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The impact of natural products on the treatment of cancer therapy

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ABSTRACT:

In this entire present reality, on the off chance that individual fear whom, it is malignant growth sickness. Albeit impressive advancement has been made in the therapy and control of disease movement, critical weaknesses and opportunity to get better remain. Now and again numerous undesirable secondary effects happen during chemotherapy. Normal cures, for example, the utilization of plant-inferred items in disease treatment, can decrease antagonistic incidental effects. At present, some plant items are being utilized to treat malignant growth. Nonetheless, a few plant items exist that have shown exceptionally encouraging anticancer properties *in vitro*, however, have not yet been assessed in people. Further investigations are expected to decide the adequacy of these plant items in the therapy of disease in people. This audit will zero in on different plant-inferred synthetic mixtures that, as of late, have shown guarantee as anticancer specialists and will lay out their possible systems of activity. The Present article deals with Natural product and their therapeutic advantages for the successful management of Cancer.

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INTRODUCTION:

Cancer is responsible for one in eight deaths worldwide—more than AIDS, tuberculosis, and malaria together [1]. However, cancer remains a leading cause of death worldwide. In the United States, for example, 589,430 deaths and 1,658,370 new cases of cancer are projected for 2015. Given the morbidity and mortality associated with the disease, as well as the significant economic burden, there continues to be a critical need for more effective strategies. In an ideal world, cancer chemoprevention would work as well as vaccines for the prevention of human ailments. Although this has yet to be accomplished, proof of principle has been established by seminal clinical trials conducted for the prevention of breast cancer with tamoxifen, and more recently with

tamoxifen relatives such as raloxifeno and a separate class of aromatase inhibitors. Agents such as finasteride have shown promise for the prevention of prostate cancer. In terms of drugs under investigation, as is the case with cancer chemotherapeutic agents, natural products have played a critical role in cancer chemoprevention studies. An overview is presented herein. Medicinal herbs and their derived phytocompounds are increasingly being recognized as useful complementary treatments for cancer. Because people are using more organic things nowadays biochemical and cellular mechanisms of herbal medicines in specific tumor microenvironments and the potential application of specific phytochemicals in cell-based cancer vaccine systems. This review should provide useful technological support for the evidence-based application of herbal medicines in cancer therapy. Various methods are used for cancer treatment such as chemotherapy, but in this method, because of the non-selectivity of medicines, a high percentage of healthy cells will be lost with cancer cells. The most important problem in cancer treatment is destroying tumor cells in the presence of natural cells, without damaging natural cells. In order to prepare anticancer medicines from natural resources like plants, testing cytotoxic compounds and screening raw extracts of plants is necessary [1,2].

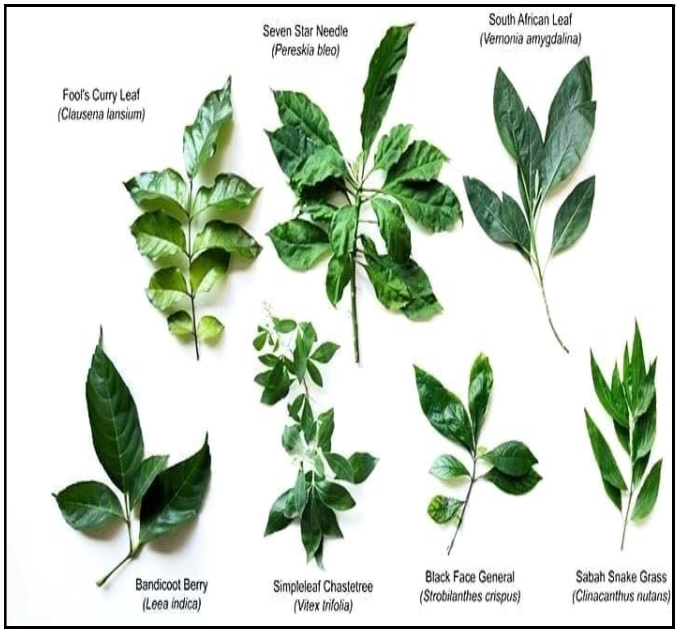

Fig 1. Some of the herbs and plants exhibit anticancer activity.

