

## REVIEW ARTICLE



## International Journal of Futuristic Research in Health Sciences

Journal homepage: [www.ijfrhs.com](http://www.ijfrhs.com)

### A REVIEW ON CANCER THERAPY

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#### Abstract

Cancer is a disease that involves the abnormal growth of cell having potential to spread or invade to other parts of body. The constant methods of treatment for causes are chemotherapy, radiation therapy, surgery and targeted therapy. Keeping aside the constant methods of treatment for cancer there are many new inventions for treatment which revolves around reducing the risk factor and also for the treatment. The measures include by using BIOMARKERS the substance that indicates the presence of cancer in the body of an individual. Found in blood, urine or body tissues of a person with cancer. CAR-T CELL THERAPY this is one of the ADOPTIVE CELL TRANSFER, these are the T-cells which is genetically modified for producing an artificial T-cell receptor proteins modified to give T-cells new ability to target specific protein. SALVIA MILTIORRHIZA (dance) used in the gastric cancer. It shows significant effects in the terms of inhibiting tumor cell proliferation and promotes apoptosis in breast cancer, clear cell ovary carcinomas, promyelocytic leukemia, hepatocellular carcinomas. Research studies show that PROPOLIS has antitumor activity. The ester of coffee acid (CAPE) is an active compound of poplar based propels. The ant metastatic effect of CAPE should be either due to cytotoxicity, inhibitory activity against tumor cells.

**Keywords:** Cancer, Biomarkers and CAR-T therapy

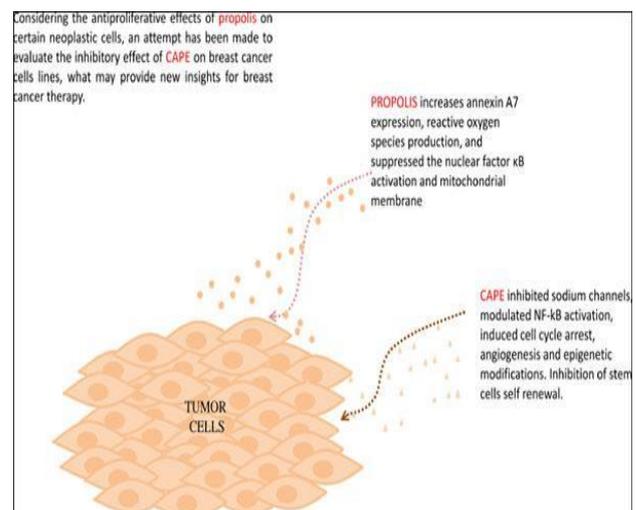
#### Introduction

Cancer is a group of diseases that which involves the abnormal growth of the cell with the ability to invade or spread to other body parts [1]. Cancer is a contrast benign tumor, which do not spread. The constant treatment used for cancer is radiation therapy, surgery, chemotherapy, and targeted therapy. the signs and symptoms which are possible are a lump, abnormal bleeding, prolonged coughs, bowel movement these symptoms may also have other causes [2]. Over 100 types of cancer affect human. TOBACCO use is the cause of about 22% of cancer deaths. Another 10% are due to obesity, poor diet, lack of physical activity or excessive drinking of alcohol. In this, besides the constant treatments we will get to know about some different methods to reduce the risk factors and also for treatment.

#### PROPOLIS IN CANCER TREATMENT:

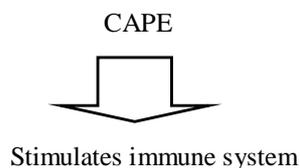
Recent studies in china concentrated on the efficacy of propels in the prevention of cancer and its treatment [3].

Coffee acid phenethyl ester, one of its constituents is of the particular interest. Propels is a reddish brown substance [4-5].

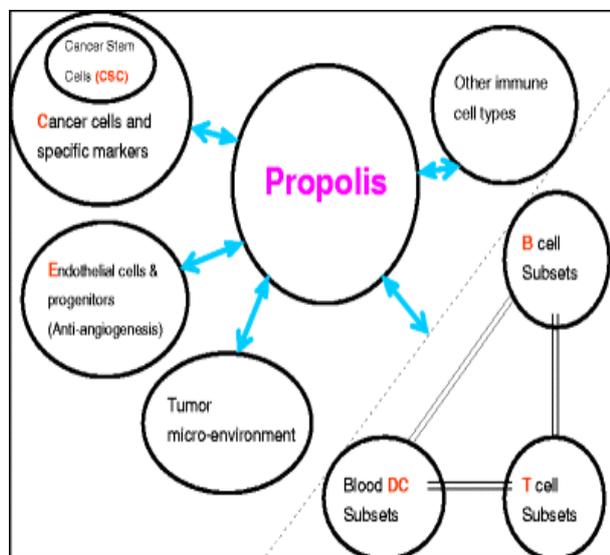


**[Fig 1. Effects of Propolis and Caffeic Acid Phenethyl Ester (CAPE) on Breast Cancer Cells]**

The composition of propolis is dependent on the source, but a typical sample comprises 50% resinous substances, 25% wax, 10% essential oil and 5% pollen [6-8]. It is produced by bees and derived from resinous substances collected from the barks of trees. Used as cement to stabilize the internal structure of the hive and make it more defensible by sealing gaps that may be exploited by intruders.



