

# **ORIGINAL RESEARCH PAPER**

## Oncology

Antiangiogen

# IS COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM), NEW HOPE IN FIELD OF ONCOLOGY?

## **KEY WORDS:** Cam, Phytoestrogens, Isoflanoids,

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ABSTRACT

Awareness of Complementary and alternative medicine (CAM) is increasing and has been frequently used by cancer patients. The benefit of complementary medicine is that it helps in enhancing the quality of life in patients, can reduce the side effects of conventional therapy. Due consideration of side effects and interactions with the Chemotherapy and radiation should be considered as it may reduce the effectiveness of cancer therapy and jeopardize the outcome of therapy. Evidence regarding the efficacy and safety of CAM is reviewed. Oncologists should have knowledge about the most commonly used remedies, or at least be able to direct patients to reliable sources of information

#### INTRODUCTION

CAM has been defined as therapeutic intervention that does not belong to conventional therapeutic approach.



### History:

US congress established the office of CAM in 1992 with the NATIONAL INSTITUTE OF HEALTH with budget of 2 million Dollars. In 1998- U S Congress further elevated the office of CAM & clubbed it with National Institute of health centre. In October 1998 (NCI) National Cancer Institute of USA established the office of CAM in order to enhance high quality cancer research. CAM started functioning as NCCAM with increase in budget of 50 million dollars which was further increased to budget of 122 million in 2016. In the National Institute of Institute of

#### Prevalence-

Surveys published suggest that 25% to 83% of US cancer patients have used CAM therapies at some point of time after diagnosis. Interestingly, CAM was used high among higher education level patients & High Socioeconomic group of patients, as well as females of younger age group. Use of CAM among cancer patient outside of USA, include CANADA, EUROPE, ISRAEL, SOUTH AMERICA and ASIA overall data is approximately 30%.<sup>3</sup>

#### **DISCUSSION:**

### Patient clinician communication:

Research has shown that, patients do not disclose/discuss to the Oncologist about CAM therapy, with the treating doctors as their initial belief is that the doctor might not approve of the same. Treating Doctor should guide patients about selection of which type of CAM would be beneficial for patients as CAM supplements in the outcome conventional therapy.<sup>4</sup>

**Drug Interaction:** Many chemotherapy agents are metabolized in liver with the help of Cytochrome 450 Systems. Many herbs like St Johns wart (Hypericum perforatum) taken during chemotherapy inhibits cytochrome P450. <sup>5</sup>Likewise Irinotecan given along with St.

Johns wart reduces 50% of this drug active metabolites. Other agents which inhibit Cytochrome P450 enzyme are Cannabinoids, Grape fruit juices. Herbs inducing the activity of Cytochrome 450 are blood roots (San Guinaria), Cana Densis which leads to decrease in active metabolites of chemotherapeutic drugs.

# ANTIOXIDANT INTERFERENCE WITH CHEMOTHERAPY OR RADIATION

Some chemotherapy agents & Radiotherapy action depends on free radical damage. Supplementation with Vitamin A, E, C, Lycopene, Green tea, grape seed extract, melatonin, selenium. 4-5

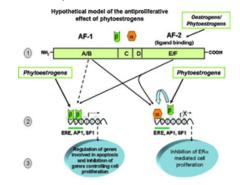
#### **INCREASES BLEEDING RISK**

Multiple herbs & Supplements carry an increased risk of bleeding like using Ginkgo Biloba, Saw Palmetto (Serenoa Repens), Garlic (Allium Sativam) using alone or with aspirin or warfarin can increase risk of bleeding. 4-5

### PRIMARY PREVENTION OF CANCER BY CAM-

It has been suggested that agents contains antioxidants acts by preventing oxidative damage of cells which decrease the risk of cancer.