Therefore, the availability of natural products with higher effectiveness and lower side effects is desired. Medicinal herbs are important for cancer treatment due to their multiple chemical compounds for discovering new active materials against cancer [3].

In an ideal world, cancer chemoprevention would work as well as vaccines for the prevention of human ailments. Although this has yet to be accomplished, proof of principle has been established by seminal clinical trials conducted for the prevention of breast cancer with tamoxifen, and more recently with tamoxifen relatives such as raloxifene, and a separate class of aromatase inhibitors. Agents such as finasteride have shown promise for the prevention of prostate cancer. In terms of drugs under investigation, as is the case with cancer chemotherapeutic agents, natural products have played a critical role in cancer chemoprevention studies. An overview is presented herein [4,5].

Herbal products and other plants in cancer treatment and prevention:

According to the two famous Islamic physicians (Rhazes and Avicenna), diseases need to be treated by using a scheme that consists of three options; the first option will be by using physiotherapy and diet, the second one will be by using drugs, and the last option will be surgery. Drugs used at that time have been classified as simple and compound drugs. Treatment of any disease will start with the simple one to avoid drug-drug interaction; unless it did not work, then the physician will use the compound drugs, and when the second option failed too, then surgery will be used [6].

Current Trends in NHP Research and Cancer:

Even with all the incoming evidence, herbal drugs and other NHPs and NPs are usually shunned during systemic chemotherapy because of herb-drug interaction and exaggeration of chemotherapy-related toxicity. Current research is focused on the development of new and more effective chemotherapeutic agents that have little to no associated toxicity to the patient. Lately, this focus has been centered on NHPs and herbal formulations, mainly in the form of plants and other biological sources around the world. NHPs have been used for centuries by a variety of cultural backgrounds for a great number of illnesses; some of which continually provide new medicinal applications and intriguing anecdotal evidence, that merits further investigation. Today, there are numerous natural health products that fall under the umbrella of traditional medicine, such as the Indian herbs Tulsi (*Ocimum sanctum*), Neem (*Azadirachta indica*), and

Ashwagandha (*Withania somnifera*), commonly known as Indian ginseng or winter cherry. These herbs have shown an incredible diversity of treatments for diseases in both ancient and modern times as well. Ayurvedic medicine has been very informative in the introduction of numerous NHPs. Tulsi, also referred to as "Holy Basil," has in past decades been studied for its many health benefits, which include but are not limited to treatments for bronchitis, pain, malaria, asthma, arthritis, cancer, diabetes, and numerous microbial infections [7,8].

The study claims that it is primarily the phenolic compound, eugenol, to which the health benefits of Tulsi are owed, however more recent research suggests that there is an additional range of compounds at work, including the phytochemicals rosmarinic acid, apigenin, myretenal, luteolin, β-sitosterol, and carnosic acid; all of which have been shown to be valuable in the reduction of chemically induced cancers through initiating apoptosis and maintaining antioxidative and antiangiogenic effects [7,9].

On the same page, Neem leaves have been shown to possess a strikingly similar range of pharmacological effects to Tulsi and in one study are referred to as a "living pharmacy" in itself [10]. The benefits of Neem range from reductions in inflammation, microbial infection, progression of diabetes, oxidative stress, cancer proliferation, and tumor development, indicating chemopreventive benefits. Some of the active compounds within Neem are Azadirone, Nimbidin, Nimbolide, and the Polysaccharides GIa and GIb [11,12].

Ashwagandha has been a staple in traditional Indian medicine for decades and has been widely used, owing to the various properties that have been attributed to it. Ashwagandha is proposed to have antioxidant, anti-inflammatory, anticancer, antistress, and adaptogenic properties [13,14]. The extracts of this plant have been studied intensely to validate the claims that have been the backbone of its use in ayurvedic medicine. A recent study in 2013 showed the efficacy of Withania extract against metastatic breast cancer. The ethanolic extract of this plant was efficient in preventing the invasion of breast cancer cells in a spheroid invasion assay while inhibiting the metastasis of breast tumors to the lungs and lymph nodes in animal models [15]. In Phase II clinical studies, this herb was shown to promote the general well-being of patients when used in combination with chemotherapy, as well as enhance the cytotoxicity of chemotherapy in breast cancer patients. This combination of treatments led to an increase in the quality of life of the breast cancer patients in this study [16,17].

