# Ph.D. SYNOPSIS (2017-18)

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<td>Ph.D. SYNOPSIS TITLE</td>
<td>“MANAGEMENT OF SIDE EFFECTS IN ANTI-CANCER THERAPY BY USING COMPLEMENTARY AND ALTERNATIVE MEDICINE”</td>
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SYNOPSIS SUBMITTED FOR THE REGISTRATION OF DEGREE OF

DOCTOR OF PHILOSOPHY

In the Faculty of Pharmaceutical Sciences & Technology

Submitted

By

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(2017-2018)
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1. **Abstract of proposed work plan:**

Cancer is one of the most life threatening diseases and possess many health hazard in both developed and developing countries. It is characterized by irregular proliferation of cells. Cancer occurs when a single progenitor cell accumulates mutations and other changes in the DNA, histones, or other biochemical compounds that make up the cell's genome. Cancer is usually treated with chemotherapy, radiation therapy and surgery. Chemotherapeutic drugs are chemically designed to target cells that are dividing and growing rapidly. The ADR are divided in to many of the side effects among which Musculo skeletal and connective tissues disorders are commonly observed which includes body ache, muscle cramps, muscular weakness, and weight loss. The other side effects are on Heme and lymphatic system which shows effects on bone marrow depression, anaemia, thrombocytopenia and leukopenia. The most affected organ system was GIT (34%, 38%) followed by skin (15%), musculoskeletal (12%, 14%), Heme (10% and 9%) and nervous system (10% and 8%).

To deal with and minimize the different side effects the complementary and alternative medicine (CAM) is used in cancer treatment and increasingly being demanded by patients, and more physicians.

The present study would focus on evaluating the efficiency of the different CAM treatments like ayurveda, herbal medicine. It also involves analysis of the combination of herbal drugs and given in forms to evaluate the effective form in treatment of side effects of cancer treatment.
1. INTRODUCTION
Cancer is a major public health burden in both developed and developing countries. It is the second leading cause of death in developed countries and is one of the three leading causes of death for adults in developing countries. Cancer, known medically as a malignant neoplasm, is a broad group of various diseases, all involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invade nearby parts of the body.

It may also spread to more distant parts of the body through the lymphatic system or bloodstream. Many things are known to increase the risk of cancer, including tobacco use, certain infections, radiation, lack of physical activity, obesity, and environmental pollutants. These can directly damage genes or combine with existing genetic faults within cells to cause the disease.

Cancer occurs when a single progenitor cell accumulates mutations and other changes in the DNA, histones, and other biochemical compounds that make up the cell's genome. The cell genome controls the structure of the cell's biochemical components, the reactions that occur within the cell, and the biological interactions of that cell with other cells. Certain combinations of mutations in the given progenitor cell ultimately result in cell displaying a number of abnormal, malignant cellular properties with characteristics as follows:

- The ability to continue to divide perpetually, producing an exponentially (or near-exponentially) increasing number of new malignant cancerous "daughter cells" (uncontrolled mitosis).

- The ability to penetrate normal body surfaces and barriers, and to bore into or through nearby body structures and tissues (local invasiveness).

- The ability to spread to other sites within the body (metastasize) by penetrating or entering into the lymphatic vessels (regional metastasis) and/or the blood vessels (distant metastasis).

Cancer can be detected in a number of ways, including the presence of certain signs and symptoms, screening tests, or medical imaging. Once a possible cancer is detected it is diagnosed by microscopic examination of a tissue sample. If the cancer is found to be localised it can be removed out by surgery and if it is locally advanced then chemotherapy
and radiotherapy is the choice of treatment available. Majorly chemotherapy is the commonly used as first line of treatment.  

Chemotherapy is a kind of treatment that uses drugs to attack cancer cells. It is called a "systemic treatment" since the drug, entering through the bloodstream, travels throughout the body and kills cancer cells at their sites. These drugs are chemically designed to target cells that are dividing and growing rapidly. Once they reach the cancer cells, they act to retard their growth, eventually resulting in their destruction.

