

Theoretical-based Mechanisms of Action of Ayurveda Therapy in Cancer-related Symptoms

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Abstract

In Ayurvedic science, the clinical entities of *Granthi* (glandular cyst) group of diseases include cancer (*Arbuda*) and the progressive stages of cancer. Theoretical based mechanisms of action of Ayurvedic therapy is supposed to treat and prevent these entities well fully by which patient's quality of life improves. In the Bruhataryi (foremost texts) of Ayurveda; Charaka, Sushruta and Ashtanga Hridya samhita, the absolute explanation of cancer related signs and symptoms are seen in scattered ways which are explained in a single chapter of contemporary sciences. New findings gained through scientific developments add up to Ayurvedic science that develops an integrated approach to manage cancer and its related symptoms. Review of literature on anticancer drugs of plant origin revealed identification of newer Ayurvedic drugs that are not mentioned in the ancient texts. Many of herbals and traditional compounds are being screened worldwide to validate their use as anti-cancerous drugs on various cancer cell lines and in vivo study. Clinical studies established that the use of Rasayana drugs of Ayurveda is helpful to reduce side effects of chemo and radio therapeutic agents while adjoining with these therapies.

Hence, an attempt is made in this review to discuss about the pathology and the principle of therapeutic management of various cancers described in Ayurveda.

Keywords: Arbuda; Ayurvedic principle; Cancer; Rasayana.

Introduction

The world is facing second cause of death by survival of cancer.[1] Cancer is a chronic disease & affects patients of both sexes and all age groups, more in later age of life. Though cancer is not directly mentioned in Ayurvedic texts, but symptoms related to *Granthi* (glandular cyst) - *Arbuda* (cancer or tumour) group of diseases are well matched with various types of cancer or cancer related symptoms.[2] The treating cancer has more challengeable to medical scientists due to known adverse effects with three principal modes of treatment viz. Surgery, chemotherapy and radiotherapy, because each of these has its own limitation.

The Ayurvedic literature describes how this therapy aims to restore a balance of humours (Dosha), bodily tissues (Dhatu) and spirit for good health.[3] *Naishthika chikitsa* (spiritual healing) along with the main treatment gives complete wellness of humanity in such life hold diseases.[4] Ayurveda offers treatment with many single and poly herbal or herbo-mineral preparations which promote immunity and manage cancer and its related symptoms. By adjuvant with established treatment, Ayurveda provide better quality

and prolonged life.[5] Ayurvedic therapeutic approaches, such as changes in lifestyle, diet, drugs, Panchakarma (body cleansing mechanism), exercise, and meditation help to strength and purity the body and mind. These holistic treatment procedures not only cure several diseases; but also improve the bodily resistance and rejuvenate the tissues of the body through Rasayana (restoration of normal function of tissue) therapy. The positivity of health is feeling by the patient and patient may get relief with his/her pain and anxiety. The health promotive, disease preventive and rejuvenation approach Ayurveda is gaining greater attention and popularity in many regions of the world.

Probable Pathogenesis of Cancer in Ayurveda

According to Ayurvedic principles, the disease cannot be named on its own because it differs between persons in terms of illness, clinical presentation and also the treatment required.[6] Ayurveda is explained each individual has a unique combination of bioenergetics principles called Doshas which involve in pathogenesis of diseases. Each individual's health is influenced by the innate proportion of the three Doshas, known as Prakruti (genotype- nature), and by the state of disequilibrium of these Doshas, known as Vikruti (i.e., the current state of imbalance of the Doshas). Agni (biologic fire of the body), which is present in each and every cell, is responsible for digestion and metabolism in human body. The decrease in Agni is the responsible for production of Ama (Autotoxins) which leads to impairment of body channels (Srotamsi). Thus inverse proportional of the related tissue form which leads to manifestation of Arbuda. Therefore in Arbuda, the decreased state of Dhatwagni (deranged metabolism) will result in excessive tissue growth. Vata can be correlated with the anabolic phase of growth whereas Kapha to the catabolic phase. Cancer originates due to a metabolic crisis, i.e. aggravation of Vata forces and suppression of Kapha forces, both interacting with one another resulting in proliferation. However, the abnormal

cancerous growth at a specific organ (Ekadesavridhi) is managed by compensation from other parts of the body (Anyasthaniyakshaya), e.g. body weight loss (cachexia).[7]

Thus, Vikriti turns into disease. Sushruta has proposed six stages in the pathogenesis of all diseases (Shatha Kriya kala) but this concept suits more to the pathology of the tumour than pathogenesis itself.

