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Pharmacothrapy of Cancer in Ayurveda

Dr. Sudeep Kumar Brahma

Abstract
Cancer is an uncontrolled growth disorder of cells characterized by the formation of tumor, invasiveness, metastasis and anaplasia. The disease is a major cause of motility and morbidity across the world. Despite a huge advancement in the therapeutic strategies, it is still a major cause of death worldwide. Ayurveda describes a variety of clinical conditions which have approximate similarities with cancer. Out of them description of Granthi and Arvuda by Sushruta and delineation of their characteristic features apparently denote to benign and malignant tumors respectively. The treatment strategy in Ayurveda consists of surgical, parasurgical as well as medicinal treatments. Therefore it is judicious to design a proper treatment strategy for the treatment of cancer with special reference to Arvuda in Ayurveda. In this paper attempts have been made to design a suitable medicinal strategy for the treatment of cancer on the basis of their mechanism of action with special reference to the pharmacodynamical factors of drug action mentioned in Ayurveda.

Keywords: cancer, metastasis, Arvuda, Granthi, Medo Dhatu, Kapha Dosha

Introduction
Cancer is a group of disease involving uncontrolled cell growth with potentials to invade the nearby tissues and spread to other parts of the body called metastasis. They form a subset of neoplasm or tumors. As per a definition given by British oncologist R A Willis- **"**A tumor or neoplasm is an abnormal mass of tissues, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner even after the cessation of stimuli which evoked the change" [1]. The word tumor literally means a swelling or mass in practice. But it has become synonymous with neoplasm. Tumors are grossly two types including benign and malignant. Sometimes mixed and localized tumors are also seen. Oncology is the study of tumors. Benign tumors represent the accumulation of cells which has been transformed to reproduce in abnormal numbers but under circumstances where they remain within the tissue of origin. Malignant tumors are comprised of cells which are capable of invading adjacent tissues called as invasiveness and leaving the tissue of origin to disseminate and to form metastases [2].
Surgery, radiotherapy, chemotherapy, immunotherapy are the main stay of modern cancer management. Despite a significant advance in research, cancer still is the major cause of morbidity and mortality in entire world. In Ayurveda although various clinical conditions like Granthi, Arvuda, Apachi, Dusta Vrana etc. resemble various types of cancers in their symptomatology, their drug therapy is described individually in their respective chapters in the respective Ayurvedic classic. No single unified study is available so that a proper treatment strategy can be designed with a special reference to the pharmacodynamical properties of the individual drugs and their mechanism of action in cancer. This is the first such study which has attempted to design a proper medicinal treatment strategy along with mechanism of action of the drugs for the treatment all kinds of malignant conditions in general.

Characteristics of Malignant tumors
Malignant tumors infiltrate or invade the tissue or organ in which it grows. They grow very faster and spread to distant places called as metastasis or secondary deposits. The metastasis happens mainly through lymphatic and through vascular channels and along natural cavities and passages. As a general rule sarcomas spread through blood while carcinomas through lymphatic. The malignant tumor is monoclonal mass of cells. Anaplasia or undifferentiated growth is another integral character of malignant tumors which means the tumor cells do not differentiate or behave like the mother cell or tissues from which it has been arisen. They grow only in numbers but do not differentiate [2].

Difference between benign and malignant tumors [3].

Serial number	Properties	Benign	Malignant
1	Age	May occur at any age	Usually seen after 40 years or in the first decade of life.
2	Size	Usually of small size, but occasionally of enormous size	Usually large size
3	Tumor edge	Well defined, well cicumscribed	Ill defined, less circumscribed
4	Encapsulation	Usually encapsulated	Usually not encapsulated
5	Growth	Slow, expansive, erratic growth with a tendency to cease.	Rapid, invasive, progressive, relent less growth until death occurs.
6	Histology	1. Well differentiated, closely resemble with the parent tissue. 2. With well formed stroma, 3. Cells regular. 4.Few in the state of mitosis	1. Less well differentiated and sometimes completely anaplastic, 2. Stroma often poorly formed. 3. Cells are often pleomorphic 4. Mitosis is often numerous
7	Fixity	Usually not fixed to the surrounding structures	Usually fixed to the surrounding structures due to local invasion
8	Invasiveness	Surrounding structures are not invaded	Usually invades the surrounding structures and is a characteristic feature.
9	Hemorrhage and ulceration	Usually do not show any tendency for hemorrhage and ulceration	Malignant tumors show more tendencies towards hemorrhage and ulceration due to increased vascularity.
10	Metastasis	Metastasis never occurs.	Metastasis frequently occurs.
11	Cause of death	Usually not fatal. If death occurs due to mechanical pressure and obstruction.	Almost invariably fatal if left untreated. Cause of death is a combination of mechanical and destructive effects together with blood loss, secondary infection starvation, cachexia, marrow replacement by metastasis, anemia, malnutrition etc.

Incidences

Global scenario

Cancer of lungs, female breast, colon and rectum are the top three cancers types in terms of number of new cases worldwide in 2018 followed by prostate cancer in fourth and stomach cancer in the fifth position among all the newly diagnosed cases. Mortality due to cancer of lungs is highest among all cancer related mortalities followed by colorectal in the second position while number of death due to breast cancer is placed in the fifth position around the world. Together these three cancers constitute one third of the total cancer incidences worldwide. They also together contribute one third to the total cancer related mortalities around the world [4].

The global cancer burden was increased to 18.1 million new cases and 9.6 million deaths in 2018. One in 5 men and one in 6 women worldwide will develop cancer during their life time and one in 8 men and one in 11 women will die from cancer. Asia contributes around 60% to the global population. Accordingly it has contributed at least 50% of total new cancer cases and 50% of cancer related deaths in the year 2018 [4].

Indian scenario

India had an estimated 1.16 million new cancer cases in 2018 as per World Health Organization (WHO). WHO also forecasts that one in ten Indians will develop cancer in their life time and one in 15 will die out of it. In India the most common types of cancer are breast cancer, oral cancer, cervical cancer, lung cancer, stomach cancer, colorectal cancer. Oral cancer tops among men while breast cancer tops among women in India [4].

Etiology of cancer (malignant tumors)

The following have been reported to be the general causes of cancer.

