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Review of Anti-cancer Activity of Metals and Minerals

Nano-technology is an emerging science having a promising role in treating a number of diseases including cancer. *Bhasma* can be comparable to nano-medicine or can be considered as ethno-nanomedicine. *Arbudaharayogas* (anticancer drugs) mentioned in the classical textbook of *Rasayoga Sagur* and research works published in various journals showing the effect of nanoparticles prepared by different method in various types of cancer have been documented in this study. It can be concluded that *Bhasmas* play a strong role in the emerging era of nano-medicine and can be considered as an efficient therapeutic cure in dreadful disease like cancer.

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Review of Anti-cancer Activity of Metals and Minerals

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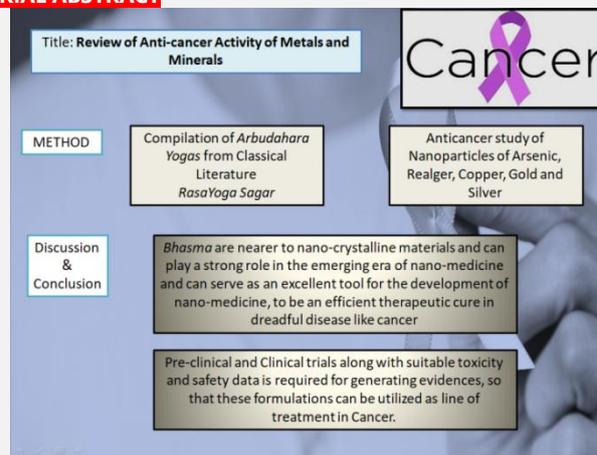
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ABSTRACT

Introduction: Cancer has been considered as the second leading cause of death worldwide. The current interventions employed to combat the disease includes chemotherapy, radiation therapy, surgery and immunotherapy. Though these therapies are considered for treating the dreadful disease, they does not promise perfect cure and also have devastating effect on the quality of life of cancer survivors. Nano-technology is an emerging science having a promising role in treating a number of diseases including cancer. Various works has been done by different scholars in the field of nanotechnology and its role in cancer using varied techniques and procedures. In Ayurveda, the Herbo-metallic or Herbo-mineral compound formulations, *Bhasmas*, can be considered as biologically produced nanoparticles. **Method:** In this present paper a review has been done to collate the evidences related to anti-cancer activity of nanoparticles of various metals and minerals along with it, an effort has been made to recapitulate all the *Arbudaharayogas* (anticancer drugs) mentioned in the Classical textbook of *Rasayoga Sagar*. **Result and Conclusion:** Ayurvedic *Bhasmas* can play a strong role in the emerging era of nano-medicine and can serve as an excellent tool for the development of nano-medicine, to be an efficient therapeutic cure in dreadful disease like cancer. There is a lack of clinical trials and publications by the practising physicians, which is a matter of great concern.

KEYWORDS Nanotechnology, Nanomedicine, Cancer, *Arbudahara Yogas*.

PICTORIAL ABSTRACT



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1. INTRODUCTION

Cancer is a term for a large group of diseases characterised by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs^[1]. Cancer can affect almost any part of the body and has many anatomic and molecular subtypes that require specific management strategies. The most common types of cancer in males are lung, prostate, colorectal and stomach cancer. In females commonly found cancers are breast, colorectal, lung and cervical cancer, whereas in children the incidence of acute lymphoblastic leukemia and brain tumors are more^[1].

The slot of major public health burden in both developed and developing countries has been acquired by Cancer. It is the second leading cause of death globally after the cardiovascular diseases. In 2018, around 18 million people were suffering from cancer accounting for a death of about 9.6 million people worldwide. It is predicted that the number of cancer cases will rise up to 29 million by the year 2040^[2].

In India, the number of people living with cancer is 22 million; with an increase in the number of new cases in both sexes is 1.15 million in all ages having an incidence rate of 89.4 %. The number of cancer related deaths accounts for over 7.8 lakhs nationwide^[3]. The increase in the prevalence of risk factors such as use of tobacco, alcohol, unhealthy diet and physical activity along with rapid growth in population and aging are the contributing factors towards the rise in number of incidences and mortality related to cancer.

Current therapies employed for the treatment of cancer include chemotherapy (cytotoxic anti-neoplastic drugs), radiation therapy (use of ionizing radiation), immunotherapy and surgery. These methods have been accepted and practiced for decades, but they have their drawbacks and side effects. There is a need to search for newer options of cancer therapy.