Some well-known plants used in anticancer:

Herbal medicines are desirable for cancer treatment because they are natural and readily available. They can easily be administered orally as part of a meal by the patient [18,19]. In addition, as naturally derived compounds from plants, they are generally more tolerable and non-toxic to normal human cells [20]. However, there are exceptions such as e.g., B. cyanogenic glycosides, lectins, saponins, lignans, lectins, and some taxanes [20,21]. Although herbal preparations can show selectivity in studies, are non-toxic to normal cell lines, and show cytotoxicity towards cancer cell lines, these drugs can be the subject of clinical studies for further therapeutic development. Herbal medicines can belong to four classes of medicines with the following activities; Methyltransferase inhibitors, drugs or antioxidants to prevent DNA damage, histone deacetylase (HDAC) inhibitors, and mitotic disruptors [20].

Achillea wilhelmsii:

Achillea plant with the scientific name Achillea wilhelmsii is from the *Asteraceae* order and Compositaea genus. Achillea has different species but Achillea wilhelmsii is more frequent in Iran and grows in different areas. *Achillea wilhelmsii* is a gramineous, perennial, and short plant of 15 to 40 cm.

The research study revealed that the methanol extracts and essence of leaves of this plant have cytotoxic effects on colon cancer cells (HT-29) and cytotoxic effects of essence are higher [18]. In other studies, the effects of methanol extracts from plant leaves against cell lineage of colon cancer and cancer of the stomach and breast are shown [19]. Methanol extract of the plant contains phenol compounds, especially flavonoids, which suppress the reproduction of cancer cells by inducing apoptosis [20,21]. One of the most important monoterpene compounds of this plant that causes apoptosis in human melanoma cells is 1,8-cineole and α-piene in plants' leaf essence [22].

Allium sativum:

Allium sativum is a plant of the Aparagales order, *Amaryllidaceae* family, and Allium genus. Allium sativum is a perennial plant harminus, the stem size is 40 cm. The underground part is blown out and consists of 5 to 12 parts surrounded by thin and thin membranes of grey and white color. Its leaves are thin and the fillets

are dark green, and the flowers are small, pink, like an umbrella at the end of the stem.

Several studies have shown that *Allium sativum* and organosulfur compounds reduce the risk of cancers of the breast, larynx, colon, skin, uterus, esophagus, bladder, and lungs. The sativum compound, i.e., allicin, the antitumor properties of this compound have been demonstrated in breast and prostate cancers. This compound causes the death of striatum cells and plays an anticancer role [23,24]. When *Allium sativum* is crushed and broken down, allicin is converted by an enzyme to allicin. Allicin is an inhibitor of the proliferation of human malignant cells. Ajoen is another compound that prevents the spread of leukemia and causes planned cell death.

Artemisia absinthium:

Artemisia is a plant in the *Asteraceae* family. Artemisia has 200 to 400 species that have clustered and bitter flowers. One species, Artemisia absinthium L, is native to Asian moderate areas, north of Africa, and vast areas of America. The size of this plant is 80 to 120 cm. The flowers of this plant are yellow and clustered [25].

Research on breast cancer cells MCF-7 has been reported [26]. Similar results related to the anticancer characteristics of this plant on 3 cancer cells HeLa, HT-29, and MCF7 have been reported. In a study about the Artemisinin effect of this plant on breast cancer cells, it was determined that plethoric reaction in cancer cells involves inhibiting cell growth, apoptosis, preventing angiogenesis, preventing cell migration, and decreasing responses of core receptors. Quercetin, isorhamnetin, kamfrolinalol, alphapinin, limonene, and myrecene are the other compounds of this plant [27].