- Drugs used in Cancer Chemotherapy belongs to following categories
  - Cytotoxic Agents
  - Alkylating Agents
  - Antimetabolites
  - Cytotoxic antibiotics
  - Plant derivatives - Hormones
  - Miscellaneous (mostly target oncogene products)

The treatment of anticancer majorly involves many of the chemotherapeutic agents which working from different mechanisms are commonly classified anticancer drugs are as follows

Table No.1: Classification of anticancer drugs

<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Mode of action</th>
<th>Example</th>
</tr>
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<tbody>
<tr>
<td>Alkylating agents</td>
<td>Damages DNA and result in death of growing cells</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>Interferes with intermediary metabolism of proliferating cells</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Antitumor antibiotics</td>
<td>Binding DNA to prevents DNA and/or RNA synthesis</td>
<td>Vinca alkaloids</td>
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<tr>
<td>Antimitotics</td>
<td>Blocks blood-vessel formation to tumor (affect protein synthesis)</td>
<td>Paclitaxel</td>
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<tr>
<td>Molecular targeted agents</td>
<td>Gene expression, monoclonal antibody, kinase inhibitor, proteasome inhibitors</td>
<td>Pertuzumab</td>
</tr>
<tr>
<td>Topoisomerase</td>
<td>Stops DNA replication, blocks topoisomerases 1</td>
<td>Etoposide</td>
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Side effects and complications of cancer therapy.

Chemotherapy is known to have substantial short and long term side effects. They include fatigue, phlebitis, alopecia, nausea, vomiting, mucositis, anemia, and myelosuppression or neutropenia. Long term side effects include premature ovarian failure, weight gain, cardiac dysfunction, leukemia and possibly cognitive dysfunction\textsuperscript{4,5}.

Table No.2: Side effects of cancer

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>GIT</td>
<td>Nausea, Vommiting, Diarrhoea, Constipation, Mucositis</td>
</tr>
<tr>
<td>Heme and lymphatic</td>
<td>Neutropenia, Anaemia, Thrombocytopenia, Leukopenia</td>
</tr>
<tr>
<td>Nervous system changes</td>
<td>Body ache, Fatigue</td>
</tr>
<tr>
<td>Dermatological disorders</td>
<td>Alopecia, Nail discoloration, Dermatitis, Photosenstitivity</td>
</tr>
<tr>
<td>Gonadal dysfunction</td>
<td>Oligospermia and premature menopause</td>
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The prevalence of cancer-related fatigue increases to 80 to 96\% in patients undergoing chemotherapy. The physiological factors like anaemia, infection, electrolyte imbalance, sleep disorders, pharmacologic treatment and psychological factors such as mood disorders, stress contribute in occurrence of fatigue. The other complications like neutropenic complications associated with myelo suppression are also significant cause of morbidity and mortality. The chemotherapy suppresses the hematopoietic system, impairs the protective mechanisms which limits the dose window of chemotherapeutic drugs.\textsuperscript{5}
Pathophysiology of Side effects

1. Muscle fatigue
The major side effect of chemotherapy is experience of fatigue, which is connected with feelings of debilitating tiredness or loss of energy. Around more than 75% of patients reports fatigue as a principal complication to lead day to day life. The prevalence of cancer-related fatigue increases to 80 to 96% in patients undergoing treatment of chemotherapy. Fatigue has a constant presence following chemotherapy, increases incrementally with consecutive cycles of chemotherapy, and may persist for years after treatment completion. Although cancer-related pain can be managed with opioids, no effective therapy for fatigue has yet been identified. It is a multifaceted condition which may arrive due anaemia, insomnia, depression, metabolic disorders, etc. The major etiological factor as, oxidative stress and increased production of free radical due to chemotherapeutic agents are thought to contribute to chemotherapy-related weakness and fatigue. Along with this other physiological and psychological factors related to development and progression of cancer are also responsible.

Muscle cramps is a type of fatigue may also develop as a symptom of a systemic disease, such as uremia. The cramps related to fatigue probably originate in the distal portion of the motor nerve. Hence, membrane-stabilizing agents, such as quinine, phenytoin or carbamazepine are drug of choice which may be selected according to the intensity of fatigue and cramps. It is also documented that intensity of fatigue is not dependent on age, disease stage, and type of surgery.

2. Inflammation
The chemotherapeutic drugs induces oxidative stress, apoptosis, and inflammation. The chemotherapeutic agent triggers renal oxidative stress, and inflammatory response by increases the expression of multiple genes that are important in proliferation, adhesion, and metastasis, such as chemokine IL-8 and growth factors. Several drugs induced TNF-arelease from multiple tumor cell leading to release of inflammatory cytokine production which leads to inflammation.

