



An Ayurvedic concept of *Shatkriyakala* with special reference to Cancer Pathogenesis

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ABSTRACT

Acharya Susruta describes about the various stages in the development of malignant tumors and also recognizes recurrence as well as metastasis. The concept of *Shatkriyakala*, is an objective approach of *Ayurveda*, which gives a sign about the consecutive phases of the disease for distinguishing the particular disease and to institute appropriate therapeutic intervention, and accordingly preventive measures can be described to overcome complications as well as advancement of the disease. *Shatkriyakala*, in which disease state is not an instantaneous occurrence, evolves through a sequence of certain phases in relation to the *tridoshas*-pathophysiologic rhythm. In respect to cancer pathogenesis, it is a hyper-proliferative disorder develops due to genetic dysregulation of growth of cells and tissues that encompasses many stages such as transformation, derange of apoptosis, proliferation, invasion, angiogenesis and metastasis (almost final stage). The physician must acquire the knowledge to recognize early stages of the diseases and accordingly initiate the needful management to contain the further progression of the diseases. In this article critically correlate the concept of *Shatkriyakala* (stages of progression of disease) in respect to cancer pathogenesis based on the probable involvement of *tridoshas* (*Vata*, *Pitta* and *Kapha*), *Dushyas* (*dhatu*s, *upadhatu*s & *malas*), *Agni*, *Srotas* etc.



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INTRODUCTION

The concept of *Kriyakala* is one of the important original contributions of *Sushruta*. *Shatkriyakala* includes two words– *kriya* and *kala*. *Kriya* means treatment and *Kala*-appropriate time for identifying the stages of the disease and their management strategies as per different stages (Srikantha, 2005b). Malignant growth is the subsequent driving reason for death globally and is evaluated to represents 9.6 million (deaths) in 2018 (WHO, 2018). *Ayurveda*, the oldest Indian medical system understands cancer as the derangement of *tridosha* as a whole of neuro-humoral, metabolic and adaptation