Curcuma longa:

Curcuma longa is popularly known as turmeric in English, haridra in Sanskrit, and haldi in Hindi. The rhizome of the plant is traditionally used in cooking. The active ingredient of this plant is curcumin, a polyphenol derived from the rhizome of the plant [27]. Turmeric is used for both cancer prevention and treatment [28]. The anticancer potential of curcumin is associated with its ability to inhibit proliferation in a wide variety of tumour cell types [28,29]. The antiproliferative properties of curcumin may be related to its ability to down-regulate the expression of a number of genes, including NF-kappa B, Activator Protein 1 (AP-1), Epidermal growth receptor 1 (EGR-1), cycloxygenase 2 (COX2), lysyl oxidase (LOX), nitric oxide synthase (NOS), matrix metallopeptidase 9 (MMP-9), and tumor necrosis factor (TNF) [28-30]. Moreover, turmeric reduces the expression of various chemokines, cell surface adhesion molecules, cyclins, and growth factor receptors, including epidermal growth factor receptor (EGFR), and human epidermal growth factor receptor 2 (HER2) [28]. In addition to its effects on gene expression, turmeric inhibits the activity of c-Jun N-terminal kinase, protein tyrosine kinases, and protein serine/threonine kinases [28]. Turmeric has also been shown to inhibit tumor cell invasion and metastasis in vitro by reducing MMP-2 activity and by inhibiting HEp2 (epidermoid carcinoma cell line) cell invasion [31].

Ammi majus:

A white flower with the scientific name Ammi majus belongs to the *Apiaceae* family, and it is an annual and dicotyledonous plant with autumn germination. It is a long and thin plant that grows to 100 cm in general conditions, in wet and soft lands, saline grassland, and coastal areas. This plant is cultivated in Europe and the Mediterranean area, western Asia, and even in India [32].

The effect of ethanol extract of this plant on HeLa and MCF7 was studied and results showed that this plant's extract has a toxic effect on these cells. Comorian compounds (as part of phenol compounds) are major compounds of this plant, and the main biological activities of this plant are attributed to them. Research has referred to cell toxicity of coumarin compounds on cell lineages, and apoptosis induction by these compounds is studied and confirmed. Psoralens are the most important coumarin compounds of this plant that can play an anticancer role, inhibiting cytochrome p450 activity [35].

Ammi visnaga:

Ammi visnaga L is a gramineous and perennial plant that grows in Mediterranean areas. This species is divided into 3 components: alegrian, furanochromones, and flavonoids [20]. It is seen in the north of Iran in Geilan, Roudbar, Manjil, and in the south of Iran in Bushehr and Shahbazan at a height of 800 meters. Its leaves have more cuttings and its flowers are white and umbellate. This odorant plant is of *Apiaceae* family, and its antibacterial, antifungal, and therapeutic effects on vitiligo have been published [22-23].

The killing activity of different extracts of the above-ground part of this plant on T47D cancer cells has been studied [24]. Also, the inhibitory and dose-dependent effect of this plant on 2 human cell lineages, pelvic

rhabdomyosarcoma and L20B of mice, have been proven [24]. Khellol, visnadine, cimitugin, and β-sitosterol are the most important compounds of this plant. Flavonoids like quercetin and kaempferol are isolated from the aqueous extract of this plant, and these compounds can justify the anticancer effects of this plant [23].

Ayurvedic Concept of Cancer:

Cancer was described as granthi and arbuda in Charaka and Sushruta Samhita by two great Indians and explained the disease conditions and reasons responsible for the cause of cancer [32,33]. Charaka and Sushrutha explained cancer as inflammatory or devoid of inflammation, based on the doshas involved [33]. Three doshas Vata, Pitta, and Kapha in the body are responsible for disease and the balanced coordination of these doshas in the body, mind, and consciousness is the definition of health in Ayurveda [34]. A morbid condition that arises in cancer is the state where all three major body humor loses mutual coordination and it is explained as Tridoshicarbudas in Ayurveda. In Ayurveda, the concept of Neoplasm shows various clinical symptoms. Various types of cancers were much earlier classified into three groups in Ayurveda. The three groups are divided in Ayurveda based on their occurrence [34].