3. Heme related disorder
Hematologic toxicity induced by chemotherapy is called cytopenia. Cytopenia (Pancytopenia) is described as decreasing of all three types of blood cells including Red blood cells (Anemia), White blood cells specially neutrophils (Leukopenia-Neutropenia) and Platelets
(Thrombocytopenia). Neutropenia is known as the most serious adverse effect of chemotherapy it occurs due to decreased amount of neutrophils in blood, there is a higher risk for dangerous infection. On the other hand thrombocytopenia increases the risk of bleeding and sometimes makes physician decrease the dosage of chemotherapy drugs which in turn compromises treatment results. The chemotherapy shows potential contribution of bone marrow-derived endothelial progenitor cell leading to heme related disorders.¹¹,¹²

- **Complementary and alternative medicine (CAM) and its approach to treat side effects of cancer treatment**

  The National Centre of CAM defines CAM as “a group of diverse medical and healthcare systems, practices, and products that are not currently part of conventional medicine."¹³ The complementary and alternative therapies within four domains as biologically based, energy therapy, mind and body medicine, and whole medical system such as Ayurveda, Homeopath etc. CAM can also be defined as complementary therapy where it is used along with conventional therapy and alternative therapies are methods that are used in place of conventional therapy.¹⁴ CAM encompasses a variety of discipline viz. acupuncture, yoga, hypnosis, guided imagery, biofeedback, aromatherapy, herbal remedies, massages and many others. CAM possibly due to dissatisfaction with conventional medication, desperation, compatibility.¹⁵ In India, there is a high degree of reliance and cultural acceptability of Ayurveda medicine in favor of traditional systems of medicine. Herbal medicine is still the mainstay of about 75–80% of the world population, mainly in developing countries, for primary healthcare.¹⁶

In different types of CAM therapy majorly used are ayurvedic system which well known and established traditional system providing the interventions and pathophysiology of the disease. The other efficiently used CAM is herbal medicine which is a part of conventional systems involving the conventional formulation.

Medicinal herbs mitigate numerous symptoms related to conventional therapies used in cancer patients like improve digestion, reduce nausea, anxiety, insomnia or constipation, are very wide-spread.
Many herbal drugs are used to treat different side effects like *Panax ginseng*, *Paullinia cupana*, both of which are used to fight fatigue; also highly studied is Aloe (*Aloe vera*) as treatment for mucositis related to anticancer therapies. Very important is *Cannabis sativa* to control pain in cancer patients, and Ginger extracts *Zingiber officinale* to treat nausea and vomiting post-chemotherapy. They can also be used as anti-inflammatory activity, such as extracts of *Ribes nigrum* leaves and *Boswellia serrata* resin. Also *Withania Somnifera* is being used to treat fatigue related to chemotherapy. Some herbs act as radioprotector and chemoprotector which helps to minimize the side effects of cancer treatment are *Tinospora cordifolia*, *Curcuma longa*, *Acacia Arabica*, *Punica pomogratum*, *Ocimum sanctum* etc.

The ayurvedic preparation containing different herbs are used in management of side effects of chemotherapy. Few drugs listed are as follows Terminalia chebula, *Phyllanthus emblica*, *Elettaria cardamomum*, *Cyperus rotundus*, *Curcuma longa*, *Piper longum*, *Santalum album*, *Glycyrrhiza glabra*, *Centella asiatica*. *Withania somnifera*, *Glycyrrhiza glabra*, *Ipomoea digitata*, *Asparagus adescendens*, *Emblica officinalis*, *Tinospora cordifolia*, *Asparagus racemosus*, *Convolvulus pluricaulis*, *Vitex trifolia*, *Argyreia speciosa*, *Curculigo orchoides*, *Capparis aphylla*, *Acacia arabica*.
2. REVIEW OF LITERATURE:

1. R Das, D. K. Mehta, A.K. Chaudhary and M.U. Khan The above survey reveals the role of Indian medicinal plants and the various phytochemicals that may be used effectively for cancer treatment. This article reveals a detailed review of important herbs in cancer from Indian medicinal plants which will be useful to treat various types of cancer. It will be helpful to explore the medicinal value of the plants and for the new drug discovery from them for the researchers and scientists around the globe.

2. P Paramasivan, E. Thomas Ayurveda, the traditional Indian holistic medicine, uses plant derived products for cancer care, is not merely a system of medicine. The Ayurvedic science is believed to add a step on to the curative aspects of cancer and lead to healthy living by fostering healthy cells in addition to controlling/killing the cancer cells. The scientific evidence of Ayurvedic medicine is increasing, and a number of plants used in Ayurveda have scientifically proven to possess anticancer effects. In this editorial, we emphasize on combining the modern western and traditional medicines such as holistic Ayurveda which would be of great advantage to manage symptoms, control side-effects and improve the state of mental wellbeing.