1. Polycyclic hydrocarbons benzpyrene (present in tar) group, cholanthrene, methyl colanthrene, napthylamine, benzidine, dimethylaminoazobenzene, nitrosamine, vinyl chloride, asbestos, nickel, chromium and numerous other chemicals are carcinogenic. Aniline dye containing beta-napthylamine causes bladder cancer. Most of them have to be modified in the body in the liver to become carcinogenic. This activation occurs at the site of liver by the oxidase group of cytochrome -P-450 microsomal enzymes [2].
2. Among the natural carcinogens sex hormones like estrogen, progesterone and testosterone have been implicated in the cancers of breast, endometrium, ovary and prostate [5].
3. There are many viruses which can cause cancer in both humans and animals. RNA virus like human T - lymphotrophic virus type-1 can cause human T cell leukemia while hepatitis C virus can cause hepatocellular carcinoma. Among the DNA viruses Epstein Barr virus can cause Burkitts lymphoma and nasopharyngeal carcinoma. Herpes simplex II virus can cause cancer of cervix and Caposi's sarcoma in AIDS patients. Human papilloma virus (HPV) can cause skin cancer, cancer of cervix, squamous cell carcinomas of head and neck in man. Bovine papilloma virus (BPV) can cause various types of cancer in cattle. Hepatitis B virus is a DNA virus that can cause cancer of liver [6]. Besides bacterial pathogens like *Helicobacter pylori* is indicated in stomach cancer [7].
4. Aflatoxins, a toxin developed by a fungus *Aspergillus flavus* can cause liver cancer and toxic hepatitis in humans [8].
5. Radiations in all its forms can cause cancer including ultraviolet radiation; ionizing and non-ionizing radiations. They can cause skin cancers including melanoma [9].
6. Smoking and chewing tobacco are risk factors for lung cancer and oral cancer respectively [10].
7. Immunodeficiency states either naturally or artificially or genetically increases the chances of lymphomas and leukemias [11].
8. Chronic irritation-Kangri cancer in the natives of Kashmir due to holding hot basket charcoal under their

clothes for the purpose of warmth as a result of thermal irritation [12].

9. Besides there is also involvement of dietary habits, alcohol consumption, sedentary lifestyle, lack of physical activity, water contamination, reproductive factors etc as risk factors for various types of cancers [13].

Genetic factors in cancer

Recent evidences suggest all the etiological factors end up in producing a genetic alteration in the cells. There has been the involvement of three kinds of genes in cancer pathogenesis [14]. They are

1. **Proto-oncogenes:** These are normal genes when subjected to mutations or increased expression converted into an oncogene thus transforming a normal cell into a malignant cell along with uncontrolled proliferation of that particular cell type. The greater is the activation of oncogene, poorer is the prognosis. A group of proto-oncogenes unregulated after getting mutated provide signals that lead to uncontrolled cell division while another group of proto-oncogenes also regulate programmed cell death or apoptosis. Some of the important proto-oncogenes are RAS, WNT, MYC, ERK,TRK etc. [15, 16].
2. **Onco-suppressor genes:** Onco-suppressing genes or tumor suppressing genes are responsible for inducing apoptosis or programmed cell death as a routine function within the cell. A mutation in the onco-suppressor genes will interfere with the apoptosis (programmed cell death) of the cancer cells as well as senescent cells thus giving rise to uncontrolled proliferation. Oncosuppressor genes are three types. Care taker genes- which ensure genomic stability via DNA repair and subsequently when mutated allow mutations to accumulate. Gate keeper genes directly regulate cell growth by either inhibiting cell cycle progression or inducing apoptosis. Lastly the land scaper genes regulate growth by contributing to the surrounding environment. When mutated can cause an environment that promotes unregulated proliferation. Tumor suppressor genes or the proteins for which they encode can have either a repressive effect on regulation of the cell cycle or can promote apoptosis or sometimes both [16, 17].
3. **DNA repairing genes:** Effective DNA repair is at the back bone of cancer free survival. These are a group of genes which are responsible for the repair of the DNA damages either due to endogenous sources like free radicals or due to exogenous sources like UV radiations. A cell when accumulates large amount of DNA damages or mutations, the cell looses its DNA repairing ability and can enter into three possible fates. 1. Senescence 2. Apoptosis 3. Unregulated cell division that can lead to the formation of a tumor which could be cancerous. Alteration or mutations in the DNA repair genes will lead to increased inactivation of the other tumor suppressor genes and activation of oncogenes. DNA repair ability of the cell is vital to the normal function of that organism. [17]

Concept of cancer in Ayurveda

Cancer as a single disease is not described in Ayurveda. But many clinical conditions which have approximate similarities with the clinical cancer are described. They are mentioned under the context of Arvuda (tumors), Shotha (inflammations), Udara (enlargement abdomen including ascites), Gulma (various kinds of abdominal lumps), Granthi (glandular swellings), Apachi (cervical lymphadenitis), Vidradhi (abscess), Stanaroga (diseases of the breast), Ostharoga (diseases of lips), Mukharoga (diseases of oral cavities), Asadhya Vrana (incurable or malignant ulcers) etc. whose symptoms sometimes resemble with the cancer of the respective organ. Out of them Arvuda is most interesting to study as it apparently denotes tumors of malignant origin [18] Charaka has mentioned a typical term called as Utsheda which can be correlated with any kind of tumorous growth including Adhimansa, Arbuda, Granthi, Apachi etc. [19].

Concept of Arvuda (malignant tumor)

The word Arvuda literally means a billion indicating billions of cells involved in the growth of a tumor. Arvuda itself also means a tumor or a swelling or a polypus. Another meaning of Arvuda is a mountain with unequal peaks which perhaps refers to the un-circumscribed unequal irregular margins of the malignant tumors. Here three relevant meanings of Arvuda have been presented [20].

Concept of Granthi (benign tumors) in Ayurveda

In Ayurveda Granthi is a group of disease characterized by circular, well circumscribed surface (Vritta), elevated (Unnata), hard, glandular (Vigrathita) and encapsulated (Sakosha) swellings perhaps refers to a benign tumor or a cyst [18, 21]

Aetio-pathogenesis and symptomatology of Arvuda in Ayurveda

Murchita (abnormal) Doshas being situated inside the body vitiate the Rakta (blood), Mamsa (muscle tissue), Medo Dhatu (asipose tissue) and produces Vritta (round), Sthira (stable or immobile). Mandaruja (mild pain), Mahan (bigger in size), Analpamula (deep rooted), Chira Vriddhi (continuously growing due to uncontrolled cell division), Apaka (without undergoing suppuration), produces accumulation of Mamsa (Kurvanti Masopachayam) or muscle tissues. The tumor characterized by these clinical features is called as Arvuda. [22] The symptoms Sthira (stable), Vritta (round), Mandaruja (mild pain), Mahan (big size), Analpamula (deep rooted) are all the manifestations of Kapha Dosha [18]. The term Chiravriddhi refers to uncontrolled cell division and continuous growth of the tumor which is controlled by Vayu. Metastasis is the mechanism of separation of tumor cells and transportation to the other parts of the body through blood vessels and lymphatics (Srotas) which is again controlled by Vayu. Therefore along with Kapha Dosha, Vayu plays a significant role in the formation, invasion and metastasis of malignant tumors. Arvuda can be equated with malignant tumors on the basis of the gross morphological features and the behavior of the tumor. Among the gross morphological features irregular margin, uncircumbscribed surface and lack of a capsule around the tumor are specifically important. Among the behavioral characters Chira Vriddhi (continuous growth and uncontrolled cell division), Mahan (bigger in size), Analpamula (deep rooted) are important [18].