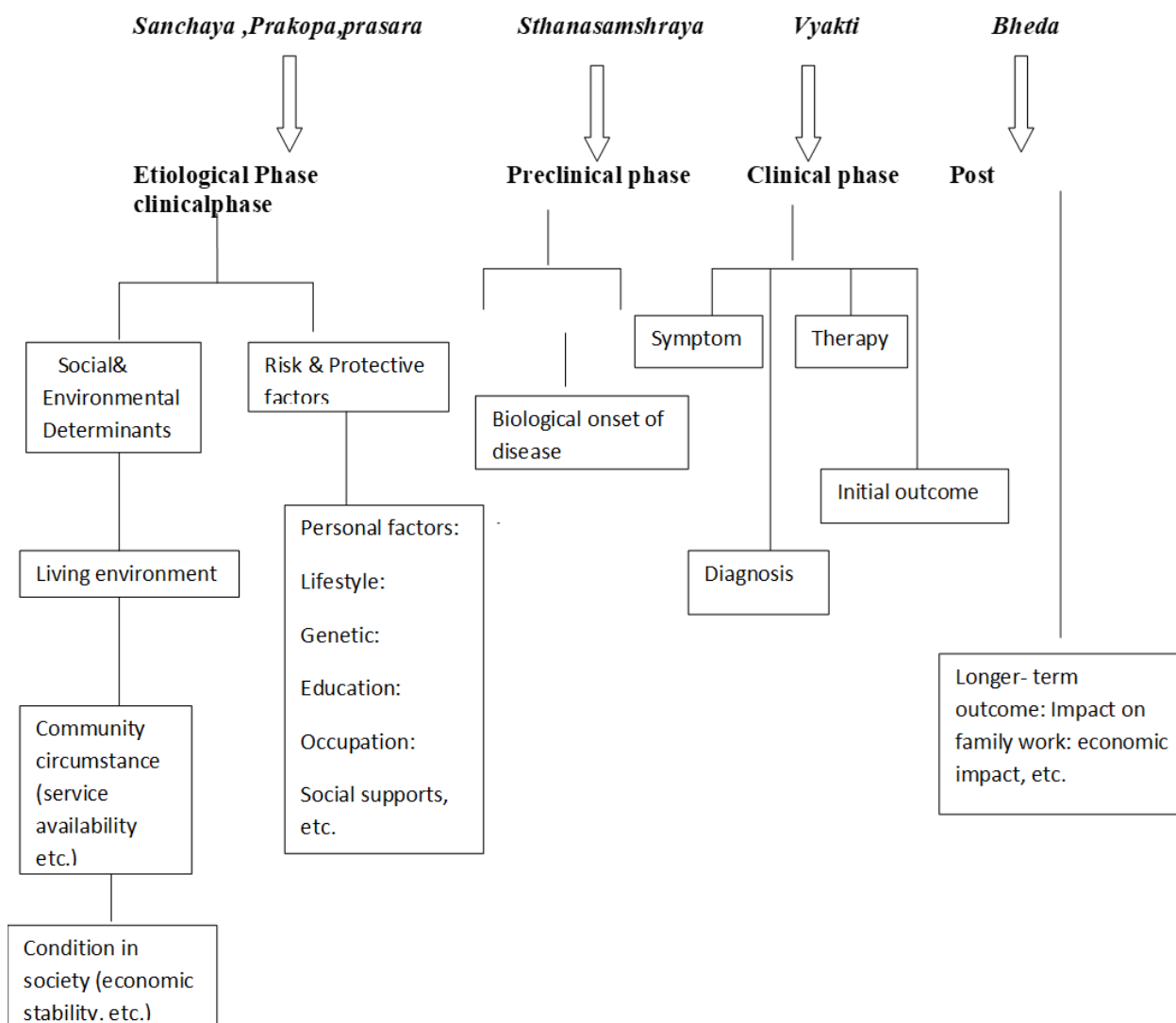


Figure 1: Description of six stages of Vyadhi (point of view of various diseases Management)

of unwhole some measures in respect to diet, conduct and activities that causes loss of shared coordination in homeostasis and disturbs the normal tissue and cell tissue multiplication (Rabinarayan and Das, 2017). Malignant growth include anomalous cell development with the possibility to assault or spread to different parts of the body.

Cancer develops in a prolong, multistep process in a group of malignant, autonomously growing abnormal clone cells, through the sequential acquisition of primarily somatic mutations in critical genes, due to exposure of DNA damaging chemicals such as deranged diet and lifestyle (Harrison et al., 2001). This study also explains that *Shatkriyakala*, is mentioned in *Sushruta Samhita* texts, gives an thought about the succeeding stages of diseases and a significant role in the point of view of *chikitsa* (treatment modalities) for application in management of various stages of the diseases.

An early diagnosis of all phases of disease will help understanding the pathophysiology of disease and prevents to advance progression of the diseases by subsiding of *Nidanas* (etiological factors). Holistic approach to cure, prevention and improvement of quality of life. Impairment of diet, erratic life style and other environmental factors stimulate the abnormal cell proliferation (Singhal et al., 2007).

Concept of *Shatkriyakala*

According to changes in the *Doshas* different stages of progression of disease are described.

1. *Sanchaya* (stage of accumulation)
2. *Prakopa* (stage of aggravation)
3. *Prasara* (stage of spread)
4. *Sthanasamsharaya* (stage of localization)
5. *Vyakti* (stage of manifestation)

6. *Bheda* (stage of differentiation and development of complications)
7. *Sanchaya* and the other five stages develop one after the other more strongly and their advancement of stages is the base for the progress of the disease is termed as *Samprapti*. During these *Sachayadi* stages the *Dosas* getting aggravated greatly and create abnormalities or pathological changes in *Dhatus, Malas, Agni, Srotas, Ojas* etc. Thus produces severity of the symptoms and the incurability of the diseases which depends on the degree of involvement of disease producing fundamental factors.

Sanchaya-Accumulation

It is the first stage of *Kriyakala* and initial component for disease manifestation. In this stage due to excessive intake of *Nidanas* (etiological factors) leading to gradual accumulation of *Doshas* in their respective places and exhibit certain features (Byadgi, 2018b).

