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REVIEW ARTICLE

*Shilajit*in Cancer Treatment: Probable Mode of Action

Akhilesh Kr Verma*[1], Neeraj Kumar[2], L.N. Gupta[3], Sunil Chaudhary[4]

[1]*Research Scholar, Department of Rasa Shastra, Faculty of Ayurveda, IMS, BHU, India*
[2]*Professor, Department of Rasa Shastra, Faculty of Ayurveda, IMS, BHU, India*
[3]*Assistant Professor, Department of Rasa Shastra, Faculty of Ayurveda, IMS, BHU, India*
[4]*Assistant Professor, Department ofRadiotherapy & Radiation Medicine, IMS, BHU, India*

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ABSTRACT

Cancer is a horrible disease which is leadingcause of death after cardiovascular disease. The principal etiological factor for cancer comprise mutagens, toxins, free radicals, radiations apart from many other causes, inflammation can increase the threat of cancer development and progression. Indian medical system i.e.*Ayurveda* was used as a means for the prevention of the effects of aging and generation of disease. *Shilajit*is a potent rejuvenator and havingadaptogenic action. Since thousands of years many therapeutic assets have been ascribed to it, some pharmacological properties have been verified by modern scientific evaluation. *Shilajit* has been attributed with many miraculous restorative properties,improve the quality of life and it seemed to cure all diseases. *Shilajit* is a brownish-blackcoloredherbo-mineral medicine, collected from the high altitude mountains of many parts of the world. In this review we have focused on the cancer preventive and therapeutic properties of active principles of*Shilajit*. *Shilajit* possess anti-inflammatory, antioxidant, anti-mutagenic, immuno-modulator, antitumor, and photo-protective properties. These assets make *Shilajit* useful agents for cancer therapy and prevention.

Keyword: *Shilajit*, Adaptogenic, Anti-oxidant, Anti-inflammatory.

INTRODUCTION

Cancer is the leading cause of death after the cardiovascular disease and is the major health disaster, causing approximately 7 million deaths every year worldwide. Now a daywe acquire surgical intervention which is not able to cope up effectively with this horrible disorder. The conventional therapies i.e. chemotherapy, radiotherapy, immunotherapy for cancer treatment are not so efficient. Thus, there is a vital obligatory to approaches for the cancer management by natural agent like *shilajit*. *Shilajit* is brownish black herbo-mineral compound mainly composed of humic acid and fulvic acid. Humic andfulvic acid have been well reported to retain cancer preventive properties[1]. These compounds can constrain mutagenesis and having free radicals scavenging, photo-protecting and anti-inflammatory properties that can prevent the cancer progression. *Shilajit* is non-toxic, natural compound which can be taken orally for preserving good health. Therefore, it is necessary that future clinical research work should focus on phyto-constituents and pharmacological action of shilajit in reference of cancer treatment as an alternative. In this review, we address the use of *shilajit* and its components for the inhibition and controlling of cancer[2]. *Shilajit* is considered as a vibrantmedicament in the ancient classics as remedies and presently also extensively used by the *Ayurvedic* physicians for a various disorder.In*Ayurvedic*classical texts like *CharakaSamhita*and *SusrutaSamhita*describe the use of *shilajit* as a treatment for all ailment of our body as well as a *rasayana* (rejuvenative) to increase the endurance[3]. *Shilajit*encompasses a humic substance i.e. fulvic acid (FA) and humic acid (HA) (60-80%), minerals (20-40%) and up to 5% of trace elements (Fe, Ca, Cu, Zn, Mg, Mn, Mo, P)[4,5]. The chief and active constituents responsible for the *shilajit* activities is the fulvic acid and humic acid. By virtue of the FA *shilajit*

***Corresponding Author:**AkhileshVerma, **Email:** akvbhu1980@gmail.com, Phone No: +91-8423524864

has many biological functions and uses [6, 7] which acts as carrier molecule. The low molecular *shilajit*. *shilajit* has been used for the treatment of hypersensitivity, diabetes, digestive disorder, nervous ailment, tuberculosis, chronic bronchitis, asthma, anemia, eczema, bone fractures, genitourinary ailment and many other diseases [8, 9] . The humic compounds of *shilajit* can be a potential cancer preventive agent. Anti-inflammatory, anti- oxidative, anti-mutagenic, immuno-modulatory and several other effects of *shilajit* have been already reported.