Sushruta denotes six different time periods/opportunities for action to treat a disease on the basis of six different stages of pathogenesis. They are Sanchaya (accumulation), Prakopa (aggravation), Prasara (expansion), Sthanasansraya (localization), Vyakta (clinical manifestation), Bheda (complications and prognosis. The pathogenesis of cancer follows exactly the six step pathogenesis as described in Ayurveda [22].

1. **Sanchaya:** Can be correlated with the accumulation of mutation due to accumulation of oxidative free radicals and other carcinogens [22].
2. **Prakopa:** Can be correlated with the uncontrolled cell division and initiation of tumor formation due to the action of various promoters and growth factors [22].
3. **Prasara:** Can be correlated with both stage of invasion and metastasis or spreading to distant organs through Rakta Vaha (vascular channels), Lasika Vaha (lymphatics) and natural cavities of the body like abdominal cavity (Udara), cranial cavity (Shira), thoracic cavities (Uras) [22].
4. **Sthana Sansraya:** Localisation of the metastatic cells at a particular site or organ or Dhatu due to Sanga or obstruction of Srotas specifically in the Rakta Dhatu, Mamsa Dhatu and Medo Dhatu because Sushruta includes Arvuda, Granthi, Vriddhi, Galaganda etc in the Rakta, Mamsa and Medo Pradoshaja Vikara [22, 23].
5. **Vyakta:** It is the stage of appearance of tumor or Arvuda at the lodged site. In this phase there is clear expression of symptoms of diseases like Sopha (inflammation), Arvuda (malignant tumor), Granthi (benign tumor), Vidradhi (abscess), Visarpa (erisypelas), Jwara (fever), Atisara (diarrhea) etc. This is the phase of clear clinical expression of the disease [22]
6. **Bheda:** It is the stage of complications. Malignant tumors burst open and results in ulceration, hemorrhage and necrosis. Patient suffers from anemia due to blood loss. Other symptoms found at this stage may include cachexia, malabsorption, starvation and secondary infections. Patient may end up with death if left untreated or if the treatment does not respond [22].

Model of Pathogenesis of Cancer in Ayurveda

Nidana Sevana (adopting to aetiological factors)→ Dosha Samchaya (accumulation), mainly of Kapha and Vayu→ Mandagni (derangement of enzymatic activity) →Ama formation (generation and accumulation of toxins, free radicals and other oncogens resulting in accumulation of mutation) → Prakopa (aggravation and proliferation of Kapha and Vayu) (phase of rapid cell division and initiation of tumor formation)→ Prasara (spreading and expansion of excited Kapha and Vayu resulting in invasion and metastasis)→Srota Dushti→ Sanga (obstruction of Rakta Vaha, Lasika Vaha, Mamsa Vaha, Medo Vaha Srotas) and Vimarga Gamana (invasion and metastasis) → Sthana Samsraya at Rakta, Mamsa, Meda Dhatu (localization at blood, muscles and fat tissues) and other body parts→ Dosha Dushya Samurchana (appearance of Poorva Roopa or premonitory signs and symptoms) → Vyakta (Roopa) (manifestation of full fledged clinical cancer with other symptoms→Bheda (complications including bleeding, anemia, necrosis, secondary infections, malnutrition, cachexia and death.)

Classification of Arvuda in Ayurveda

Various types of Arvuda: These malignant tumors (Arvudas) are of six different types including 1. Vataja, 2.Pittaja, 3. Kaphaja. 4. Raktaja. 5. Mamsaja. 6. Medoja [18].

Out of them Vataja, Pittaja and Kaphaja, Medoja Arvudas produce symptoms equal to their respective Granthis (benign tumors). However Sushruta distinctly describes the symptoms of the other two varieties of Arvuda including Mansarvuda and Raktarvuda [18].

Symptoms of Vataja Granthi/Arvuda

Vataja Granthis and Arvudas are characterized by stretching type of pain (Ayamyate), rigour (Vyathita), Toda (pin pricking type pain), tearing or cutting type of pain (Pratyasyate). black in color, hard (Amrudu) in consistency. It is inflamed like a bladder and produces serosanguinous fluid on bursting [18].

Symptoms of Pittaja Granthi/Arvuda

Piitja Arvuda and Granthis are characterized by stiff burning type pain (Dandahyate), elevated temperature (Dhupyati), sucking type of pain (Chusyati), suppuration (Papachyate), burning sensation (Prajwalati), reddish or yellowish in appearance and oozing of profuse warm blood on brusting [18].

Symptoms of Kaphaja Granthi/Arvuda

The Kaphaja Arvuda and Granthi are cold to touch (Sheeta), without any discolouration of the skin (Avivarna), with mild pain (Alpa Ruja) and severe itching (Atikandu), stony hard consistency (Pashanabat Samhanana), bigger in size (Upapanna), Chirabhivriddhi (continuous but slow growing) and produces white thick discharge on bursting (Shukla Ghanam Puyam) [18].

Symptoms of Medoja Granthi/Arvuda

The tumor grows or reduces on the basis of growth or reduction of fatty tissues (Meda), Snigdha (smooth), Mahan (big in size), Alpa Ruja (mild pain), Atikandu (severe itching), on bursting gives rise to oil cake or clotted Ghee like secretions [18].

Aetiology and symptomatology of Raktarvuda

Vitiated Dosha by vitiating Rakta Dhatu (blood) and constricting Shiraa (blood vessels) (Sampidya, Sankochya) does not undergo suppuration. It produces a tumor along with number of polyps (Mamasankura). This tumor grows very rapidly (Ashu Vriddhi). There is continuous and profuse bleeding of vitiated blood (Sravati Ajasra Rudhiram) from the tumor due to ulceration on the surface. Due to continuous and profuse bleeding the patient becomes anaemic (Pandu). This tumor has been said to be incurable (Asadhya) [18].

Aetiology and Symptomatology of Mamsarvuda

Fist blow (Musti Prahara) or any other kind of contusion injury vitiate the Mamsa Dhatu and produces a tumor there. This swelling is painless (Avedana), Snigdha (unctuous or smooth), resembles to the skin colour (Ananya Varna), Apakam (does not undergo suppuration), stony hard in consistency (Asmopamam), Aprachalyam (fixed or immobile), This Mamsarvuda is found more frequently in case of the meat eaters due to the vitiation of their Mamsa Dhatu. This is called as Mamsarvuda and is incurable [18].