Sign and Symptoms

These symptoms are causes of accumulated *Doshas*.

Vata Sanchaya features (*Vata* accumulating features) such as Stability and fullness of *kostha* (Gastrointestinal tract and other associated complain in abdomen)

Pitta Sanchaya features (*Pitta* accumulating features) such as *Pitavabhasata* (Yellowish discoloration of body parts), *Mandosmata* (mild elevation of temperature)

Kapha Sanchaya features (*Kapha* accumulating features) likes *Angagaurav* (Feeling of heaviness of the body), *Alasya* (lassitude) (Sharma, 2000c).

To conclude in this stage person develops aversion towards the causative factors which are responsible for the accumulation of *Dosha*. If person understand this phenomena of the body and acts accordingly as a result *Sanchaya* stage do not undergo further stages, otherwise in the successive stages they become powerful and produce diseases. In this stage one should also adopt the measures to eliminate the accumulated *Doshas* to prevent the further progression of the disease (Byadgi, 2018b). If combination of two or three *Doshas*, then firstly dominant *Dosa* should be treated without antagonizing with the less powerful other *dosas*. According to *Sushruta Samhita* certain measures should be adopted soon to prevent the further progression of the next stage.

Prakopa -Aggravation/excitation

It is the second stage of aggravated *Doshas* due to continue consumption of *Nidanas* (etiological fac-

tors).

In this stage the movement of *Doshas* from their original site to other site but don't spread all over body. In this series aggravation of *Doshas* into next stages depends on intake of causative factors.

Sign and Symptoms-Aggravated *Dosas* produces following symptoms

Vata Prakopa features (*Vata* aggravating features) such as *Kostha toda* (Pain in *Mahasrotas*) and *Sancharna* (Movement of *Vata*)

Pitta Prakopa features (*Pitta* aggravating features) such as *Amlika* (Sour eructations), *Pipasa* (Excessive thirst) and *Paridaha* (Burning sensation all over body)

Kapha Prakopa features (*Kapha* aggravating features) as *Annadvesa* (Aversion of food) and *Hridayotkleda* (Excessive salivation in mouth) (Sharma, 2000d).

Prasara -Spread of disease producing components to other places

This is the third stage of progression of the disease. This stage happens due to continuous intake of causative factors and not adopting the precautionary measures.

In this stage the overflow of increased *dosas* to other places from their own sites to different organs and tissues.

Sign and Symptoms

Vata Prasara features (*Vata* spreading features) likes *Vayuvimargagamana* (Movement of *Vata* in abnormal channels) and *Aatopa* (Tender/tympanitis)

Pitta Prasara features (*Pitta* spreading features) such as *Oosha* (Localized heat), *Chosha* (Sucking pain), *Paridaha* (Generalized burning sensation) and *Dhumayana* (feeling like emitting smoke)

Kapha Prasara features (*Kapha* spreading features) as *Aruchi* (Anorexia), *Arochaka* (Indigestion), *Angadaha* (Lassitude) and *Chardhi* (Vomiting) (Sharma, 2000a).

The aggravated and excited *Doshas* blowout to the different body parts and create the disease like the clouds in the sky which cause rain. If the preventive measures are not taken at this stage leading to the further progression of the condition and favoring the complete development of the disease. In certain conditions comorbid factors stays hidden in its path for a while and later on aggravates when favorable condition prevails. Symptomatic treatment and avoid the causative factors is the key treatment in this stage.

