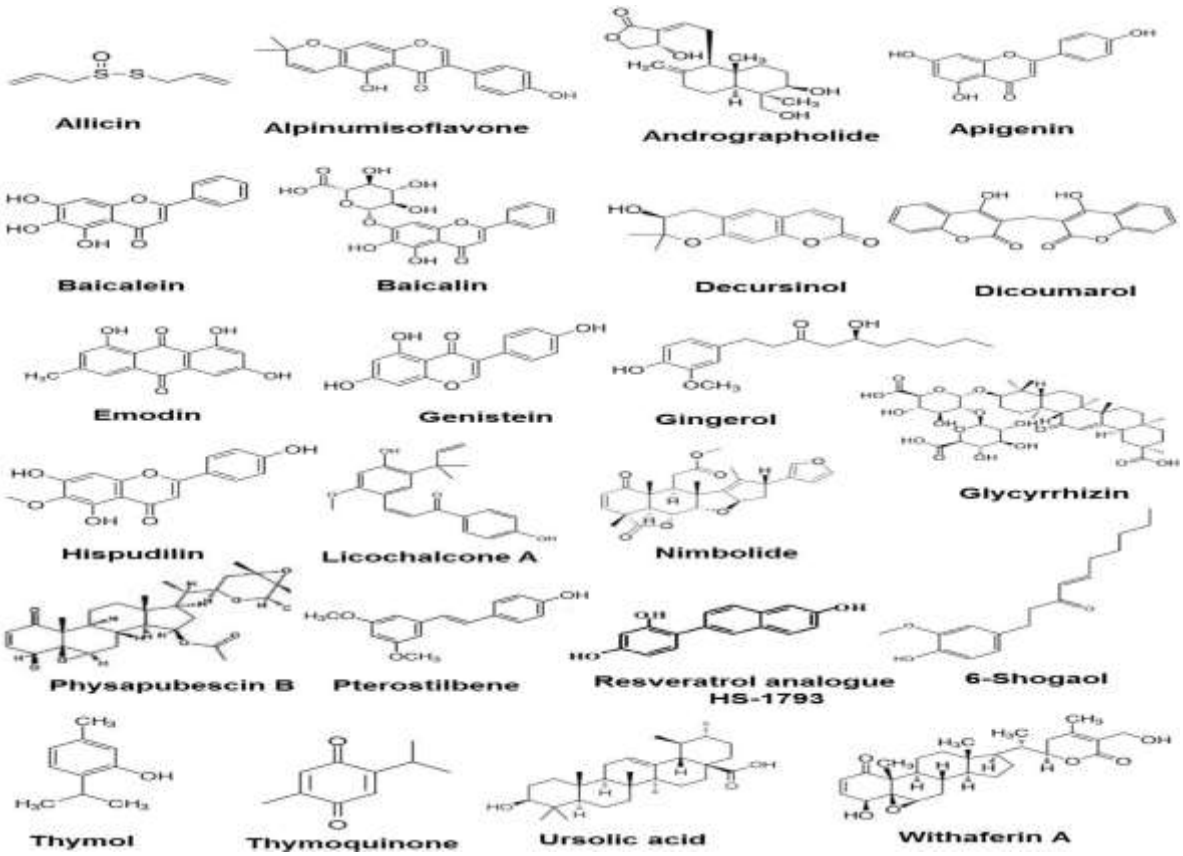

Table 3. Various Phytocompound is used for carcinoma.

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Sr. No	Class of phytochemical	Pharmacological action	Type of cancer	Molecular targets	Reference
1	**Vinca alkaloids** Vinblastine Vincristine Vindesine Vinflunine Vinorelbine	Inhibit microtubule polymerization and assembly, leading to metaphase arrest and cell death.	Non-small-cell lung carcinoma (NSCLC), breast, lung, leukemia, Hodgkin and non-Hodgkin lymphomas, testicular carcinoma, Kaposi's sarcoma, and second-line transitional cell carcinoma of the urothelium (TCCU)	Tubulin	**[36]**
2	**Camptothecin** Irinotecan Topotecan	Stabilizes topoisomerase I-DNA complex thereby preventing religation of single strand breaks resulting in lethal double-stranded breaks in DNA.	Ovarian, cervical, colorectal, and small cell lung cancer (SCLC)	Topoisomerase I	**[37]**
3	**Podophyllotoxin** Etoposide Teniposide	Inhibits DNA synthesis by forming a complex with topoisomerase II and DNA	Osteosarcoma, NSCLC cervical, nasopharyngeal, colon, breast, prostate, and testicular cancer	Topoisomerase II	**[38]**
4	**Taxanes** Cabazitaxel Docetaxel Paclitaxel	Inhibit microtubule function resulting in cell cycle arrest and aberrant mitosis	NSCLC, head and neck, breast, prostate, gastric adenocarcinoma	Tubulin	**[39]**
5	Ingenolmebutate	Rapid induction of cell death and activation of inflammatory response	Actinic keratosis	Protein kinase C	**[40]**
6	Homoharringtonine	Binds to large ribosomal subunit, which affects chain elongation and prevents protein synthesis	Chronic myeloid leukemia	Ribosomoal protein	**[41]**

Perspectives: Phytochemical Combination Studies For Chemotherapy –

Many of these herbs and their extracts are still adulterated and regulated in Asian countries for chronic diseases such as arthritis, diabetes, and cancer. There have been many complaints from practitioners in India, China, and other Asian countries, about curing cancer. The senior author met some of them, visited their "clinic", saw their "patients" who are said to have been saved from end-stage neuroblastoma and adenocarcinomas. The common characteristic of these students was their reluctance to submit herbal preparations for clinical trials using parameters (double-blind, randomized, crossover, or case-control study). In the United States, they are not approved by 3444

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regulatory agencies such as the FDA to treat specific diseases but are widely sold over-the-counter as a nutritional supplement [42].