1. *Sanchaya (Stage of Aggravation)*: early stages of localized neoplastic changes.
2. *Prakopa (Stage of Accumulation)*: transformation of primary growths into metastatic tumours.
3. *Prasara (Stage of Overflow)*: metastasis.
4. *Sthana Samsraya (Stage of Relocation)*: complete metastasis and secondary growth.
5. *Vyakti (Stage of Build-up in a New Location)*: clinical signs and symptoms are expressed.
6. *Bheda (Stage of Manifestation)*: the stage where differentiation of growth occurs on the basis of histopathology.[7]

Basic Classification of Cancer and its Related Symptoms

Ayurvedic classification of neoplasm depends on various clinical symptoms in relation to Tridoshas.[8,9]

- *Group I*: Diseases that can be named as clear malignancy, which includes Arbuda and Granthi, e.g. Mamsarbuda (melanoma) and Raktarbuda (leukemia), Mukharbuda (oral cancer), etc.
- *Group II*: Diseases that can be considered as cancer, such as incurable ulcers with e.g. Tridoshaj Gulmas (abdominal tumours like carcinomas of the stomach and liver or lymphomas).
- *Group III*: Diseases with the possibility of malignancy, e.g. Visarpa (erysipelas), Asadhya Kamala (incurable jaundice) and Nadi vrana (sinusitis).

Principles of Ayurvedic Healing

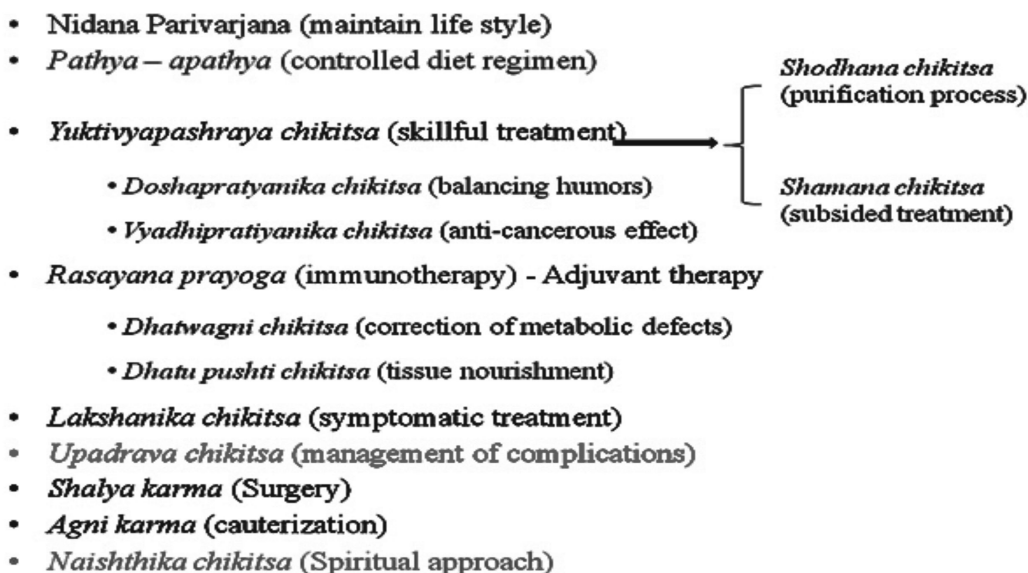
The causative factors which upset the balancing of Dhosha and Dhatu of human system and leads to disease like cancer. It classifies disease development into six stages that include aggravation, accumulation, overflow, relocation, build-up in a new location, and manifestation into a recognizable disease. The aim of Ayurvedic therapy is to diagnose an illness at even initial stages of disease and maintain a balance by supplying deficient substances as well as reducing the excessive ones.[10] The foremost physician of Ayurveda, tried to achieve equilibrium state of vitiated humors and related tissues (Doshadushya Sammmurchhana) by destruction in pathogenesis (Samprapti-vighatana) of disease which brings the cure. The Ayurvedic system of medicine was well founded on the basic principles of nature and its elements after a careful and thorough study of human physiology (Loka- purusha samtavada). This is the first system to emphasize health as the perfect state of physical, psychological, social and spiritual component of a human being. The therapeutic approach of Ayurveda has been divided into four categories as Prakritisthapani chikitsa (health maintenance), Roganashani chikitsa (disease cure), Rasayana chikitsa (restoration of normal function) and

