Ayurveda as an adjuvent therapy in cancer management

Afzal Nishat1, Rani Mukesh2, Sharma Sudhir Kumar3, Shukla Gyanendra Datta4

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Abstract
A review articles published in reputed journals of cancer suggests that patients under combined therapy (coordination of medical/radiation oncologist & surgeon) of cancer treatment experience adverse events included constitutional symptoms, gastrointestinal complications & pain. The most common reason for withdrawal was disease progression, followed by adverse effects. Complications during cancer treatment include- complications due to disease/ treatment & psychosocial problems. Ayurvedic formulations including single drugs like Gvarras, Panchatulasiras & combination drugs like Rasayan Churna, Yastimadhu Ghrita etc. have proven to be effective medicines when given in between consecutive chemo/radiation therapies. Ayurvedic interventions with combined therapies reduce cost of treatment with decrease in relapse of disease & decreased AEs.

Key words: Cancer, Gvarras, Palliative therapy, Panchatulasiras, Rasayan Churna, Supportive therapy.

Introduction
Sedentary and irregular life style, dietary factors, pollution, lack of exercise, industrialization and stress are most important factors responsible for many serious diseases & cancer being one of them. Description with similar characteristic to this disease is given under different context in Ayurveda. Vivid elaboration of these in texts shows that early Ayurvedic physicians had a good understanding of etiology & clinical manifestation of cancer. Cancer is on rise in India affecting most of the people. It is the most dreaded disease of the 20th century and affecting continuously with drastic increase of incidences in 21st century (Goel et al., 2015). Chemotherapy, radiotherapy and surgery being the main line of treatments for cancer in modern science have its limits. Chemotherapeutic drugs which may be either cytotoxic or immunomodulatory are currently used for the treatment of an estimated 535,767 people dying of the disease in the year 2011. As per the latest estimates of Indian Council of Medical Research (ICMR), the prevalence of cancer in the country is about 27 lakh. The incidence of new cancer cases every year in the country is about 11 lakh and about 5 lakh people die every year from the ailment (Balachandran and Govindarajan, 2005). Cancer is one of the distressing diseases globally and its death toll may be reduced by subsiding the side effects of chemotherapy and radiotherapy. Chemoprevention is a rapidly growing area of oncology which focuses towards the cancer prevention strategy of natural and synthetic interventions. Chemoprevention also deals with the chemotherapy of pre-cancer lesions which are called pre-invasive neoplasia, dysplasia or intraepithelial neoplasia depending on the organ system. Chemoprevention by synthetic agents can produce toxic side effects, which have limited their extensive use (Perboni et al., 2008). Ayurvedic drugs works as a immunomodulatory and also helps in minimizing the side effects of chemotherapeutic drugs. Many Ayurvedic drugs have scientifically proven for their anticancerous activities e.g., Tinospora cardifolia, Semicarpus anacardium, Piper longum, Andrographis paniculata, Phyllanthus niruri (Arbabi et al., 2012). This review study describes the anticancerous properties of single drugs and combination drugs and also when used with chemotherapeutics it not only reduces the side effects but also stimulates the immune response of the body. In the armory of modern medicine, the...
components of synthetic drugs or the medicinally accepted plants are evaluated for their efficacy against certain diseases thus forming a valuable source of therapeutic agents. Plants used against cancer lists more than 3000 species that have reportedly been used in the treatment of cancer (Debabrata et al., 2011). Ayurvedic therapy used as decreasing the side effects of chemotherapy and radiotherapy and also helps to improve the condition of patient by inducing the immune system of the cancer patients.

This review study aims at compiling the evaluation of efficacy of the Ayurvedic drugs which is in practice used as adjuvants to the chemotherapeutic drugs.

**Material and Method**

This study is done by reviewing different classical texts of Ayurveda as well as various articles, journals, research papers and relevant sites.

**Common chemotherapy side-effect in cancer patient and its Ayurveda based management:**

**Anorexia:**

Nearly 80% of cancer patients develop anorexia-cachexia syndrome in advanced stage which is worsened further with the administration of chemotherapy (Julie et al., 2012). Anorexia is most common side effect of chemotherapy and is associated with weight loss; fatigue and decreased appetite. To overcome this side effect Ayurvedic drug used as adjuvant drug. As per Sharangdhar Samhita Lavangadi churna is herbal preparation indicated in the patient of anorexia suffering from chronic illness (Alexander et al., 2010).