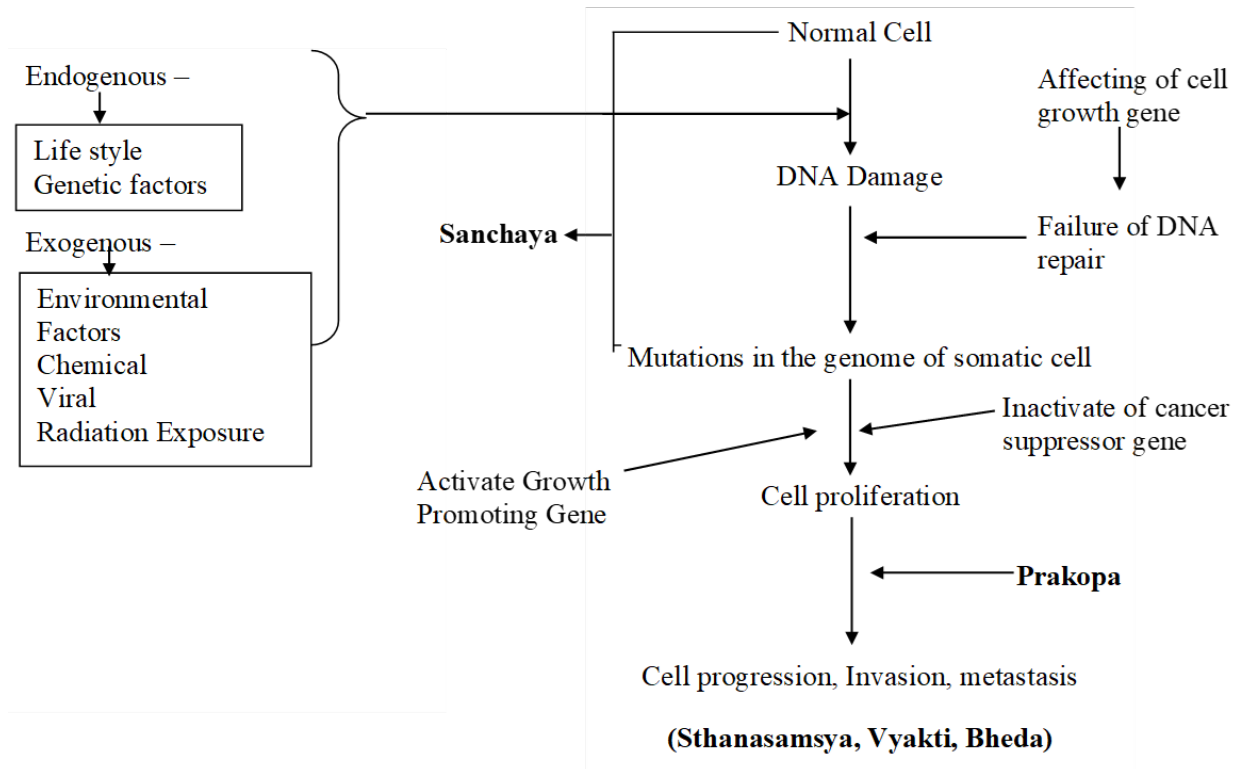


Figure 2: Correlation of Cancer pathogenesis with Shatkriyakala (Stages of Vyadhi)

Sthanasamsharya - Antigen-antibody interaction stage

It is a prodromal phase of a particular disease due to interaction between *Doshas* and *Dushyas* in a particular place due to vitiation and obstruction inside the body channels and accordingly progression of disease takes place. The interaction between antigen and antibody is the key factor in this stage and accordingly disease develops. The strength of interaction between antibody and antigen at single sites leading to inflammatory process in that place and responsible for disease progression. The segregation of the disease producing factors in one particular site leading to the initiation of inflammatory process leading to development of the diseases in that place. The greater the interaction, the stronger the affinity. Voracity is perhaps a more helpful measure of the overall immovability or strength of the antibody-antigen complex.

Antibody epitope affinity, the valence of both the antigen and antibody, and the structural arrangement of the interacting parts are the three major factors controls the overall interaction of antigen and antibody. Eventually these influences outline of the specificity of the antibody leading to the binding to a precise antigen epitope. Treatment must be employed to correct the comorbid factors involved in the disease genesis.

Vyakti -Actual manifestation of the disease

Accurate development of the disease along with the appearance of classical signs and symptoms.

Bheda -Chronicity and advancement of the disease

This stage represents the advanced stage of the disease leading to chronicity of the disease along with development of complications. This stage represents the incurability of the disease. In this stage comorbid factors attacks vital organs and deeper tissues and cells leading to development of disability and deformity. Many chronic diseases are not instantaneously lethal but can have a severe influence on patient’s physical ability, emotional state and social activity on a day-to-day basis. Many of the most common chronic diseases like cancer, heart disease, hypertension, stroke and diabetes mellitus are often linked with ageing populations and unhealthy lifestyles. The large number of people living with chronic diseases frequently affects their quality of life.