3. S. Malvika, S. Sharma Ayurveda is being used as chemoprotector during the treatment and analyses the side effects as aggravation of pitta dosha categorized as ratakappa and raktadushti. It specifies the use of different herbs as chemoprotector and radioprotector with an ayurvedic perspective.

4. Zhang M, Liu X, Li J, He L, Tripathy D This article provides prevalence of chemotherapy side effects along with report of different Chinese herbs combined with chemotherapy to treat the side effect like phlebitis, alopecia, nausea and vomiting, and in fatigue heme related disorder. Chinese medicinal herbs in alleviating chemotherapy induced short term side effects like bone marrow improvement and quality of life, but the evidence is too limited to make any confident conclusions.

5. Anitra C. Carr, Margreet C. M. Vissers, and John S. Cook Cancer patients commonly experience a number of symptoms of disease progression and the side-effects of radiation therapy. In this mini review the methods commonly used to assess
health-related QOL in cancer patients by examining the effects of IV vitamin C on cancer- and chemotherapy-related QOL.  

6. Siegal T  This study reveals the approach of muscle cramp as major side effect of cancer treatment.  

7. Kristine A. Donovan  This article defines fatigue in relation to patients receiving chemotherapy and radiotherapy. Comparisons of fatigue during initial treatment in women who received chemotherapy reported greater fatigue severity and disruptiveness than women receiving radiotherapy. The results indicate that majorly chemotherapy interventions are more likely to occur than radiotherapy.  

8. Dinesh Vyas, Gieric Laput, and Arpitak K Vyas  This article deals with the finding of the different mechanism of inflammation and its complication related to certain chemotherapeutic agents like Doxorubicin, 5-fluorouracil, cisplatin, and paclitaxel are the first-line therapy in various cancer to analyse toxicity, resistance, and treatment failure limit their clinical use.  

9. Edwardson DW, Boudreau J  This article deals with inflammatory cytokine production in tumor cells upon chemotherapy drug exposure and accordingly drug resistance. It show significant account of changes in drug therapy.  

10. Shahrasbi A, Armin A, Ardebili A, Rafie KS, Ansari M and Rabani  The explains anemia as most adverse effect following systemic chemotherapy in both hospitals. It also provides the overall prevalance rate of heme related disorder where cytopenia was more prevalent in the university hospital than private hospital.  

11. Wei Liu, Cui-Cui Zhang, Kai Li  they study the Chemotherapy as the standard treatment for small-cell lung cancer (SCLC), and leukopenia is a common side effect. This study assesses whether chemotherapy-induced leukopenia is a predictor of efficacy and whether it is associated with the survival of SCLC patients.  

12. Rose M. Bell  This article is to provide oncology nurses with an understanding of the use of CAMs in cancer survivorship. By understanding the characteristics of typical users, the reasons for their use, and ethnic- and gender-related considerations, nurses can identify patients in this population and safely guide their use of CAM throughout survivorship.
13. Maryam Farooqui, Mohamed Azmi Hassali The current study aimed to evaluate the patterns of CAM use among cancer patients from a local hospital in Malaysia. In addition, the study focused on the information seeking behavior and CAM use disclosure to doctors. Of 393 patients, 184 (46.1%) had used CAM for their cancers. CAM usage was significantly associated with gender, level of education, employment status and monthly income. This helps to analyses the affordability and acceptance of CAM.

14. Priyanka Singh and Aditi Chaturvedi This paper reviews complementary and alternative therapy approaches for cancer pain and its impact in improving the QoL of cancer patients. Cancer pain is multifaceted and complex to understand and managing cancer pain involves a tool box full of pharmacological and non pharmacological interventions which hamper the quality of life.

15. Dinesh Kumar, Naveen Krishan Goel, Awadhesh Kumar Pandey, and Sandeep Singh Sarpal The present study was conducted to find prevalence rate of CAM use among cancer patients undergoing allopathic treatment in a health facility and to compare the CAM usage patterns among different subgroups of patients at different stage. Also had analysed CAM is a group of diverse medical and healthcare systems, practices, and products that are not generally considered part of conventional medicine.