Pharmacological Actions of *Shilajit* (Humic&FulvicAcid) in Cancer Prevention:

It is assumed that *shilajit* can play an important role in cancer prevention and possibly in its treatment. The general pharmacological actions of *shilajit* in relation to cancer therapy are summarized below.

Anti-Oxidant Properties:

Free radicals are molecules with incomplete electron shells, which make them more chemically reactive than those of complete electron shells. Exposure to various environmental factors, including tobacco smoke and radiation, can also lead to free radical development. In humans, the most extensive form of free radicals is oxygen. When an oxygen molecule (O_2) becomes electrically charged, it tries to take electrons from other molecules, and thus can cause damage to DNAproteins and cell membrane[10]. Such damage specially damage in DNA could become irreversible and might lead to illness including cancer[11]. Antioxidants are substances that may protect cells from the damage caused by unstable molecules (free radicals) by neutralizing their electrical charge and thus can prevent the free radical damage in cells[11]. Free radicals which are generated during cancer chemotherapy and radiation therapy, can damage the normal cell around the vicinity of the tumor cell, which makes the cancer treatment rather painful. The anti-cancer drugs damages the cellular DNA by producing the reactive oxygen species (ROS) hence the antioxidants can be used with the cancer therapy to reduce the pain and the severity of the side effects [11]. HA compound are brilliant antioxidantsalong with anti-lipid per-oxidative activity [12]. *Shilajit* has free radical scavenging or antioxidant properties against the NO &OH and this antioxidant activity depends on the increasing concentration of the humic compounds present in *shilajit*[01]

weight bioactive organic compound such as oxygenated dibenzo-α-pyrones is also present in

Anti-Inflammatory Properties:

The inflammation is measured to induce the cancer progression, development and the metastasis [10]. It has been shown that the HA matters has anti-inflammatory properties [01]. *Shilajit* has anti-inflammatory properties confirmed in the study of the Goel et al[13]. They have shown that the *shilajit* can reduce the inflammation such as pedal oedema and granuloma pouch in rats induced by the carrageenan. In addition, *shilajit* can also reduce the adjuvant induced arthritis in rats. In another study the humic compounds derived from the coal was found to inhibit the inflammation responded ear swelling in the rats [14]. Lowen et al have described that HA alone or HA combined with other anti-inflammatory drugs such as indomethacin were beneficial for the chronic and acute inflammation in the male SparagueDwleyrats[15]. Van Rensburg et al have shown that the presence of potassium humate reduces the level of pro-inflammatory cytokines like TNF-α, IL-1β, IL-6 and IL-10 produced by mononuclear cells and also the compliment activation[16]. HA can inhibit the degranulation of the neutrophils during inflammation, moreover it is an anti-allergic agent [17,18]. It has been oxifulvic acid may be beneficial in the clinical treatment of inflammatory skin conditions in humans as, FA possesses anti-inflammatory properties [19].

Photo Protective Properties:

The exposure to the radiation as the ultraviolet (UV) rays can leads to the long-term DNA damage by forming the thymine dimer in the DNA which can lead to mutations and cancer. *Shilajit* can function as photo-protective agent, as reviewed by Meena et al 2010[20]. The humic compounds have been proved to be excellent agents for reduction of gene mutation caused by pollutants and mutagens. Toxins, pesticides, radioactive metals, petroleum products, polyaromatic hydro-carbons and heavy metals can be inactivated by HA[21]. Moreover, it reduces bioavailability of the hazardous matters and averts the formation of the mutagenic or carcinogenic compound and prevent DNA damage in the cell[22]. Marova et al have shown that processed HA can inactivate the mutagens which were tested on the yeast[23]. They used 4-nitroquinoline-N-oxide (4-NQO), a mutagen on Saccharomyces cerevisiae D7 to check the anti-mutagenic