Naishthiki chikitsa (spiritual approach).[11] Surgery is considered only for advanced cases.[12] Finding the cause of an illness is the basic goal of Ayurvedic therapy through Yuktivyapasraya chikitsa (skillful treatment by physician) and in cancer. [Figure]

Pathya-apathya (Life Style and Dietary Management)

Ayurvedic anticancer therapy includes recommendations for lifestyle and use of specific foods and herbs which are very helpful not only in preventing the progression of the disease but also makes the patients feel better and comfortable overcoming the symptoms. Allium sativum (garlic) could be helpful to manage pain and ache. Bacopa monniera strengthens mental faculties and helps to manage insomnia or sleeplessness due to stress.[13] Dietary agents also synergize with chemotherapeutic drugs, thereby reducing the toxicity of chemotherapeutic drugs. Some of the dietary agents that are known to modulate p53 activity are curcumin.[14] Curcumin is a powerful inhibitor of tumor cell proliferation. Curcumin also inhibits cell cycle progression of immortalized human umbilical vein endothelial cells by up-regulating the cyclin-dependent kinase inhibitors, p21WAF1/CIP1,

Fig. Theoretical based action of Ayurvedic therapy for cancer



p27KIP1, and p53.[15] Dietary agents such as curcumin, genistein, and green tea can interfere with the non-receptor tyrosine kinases such as Src and FAK, thereby inhibiting the downstream PI-3 kinase signaling responsible for the induction of such angiogenic target genes as COX-2, VEGF, IL-8, and the MMPs.[16]

The active principle identified in fruit and vegetables and the molecular targets modulated may be the basis for how these dietary agents not only prevent but also treat cancer and other diseases.[17] From this discussion it is clear that numerous agents in fruits and vegetables can interfere with multiple cell-signaling pathways. These agents can be used either in their natural form for the prevention and perhaps in their pure form for the therapy, where large doses may be needed. While these agents are pharmacologically safe in most situations, one of the concerns commonly expressed is the lack of bioavailability.

Experience again indicates that these agents exhibit bio-response at serum concentrations that are insufficient to demonstrate in vitro response; thus suggesting that their bioavailability should not be evaluated in the same manner as synthetic compounds. Most modern medicines currently available for treating cancers are very expensive, toxic, and less effective in treating the disease. Thus, one must investigate further in detail the agents derived from natural sources, described traditionally, for the prevention and treatment of cancer and disease. More clinical trials are also needed to validate the usefulness of these agents either alone or in combination with existing therapy.[17] Ginger has been traditionally used in different ailments to aid digestion and treat stomach upset, diarrhoea, and nausea. Some pungent constituents present in ginger and other zingiberaceous plants have potent antioxidant and anti-inflammatory activities, and some of them exhibit cancer preventive activity in experimental carcinogenesis.[18] The anticancer properties of ginger are attributed to the presence of certain pungent vallinoids,

viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc.[19]

Yuktivyapasraya Chikitsa (Skillful Curative Approach) in Cancer

The technique applied to treat the disease and protect the progress of disease is known as Yuktivyapasraya chikitsa. In which skill based treatment approach is adopted by a physician to manage the disease condition. Shodhana chikitsa (purification process), which eliminates vitiated Doshas, have been primarily used for medical management of cancer. When both internal and external medications were given then it is called as Panchakarma chikitsa. Detoxification on cancer patients showed the increased body weight, improved serum immunoglobulins, increased hemoglobin levels and normalized liver functions. It was found helpful in minimizing the adverse effects of chemotherapeutic agents. The other type of curative therapy is called Shamana chikitsa (subsided treatment), which pacifies dosha and gradually relieves the disease. Shamana chikitsa is based on the properties of drugs which having taste like Tikta (bitter), Kashaya (astringent) act as Dhatu Vriddhikara (tissue nourishment) and Rakta Prashadhaka (improve circulation) and Lekhana (reduced the extra growth of tissue and normalized the cells) action simultaneously. Rasayana prayoga (immunotherapy through rejuvenating drugs), certain poisonous plants, mercury like metals and animal products were rendered non-toxic and harmless by the use of some specific pharmaceuticals known as Shodhana and are used as rejuvenating drugs. Other methods of treatment include, Dhatwagni chikitsa (correction of metabolic defects), Vyadhipratyanika chikitsa (specific anti-cancerous drugs), Lakshanika chikitsa (symptomatic treatment)[10,20] and Upadrava chikitsa (treatment of complications).