16. E.Rossi, M.Di Stefano, F. Firenzuoli, M. Monechi, and S. Baccettisome CM will be introduced in Cancer Departments in Tuscany to additional treat cancer-related symptoms and side effects of conventional cancer therapy: acupuncture for nausea and post-chemotherapy and post-surgery vomiting, pain, hot flashes of iatrogenic menopause, xerostomia; homeopathy for hot flashes of iatrogenic menopause and the side effects of radiotherapy; herbal medicine for cancer-related fatigue, nausea and vomiting, pain, mucositis, anxiety, and depression.

17. A. Saxena, S. Dixit, S. Aggarwal, V. Seenu, R. Prashad, S M Bhushan, V. Tranikanti Chemotherapy is associated with significant side effects and toxicities, resulting in high dropout rates and morbidity. There is a need to explore an ideal chemo-protective agent without toxic effects. The study has analysed an
ayurvedic formulation named Maharishi amrit kalash profoundly used in the management of side effects of breast cancer.\textsuperscript{18}
4. Objectives of Research/ Proposed Hypothesis:

1. To identify and document the possible new approach for management of anticancer therapy related side effects with Complementary and alternative medicine.

2. To identify and document the efficiency of Ayurvedic formulation with specifically identified drugs to be used in management of side effects of cancer treatment.

3. To optimize the dosage regimen of CAM for better therapeutic outcome.

4. To identify and document the efficiency of herbal formulation with specifically identified drugs to be used in management of side effects of cancer treatment.

5. To provide suggestive modification with relation to CAM in currently practiced anticancer regimen.

6. To provide the comparative analysis of ayurvedic and herbal preparation.

7. To formulate and analyses a novel approach of drug delivery in herbal medicine.

8. To analyses the behavior of the selected drug candidate with conventional anticancer drug.
9. Methodology to be adopted:

1. Selection of drug candidate
2. Procurement and authentication of the drugs
3. Preliminary study
   A. Raw material analysis
      • Pharmacognostic analysis of drug
   B. Extraction of the drug
      • Analysis of the extract
4. Formulation and development
   A. Formulation with different combination
   B. Analysis of the formulation
5. Pharmacological screening

This involves different approaches to verify the activity of the drugs which is contributing to improve the side effects.

A. Screening models for evaluating muscoskeletal strength:-

1. Locomotor Activity: The spontaneous locomotor activity for muscle fatigue was assessed with the help of a photoactometer. Each animal was observed for a period of 5 min in a square closed field arena (30 cm × 30 cm × 30 cm) equipped with six photocells in the outer wall. Interruptions of photocell beams (locomotor activity) will be recorded by means of a six digits counter. To see the locomotor activity, each mouse was placed individually in the activity cage for 5 min. The basal activity score for all the animals will be noted. The percentage decrease in motor activity was calculated\(^{15}\).

2. Rotarod Test: The grip of animals to be on the rotating rod is use as a parameter where animals remained on Rotarod (25 rpm) for 5 mins. After the administration of control, standard, and test material, the fall off time from the rotating rod will be noted after 30 min. The difference in the fall off time from the rotating rod between the control and the treated rats will be taken as an index of muscle relaxation\(^{15}\).
B. Screening models for evaluating Inflammation related disorder:

1. **Caragenen induced paw edema**: Paw oedema was induced by injecting 0.1ml of 1% Carrageenan in physiological saline into the sub plantar tissues of the left hind paw of each rat. The extracts were administered orally 30 min prior to Carrageenan administration. The paw volume was measured at 60, 120, 180, 240, minutes by the mercury displacement method using a plethysmograph. The percentage inhibition of paw volume in drug treated group was compared with the control group. Diclofenac sodium was used as reference standard. 

2. **Carrageenan-induced pleurisy in rats**: Groups of six rats each were pretreated with the test Extract. One hour later all animals received an intrapleural injection of carrageenan (0.25 ml of 1% solution in 0.9% saline) on the right side of the thorax. Three hours later the animals were anaesthetized with ether and killed by bleeding through the portal vein. The pleural exudate was collected and the pleural cavity was washed with 1.0-ml saline containing eparin (10 IU/ml). The number of migrating leukocytes in the exudate was determined with a Neubauer chamber. Results were expressed using suitable statistical approach. 

C. Screening models for evaluating Heme related disorder

1. **Erythropoetin assay**: Anemia was induced by venoclysis in rat tails for 4 days at a concentration of 10 mg/kg using melted phenylhydrazine in sterilized normal saline. The rats were divided into 10 groups including a normal control group, control anemia group treated with PHZ and other groups injected with 300 mg/kg of the extracts after the PHZ treatment. The extracts were administered orally administration for 1 week after anemia was induced in normal saline, with the same amount of saline administered orally to the normal control group and the PHZ-treated anemia control group. Serum EPO concentrations were measured in accordance with the recommendation from the manufacturer of the Rat EPO Enzyme-linked Immunosorbent Assay (ELISA) kit.