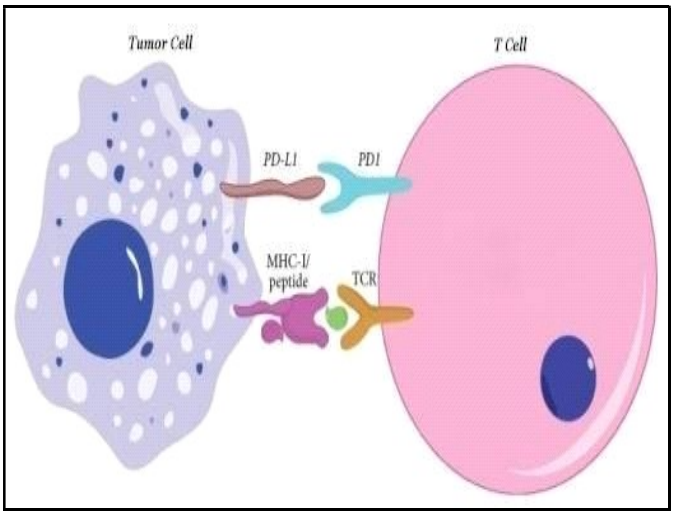

Fig 2. The immunological mechanism of T-Cell for invading the tumour cell.

Group I: malignancies which include sarcomas, leukemia, oral cancer, and incurable or malignant ulcers.

Group II: Inflammatory conditions that can be altered to probable malignancies, such as ulcers and growths under certain influences like radiation, change in dietary habits, stress, smoking, etc. Examples of these are the growth of lips, incurable thyroid tumors, and abdominal tumors like carcinomas of the stomach and liver or lymphomas.

Group III: Diseases in which there is a possibility of malignancy, such as incurable jaundice, or untreatable sinusitis [35].

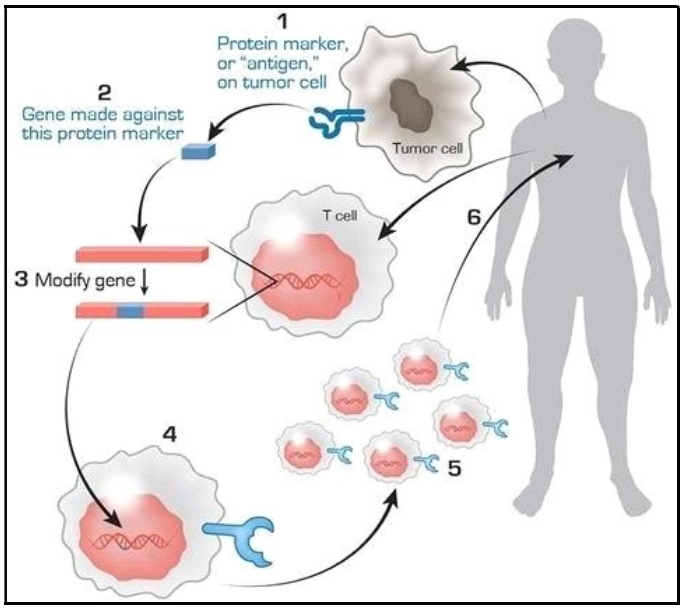

Fig 3. The mechanism that the Cholesterol-Lowering Drugs Improve Cancer Immunotherapy?

Immune checkpoint inhibitors work well and even cure some people with advanced cancer. But for most patients, these immunotherapies only work briefly or not at all. Now researchers have evidence that cholesterol-lowering drugs may offer a way to improve these success rates.

In a study in rats, two cholesterol-lowering drugs slowed tumor growth on their own and in combination with an immune checkpoint inhibitor, a Duke University team found. The two drugs, evolocumab (Repatha) and alirocumab (Prulent), are used to treat certain people with high cholesterol.

What's exciting is that these drugs have been approved by the FDA since 2015 and have been used by thousands of patients around the world, said lead researcher Chuan-Yuan Lee, DSc, Duke University Medical Center. They are generally very safe, said Dr. Lee.

There may be other benefits, including allowing patients to take their medications at home. The drugs are also cheaper than most cancer treatments, said James Gulley, MD, PhD, head of the immunotherapy group at NCI's Center for Cancer Research.

"This opens up the possibility of doing a study to investigate this combination" in people with cancer, said Dr. Gulley. dr. Lee and his colleagues hope to start a clinical trial on the drug combination.

Evolocumab and alirocumab both inhibit the activity of PCSK9, an enzyme that regulates the levels of "bad" cholesterol, also known as LDL cholesterol. But the researchers found that the drugs' effects on tumors had nothing to do with cholesterol. Instead, blocking PCSK9 made cancer cells more visible to cancer-fighting immune cells. The results of the NCI-funded study were published Nov. 11 in Nature.

Researchers are still investigating the role of PCSK9 in cancer. Proteins have many functions in healthy cells, said Dr. Li, so they may also play other roles in cancer cells.