properties of the sodium or potassium humate and found that the sodium humate have significant anti-mutagenic property against the 4-NQO. Furthermore, Zhang et al checked the toxicity and the HA [24]. These results illustrated that the HA reduces the bioavailability and toxicity of these two ILs and also HA increases the viability around 50% of HepG2 cell line against the two ILs.It has been shown that HA possesses significant cytotoxic activity in the CEM (acute T lymphoblastic leukaemia) cell line[25]. HA have been found to exert anti-proliferative action and growth inhibition on HL-60 cells through induction of apoptosis by activating the caspase-3 and mitochondrial cytochrome-c in these cells [26]. HA has also been found to induce the apoptosis and inhibit the growth in the human smooth muscle cells. Hseu et al, have reported that HA has been found to inhibit the proliferation of the smooth cells in the G1 phase of the cell cycle and led to the apoptotic cell death of smooth muscles cells [27]. *Shilajit* and HA matters are immune-modulatoryagents[28]. *Shilajit* helps the immune system for increased cytokine production by activated immunological cells and maintains the cell integrity [29]. All biological molecules are prone to oxidative damage by free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS). This oxidative damage leads to various diseaseconditions, viz., heart disease[30],autism[31],cancer[32,33],diabetes [34],Arthritis[35],Alzheimer'sdementia[36],Parkinson 'sdisease[37],cataracts[38],andaging[39]. Antioxidants are the compounds that prevent thisoxidative damage by different mechanisms [40]however synthetic antioxidants possess adverse effects[41].

Immuno-Modulatory Activity:

Shilajit as an immune-modulator agent was studiedin mice that were given either *shilajit* extract or a placebo.The white blood cell activity was studied and monitored at intervals after receiving the *shilajit* extract or a placebo. It was found that the white blood cell activity was increased after administration of*shilajit* extract. The activity increased as the dose of *shilajit* extract and time of exposure was increased [42]. *Shilajit* and its combined constituents elicited and activated to different degrees, murine peritoneal macrophages and activated splenocytes of tumor-bearing animals at early and later stages of tumor growth. In another experiment, the effect of *shilajit* was determined on the levels of brain monoamines in rats. It was found that *shilajit* at a dose of 25 and 50 mg/kg i.p. for 5 days bioavailability of the ionic liquids (ILs), 1-butyl-3-methylimidazolium chloride and 1-octyl-3-methylimidazolium chloride, in the presence of

significantly reduced the level of 5-hydoxy tryptamine and 5-hydroxy indole acetic acid and increased the level of dopamine, noradrenaline and their metabolites in rat brain. These changes in neurotransmitter levels are similar to those seen in cases of increased humoral (immune) activity and hence validate its use as an *Ayurvedicrasayana*. [43].

Ayurvedic View:

The *CarakaSamhita*deliberates*shilajit* in a chapter as rejuvenation therapy (*rasayana*). It has been suggested that the contemporary of*rasayana* is an adaptogenic substance [44].The *CarakaSamhita*states that there is no curable disease in the universe, which is not effectively cured by *shilajit* when it is administered at the appropriate time, combination with suitable drugs and by adopting the prescribed method. When administered to a healthy person, with similar conditions it produces immense energy. In the *SushrutaSamhita*, it is noted that there is no physical distemper, which does not yield by highly therapeuticqualities of *shilajit*. When gradually taken, (in adequate doses) it tends to improve the strength and complexion of the body[45].The ancient *Ayurvedic*text *AstanaHrdayam* also states that it is the best rejuvenator [46].

CONCLUSION

Humic and fulvic acid have been reported to possess cancer preventive properties. It has been shown that these compounds can inhibit mutagenesis and have free radicals scavenging, photo-protecting, anti-inflammatory and toxic compound removing properties that can inhibit the cancer development. *Shilajit* is non-expensive, non-toxic compound which can be taken orally. Therefore, it is rational that future clinical studies should focus on examining the efficacy of *Shilajit*and its active constituents in cancer prevention as an alternative pharmacological agents. In this review, we address the use of *Shilajit* and its constituents for the prevention and management of cancer. *Shilajit* is one such compound, which has been used in *Ayurveda* for centuries. The humic compounds of *Shilajit* can be a potential cancer preventive agent. Anti-inflammatory, anti- oxidative, anti-mutagenic, immuno-modulatory and several other effects of *Shilajit* have been already reported.

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