Prognosis of Arvuda

Out of the Sadhya or curable Arvudas, those which produce secretions or oozing, those which are formed at the vital spots (Marma Sthanas), those which are present inside the Srotas (blood vessels and natural cavities), those which are Achalya (fixed) are considered incurable by the Arvudajnas (oncologists). That which is being formed above another tumor is called as an Adhyarvuda (superimposed tumor). The tumor raised near another tumor is called as Dwirarvuda (collision tumor). Both are said to be incurable. The use of the word Arvudajna refers to oncologist. It indicates specialized

oncologists to treat tumor related diseases existed in the past. [18]

All Arvudas are characterized by excessiveness of Kapha Dosha and Meda Dhatu (fatty tissues), Sthiratwa (immobility) and Grathita (glandulation or knotting) features which prohibits them from undergoing suppuration (Paka) [18].

Principles of treatment of Cancer in Ayurveda

The above principle of pathogenesis is very much applied to the treatment of cancer. If the disease can be detected at the time of accumulation of free radicals and other carcinogens, resulting in genetic mutation it can be either prevented or treated with respective drugs and cannot proceed to the level of Prakopa or state of cell division and initiation of tumor formation. Both cancer promoters and growth factors work at the level of Sanchaya in order to start the cell division resulting in the initiation of tumor formation. Therefore if it is treated at the stage of cell division or initial appearance of tumor, it cannot proceed further to the stage of Prasara or distant spreading or metastasis and invasion. If the tumor cells are killed at the time of Prasaravastha or metastasis they cannot lodge or localize at a particular site to form a new tumor. If it is already localized and lodged (Sthana Samsraya) at a particular site or organ, immediate treatment should be started with a view to prevent it from further aggravation to stage of Vyakta or full fledged clinical manifestation of cancer. At the state of Vyakta Avastha still there is a scope to treat the tumor medico-surgically to prevent the stage of complications. At the stage of complications or Bheda Avastha the oncologist should attempt for the survival of the patient irrespective of the consequences.

Therapeutic strategy for cancer in Ayurveda

1. Nidana Parivarjana (avoidance of the etiological factors that causes aggravation of Vayu and Kapha). In other words etiological factors that cause accumulation of free radicals, carcinogens and other oncogens resulting in mutation should be avoided. (24)
2. Amanashaka and Agnivardhaka Chikitsha (To prevent accumulation of free radicals)-Ushna Veerya, Katu, Tikta Rasa Dravyas) like Rasna (*Alpinia galanga*), Sunthi (*Zingiber officinale*), Guggulu (*Commiphora mukul*), Chitraka (*Plumbago zeylanica*), Bhringaraja (*Eclipta alba*), Ativisha (*Aconitum heterophyllum*) etc. Ushna Guna, Tikta and Katu Rasa drugs helps in the digestion of Ama accumulated in the form of free radicals by enhancing their metabolism at the tissue level (Dhatu level) by increasing the respective Dhatwagni or anti-oxidant enzymes. Formation of Ama is always triggered by Mandagni or low level of digestive enzymes [25, 26]
3. To arrest aggravation of Vayu and to arrest cell division and metastasis-Vatanashaka drugs mainly of Ushna Veerya origin like Guggulu (*Commiphora mukul*), Gandira (*Coleus forskohlii*), Rasna (*Alpinia galanga*), Vidanga (*Embelia ribes*), Bhallataka (*Semecarpus anacardium*), Nirgundi (*Vitex negundo*) etc should be employed. Vayu is the responsible agent for all kinds of Bibhajana or division including the cell division, all kinds of transportations including the metastasis or distant spreading. It is also the factor involved in invasion or local spreading or invasion to the nearby tissues. Madhura (sweet taste), Amla (sour taste), Lavana (salts), Snigdha (unctuous) properties should not be adopted here because they have the ability to aggravate both Kapha and Meda which are the prevailing Dosha and Dhatu in cancer respectively. These drugs should be administered in the forms of Snehana (oleation), Swedana (fomentation/sudation), Asthapana (dry enema), Anuvasana (oily enema), Nasya (as nasal drops), Bhojana (internal administration), Abhyanga (massage), Utshadana (coating), Parisheka (fomentations) etc. [26-28]
4. Kapha Nashaka Chikitsha (to regress the growth of the tumor)- Since Kapha is the prevailing Dosha in cancer, it should be treated by the administration of Ushna Veerya (hot), Tikshna (sharp), Laghu (light), Ruksha (dry) Gunas, Katu (pungent), Tikta (bitter), Kashaya (astringent) Rasa drugs. [29] Ayurveda holds the concept that drugs exhibit their pharmacological actions either by virtue of their Rasa (taste) or by Guna (physical properties) or by Veerya (potency) or by Vipaka (digestive end product) or by Prabhava (specific pharmacological effect). [30] Kaphanashaka drugs should be administered in the form of Swedana (sudation), Vamana (emesis), Shirovirechana (nasal drop therapy), Samana (palliative treatment). Simultaneously Ushna and Tikshna Guna can exhibit Lekhana Karma or scrapping action by reducing both Medo Dhatu and Mamsa Dhatu [31].
5. Sophanashaka Chikitsha (anti-inflammatory therapy)-In this phase all the seven procedures of treatment like Vimlapana (light massage), Avasechana (blood letting), Upanaha (poultice), Patana (operative procedures), Shodhan (antiseptic), Ropana (healing measures), Vaikrutapaha (restoring the normal colour of the skin) can be adopted as a measure of treatment of Arvuda because all Arvudas are included under the heading of Shopha as per Sushruta. Drugs which can be administered for these purposes are Haridra (*Curcuma longa*), Bhallataka (*Semecarpus anacardium*), Kupilu (*Strychnos nox-vomica*), Vatshanabh (*Aconitum ferox*), Arka (*Calotropis procera*) etc.[32, 33]
6. Dhatu Nashak Chikitsha (cytotoxic therapy) of the vitiated Dhatus involved including Rakta, Mamsa and Medo Dhatu. Lekhana Karma (scrapping therapy) reduces both the Medo and Mamsa Dhatus. For the purpose of Lekhana Karma drugs with Laghu, Ruksha, Ushna, Tikshna properties, Katu, Tikta, Kashaya Rasas should be taken for administration. Drugs like Yava (*Hordeum vulgare*), Ativisha (*Aconitum heterophyllum*), Sunthi (*Zingiber officinale*), Pippali (*Piper longum*), Vidanga (*Embelia ribes*), Amalaki (*Embelica officinalis*), Shilajit (*Asphalt*) etc can reduce both Mamsa and Medo Dhatu. [34] Administration of Tikta, Kashaya Rasas can purify the vitiated Rakta Dhatu. Drugs like Nimba (*Azadirachta indica*), Chirayita (*Swertia chirata*), Manjistha (*Rubia cordifolia*), Guduchi (*Tinospora cordifolia*) etc can be used for the pacification of vitiated Rakta Dhatu. Involvement of other Dhatus can be treated accordingly [35].
7. To prevent and treat invasiveness and metastasis: Vata Nashaka Chikitsha, Srotas Sodhan Chikitsha-Administration of Ushna [36], Tikshna [37], Ruksha [37] Dravyas (Vidanga, Vatshanabha (*Aconitum ferox*), Vacha (*Acorus calamus*), Guggulu (*Commiphora mukul*), Maricha (*Piper nigrum*), Bhallataka (*Semecarpus anacardium*), Arka (*Calotropis procera*) etc) [38] will remove obstructions of the blood vessels, lymphatics and cavities (Antarmukha Srotas) involved in metastasis while Panchakarmas like Vamana (emesis), Virechana (purgation therapy), Asthapana (dry enema), Anuvashana