"We think there's more to it," he said. The team is currently conducting experiments to see what other gene and protein changes occur in cancer cells without PCSK9 [36].

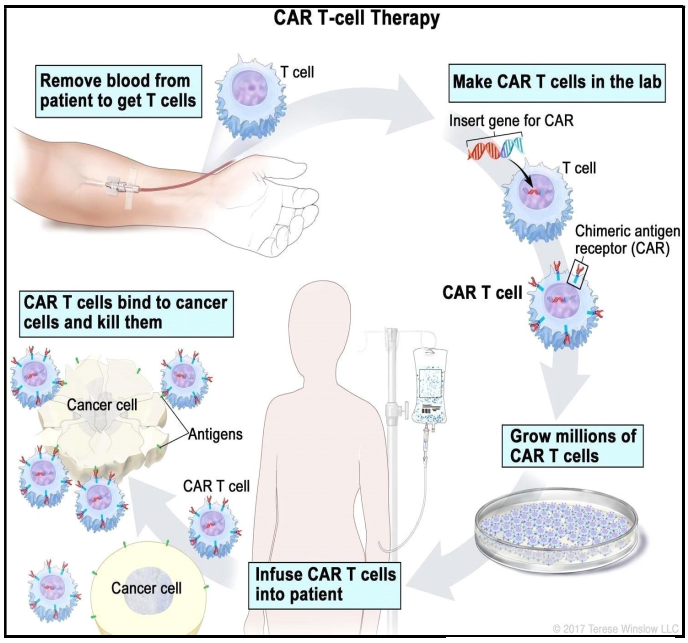

Fig 4. The figure presents the Chimeric antigen receptor T-Cell therapy.

Gut Microbes May Influence How Well Radiation Therapy?

Several studies have shown that bacterial communities in the gut can influence cancer in humans, from the rate of tumor growth and spread to respond to treatments such as chemotherapy or immunotherapy.

However, new research suggests that bacteria are not the only microorganisms in the gut that influence how tumors respond to cancer treatments. According to the study, fungi could also be an important component.

In studies in mice, scientists at Cedars-Sinai Medical Center found that the fungi migrate when normal bacterial communities in the gut are disturbed. These fungi, in turn, disrupt the tumors' immune response, which may be important for radiotherapy to work more effectively. The researchers also identified a fungi-sensing protein in tumors that may play a role in this phenomenon. Using samples from human tumors, they found that people with breast cancer or melanoma that had higher levels of this protein did not live as long as those who had lower levels.

Scientific studies on anticancer activity:

The details of how the immune system helps fight cancer are still being uncovered. Early work in the field led to the rise of immunotherapies: cancer treatments that coax the immune system to attack and kill tumor cells. These therapies have already revolutionized the treatment of several types of advanced cancer, including melanoma and lung cancer.

But recent research has revealed that the immune system can also influence how well chemotherapy and radiation therapy work. Research has shown that the microorganisms normally found in the human gut - known as the gut microbiome - affect how immune cells do their job throughout the body.

The new study, led by Stephen Shiao, M.D., Ph.D., and David Underhill, Ph.D., both of Cedars-Sinai Medical Center, sought to build on this earlier research.

The role of the immune system in controlling cancer after radiation therapy has been under intensive study, Dr. Underhill explained. Without the contribution of immune cells, cancer cells are likely to grow back right after treatment [37].

Extra or Missing Chromosomes May Help Cancer Cells Survive Treatment

Most cells in our bodies have 46 chromosomes. When a cell is getting ready to divide, it makes a copy of each chromosome. The chromosomes are then paired up and evenly split between the two resulting cells. Around 90 % of tumors have cancer cells with extra or missing chromosomes - a phenomenon known as aneuploidy. Despite this frequency, scientists have struggled to understand whether aneuploidy is harmful or helpful to cancer cells. But a new NCI- funded study has shown that the gain or loss of chromosomes may actually benefit cancer cells, particularly when they are exposed to cancer treatments.

Scientific evidence:

The new study, published August 4 in Developmental Cell, found evidence to support that idea. In lab experiments, aneuploidy helped human cancer cells survive treatment with cancer drugs like chemotherapy

and targeted therapy. What's more, the cells that thrived tended to have the same pattern of extra or missing chromosomes.