**1.PHYTO ESTROGENS:** Plant based compound structurally similar to estradiol, capable of binding estrogen receptor as agonist. In estrogen antagonist popular herbs that contain **Phytoestrogen** such as, Black Cohosh (Cimicifuga Racemosa), Soy (Glycirne Max), Red Clover (Trifolium Pretense), Soya Food Consumptions widely in Asian countries has shown decrease in Breast cancer in Asian population in comparison to western countries. <sup>6-8</sup>



#### 2.CAROTENOIDS:

**Carotenoids** have antioxidant and proliferative properties; lycopene intake study says it causes reduction in prostate cancer risk.<sup>6-7</sup>

#### 3.SELENIUM:

Selenium is trace mineral found in soil, water & some foods. It has antioxidant, anti-angiogenesis and Proapoptosis properties. Selenium promotes antioxidant activity in body via glutathione peroxidase enzyme acting as catalyst. Evidence shows that selenium supplementation reduce the risk and has protective properties against prostate cancer, it helps in normalization of serum PSA level, decreasing androgen receptors.<sup>7</sup>

#### 4.GREEN TEA:

Green tea is a product of dried leaves of camellia sinesis which is a perennial ever green shrub. It has antioxidant (poly phenols), Antiangiogenasis and Proapoptotic properties as well as decrease serum estrogen levels.<sup>7-8</sup>

**5.VITAMIN A:**Vitamin A is comprised of retinol and carotenoid precursor's (Trans retinoic acid). Its role well established in acute Promyelocytic leukemia and also in decreasing risk of Head and Neck cancer. <sup>6-8</sup>

**6.VITAMIN E:**Also known as Alfa-Tocoferal, a fat soluble Vitamin having powerful antioxidant properties proven to decrease risk of breast, Lung and Prostate cancer.<sup>6-8</sup>

# CAM THERAPIES USED FOR CANCER TREATMENT IN SECONDARY PREVENTION:

#### **COMMONLY USED HERB FOR CAM**

- **1.GARLIC & ONIONS:**Garlic & Onions have Allicin and Sulfuric Compounds, manganese, Vitamin B6 and C, Copper and Selenium which stimulate production of glutathione (the potent antioxidant of liver) and detoxification of entire digestive system. Major action of garlic and onion are antibacterial, antiviral, antifungal, anti-Inflammatory properties, it also stimulate production of Natural killer cells. <sup>9-11</sup>Hence people whose diet is rich in Garlic & Onions (according to Italian research) have significantly lower risk of developing certain cancers like Colon Cancer, Ovary Cancer, Kidney Cancer, Head & Neck Cancer.
- **2.ST JOHNS WORT:** It's a yellow flowing plant which used in elevating depression. It activates Cytochrome P450 thus helpful in detoxification of carcinogens in the liver. <sup>9-10</sup>
- **3.CANNABINOIDS:** It is the chemical component of cannabis plant and shows its antitumor effects by various mechanism like Induction of Apoptosis and Anti-angiogenesis. <sup>9-11</sup>
- **4.BLOOD ROOTS (SANGUNERIA):** It's a white flowing plant found mostly eastern part of USA. Blood Roots have cancer killing properties as they promote apoptosis and have Anti-angiogenesis properties. <sup>9-11</sup>
- **5.SAW PALMETO:**It is basically an American Palm tree. Supplementation Inhibit growth of prostate cancer as it acts by inducing apoptosis, countering the effect of androgen in prostate cancer and also used as Radiation sensitizer during radiotherapy of prostate cancer.<sup>9-12</sup>
- **6.TERMIRICO (TURMERIC):**Curcumin is main ingredient of turmeric which has antioxidant and anti-inflamatory action. Acts by altering cell signaling pathway, proapoptosis and antiangiogenesis properties. It also interferes in proliferation of cancer cells by inhibiting cycloxygenase and lipoxygenase enzymes. Used in Breast cancer, Bone cancer, Stomach cancer, Skin cancer. <sup>9-12</sup>
- **7.OLEANDER:** Oleander extract is used against cancer as it has tremendous immune boosting and Inhibits angiogenesis. Used in chemotherapy & radiotherapy induced side effects. Available capsule or extract can be consumed as soup. it can be used. <sup>10-12</sup> It is a cardiac glucoside hence should not be used along Digitalis, warfarin or Vita K preparation.
- **8.GINGKO BILOBA**: Gingko Biloba extract has anti cancerous properties by anti-angiogenesis effect, Promoting Apoptosis, anti-

inflammatory, anti-oxidant properties and also helps in protecting the DNA damage in the normal cells. 9-12

- **9.GINSENG:** Ginseng reduce systemic inflammation and stress by inducing cortisol production thereby reducing chemotherapy or radiotherapy side effects. Precaution should be taken not to give along with warfarin or Vitamin K. Ginseng has estrogenic receptor stimulating activity hence should be avoided in estrogen receptor positive breast cancer. <sup>10-12</sup>
- **10.ZINGER:** Zinger is a root of vegetable. Useful in chemotherapy induced nausea & vomiting, radiotherapy side effects, Antioxidant properties, promotes apoptosis. It also helps in DNA repairing in normal cells during radiotherapy or chemotherapy and boost natural immune system. <sup>9-12</sup>