(oily enema), Shirovirechana (nasal drop therapy) and Rakta Mokshana (blood letting) can be adopted for the treatment of metastasis and invasion present in the Sthula Srotas (bulk cavities) like Stomach, intestine, nasal cavities, oral cavity etc. Out of these, Vamana and Shirovirechana can pacify Kapha [31] while Asthapana and Anuvasana can pacify Vata [28]. Virechana and Rakta Mokshan can pacify Rakta [39]

8. To preserve Rogi Vala and Vyadhikshamatwa (immunomodulatory/Rasayana therapy)-In treatment of Shotha Chikitsha Sushruta has mentioned that Rogi Bala (strength and immunity of the patient) has to be preserved which will neutralize the Vyadhi Bala or virulence of the Disease [40]. Therefore Rasayana Chikitsha mentioned in Ayurvedic literature should be adopted as per the procedure which conserves the strength, immunity, Vitality and stamina [41] Some of the common Rasayana drugs are Chyawanprash, Aswagandha (*Withania somnifera*), Satawari (*Asparagus racemosus*), Guduchi (*Tinospora cordifolia*), Shilajit (*Asphalt),* Amalaki (*Emblica officinalis*), Haritaki (*Terminalia chebula*), Punarnava (*Boerrhavia diffusa*) etc. Some of them have shown anti-cancer potential also. [41, 42]
9. Surgical treatment to remove the tumor including the Sashtra Karma (Chedana/excision, visravana/drainage etc), Agni Karma (cauterization), Kshara Karma (alkalization) etc should be adopted. The tumor should be surgically removed in such a manner that it should not recur further due to left over tissue (Saseshaani Doshaani) in the tumor area. This theory resembles to the stem cell theory of cancer. If the lesion is very big in nature surgical removal is the main line of treatment along with prevention of recurrence through medicinal treatment. But if the size of the tumor is small in size or the cancer is in preliminary stage medicinal treatment can be initiated [40, 43].
10. Other symptomatic treatments.

Pharmacodynamics of drugs used for the treatment of Arvuda.

On the basis of pathogenesis and principles of treatment of cancer as mentioned above, pharmacodynamics of anti-cancer drugs in Ayurveda will be chiefly determined by Ushna Veerya, Tikshna, Laghu, Ruksha Gunas (properties) and Katu, Tikta Rasas (tastes). The following analysis of the pharmacotherapeutic properties of the above mentioned pharmacodynamical factors on the basis of Ayurvedic literature will substantiate the claims made above.

Katu Rasa (pungent taste)

The taste which produces mental and psychological irritation and burning sensation (Daha) on coming in contact with the tongue, enhances the secretions from the nostrils, eyes and mouth is called as the Katu Rasa. [35] It is dominant of Vayu and Agni Mahabhuta. The pharmacotherapeutic actions of Katu Rasa are purification of the mouth, stimulation of the Agni (digestive and enzymes including those which wok as anti-oxidant enzymes), pacification of the inflammation (Swayathu Hara), pacifies the Upachaya (accumulative growths like tumors/cancers), penetrates and removes the obstruction of Srotas or channels including the blood vessels, lymphatics and the natural cavities of the body. It removes the unctuous molecules from the skin and the Srotas including cholesterol and the metastatic cells. The drug with Katu Rasa decreases itching on the tumors, improves appetite, heals up the ulcers and wounds. It kills or inactivates the microbes including the worms. Katu Rasa reduces the Mamsa Dhatu, opens and dilates the Srotas, pacifies the Kapha Dosha. It is also characterized by lightness (Laghu), Ushna (hot) and Ruksha (dry) properties [35].

Tikta Rasa (bitter taste)

The taste which disturbs the gustatory sensation of the tongue for a transient period, affords good psychological feeling by eliminating the Mukha Vaisadya (tastelessness of the mouth) is called as Tikta Rasa [35]. Bitter taste eliminates anorexia, pacifies poison, kills microbes including the worms, pacifies Murcha (fainting), Daha (burning sensation), Kandu (itching and pruritus), skin diseases (Kustha), stabilizes the Twak and Mamsa Dhatu (skin and muscle tissue), stimulates the digestive fire (Dipana), Pachana (digests the Ama or the free radicals), Lekhana (reduces the Mamsa Dhatu and Medo Dhatu). Simultaneously it dries up Kleda (moisture), Meda (adipose tissue), Vasa (fat), Lasika (lymph), Puyah (pus), Sweda (sweat), Mutra (urine), Purisha (stool), Pitta (bile), Kapha (phlegm). It is also characterized by Laghu (light), Ruksha (rough) and Sheeta (cold) properties [35].

Ushna Veerya Karma (functions of hot potency)

The property of the drug which alleviates cooling sensation from the body and induce perspiration (Swedana), burning sensation (Daha), vertigo (Bhrama), thirst (Thrishna), anxiety (Glani), induce quick suppuration of wounds (Ashupaki) is called as Ushna Veerya or hot potency. They pacify both Vayu and Kapha Dosha and simultaneously aggravate Pitta Dosha. Ushna Guna lequifies the Doshas accumulated inside the Srotas. Therefore both cytotoxic and anti-metastatic activities could be mediated through Ushna Guna [44].

Tikshna Guna (sharp properties)

The drugs which penetrate the channels and expel the Doshas and Malas accumulated within the channels is called as Tikshna. It is having Agni and Akasha Mahabhuta dominance. The cytotoxic properties may be mediated through Tikshna Guna [37].

Laghu Guna (light-ness)

The drugs which create lightness within the body is called as Langhana Dravya. They are of Agni and Vayu Mahabhuta dominanace. It is opposite to Guru Guna or heaviness. It acts always in the upward direction and helps in the tumor regression due to its lightness. It also pacifies the Kapha and Meda [37, 45].