Research in this interesting area was intense and was able to identify some operating compounds (as described in this evaluation), purification, structure, and lightening characteristics of compounds this and these results studies lead to many similar solids. The activity molecular mechanism of these compounds has been deeply studied. Many of them have been tested separately and match 2 or 3 together and show Sononance and Synergistic Properties. However, combined studies used have not been discovered together and the molecular mechanism of this combination must be asurvey [43].

So manycapabilities are combined to cause the complete and permanent cancer relief must be evaluated. The article's previous discussion of different 4044 phytochemicals demonstrates that each of these 4044 phytochemicals has multiple uses and purposes.Compounds,characteristic specifically for low toxicity with regard to effective absorption when taken orally,some of these compounds had no effect on but different types of cancer, andeach of the phytochemicals have many mechanisms in common, with another, and act on channels on their own [45].

The molecular mechanism of action of of these compounds has been studied extensively. Many of them have been tested individually and a combination of 4044 of the two and have shown a resonant and synergistic nature of 4044. However, studies combiningusing some of them together have studies could not be performed and the molecular mechanism of of these combinations needs to be elucidated. The ability of many such combinations with 4044 to induce permanent cancer remission needs to be evaluated [46].

Table 4. Phytochemicals clinically tested in cancerous patients.

Sr. No	Phyto chemical	Patients	Study Design	Intervention	Effect	Reference
1	Allium sativum	Patients with inoperable colorectal, liver, or pancreatic cancer	Randomized double-blind placebo controlled trial	4 garlic capsules per day for 12 weeks, 4 capsules contained 500 mg of aged garlic extract	Increase of number and activity of natural-killer cells	**[47]**
		Patients with colorectal adenomas	Randomized double-blind trial	3 capsules twice a day for 12 months, 6 capsules containing the equivalent of 2.4 ml of garlic	Suppress of size and number of colon adenomas	**[48]**
2	Camptothecin	Patients with refractory cancers	Phase I clinical trial	Camptothecin: 3 weeks on drug with a 1-week rest; Nitrocamptothecin: 5 consecutive days with a 2-day rest period	Both compounds lead to tumor regression in a number of patients with breast, prostate and melanoma cancers	**[49]**

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3	Curcumin	Patients with urinary bladder cancer, uterine cervical neoplasm, or intestinal metaplasia	Prospective phase I/II clinical trial	500 mg/day, orally, for 3 month	Histologic improvement in 1 out of 2 patients with bladder cancer, 1 out of 6 patients with intestinal metaplasia and 1 out of 4 patients with uterine cervical neoplasm	**[50]**
		Patients with advanced pancreatic cancer	Nonrandomized open-label phase II trial	8 g/day curcumin, orally, for one mouth	Among 21 patients, 1 had stable disease for >18 months and 1 had tumor regression	**[51]**
4	Green tea	Patients with high-grade prostate intraepithelial neoplasia	Double-blind placebo controlled trial	600 mg/day green tea catechins, orally, for one year	After 1 year, the incidence of tumor development was 3% and 30% in treated and control men, respectively; quality of life improved	**[52]**
		patients with histologically confirmed	Case-control study	Usual tea consumption	The prostate cancer risk	**[53]**

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		adenocarcinoma of the prostate			declined with increasing frequency, duration and quantity of green tea consumption green tea	

II. CONCLUSION-

Cancer is often fatal and is becoming more urgent in the world. They have to find new treatments. Medicine Plants have been an important source of information for discovering new things to treat human diseases. Therefore, this source could be a goodcandidate for newanti-cancer drug development. Among hundreds of plants studied for cancer some of these are present in vitro Experimental and animal studiesIn the context of clinical studies. Based on our literature search, Allium sativum, Camptothecin, curcumin, green tea, ginseng, resveratrol, rhusverniciflua, Viscum, the album contains satisfactory clinical examples to support its anti-cancer effect. There wasevidence. Therefore, it seems that they can be used as adjuvant therapy,along with common chemotherapeutic agents, and in various cancers. However,many other phytochemicals should be added to this list until further clinical studies support their anti-cancer effects. Complete WeaknessesPhytotherapy for CancerMostly Related studies exist systematicallygroups includingcontrols or lack of placebo, small sample size, and short study duration.

CONFLICTS OF INTEREST-

There are no conflicts of interest and disclosures regarding the manuscript.

ACKNOWLEDGMENT-

I would like to thank [Name of Guide] for her help and assistance in writing thismanuscript. I would also like to thank [Name of Principal]. Principal of [Name of college] his support on the manuscript.

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