**Mucositis:**

Oral mucositis is one of the common and serious complications of chemotherapy. Chemotherapy induced mucositis is highly painful condition without any definite cure; this condition is an important cause of poor quality of life in cancer patients receiving chemotherapy (Surendiran et al., 2010). Recent scientific study showed that local application of Yashtimadhu powder (mixed with honey) in oral cavity, prior to radiotherapy, reduced radiotherapy induced mucositis (Sastri and Chaturvedi, 2011; Stanković et al., 2010 and Stanković et al., 2012).

**Nausea and Vomiting:**

They are the most common occurrence during Chemo-Radiotherapy. Inspite of using anti-emetic drugs, 70% of patients show persistent symptoms. The treatment mentioned in Ayurveda as follows: Powder of Haritaki (Terminalia chebula) mixed with honey and Jamun (Syzygium cumini) are all are indicated in Nausea and Vomiting (Renault et al., 1999 and Stanković et al., 2012).

**Diarrhoea:**

Fifty to eighty percent of patients receiving chemotherapy suffer from diarrhea which is contributor to poor quality of life and reduced treatment output. Ayurvedic treatment mentioned in Charak Samhita is Pepper powder with honey or butter milk with the powder of chitraka has potential to cure all kind of diarrheas (De Luca and Laflamme, 2001 and Uma, 2001).

**Constipation:**

Constipation is another major problem in patients receiving specific chemotherapeutic agents such as Cisplatin. In Ayurvedic literature treatment of constipation is Triphala with warm water and ghee is considered as good remedy for constipation (Aruna and Sivaramakrishnan, 1990; Uma et al., 2002 and Ganasoundari et al., 1997).

**Review list of some other Ayurvedic drugs which are useful in treatment of cancer**

**Single drugs**

**Sadabahar (Catharanthus roseus):**

Catharanthus roseus is a very important medicinal plant in this direction as availability and its property both are fortunate things for human being. Catharanthus roseus commonly known as the Madagascar periwinkle is a species of Apocynaceae family. It is also known as Sadabahar means always “Bloom”. The main active constituents in this herb are phenolic acid, flavonoids and alkaloids. These active constituents perform many protective functions and are involved in many anti-oxidative and anti-carcinogenic activities (Hidvegi et al., 1999; Baral and Chattopadhyay, 2004 and Dhama et al., 2013). In this many active constituents vincristine and vinblastine are the two alkaloids which are helpful to treat cancer. Vincristine and vinblastine both require aerial and root part of plant to be synthesized. Methanolic
extract have cytotoxic activity and ethanolic, methanolic and aqueous extract of leaves, stem, root & aerial part of plant have anticancerous activity (Othman et al., 2011; Ahmad et al., 2008; Chen et al., 2009; Karthikeyan et al., 1999; Shi et al., 2004).

**Panchatulsi Ras:**
Ocimum sanctum also known as “Holy basil” family Labiatae. Aruna and Sivaramakrishnan, based on their finding that the leaves of ocimum sanctum suppressed in benzo(a) pyrine induced chromosomal aberration in bone marrow and elevated glutathione and glutathione-s-transferase activities in liver of mice, suggested a possible role of plant in protecting against cancer. Ocimum leafs extract as well as their flavonoids orientin and vicenin have shown strong antioxidant activity in vitro, which strongly suggest free radical scavenging as a major mechanism by which ocimum product protect. The alkaloids of Ocimum sanctum such as eugenol, linolenic acid, rosmarinic acid, orientin and vicenin are effective against cancer like papillomas, breast cancer, liver cancer and fibrosarcoma (Kumar et al., 2002 and Bhattacharjee and Sil, 2002).

**Giloyras (Tinospora cordifolia):**
Tinospora cordifolia belonging to the family menispermiacae, this is commonly known as *Guduchi* or *Giloy or Amrita*. The whole plant is used as rasayana or rejuvenating drug in *Ayurveda* to improve immune system of our body. Alkaloids like berberine, palmatine, tembaterine and magnoflorine isolated from the stem of T.cordifolia and shown effect on human cancerous cells. Out of the different alkaloids of T. cordifolia palmatine have anti-cancerous effect on melanoma cells, Dalton’s lymphoma, leukemia, and skin & neck cancers.