2. **ALAD Activation assay**: ALAD is an enzyme that catalyzes the synthesis the porphobilinogen from δ-aminolevulinic acid (ALA), and is the initial synthesis process for Hbg. Hemolytic anemia inhibits ALAD activation and increases urinary
excretion of ALA to inhibit hematopoiesis. The ALAD concentration in the liver tissue was measured based on the manufacturer’s recommendations from the Rat Aminolevulinate Delta Dehydratase EPO ELISA kit 16.
6. Importance of study/ Society application:

1. Cancer treatment and related side effects are well established and required to be explored for betterment of disease.
2. Various CAM are being practiced in India where principally Ayurveda and herbal medicine are known.
3. Quality of life can be improved by combining different system of medicine
4. Optimization of dosage regimen for the intended formulation to act as a chemo protector.
5. The combat use of CAM with conventional treatment is the interest of intervention.

► International status:

• Complementary and Alternative Medicine (CAM) include a wide range of products (herbs, vitamins, minerals, and probiotics) and medical practices, developed outside of the mainstream Western medicine. In the US, the use of CAM is constantly increasing with the largest practice being among the non-hispanic whites and in the rural areas (rate of use up to 63%) compared with the cities in terms of geographic areas the highest rate of use was observed in the Mountain Regions and in New Mexico. the average one-year prevalence is 41.1% and the average lifetime prevalence is 58.1%.27

• A European survey conducted by Molassiotis A. et al., demonstrated that the use of CAM in the EU is about 35.9% of the total patient population. The use of CAM has increased steadily over the past 15 years or so; undoubtedly it has gained medical, economic and social importance. The available studies report that the prevalence of CAM use among cancer patients is in the range of 12.5-73%. This enormous variability is, at least partially, justified by the inconsistent definition of CAM, with some authors including only herbal medications, while some others considering also including dietary supplements and unconventional medical practices (massages, acupuncture)26,27.

• According to Italian survey, 75.6% said they knew what CAM was, but only 27.6% were aware of the difference between alternative and complementary medicine which they had practiced.

• The usage of Chinese medicinal herbs varied widely; however the majority reported high
usage of 94.4% , 93.75% , 86.4% , 76.75% and one low rate of 2.48%.%

- Increasing prevalence of CAM usage by cancer patients reflects the growing use of CAM over time. Our review suggests a higher CAM prevalence compared with a prevalence of 31.4%, and a range of 7-64%. However, unlike Ernst, we were unable to access non-English language publications.

► National Status:
The use of Complementary and Alternative Medicine for health maintenance, disease prevention and treatment is prevalent among healthy individuals as well as patients with chronic diseases. The cumulative incidence rate of CAM use among cancer patients is in the wide range of 14.5 to 91% it supports and improves the quality of life of cancer patient during and post treatment. CAM therapy's usage pattern among males was found to be the highest for Ayurveda (18.8%) followed by spiritual therapy (12.6%) and yoga/meditation (11.6%); whereas, among females, user rates of these therapies were reported to be 15.5, 13.1, and 13.1% respectively. The most common CAM therapy in use was found to be ayurvedic treatment reported to be (16.7%).

► Significance of the study:
- The use of CAM mainly derived from an auto-prescription (67%), most patients were not aware of the potential side effects, the substance was bought by the patient himself depending on personal research or by suggestion. Hence it becomes important elite the interventions of CAM with conventional treatment with respect to its side effects.
- The multivariate analysis indicated that the only factors which were confirmed to be significantly associated with the use of CAM were a high educational level 1.96 95% receiving treatment in a specialized cancer center rather than in a peripheral hospital/clinic, Hence the CAM is being studied to cross the class barrier and use its profound benefits to manage the side effects of cancer treatment.
- The vast knowledge available in ancient texts of Ayurveda makes it a profound ,available ,affordable with specific and controlled study
7. Proposed work Plan/ Formulation and Structure of Study:
Year-wise Plan of work and targets to be achieved:

<table>
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<tr>
<th>Sr. No.</th>
<th>Expected target to be achieved</th>
<th>1-6 months</th>
<th>7-10 months</th>
<th>11-13 months</th>
<th>14-20 months</th>
<th>21-28 months</th>
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