Ruksha Guna (dryness)

The drugs which have the capacity to absorb moisture or water content are called as Ruksha Dravyas. It is opposite to Snigdhatwa or lubricating or unctuous property or oily property and helps in the regression of the tumor by drying up the Mamsa and Meda Dhatu [37].

Anti-cancer studies on Ayurvedic drugs

Randomly five drugs were selected which are having common pharmacodynamical properties (Ushna Veerya, Laghu, Ruksha, Tikshna Gunas, Katu, Tikta Rasas) required for anti-cancer potential. These drugs are Vidanga (*Embelia ribes*), Bhallataka (*Semecarpus anacardium*), Arka (*Calotropis procera*), Guggulu (*Commiphora mukul*) and Chitrak (*Plumbago zeylanica*). Their anticancer potential has been reviewed in the terms of their anti-oxidant, anti-mutational,

anti-inflammatory, immunomodulatory and cytotoxic activities on the basis of available published literature. Another very commonly used Ayurvedic Rasayana formulation Chyawanprash has been reviewed in order to justify the role of Rasayanas/immunomodulators in the treatment of cancer.

Vidanga (*Embelia ribes* Burm f). Family-Myrsinaceae

The fruits of Vidanga are indicated in several clinical conditions like Krimi (worms), Kustha (skin disease), Shula (colicky pains), Adhmana (tympanitis), Udara (ascites), Shleshma (diseases due to Kapha), Vata (diseases due to Vata) and Vivandha (constipation). It is used as a Trptighna (anti-satiety) and Shirovirechana (errhine) drug. It has been attributed with Ushna Veerya, Katu, Kashaya Rasa, Laghu, Ruksha, Tikshna Guna, Katu Vipaka. It alleviates Vata due to its Ushna Guna and pacifies Kapha due to its Laghu, Ruksha Guna, Ushna Veerya, Katu Rasa and Katu Vipaka. (38) Its anti-cancer potential has been widely studied and published by a number of investigators.

Anti-cancer potential

1. Embelin obtained from *Embelia ribes* (ER) has been reported to possess anti-cancer potential by binding to the BIR3 domain of XIAP (X-linked inhibitor of apoptosis protein) preventing the association of XIAP and caspase-9 which results in suppression of cell growth, proliferation and migration of various types of cancer cells. Furthermore embelin modulates anti-apoptotic pathway by suppressing the activity of NF-kB, Pl3 kinase/AKT, JAK-STAT pathways. [46]
2. Embelin has been found to inhibit the growth of leukemic cell lines K562 and U937 by suppressing the AKT signaling pathway and down regulates XIAP expression resulting in mitochondrial caspase mediated apoptosis. In addition embelin has suppressive effects on the growth of various other cancer cell lines including osteosarcoma, bladder cancer, breast cancer, human glioma etc. [47].

Bhallataka (*Semecarpus anacardium* Linn).Family-Anacardiaceae

Semecarpus anacardium (SA) in Ayurveda is a very well known drug for its hot potency and Katu Tikta Kashaya Rasa. It is associated with Madhura Vipaka and Laghu Snigdha Tikshana Guna. The fruits of the plant are used in medicine. The plant is bestowed with Chedana (expectorant), Bhedana (penetration), Bahnikara (stimulates digestive fire), Medhya (intellect promoting) actions and indicated in Vrana (ulcers), Udara (enlarged abdomen), Agnimandya (dyspepsia), Kustha (skin diseases), Arsha (piles), Grahani (sprue), Sopha (inflammation), Anaha (tympanitis), Jwara (fever), Krimi (worms). The fruits are toxic in nature and cause blisters if used in dried form. Therefore it requires purification. Always purified Semecarpus nuts are used in medicine [33].

Anti-cancer potential

1. Semecarpus nut extract has shown inhibitory effects on human breast cancer cell lines (T47D) characterized by the downregulation of Bcl2 and up regulation of Bax, cytochrome C, Caspases and PARP cleavage and ultimately by internucleosomal DNA fragmentation. SA triggers apoptotic signals in T47D cells [48].
2. In another experiment, a group of investigators studied the anticancer potential SA in leukemic mice along with imatinib mesylate as the standard drug. SA administration to the leukemic animals resulted in the clearance of the leukemic cells from the bone marrow and internal organs. Leukemia bearing mice showed a significant increase in the LPOs, glycolytic enzymes and a decrease in gluconeogenic enzymes and a significant decrease in the activities of TCA cycle and respiratory chain enzymes as compared to control animals. Pretretament with SA reversed all the above parameters due to leukemia [49].

Arka (*Calotropis procera* Aiton. W.T.) Family-Asclepiadaceae

The root bark, latex, leaves, flowers of *Calotropis procera* (CP) plant has been used in Ayurvedic system of medicine. The plant has been attributed with the properties like Laghu Ruksha Tikshna Guna, Katu Tikta Rasa, Katu Vipaka and Ushna Veerya. On the basis of the pharmacodynamical properties, the plant has possessed the ability to pacify the Kapha and Vata. Other indications of the plant include Kustha (skin diseases), Kandu (itching and pruritus), Visha (poison), Vrana (ulcers), Pleeha (splenomegaly), Gulma (abdominal lumps including abdominal tumors), Arsha (piles), Shleshma (diseases due to Kapha), Udara (enlargement of abdomen including the ascites), Krimi (worms).

Anticancer potential

1. A protein isolated from *Calotropis procera* (CP-P) root bark has been found to suppress the proliferation by inducing apoptosis of breast cancer cells through the suppression of the NF-kB pathway. CP-P when administered individually or in combination with cyclophosphamide (CYP) in a dose 0.2 mg/Kg to rats with 7, 12 –dimethyl benzanthracene (DMBA) induced breast cancer, decreased the tumor volume significantly without affecting the body weight. The drug when administered along with the CYP (CP-P+CYP) has displayed significant enhancement of the generation of anti-oxidant enzymes like SOD, CAT, GSH and also the level of anti-oxidant vitamins like Vitamin-E and vitamin-C. The investigators proposed comparable effects for both CP-P and standard anticancer drug CYP. [50]
2. Anticancer properties of the dried latex (DL) of *Calotropis procera* was evaluated by a group of investigators in the X-15 myc transgenic mouse model of hepatocellular carcinoma. The young transgenic mice were orally fed with aqueous suspension of DL (400 mg/kg for 5 day /week) for 15 weeks. The liver was studied for the histopathological changes at 20 weeks. Serum level of the vascular endothelial growth factor (VEGF) was also measured in these animals. DL treated mice showed a complete protection against hepato-carcinogenesis. The investigators found the serum VEGF level to be significantly lower in comparison to the control. The investigators did not observe any signs of toxicity of the test product in these animals. Simultaneously the petroleum ether followed by methanol extract of DL as well as its fraction-8 induced extensive cell death in both Hepatoma (Huh-7) and nonhepatoma (COS-1) cells. But the non-transformed hepatocytes (AML-12) were not affected as investigated by the same group of investigators. The cell death was mediated by DNA fragmentation in Huh-7 and COS-1 cells. No significant change in the apoptotic markers like

Bcl-2 and caspase -3 was observed by the investigators. [51]

Guggulu (*Commiphora mukul* (Stocks) Hook.). Family:Burseraceae.