Vitiated state of Doshas pass through six stages to namely Accumulation → Aggravation → Spread → Abnormal localization and prodromal features → Manifestation of the disease and appearance of clinical symptoms → Complications and produce various disease.

All these below following Flow diagrams & tables

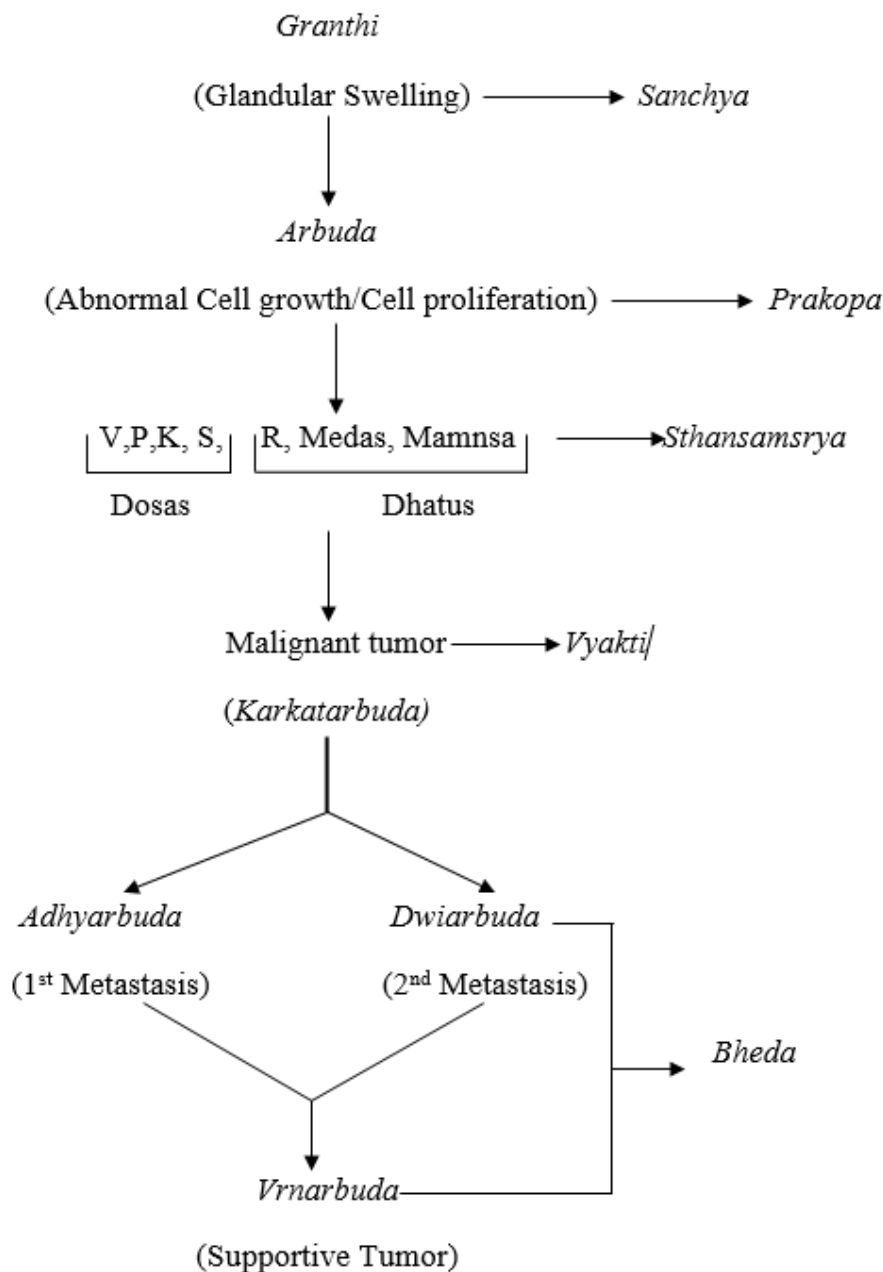


Figure 3: Ayurvedic Concept of Arbuda formation and correlated with Vyadhi Avastha