Vyadhipratyanika Chikitsa (Anti Cancerous Activity)

The search on anti-cancerous effect of medicinal plants is executed by inhibiting cancer – activating enzymes, stimulating DNA repair mechanism, promoting production of protective enzymes, including antioxidant action and by enhancing activity of the immune cells. Some medicinal plants protect the body from cancer by enhancing detoxification functions of the body. Certain biological response modifiers derived from medicinal plants are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some medicinal plants reduce toxic side effects of chemotherapy and radiotherapy.[21,22]

Most of the medicinal plants which are screened for anticancer and antitumour activity are not indicated in the treatment of Arbuda in the original texts. This confirms that cancer is not merely dealt under Arbuda. A review has been made to explain the rationality behind the ancient approach on cancer.[23]

Rasayana Therapy in Cancer

Tissue familiar Rasayana drug may protect the tissues involving in progression in pathology of disease. It may protect disease to spread. The health-related quality of life is a multidimensional construct that includes the subjective appraisal of the patient's physical, mental, and social well-being.[24,25] Quality of life outcomes are also the key goals of contemporary cancer management.[26] Rasayana preparations also increased stem cell proliferation and also prevented free radical-induced injury produced by radiation (Puri, 2003).[27] Brahma rasayana could ameliorate the oxidative damage produced in the body by radiation (Rekha *et al*, 2001).[28] Withania somnifera root produced a significant decrease in LPO, and an increase in both SOD and CAT thus indicating that Ashwagandha root powder possesses free radical scavenging activity (Panda and Kar, 1997).[29] Active glycowithanolides, sitoindosides VII-X and withaferin A of Withania somnifera (10 and

20 mg/kg, i.p.), administered once daily for 21 days, induced a dose-related increase in SOD, CAT and GSH-px activity in frontal cortex and striatum, which was statistically significant on days 14 and 21 (Bhattacharya *et al*, 1997).[30] Extract of *Tinospora cordifolia* has been shown to inhibit the LPO and superoxide and hydroxyl radicals in vitro (Mathew and Kuttan, 1997).[31] Ayurvedic concept of Rasayana seems not only to embody the principal aspects of new hypothesis centered on a immuno-endocrine psycho neuro axis but also to go beyond it by encompassing the entire human system with its diverse and complicated immunoendocrine pathway (Handa, 1993).[32] Aim to use Rasayana chikitsa, the drug should protect the cellular level (Shwasthya rakshanam).

Concept of Dhatupushti (Protect the Strength of Patient at Cellular Level)

Acharya Sushruta has been quoted that “A patient's natural resistance is one the essential factor that should be preserved for the arrest of the progress of the disease”.[33] If the immunity of a patient is naturally maintained, the intensity of disease will automatically decrease. According to Sushruta, Bala (strength) is defined as the factor due to which one obtains the nourishment and stability of Mamsa dhatu (~the muscular tissues of the body), ability to perform various tasks efficiently, good complexion, clearness and pleasantness of voice along with clear and efficient working of all the organs either external like Jnyaanendriya (sense organs) or Karmendriya (organs with motor functions) and internal like Manas (mind), Aatma (spirit), etc.[34,35]

Upadrava Chikitsa (Treatment of Complications) and Adjuvant Therapy in Cancer

Adjunct treatment with Ayurvedic herbo-mineral drugs Mauktikyukta-Kamdudha and Mauktikyukta-Praval Panchamrita and metallic drugs Svarnabhasmadi Yoga appear to have a significant effect on reducing the

toxic side effects of chemotherapy drugs in cancer patients.[36] These drugs showed significant improvement in the Karnofsky score and global score of the Quality of life by improving nausea, loss of appetite, constipation, and fatigue in cancer patients. Herbs of *Withania somnifera*[37] and *Tinospora cordifolia*[38] are also proven to be powerful immunostimulants, which could increase body resistance power during cancer associated immunosuppression. Ayurvedic Ghrita preparation, Indukant ghrita induced leukopoiesis and enhanced median survival time as well as life span in tumor bearing animals. Macrophage phagocytic capacity was also elevated. Flow cytometric analysis of lymphocyte subsets and MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphophenyl)-2H-tetrazolium salt] assay for lymphocyte proliferation, yielded promising results which reinforces its use as an adjuvant to cancer chemotherapy.[39] Primary concerns identified in the literature include the lack of control of anticipatory nausea, the inconsistent use of standardised ginger extracts and validated assessments tools, and a lack of assessment for prognostic factors that may influence individual chemotherapy induced nausea and vomiting response.[40] If successful, this trial will provide support for the efficacy of ginger as a viable adjuvant anti-emetic therapy and in doing so, help manage chemotherapy symptoms and assist in improving patient quality of life.[41]