Guggulu is one of the commonly used drugs in Ayurveda specifically for pain and inflammatory conditions. Gum resin obtained from *Commiphora mukul* (CM) aerial part is used in Ayurvedic system of medicine. Vayu is the responsible agent for both pain and inflammation and Guggulu is one of the best drugs to pacify Vata. The drug has been attributed with Lghu Ruksha, Tikshna Guna, Katu Tikta Rasa, Ushna Veerya, Katu Vipaka. It is also indicated in various tumor conditions. Kanchanara Guggulu, Amrutaadi Guggulu, Yoga Raja Guggulu are some of the formulations which are indicated in various painful and inflammatory conditions like rheumatoid arthritis, osteoarthritis, cervical lymphadenitis, swelling of the thyroid gland, chronic non-healing ulcers etc. Various bio-pharmacological studies have been conducted on Guggulu. [38]

Anti-cancer potential

1. **Breast cancer:** A group of investigators found that Gugulipid (GL) isolated from *Commiphora mukul* (CM) significantly inhibited growth of MCF-7, MDA-MB-231 breast cancer cell lines with an IC50~2 μM. The GL induced growth inhibition was correlated with apoptosis induction and evidenced by an increase in cytoplasmic histone associated DNA fragmentation and caspase -3 activity. The GL induced apoptosis was associated with down regulation of the β-catenin signaling pathways. On the other hand the normal human mammary epithelial cells HMEC compared to the breast cancer cells were significantly more resistant to growth inhibition and apoptosis induction by GL [52]
2. **Pancreatic cancer:** A study conducted on Guggulusterone (GS) isolated from CM gum resin has found to inhibit various cancer cells either in vitro or *in vivo*. Pacreatic cancer, colon cancer, head and neck cancer, esophageal adenocarcinoma, breast cancer, prostate cancer, liver, lung and ovarian cancer, hematological malignancies. It has been shown that GS prevents cell proliferation, inhibits cell motility, reduces cell invasion and induces apoptotic cell death in many pancreatic cell lines by disruption of cytoskeletal organization, inhibition of FAK and Src kinase signaling, reduction of mucin MUC 4 gene expression by inhibition of JAK kinase mediated signaling [53].
3. **Head and Neck cancer:** In head and neck squamous cell carcinoma (HNSCCC), GS treatment inhibited the proliferation of HNSCCC by inactivating NF-kB and STAT-3 signalling cascades. GS treatment of the HNSCCC prevents the NF-kB activation and leads to its degradation resulting in the inhibition of inflammatory and angiogenic responses as well as progression and metastasis. [54, 55]
4. **Esophageal adenocarcinoma:** GS treatment to the Barett's esophagus derived cell lines was found to significantly reduce the over-expression of the bile acid receptors FXR in the Barett's esophagus cell lines. The authors found a significant increase in the apoptotic cells along with increased expression of caspase-3 activity. [56]
5. **Colon cancer**: GS treatment has been found to possess anti-cancer activity against colorectal cancer. GS treatment to colon cancer cell line has been shown to block angiogenesis and metastasis by inactivation of STAT-3 activity and down-regulation of VEGF expression. [57] GS had shown increased apoptotic activity via activation of caspase cascade, down regulation of apoptotic inhibitory proteins Bcl-2 and activation of JNK kinase. [58].
6. **Anti-radiation effect:** In a study conducted to investigate the radiation sensitization effect of GS (guggulusterone) on various types of cancer cells, it was found that GS inhibits the radiation induced NF-kB activation and enhanced the radio sensitivity in the pancreatic cell line PC-Sw. GS reduced both cell cycle movement and cell growth by reducing ERα protein in colon cancer cells and pancreatic cancer cells and inhibited DNA double strand break (DSB) repair following radiation. [59]
7. **Prostate cancer**: GS treatment of human prostate cancer cell line PC-3 resulted in the efficient cytotoxic effect by inducing apoptosis without affecting the normal prostate epithelial cell lines. (PrEC) as observed by a group of scientists. This GS mediated apoptosis of PC-3 cells was correlated with the over expression of Bcl-2 family members such as Bax and Bak and sequential activation of caspase cascade. [27] Many other studies have also justified the anti-cancer activity of GS in prostate cancer *in vivo* and in vitro models [60].
8. **Liver, Lung and Ovarian cancer:** Sub toxic dose of GS and tumor necrosis factor related apoptosis inducing ligand (TRAIL), both induced apoptosis efficiently in hepatoma cells. GS also induced apoptosis in the hepatic stellate cells (HSC) by involving the regulation of the AKT and AMPK pathways resulting in the activation of the pro-apototic proteins and down-regulation of anti-apoptotic proteins. HSC cells play a significant role in liver cirrhosis. [61] GS shows inactivation of NFkB activation in LX-2 cells. [62] Studies support the anticancer activity of GS in the lungs and the ovarian cancer. Treatment with GS to the human lungs and the ovarian cancer cells resulted in the inhibition of cell proliferation and inhibition of Cyclin-D1 and cdc2 expression leading to inhibition of DNA synthesis. The investigators correlated GS mediated apoptosis with the activation of JNK, activation of caspase cascade and inhibition of the expression of various anti-apoptotic genes and inhibition of Akt pathway [63].
9. **Hematological malignancies**-These malignancies are classified into leukemia, lymphoma and multiple myeloma (MM) etc. GS has been reported for its anti-leukemic effect. [64] Sishodia and colleagues reported that treatment of leukemia, myeloma and melanoma cell lines with GS resulted in the decreased proliferation along with reduced level of cyclin-D1 and cdc-2 which inhibited the DNA synthesis. They found increased levels of cyclin dependent kinase inhibitor p21 and p27 as well as induction of apoptosis by activation of JNK, caspase cascade, PARP-cleavage and down regulation of anti-apoptotic products [63].

Chitraka (*Plumbago zeylanica* Linn.) Family: Plumbaginaceae.

Chitraka or *Plumbago zeylanica* (PL) is a commonly used Ayurvedic drug indicated mainly for the digestive and appetite stimulant properties. It is also indicated for Grahani (sprue), Kustha (skin disease), Sotha (inflammation), Arsha (haemorrhoides), Krimi (worm infestation), Kasha (bronchitis). It has the ability to pacify the Vata due to its

extreme Ushna Veerya and Kapha due to its Katu Rasa Vipaka, Laghu, Ruksha Tikshna Guna, Ushna Veerya. The root of the plant is used for the medicinal purposes [26].