explained about the correlation between *Shat-srkiyakala* (six stages of *Vyadhi*) and a tumor cell vitiation and aggravation to other places. Figure 1 describes that six stages of any diseases as a divided phases (etiological factors, preclinical and post clinical phases, Table 1 shown as a tumor cell aggravation through the penetrating of own margin and reaches to next stages at the different levels, Figure 2 explained that a normal cell changes to its genetic environment and converts to cancerous due to many etiological factors and Figure 3 mentioned that According to Ayurvedic texts, a lump

forms as a glandular swelling and aggravates into *Arbuda*, malignant tumor (*Karkatarbuda*) and *Asadhya Arbuda*.

Cancer pathogenesis

Cancer is complex, multifaceted phenomenon, characterized by the loss of growth control due to acquired capabilities of autonomy of growth signaling, deteriorations in the cell cycle regulation, insensitivity to growth inhibitory signals, evasion of apoptotic cell death, induction of tumor angiogenesis. The process and pace of cancer relies on collaborations between tumor characteristics and host character-

Table 1: Correlation of Shatkriyakala with cancer cell proliferation/progression

Correlation of <i>Shatkriyakala</i> with cancer cell proliferation /progression	
1. Sanchaya	Initial stages of neoplastic growth due to deranged Doshas
2. Prakopa	Unusual cell proliferation within primary organ site
3. Prasara	Cell migration beyond the margin of primary organ/tissue and tumour reaches distant organ through circulatory(Srotas) pathway
4. Sthanasamshraya	Where localized (Srotodusti) further starts multiplication of cell growth due to a combination of abnormal Doshas and Dushya.
5. Vyakti	Clinical manifestations of signs and symptoms of benign & metastatic tumours
6. Bheda	Advancement of disease, initiation of metastasis, differentiation of tumour growth and development of complications

istics (Joseph, 2002).

Cancer is the result of exogenous or endogenous stimuli interacting with a genetically susceptible host. The communication is affected by a myriad factors related to the stimulus identified with the upgrade and by the same number of variables including the host. There is significant evidence that cancer is a group disease instead of one disease, and that several different procedures can eventuate in cancer (Joseph, 2002).

Carcinogenesis - It is a multistep process, a series of discrete cellular changes and accumulation of multiple genetic alterations progressively resulting in more autonomous cellular processes. Acquired mutation in p53 is the most common genetic alteration found in human cancer (> 50 %) (Harrison et al., 2001).

Almost Medicine has focused on intervention only at the final stage of the long process of carcinogenesis, the invasive or metastatic stage, with arguably less therapeutic success. Hereditary instability is a feature of all cancers. There is general agreement that genetic inability is a necessary and early step facilitating carcinogenesis, rather than epiphenomena of dysregulated and rapid growth. The goal of research in carcinogenesis is the prevention of cancer formation, either by identifying carcinogenic agents so that they might be eliminated from environmental or by identifying the biochemical mechanism of carcinogenesis so that rational measures for prevention may be developed (Souhami et al., 2002). Tumor growth occurs because cell production is greater than cell loss, whereas in normal adult tissues these rates are equal.

The majority of carcinogens are also mutagens, namely they cause genetic mutations. It is generally thought that changes in gene expression in somatic cells, mostly due to mutation, which in the broadest sense includes, such as chromosomal

translocation, are the basis for malignant transformation (Souhami et al., 2002).

Invasion and Metastasis of tumor cells

Most major stages of cancers are Invasion and metastasis. These complex processes include multiple discrete advances which start with local tissue attack. After that As cancer advances and individual cancer cells in the end obtain more malignant phenotypes, under the best possible conditions, they can invade and metastasize to near and distant sites. Then it transported through haematogenous and lymphatic spread too far off destinations inside the body, where they run micrometastases that will eventually grow into macroscopic metastatic lesions (Michael et al., 1995). The growth of new blood or lymphatic vessels from ore-current vessels is important in physiological events as reproduction , development , wound-healing and immunity. However, imbalance or manipulation of these crucial processes is visible in a number of disease states and these manner are frequently concerned in cancer progression and metastasis (Folkman, 2007; Potente et al., 2011).