**Gvarras :**
Fermented wheat germ extract (FWGE) is a multisubstance composition and contains 2-methoxy benzoquinone and 2,6 dimethoxy benzoquinone which are likely to exert most of its biological effects. FWGE interferes with anaerobic glycolysis, pentose cycle and ribonucleotide reductase pathways. It has significant anti-proliferative effect and kills tumor cells by the induction of apoptosis via the capase-polymerase pathway. In addition FWGE modulates immune response by down regulation of MHC-1 and the induction of TNF-alpha and various interleukins. One of the nutrition supplements for cancer patients in current clinical use is FWGE which is available as an over the counter dietary supplements in several parts of the worlds under the brand name *avemar*. An anti-metastatic effect of FWGE alone or in combination with cytostatic drugs in a spleen-liver or muscle-lung mouse metastasis model using 3LL-HH, B16 and HCR-25 cell lines (Patel et al., 2011 and Ishihara and Sakagami, 2003).

**Neem (Azadirachta indica):**
*Neem* tree has been used successfully to reduce tumor in *Ayurveda* from centuries. Recent studies indicated that an ethanolic extract of *neem* has been shown to cause cell death of prostate cancer cells by inducing apoptosis as evidenced by a dose-dependent increase in DNA fragmentation and a decrease in cell viability. *Neem* extracts have been shown to possess potent anti-cancerous properties against oral squamous cell carcinoma. *A. indica* also have cytoprotective effect of azadiradione from the ethanolic extract of seeds of this plant. Azadiradione exhibited potent antiulcer activity through the inhibition of H+K+-ATPase (proton pump) activity via its cytoprotective effect and also via antisecretory effect (Bhattacharya et al., 2000).

**Chitraka (Plumbago zeylanica):**
Active constituent of plumbago, plumbagin was reported to act against P388 lymphocytic leukemia. Plumbagin also exhibits anticancer activity by inactivation of oncogenic transcription factors Forkhead Box M1 (FOXM1) signaling pathway in glioma cells. Plumbagin induce apoptosis in human pancreatic cancer cells primarily through the mitochondria related pathway followed by both capase-dependent and capase-independent cascades. It indicates that plumbagin can be potentially developed as a novel therapeutic agent against pancreatic cancer also.

**Kalmegh (Andrographis paniculata):**
It is used as a wonder drug in the traditional *Ayurvedic* system in Indian for multiple clinical applications. Andrographolide, a major constituent from the leaves of the andrographis, inhibited the proliferation of different tumor cell lines in various in-vitro studies. The compound exhibited direct
anti-cancer activity on cancer cells by cell cycle arrest (Wang et al., 2002).

**Haridra (Curcuma longa):**
Curcumin sulphate a major constituent of Curcuma longa induces apoptosis in various cancer cells types including skin, colon, stomach, duodenum, and ovary (Wang and Su, 2001).

**Bhumamlaki (Phyllanthus niruri):**
Phyllanthus niruri has many effective traditional uses for a variety of diseases. Many studies revealed the preclinical pharmacological activity and therapeutic effects of Phytochemical isolated from Phyllanthus niruri. The species has demonstrated an antimutagenic and anticarcinogenic action, antitumor, antioxidant activity. Phytochemical studies have shown that extracts of genus Phyllanthus contain a variety of components, including gallic acid. Furthermore, studies have demonstrated cytotoxic activity of gallic acid on the human promyelocytic leukemia HL-60 cell lines (Wang et al., 2002).