Anticancer potential

Several anti-cancer studies have been conducted on both the crude extract and plumbagin (PLB), a bioactive napthoquinone isolated from *Plumbago zeylanica* (PL).

1. In a study conducted by a group of scientists, plumbagin (PLB), isolated from roots of PL, has induced apoptosis in pancreatic cell lines Panc-1 and Bxpc-3 in a dose dependant and time dependent manner primarily through the mitochondrial related pathways followed by both caspase dependent and caspase independent cascades. Plumbagin enhanced the activation of caspase -3 but not caspase -8 and induced apoptosis via activation of caspase-3. [65]
2. Anti-cancer activity of Plumbagin (PLB), was studied in the tongue squamous cell carcinoma (TSCC) cell line SCC25. The investigators found that PLB remarkably induced apoptosis and autophagy. PLB arrested the growth of the SCC25 cell at the G2/M phase in a concentration and time dependent manner with decrease in the expression level of cell division cycle protein-2 homologue (Cdc2) and cyclin B1 and increase in the expression level of p21 Waf1/Cip1, p27 Kip 1 and p53 in the SCC25 cells. Further more PLB inhibited Phosphatidylinositol 3 kinase (Pl3K), Akt (protein kinase B), mTOR, glycogen synthase kinase 3β (GSK3β) and p-38 mitogen-activated protein kinase (p38MAPK) pathways contributing to the autophagy inducing effect. [66]
3. Plumbagin also induces apoptosis and autophagy via sirtuin -1 and Pl3K,/Akt/mTOR mediated pathways in human prostate cancer cells. [67]

Chyawanprash

Chyawanprash (CP) is a reputed anti-ageing formulation described in Ayurvedic texts. It is prepared out of more than 50 herbal constituents. Drug is indicated for mainly respiratory infections like cough, bronchial asthma, bronchitis, common cold, haemoptysis, hoarseness of voice etc. It helps in the growth and development in children. A mythological story sustains that the old Chayawan Maharishi regained his youthfulness and vitality by consuming Chyawanprash. Many Indian Ayurvedic medicine manufacturers market Chyawanprash as a general tonic. It restores the strength, stamina, vitality and immunity of the person consuming it. Its major ingredient is Amalaki (*Embelica officinalis*) which is the world's richest natural source of vitamin C. [41] Chyawanprash has been extensively studied for its various biological activities.

Anti-cancer potential

1. Chyawanprash (CP) has a potential anti-mutagenic and radio-protective effect. A study found the genoprotective effects of Dabur CP in 25 Bidi smokers on somatic chromosomes. CP when administered in the dose of 20 gms BID for a period of two months. The subjects were examined for their mitotic index (MI), chromosomal aberrations (CA), sister chromatid exchanges (SCE) and satellite associations (SA). All these parameters were found to be decreased significantly ($p<0.01$) in CP fed smokers compared to normal smokers. A significantly declined chromosomal aberrations indicated significant genoprotective activity of Chyawanprash against mutagens presents in the tobacco. [68]
2. In another cytogenetic study it was established that CP posses significant genoproptective and anti-oxidant capabilities in oral premalignant cancer lesions found in 21 betel quid chewing subjects. [69].
3. Radioprotective action of CP was studied in mice. The animals were subjected to lethal dose of gamma-irradiation. CP provided good radioprotection in mice at a minimal non-toxic dose 15mg/kg bw. Higher number of survivors was found after completion of 30 days in CP-fed group post irradiation in comparison to the CP-non-fed group [70].

Immunomodulatory potential

CP was studied for its immune-stimulatory effect in vitro by evaluating the secretions of cytokines such as TNF-alpha, IL-1β, macrophage inflammatory protein-1-alpha (MIP1-α) from murine bone marrow derived dendritic cells (DC) which plays a pivotal role in immune-stimulation. The effect of CP induced phagocytosis in murine macrophages (RAW264.7) and natural killer (NK) cell activity were also investigated by the same group of scientists. At a non-cytotoxic concentrations (20- 500 µg/ml) CP enhanced the secretion of all the three cytokines from DC. CP also stimulated both macrophage and NK cell activity in vitro. The study suggested the immune-stimulatory activity of CP in dendritic cells, macrophages and NK cells. [71]

Discussion and conclusion

Despite a huge advancement in the field of chemotherapy, surgery and radiotherapy, cancer still is a major cause of morbidity and mortality. Several plant alkaloids are in use in cancer chemotherapy like vincristine, vinblastin, vinbladin, taxol, paclitaxel etc. The WHO forecasts that one in 5 men and one in 6 women worldwide will develop cancer during their life time and one in 8 men and one in 11 women die from cancer. Cancer as a disease causes major physical, psychological, social and financial burden upon the patient, family, society and the government as well. Herbal medicine is not properly explored for the treatment of cancer. Of course it is an admissible fact that there is a tremendous surge on the front of anti-cancer drug research in the field of herbal medicine. Many Ayurvedic drugs have been investigated for their anti-cancer potentials both *in vivo* and in vitro. But their clinical trial in cancer patients is far away.

Ayurveda one of the foremost indigenous system of medicine of the world describes various clinical conditions which have apparent similarities with cancer of various organs of the body. The concept of Arvuda apparently denotes to the malignant tumors on the basis of the described morphological and clinical features. Various surgical, parasurgical and drug therapies are advised for the treatment of Arvuda. In the present review the treatment principle has been designed keeping in view the basic aetiology, pathogenesis and clinical features of various types of cancer as a whole with a special reference to those of Arvuda. Despite surgery being the main stay for the treatment of a malignant tumor of large size, medicinal therapies are essential for the treatment of small tumors and prevention of recurrence which is one of the main dogmas of cancer treatment. After a critical evaluation of Ayurvedic and contemporary modern medical literature, few pharmacodynamical properties like Ushna (hot potency), Tikshna (sharp), Laghu (light), Ruksha (drying property) Guna (properties), Katu (pungent), Tikta (bitter) Rasas

(tastes) have been found to be effective in terms of cell cycle arrest, apoptosis induction, prevention and treatment of metastasis and invasion, preventing anaplasia, prevention of recurrence and decreasing prognosis. Simultaneously the drugs with these properties have been found to have a role in the inhibition of free radicals and enhancing the antioxidant enzymes. Degradation of other oncogens is also another target of these drugs. Randomly selected drugs possessing the above five properties have all exhibited anti-cancer activities in various in vitro and in-vivo models. They may be expected to exhibit similar activities in cancer patients also. Other drugs possessing the above five pharmacodynamical properties can be studied in the similar lines. I propose selection of drugs for future anti-cancer research, both pharmacological and clinical should be carried out on basis of above mentioned pharmaco-therapeutic principles.

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