A separate research team in Europe found similar results when they examined human cancer cells with aneuploidy. Their study was also published on August 4 in Developmental Cell. This could turn out to be a common mechanism of drug resistance and might help us identify ways to counteract that resistance," said Keren Witkin, Ph.D., of NCI's Division of Cancer Biology, who was not involved in the study.

Lukow and his colleagues reasoned that cancer cells might use aneuploidy to circumvent treatments like chemotherapy. Although cancer treatments can be effective, most eventually stop working because cancer cells find ways to resist the effects of the treatment. Cancer cells use a variety of tactics to evade anticancer treatments, and scientists are still learning just how sneaky cancer can be in that regard.

CONCLUSION:

During this century, cancer has become one of the major problems and diseases which has caused predominant death. Throughout history, natural products have played a dominant role in the treatment of human ailments. All the drug discovery that has been done for cancer; everything is slowly being adjusted. That's why people's trust has shifted from chemical drugs. Now people have more faith in natural and organic cheeses. To reduce the side effects of synthetic drugs and to reduce this problem a little, more attention should be paid to natural products.

REFERENCES:

1. Costa-Lotufo LV, Khan MTH, Ather A, Wilke DV, Jimenez PC, Pessoa C, *et al*. Studies of the anticancer potential of plants used in Bangladeshi folk medicine. J Ethnopharmacol, 2005; 99: 21-30.
2. Rafieian-Kopaie M, Nasri H. On the occasion of World Cancer Day 2015: the possibility of cancer prevention or treatment with antioxidants: the Ongoing Cancer Prevention Researches. Int J Prev Med, 2015; 6: 108-112.
3. Lachenmayer A, Alsinet C, Chang CY, Liovit JM. Molecular approaches to treatment of hepatocellular carcinoma. Dig Liver Dis, 2010; 42: 264-272.
4. Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. J Nat Prod, 2007; 70: 461-477.
5. Hong WK, Sporn MB. Recent advances in chemoprevention of cancer. Sci, 1997; 278: 1073-1077.
6. Prakash P, Gupta N. Therapeutic uses of *Ocimum sanctum Linn* (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian J Physiol Pharmacol, 2005; 49(2): 125–131.
7. Pattanayak P, Behera P, Das D, Panda S. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: an overview. Pharmacog Rev, 2010; 4(7): 95-105.
8. Baliga MS, Jimmy R, Thilakchand KR, *et al*. *Ocimum sanctum* L (Holy Basil or Tulsi) and its phytochemicals in the prevention and treatment of cancer. Nutr Cancer, 2013; 65(1): 26-35.
9. Nayak BS, Jena PK, Dinda SC, Ellaiah P. Phytochemical Investigation and in vitro Evaluation of Anthelmintic Activity of *Gmnelina arborea* roxb. Fruit Extracts. Asian J Chem, 2012; 24(8): 3445-3447.
10. Atawodi SE, Atawodi JC. *Azadirachta indica* (neem): a plant of multiple biological and pharmacological activities. Phytochem Rev, 2009; 8(3): 601-620.
11. Fujiwara T, Sugishita E, Takeda T, *et al*. Further studies on the structure of polysaccharides from the bark of *Melia azadirachta*. Chem Pharm Bull, 1984; 32(4): 1385-1391.
12. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (ashwagandha): a review. Alt Med Rev, 2000; 5(4): 334-346.
13. Biswal BM, Sulaiman SA, Ismail HC, Zakaria H, Musa KI. Effect of *Withania somnifera* (Ashwagandha) on the development of chemotherapy-induced fatigue and quality of life in breast cancer patients. Integr Cancer Ther, 2012; 12(4): 312–322.
14. Jena PK, Nayak BS, Dinda SC, Ellaiah P. Investigation on phytochemicals, anthelmintic and analgesic activities of *Smilax zeylanica* Linn. leafy extracts. Asian J Chem, 2011; 23(10): 4307-4310.
15. Yang Z, Garcia A, Xuetal S. *Withania somnifera* root extract inhibits mammary cancer metastasis and epithelial to mesenchymal transition. PLoS One, 2013; 8(9): e75069.
16. Biswal BM, Sulaiman AM, Ismail HC, Zakaria H, Abdul MIJ, Muhammad KI. AOS14 PhaseII clinical study of combination chemotherapy with herb