(By increasing the presence of cells like T-lymphocytes and inhibiting the cellular growth)



**[Fig-2.** The Immuno modulatory and Anticancer Properties of Propolis]

It also prevents cellular “mistakes” in healthy cells and induces apoptosis in cancer cells. It has shown to be cytotoxic to various tumor cell lines and has antitumor properties [9]. Studies prove that propolis can arrest growth of human leukemia and different oral tumor cells. It was used in wound healing by ancient Greek and Egyptians and for thousands of years known for its antiseptic properties [10]. Many laboratory studies and clinical trials in Eastern Europe and China have demonstrated the effectiveness against bacterial, fungal and viral infections including inhibition of Hong Kong influenza and herpes simplex virus.

### **Salvia miltiorrhiza in the treatment of gastric cancer:**

Also named as Red sage, Chinese sage, Tanshen. It is an important drug whose main pharmacological actions are validation, promotion of blood circulation and elimination of stagnations [11,12]. Highly valued for its roots (perennial plant in genus SALVIA).



**[Fig-3.** *Salvia miltiorrhiza* (A); the roots of *S. miltiorrhiza* (Danshen) (B); and *Salvia officinalis* (C).]

Recent year studies show that they also have antitumor activity. 65 active components were extracted from *S. miltiorrhiza*, including dihydrotanshinone I and miltones I and II, as well as 102 potential target genes for gastric cancer [13]. Analyzed the active components and target genes of *S. miltiorrhiza* in TCMSP (Traditional Chinese medicine system pharmacology) database and analysis platform. Target genes related to gastric cancer were taken as common potential target genes of *S. miltiorrhiza*, which could act on gastric cancer [15-16]. According to degree ranking in Cytoscape 3.7.1 software, the top 10 potential target genes were protein kinase B1 (AKT1), interleukin-6 (IL-6) vascular endothelial growth factor receptor A (VEGFA), epidermal growth factor receptor (EGFR), FOS, mitogen-activated protein kinase I (MAPK1) Myc, JUN, Caspase-3 (CASP3) and signal transducer and activator of transcription 3 (STAT3). Pathway enrichment mainly involved signaling pathways such as phosphoinositide 3-kinase (PI3K)-AKT, hypoxia inducible factor I (HIF-1) and IL-17 [17].

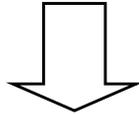
**Chimeric antigen receptor T cell (CAR-T) therapy:****ADOPTIVE CELL TRANSFER:**

Adoptive cell transfer (ACT) helps to boost the natural ability of T-cells to fight cancer [18-20]. The different types of ACT are as follows

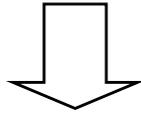
- ✓ Tumor infiltrating lymphocytes (TILS)
- ✓ T cell receptors (TCR'S)
- ✓ Chimeric antigen receptor T-cell (CAR –T) therapy

**CAR –T THERAPY-**

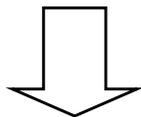
T-cells of patients are extracted (using inactivated virus as vector)



T-cells modified genetically so that it produces receptors (CARS) on cell surface capable of recognizing tumor proteins or antigens



Modified T-cells are multiplied and reinfused into blood stream of the patient.

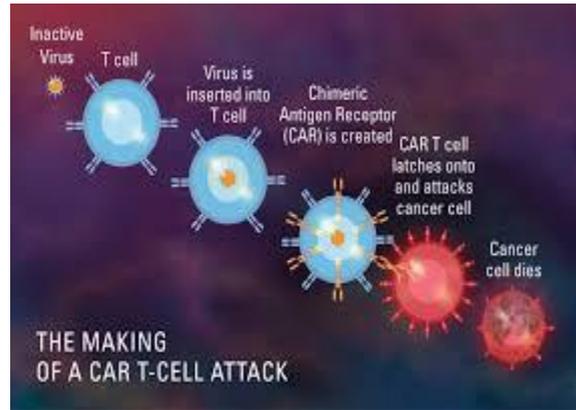


Further multiplication in patient's body and recognize and kill cancer cells via CARS [21].