At the initial stages of metastasis, many possess a tendency to metastasize to particular sites. This so called organ specificity or organ preference of metastasis occurs at early stages of metastatic progression, but at later phases of development where metastasis is across the margin and numerous secondary sites are involved, other organs and tissues are colonized by malignant cells (Michael et al., 1995).

Almost all tumors show infiltration with immune cells on pathological investigation and historically this finding was thought to represent an attempt of the immune system to eradicate the cancer. Therefore, it is now clear that tumor associated inflammatory response promotes tumor formation and cancer progression (Michael et al., 1995).

In the development of human cancer cells proto-oncogene activation might be occur by DNA rearrangement, mutation or chromosome translocation, gene amplification..Amplification play a important role in the later stages of cancer, generally appearing in cells that have metastasized and divided. This is reliable with proof that loss of the tumor suppressor gene p53, also generally a late event in tumor progression, might be lenient for amplification (Souhami et al., 2002).

Ayurvedic concept of Arbuda

Vitiated *Doshas* affects the *Mamsa* and *Rakta dhatus* leading to development of growth which is circular, fixed, slightly painful, big in size, broad based, slowly growing and it does not suppurate (Byadgi, 2018a). Comorbid factors involved in this disease *Vata*, *Pitta*, *Kapha* and *Rakta*, *Mamsa* and *Medas*. Most of the symptoms are similar to *Granthi* (Dwivedi, 2005). *Ayurveda* does not consider cancer as a awesome disorder or set of disease. The importance of infection and scientific presentation of cancer are idea to range , because every person has distinct patterns of exposure to pathogens and has dynamic adjustment in the functioning of *Dhatus* (Alyson et al., 2012).

In Modern science it's a result from sequential Genetics defect, biochemical steps, regulating cell growth and death, additionally abnormalities of epigenetic regulation, diet, environmental factors, life style and immune system considerably have an effect on the phenotype of the most cancer patients.

A better understanding of the molecular pathways and genetic alterations in most of the cancers may result in the improvement of sensitive techniques for early detection of cancer (Venil and Girish, 2012).

The science of *Ayurveda* is supposed to add a step on to the curative aspects of cancers that have resemblance with clinical entities of *Arbuda* (major neoplasm) and *Granthi* (minor neoplasm) mentioned as inflammatory and non-inflammatory swellings in *Susruta Samhita* (Srikantha, 2005a).

When excessive growth at a specific location (*Ek desa vridhi*) and there deficit situated at another site are called (*Anya sthaniya kshaya*). *Ek desa vridhi* represents tumor growth and *Anya sthana kshaya* is denoted by body weight loss (Markam and Nayak, 2018).

Ayurvedic treatment depends on an correct description of the *samprapti*. Pathophysiology of most cancers depends on tridosha theory , sapta dhatu and agni (metabolic strength). Identification of cancer genes has led to a much better information of the tumorigenesis process and has had essential repercussions on all fields.

Multiple tumors

All tumors especially malignant by nature, do not suppurate because exuberance of the *Kapha* and *Medas* as well as in the consequence of stability, condensation and compactness of the deranged *Dosas* and form the lump (Dwivedi, 2005). Even among the curable ones, the following kinds are fit to be rejected, that which is exuding greatly, that situated in the vital spots/organ develops over an earlier one, is known as *Adhyarbuda* by those having the knowledge of *Arbudas* that which is grow either simultaneously or one after another is known as *Dviarbuda*, all these are incurable (Sharma, 2000b).

CONCLUSION

Shatkriyakala helps in the understanding of progress of the disease stage by stage. It helps to understand the various ways involved in the pathogenesis of the disease. It helps to understand the prognosis of the disease based on the progression of the disease. It provides an idea for understanding the cancer pathogenesis in different levels. It is important to lay out the therapeutic procedures based on the understanding of stages as early as possible. Early diagnosis of cancer and better outcomes is possible based on *Shatkriyakala* principles.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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