**Combination of drug-**

**Rasayana churna:**
Rasayana churna is a combination of three drugs: Amlaki (Emblcica officinalis), Guduchi (Tinospora cordifolia), Gokshura (Tribulus terrestris) in same amount. Emblica officinalis have anti-mutagenic and antioxidant activity. The fresh or dried whole fruit of P. emblica is used in Ayurveda (Indian), Chinese, Tibetan traditional system of medicine as a powerful rejuvenator with anti-inflammatory effects and is widely consumed throughout india as a medicinal food. The fruit contains a series of diterpenes like gibberellins, triterpene lupeol, flavonoids, and polyphenols with potential immunomodulatory and antioxidant activities. The data obtained from same dosage form of Amalaki prepared with different method shows that freeze-dried Amalaki Rasayana has weak anti-secretory and moderate anti-acid activity, whereas freeze-dried Amalaki Churna has marginal anti-secretory moderate anti-acid and weak anti-ulcer activity. Tribulus terrestris is the another constituent of rasayan churna, belonging to the family Zygophyllaceae. Phytochemical compounds present in T.terrestris are Saponins, alkaloids and flavonoids etc. Saponin present in T.terrestris can be used as inhibitory effect on breast cancer. Third constituent of rasayan churna is Tinospora cardifolia, the anti-cancerous effects is also described in this study.

**Noni Plus Tablets:**
Noni i.e Moringa cardifolia family Rubiaceae. Its common name is Indian Mulberry. The different parts of Noni plants has been used (fruit, leaf, bark, flower, seed). There are more than 160 chemicals in Noni, the major component are scopolatin, octanoic acid, terpene compounds, alkaloids, anthraquinones, etc. It has been recently proved that Noni juice extract contained antioxidant, anticancerous, and inflammatory properties. An in-vitro experiment revealed that glycosides in noni fruit extract were responsible for the anticancerous activity. Anticancerous effect of noni extract, and or polysaccharide found in the ethanol precipitate has been tested against various cancer cell lines in vitro. Hirazumi first reported Noni fruit juice contains polysaccharides with antitumor activity that enhances the release of cytokines (INF-gamma) from thymocytes.

**Yashhimadhughrit:**
Glycyrrhiza glabra belongs to Leguminacae family. It is also called as Indian Liquorice root. Liquorice (Glycyrrhizaglabra) was potential anticancerous agent. It indicated that liquorice and its derivatives may protect against carcinogen induced DNA damage. Glycyrrhetinic acid was found to be an inhibitor of lipo-oxygenase and cyclo-oxygenase activities and it also inhibited protein kinase C, and down regulated the epidermal growth regulator factor. Glycyrrhiza glabra have a significant free radical quenching effect. Liquorice flavonoids have exceptionally strong antioxidant activity. Glycyrrhiza glabra extract has been used in herbal formulations for combating cancers like PC-SPES, a polyhedral composition used on prostate cancer (Wang et al., 2002).

**Discussion**
In this review study there are various Ayurvedic drugs have anti cancerous activity and used as an adjuvant therapy in cancerous treatment. We also deal with side effects of chemotherapy and its Ayurveda based management. Less or minimal effectiveness and toxic side effects of current cancer therapies draw the global attention towards
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herbal medicine to arrest the insidious nature of disease. There are many single and combination of drugs which are reviewed in this study. In single drug therapy Sadabahar have both anti-oxidative and anti-carcinogenic properties and the main constituents in this medicinal plant are vincristine and vinblastine which have anti-cancerous properties. Tulsi ras leafs extract have beneficial effect on human cancer. The leaves extract of Ocimum sanctum such as eugenol effective against cancer. In this study combination of drugs also effective in cancer treatment. In Rasayana churna Amlaki is the constituent and have anti-oxidative effect and effective on cancer treatment. Ayurveda plays an important complimentary role to western medicine in treatment of cancer. So Ayurveda used as an adjuvant therapy in cancer. Now a days Noni capsules are used as adjuvant drug in which Noni is main ingredient, and the alkaloids like scopolatin has anti-oxidant and anti-inflammatory properties. Ayurvedic drugs also have cytoprotective action so it is used as an adjuvant therapy in cancer patients.

Conclusion
Chemotherapy although a lifesaving modality for cancer is also a ruthless medical intervention compelling the patients to withdraw treatment before its completion. In UK, following a national audit of morbidity & mortality associated with chemotherapy, death within 30days of receiving chemotherapy is now an accepted standard. So, palliative or supportive care to cancer patients along with chemotherapy is a neo-concept on which work are being carried out. Neutriceuticals, herbal drugs or Ayurvedic herbomineral drugs have time to time proved as potent adjuvants to chemotherapy with minimizing its side effects & enhancing the quality of life.

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