Shalya Chikitsa (Surgical Management) and Agni Karma (Cauterization) in Cancer

When medical treatments practices fail, then the case was left to surgeons.[10] Surgical cancer management in Ayurveda include the principles of fomentation by means of external application, cleansing by internal medication, treatment to liquefy the contents of the swelling, opening the tumour surgically for evacuation of its contents, cauterisation to avoid recurrence and post-operative care for healing the wound.[42] Cauterisation with alkalis and acids were performed with herbal

and mineral medicines.[10] Arbuda is excised completely from its deep root seat and cauterisation done to destroy any of the remaining cell particles.[43] Otherwise metastasized (Dwiarbuda) and re occurrence (Adhyarbuda) of tumor growth takes place. These categories also come under the incurable condition of tumor.[44]

Naishthika Chikitsa (Spiritual Approach) in Cancer

The anxiety and stress leads to vitiation of Vata (Vataprakopa), which will in turn to increase of pain. Some sorts of breathing techniques, chanting of mantras, pronouncing of Omkaara and Hanuman Chalisa as a form of Naishthika chikitsa will prepare patient to face the problem in a much better way and increase the positivity to patient and his/her relatives. These exercises subsides Vata.

Plants and Bhasma (Ash of Metals and Minerals of Ayurveda- Nanomedicine) in Cancer

Plant-derived compounds have been an important source of several clinically useful anti-cancer agents. These include vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan, etoposide, derived from epipodophyllotoxin, and paclitaxel (taxol®).[45] A 70% methanol extract of *Terminalia chebula* fruit, was studied for its effects on growth in several malignant cell lines including a human (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and a non-tumorigenic, immortalized human prostate cell line (PNT1A) using assays for proliferation ([³H]-thymidine incorporation and coulter counting), cell viability (ATP determination) and cell death (flow cytometry and Hoechst DNA staining).[46] The extract obtained from *Aegle marmelos* showed activity in all assays, indicating the presence of cytotoxic substances.[47] Lambertini *et al* (2004), Lampronti *et al* (2003) Antiproliferative action of *Aegle marmelos*.[48,49] Baliga MS. (2010) proved that Ayurvedic formulation Triphala

is useful for treating and preventing cancer. [50]

In recent decades, modern technology has facilitated the study of medicinal plants/plant extracts in several aspects including extracting active components from plants (phytochemicals), studying mechanisms of actions of these phytochemicals, chemical modification of extracts to increase effectiveness and reduce side-effects, nanoparticle-packaging for the delivery and so on. Nanotechnology has been extensively used in the delivery of anti-cancer drugs. [51,52] Nanoparticles can get drugs rich in tumour site due to the special size of nanoparticles.[52] Ayurvedic bhasma are the best examples of nanoparticles and herbo-mineral formulations of Ayurvedic dosage form are the examples of nanoparticles combined phytochemicals.[53] Bhasma in accordance of classical expectation are Swarna Bhasma, Makshika Bhasma, Abhrak Bhasma, Tamra Bhasma and Louha Bhasma. X-ray diffraction, TEM and particle size analysis revealed that these Bhasma are in nanometer dimension. These Bhasma may be considered as nanomedicine and are free from toxicity in therapeutic doses.[53] Phytochemicals have been demonstrated to target cancer stem cells.[54] Nanoparticles have been used to deliver phytochemicals to increase their effectiveness. Phytochemicals may be used together with other anti-cancer agents to increase treatment efficacy and reduce side-effect.[55]

Conclusion

In Ayurveda, cancer and its related symptoms may be classified on the basis of Dosha, Dhatu, and tumor site and prognosis types.[56] Treatment modalities may be adopted accordingly. Effect of bio-mineral formulations on brain glioma (a case report), [57] tumor suppression gene level,[58, 59], and DU 145 (prostate) and COLO 205 (colon) human cancer cell lines etc.[60] are some examples which validate this ancient concept scientifically. By adopting these principles of

Ayurvedic science,[61] and use of traditional test to diagnosis of cancer patients,[62] improve the well-being of the patient, as an adjuvant to chemotherapy and radiotherapy, which increase quality of life and person may enjoy the normal life span.

Key Messages

Clinical entities of Granthi group of diseases are similar to various type of cancer, when we search review on cancer related symptoms and pathology, we find that Dosha, Dushya, site and prognosis of cancer related condition may be similar to cancer disease.

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