**Structure of CARS:**

It is composed of,

- ANTIGEN BINDING MOIETY
- EXTRACELLULAR SPACE
- TRANSMEMBRANE DOMAIN
- CO-STIMULATORY DOMAIN
- ACTIVATION/SIGNALLING DOMAIN.

**Vectors used:**

Most commonly used vectors are inactivated v-retroviral vectors derived from the murine leukemia virus and lentiviral vectors [22]. Both integrate semi-randomly into the human genome [23-24]. The other vectors being studied are DNA transposons and transfection through M-RNAs.

**Biomarkers:**

Biomarkers are substances used as indicators of disease status [25,26]. Biomarker is used to detect frequency and estimated the normal as well as abnormal biological activities, bacterial activity viral activity or land medicinal intervention [27,28]. This is a feature that is anticipated and evaluated for general, pathological and pharmacologic responses to therapeutic intervention. It is described as detecting measure of biological situation by WHO and in co-ordination with the UN and international labor organization.

Breast cancer biomarkers are of four types;

**1. MOLECULE OR BIOCHEMICAL BIOMARKERS**

Molecule or biochemical markers are organic atoms found in body liquid or tissues [29].

Protein made by prostate cells are not extensively cramped to a point restricted to a particle.

**Example:**

Estrogen receptor, progesterone receptor, human epidermal growth factor receptor.

**2. PHYSIOLOGIC BIOMARKERS**

It has to do with the practical procedures in body as imaging procedures become further developed, we are probably to see an expansion in the examination and utilization of physiologic biomarkers.

**Example:**

- ✓ CA 15-3 (carcinoma antigen)
- ✓ CA 125 (cancer antigen)
- ✓ PSA (prostate specific antigen)

**3. Anatomic biomarkers:**

Anatomic biomarkers have to do with the structure of life form and the connection of its parts.

Anatomic biomarkers involve different organ's structure. The size of certain mind structures according to each other is a biomarker for a disorder known as HUNTINGTON DISEASE

**Example:**

- ✓ oncotype DX
- ✓ CFTR (cystic fibrosis trans membrane conductance regulator)

**4. Specific biomarkers:**

Specific biomarkers are specifically identified and repeatedly shown to accurately predict relevant clinical outcomes across different treatments and populations, this use is appropriate.

**Example:**

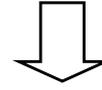
- ✓ H-MAM Human-Mamma globin
- ✓ Osteopontin
- ✓ FGFR2 Fibroblast Growth Factor Receptor 2
- ✓ PTEN Phosphatase and tensin homolog.

**Chemo + Immunotherapy:**

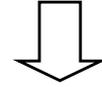
Chemo with immune therapy is one the improved technique in the treatment of the cancer. Chemotherapy causes the changes in the nature of the tumour cells when this chemotherapy is combined with the immunotherapy the results will be very beneficial to the patient.

Impact of cell death on immune response Tumor antigens must be available.

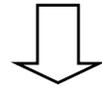
They must be presented to the immune system.



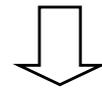
T-cells must respond to tumor antigens by reproducing themselves.



T-cells must traffic in to tumor itself.



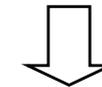
They must destroy tumor cells.



Anti-tumor CD8+ T cells (cytotoxic T lymphocytes) must differentiate into memory cells in order to prevent tumor recurrence [30].

Each of the above 6 steps could be potentiated by chemotherapy [31-34].

Chemotherapy changes the "visibility" of tumor antigens (increasing amounts of tumor antigens are released for the dead or dying cell)

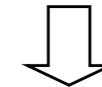


Increases spectrum of tumor antigens.

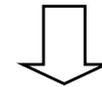
MHC CLASS I PATHWAY



Constitutively delivered to lymph nodes (process called CROSS PRESENTATION)



If tolerogenic, one would expect decrease in cytotoxic T-cell activity with ↑levels of antigen presentations.



Single protocol chemotherapy does result in an ↑ influx of tumor infiltrating T-cells. Explanations include in tumor's connective tissue following chemotherapy, ↑phagocytosis of dead tumor cell, or priming of tumor-specific helper (CD4+) T cell response

Needs some re-stimulation by "professional" antigen presenting cells in the tumor in orders to be effective [35-38].

Chemotherapy could argument the anti-tumor immune response by up-regulating the expression of so-called death receptors on tumor cells [39-40] .

### **Conclusion:**

Inspite of constant progresses made in the medical field for the treatment of cancer, cancer is not totally known, because of the etiologic complexity that involves this disease. All kinds of these treatments are uncomfortable, many times traumatic, creates great impacts on patient and their relative's lives. It is most important to figure out relevant intervention and to select a best therapeutic treatment and eventually checking the cancer type into space. All the above give methods are used to reduce the risk of death in cancer patients and to prolong their life span.

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