Withania somnifera (ashwagandha) in breast cancer. Eur J Cancer, 2012; 48(4): S8-S9.
17. Dalali IL, Monajemi R, Amjad L. Cytotoxic effects of extract and essential oil leaves of *Achillea wilhelmsii* C. Koch on colon cancers cells. Exp Anim Biol, 2013; 1(3): 1-6.
18. Uddin SJ, Grice ID, Tiralongo E. Cytotoxic effects of Bangladeshi medicinal plant extracts. J Evid Based Complement Altern Med, 2009; 111: 578092.
19. Sharma H, Parihar L. Cancer and anti-cancerous properties of some medicinal plants. J Med Plant Res, 2011; 5: 1818-1835.
20. Azadbakht M, Semnani K, Khansari N. The essential oils composition of *Achillea wilhelmsii* C. Koch leaves and flowers. J Med Plan, 2003; 2(6): 55-59.
21. Dokhani SH, Cottrel T, Khajeddin J, Mazza G. Analysis of aroma and phenolic components of selected A chillea species. Plant Food Hum Nutr, 2005; 60(2): 55–62.
22. Milner JA. A historical perspective on garlic and cancer. J Nutr. 2001; 131(3): 1027s–1031s.
23. Thomson M, Ali M. Garlic (*Allium sativum*): are view of its potential use as an anti-cancer agent. Curr Cancer Drug Targets, 2003; 3: 67–81.
24. Bianchini F, Vainio H. Allium vegetables and organosulfur compounds: do they help prevent cancer? Environ Health Perspect, 2001; 109: 893-902.
25. Nakagawa H, Tsuta K, Kiuchi K, *et al*. Growth inhibitory effects of diallyl disulfide on human breast cancer cell lines. Carcinogenesis, 2001; 22: 891–897.
26. Colic M, Vucevic D, Kilibarda V, Radicevic N, Savic M. Modulatory effects of garlic extracts on proliferation of T-lymphocytes in vitro stimulated with concanavalin A. Phytomed, 2002; 9: 117-124.
27. Ahmed N, Laverick J, Sammons J, Zhang H, Maslin DJ, Hassan HT. Ajoene, a garlic-derived natural compound, enhances chemotherapy-induced apoptosis in human myeloid leukaemia CD34-positive resistant cells. Anticancer Res. 2001; 21: 3519-3529.
28. Bora KS, Sharma A. The genus Artemisia: a comprehensive review. Pharm Biol, 2011; 49: 101-109.
29. Gordanian B, Behbahani M, Carapetian J, Fazilati M. Cytotoxic effect of Artemisia absinthium L. Grown at two different altitudes on human breast cancer cell line MCF7. Pajouhesh Dar Pezeshki, 2012; 36: 124-131.
30. Asgarpanah J, Ariamanesh A. Phytochemistry and pharmacological properties of *Myrtus communis* L. Indian J Trad Knowledge, 2015; 14: 82-87.
31. Kuttan R, Bhanumathy P, Nirmala K, George MC. Potential anticancer activity of turmeric (Curcuma longa). Cancer Lett, 1985; 29: 197-202.
32. Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. Anticancer Res, 2003; 23(1A): 363-398.
33. Shao ZM, Shen ZZ, Liu CH, Sartippour MR, Go VL, Heber D, *et al*. Endoplasmic Reticulum Stress Signaling in Cancer Cells. Int J Cancer, 2002; 98(2): 234-240.
34. Mitra A, Chakrabarti J, Banerji A, Chatterjee A, Das B. Medicinal Plants and Cancer Chemoprevention. J Environ Pathol Toxicol Oncol, 2006; 25(4): 679-690.
35. Kapoor LD. Handbook of ayurvedic medicinal plants. Florida: CRC Press; 1990.
36. Balachandran P, Govindarajan R. Cancer - an ayurvedic perspective. Pharmacol Res, 2005; 51(1): 19-30.
37. Singh RH. An assessment of the ayurvedic concept of cancer and a new paradigm of anticancer treatment in Ayurveda. J Altern Complement Med, 2002; 8(5): 609-614.

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