#### HERBS ALREADY IN USE FOR CANCER THERAPY:

**1.MAITAKE MUSHROOM EXTRACT** (GRIFOLA FRONDOSA) Popularly used in Japan, North America, Europe and Asia. Scientific basis for maitake mushroom extract is immunomodulatory properties. Polysaccharide constitute of Maitake which are beta glucans, these have been associated with host mediated antitumor activities such as induction of Nitro Oxide synthatase maitake activase, TNF, anti-angiogenesis. Evidence found Maitake powder and Beta glucan fraction was associated with tumor regression in patients of breast cancer, Lung cancer, Liver secondary. <sup>6-8</sup> Maitake induced side effects are hypoglycemia & hypotension. Interactions with above herbs with chemotherapy have not been established for which further studies are needed.

- **2.SOY (GLYCINE MAX)** This has got wide spread media coverage due to its hormone replacement therapy, cholesterol reduction, good evidence for alleviation of post-menopausal hot flashes. <sup>6-8</sup>ISOFLAVONOIDS in soy act as both Estrogen receptor agonist and antagonist. Other actions of Isoflaynoids are Tyrosin kinase inhibitor, antiangiogensis and promote apoptosis activity. Since high dose of soy acts as agonist, it should be avoided in Estrogen positive breast cancers.
- **3. MIST LTOE (VISCUM ALBUM)** Currently most popular alternative cancer therapy in Germany its biological properties are due to its compound lectines which causes increase tumor necrosis factor, increase IL-I, IL-6 (interleukins) level and increase NK cell activity hence improved cell mediated immunity. It has shown benefit in various cancers like breast cancer, lung cancer, cervical cancer, colorectal cancer, gastric, Ovarian, and Pancreatic cancer, Renal cell carcinoma, Brain tumour. 7-8

# RADIOTHERAPY & CHEMOTHERAPY SIDE EFFECTS MANAGEMENT BY ALTERNATIVE THERAPY:12-14

### a.CHEMOTHERAPY INDUCED TOXICITY:

Several CAM therapies used to combat chemotherapy toxicity

- Co-enzyme Q10 and omega 3 fatty acid used for prevention of Anthracycline based cardio toxicity.
- Vitamin E useful in Cisplatin induced neuropathy.
- In China, DANSHEN (SALVIA MILTIORRHIZA) & DONG QUAI (ANGELICA SINENSIS) have been used to treat Bleomycin induced pulmonary toxicity.
- A STRA GALUS (MEMBRA NACEUS) GINGO BILOBA, GINSENG used to combat chemotherapy induced toxicity in general.

**b.CACHEXIA:**Cancer patients usually develop cachexia, weight loss, muscle wasting and appetite suppression. DOCOSA HEXEONIC ACID (DHA) & EICOSA PENTAEONIC ACID (EPA) are used for improvement in above conditions, but no evidence has been established about use of above agents.

**c.NAUSEA** and **VOMITING:** Evidence has shown use of Zinger helpful in nausea & vomiting (especially Chemo induced), acupressure and Chinese Herbs-Decoctions of HUANGQI.

**d.CONSTIPATION:** Laxative effect of oral senna or Aloe latex, PSYLLIUM (PLANTAGO) all above very useful in chemotherapy induced constipation.

e. MUCOSITIS or STOMATITIS: Either chemotherapy or Radio therapy induced mucositis, CAM used are Glutamine, Vitamin ( A, B12, E, Folic Acid), Curcumin, Aloe Vera Extract.

**CONCLUSION:** Many cancer patients use complementary and alternative therapies as it helps in coping with the side effects of cancer treatments, ease worries of cancer treatment and related stress and feel that they are doing something more to help their own care. Patients appear increasingly willing to discuss the use of these remedies, especially when asked by their oncologists. In order to encourage open communication of CAM use by their patients, oncologists should be knowledgeable about the most commonly used remedies, or at least be able to direct patients to reliable sources of information. In some cases, patients feel that problems they perceive as important fail to receive sufficient attention. Complementary therapies improve patients' qualities of life, patient satisfaction, and the physician-patient relationship.

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