Ayurveda offers medicines and treatment which can easily be incorporated with the main stream of cancer medicines. Ayurveda opines that there is not a single substance in the

Universe which does not have a potential to be used as a drug, provided it should be used judiciously by the physician where it is required. Immunomodulatory and antioxidant properties of various medicinal plants are responsible for their anticancer activities. Phytochemicals such as vitamins (A, C, E, and K), carotenoids, terpenoids, flavonoids, polyphenols, alkaloids, tannins, saponins, pigments, enzymes and minerals have been found to elicit anticancer activities^[4]. Plants are promising and effective source of anticancer agent and over 60% anticancer agents are derived from natural resources including plants, marine organisms and microorganisms^[5]. An estimate of around 114,000 extracts of plants, marine organism and micro-organisms has been screened successfully by The National Cancer Institute for their anticancer activity^[6]. Natural products or the use of plant-derived products in the treatment of cancer will help in reducing adverse and toxic side effects and also in combating the dreadful disease.

1.1 Cancer in Ayurveda

The earliest description of malignancies was described in *Atharva Veda* (2200 BC) as *Apachi* which in later period, the term *Arbuda* (Cancer) was coined that are described as swellings, which are globular, fixed, large and deeply-seated, slow growing, little painful, non suppurative and appear like a fleshy mass. *Arbudais* classified as *Raktaja*, *Mamsaja*, and *Medoja* (i.e. arising from vitiated *Dhatus* or blood, muscle, or adipose tissues)^[7]. *Arbudais* that arise in specific organs are named accordingly. The diseases and disorders simulating cancer described in Ayurveda are *Arbuda*, *Asadhya Vrana*, *Mamsajaosthroga*, *Alas*, *MamsaKacchapa*, *Galaugha*, *Asadhya Galaganda*, *Tridoshajagulma*, *Asadhya Gulma*, *Asadhya Udaroga*, *Sahaja Arsha*, *Kshataja Kasa*, *Kshayaja Kasa*, *Lingarsha*, *Kshataja Visarpa*, *Tridoshaja Nadivrana*, *Asadhya Pradara* and *Asadhya Kamla*^[8].

Rasashastra is one the most important branch of Ayurveda dealing with the minerals, metals, precious stones, certain poisonous herbs and their processing. The *Rasaushadh* is are very potent in eliminating dreadful diseases and also for rejuvenation purposes. They occupied superior status among the Ayurvedic medicines due to their small dose, quick action, tastelessness, effectiveness on dreadful diseases and long shelf life^[9].

Bhasmas are herbo-mineral-metallic compounds which are of size of nano-dimensions (usually 5 to 50 nm), and having *Rasayana* and *Yogavahi* properties indicating its immune-modulation and target drug delivery characteristics^[10]. Nano-particles are the particles with length that range from 1 to 100nm

in two or three dimensions^[11]. The rapid expansion in nanomaterial research will increase the future prospect of the disease which will prove to be beneficial to mankind.

2. MATERIALS AND METHODS

Classical text *Rasayoga Sagar*^[12] is a compilation of all the formulations containing metals and minerals described in different classics. For present study, it was hand-searched for the herbo-minerals and herbo-metallic preparations indicated specifically in *Arbuda*. Further, the available published literature was also screened for the anti-cancer activities of nano-medicines in the databases like PubMed, Scopus etc.

3. RESULTS

3.1 Arbuda Formulations mentioned in Rasayoga Sagar

On scrutinizing the total number of *yogas* (Table 1), it is noticed that the *rasadravyas* such as *Manhashila* and *Hartala* (arsenicals), *Tamra* (copper), *Swarana* (gold), *Rajata* (silver) are widely used in the therapeutics. Hence an attempt has been made to review and collect the data published on the nano-medicines prepared from these drugs with their significant role in treating cancer.

3.2 Arsenic and its compounds

Arsenicals, a group of minerals, are an integral part of Ayurveda therapeutics comprising *Haratala* (Arsenic trisulphide), *Manahshila* (Arsenic disulphide) and *Somala* (Arsenic trioxide) mentioned with wide range of their uses. *Somal*, *Shankiya*, *Gauripashana*, *Shankhavisha* etc. are its synonyms and it is chemically arsenic trioxide (As_2O_3) or white arsenic. It is to be used in therapeutics after the *shodhana* process (purification procedures) and is said to possess *Rasayana* properties.

In a study, 15 Acute Promyelocytic Leukemia (APL) patients at relapse were evaluated after administering As_2O_3 at a dose of 10mg/d. Fourteen out of 15 patients achieved complete remission with As_2O_3 treatment alone or in combination with low-dose chemotherapeutic drug or all-trans retinoic acid (ATRA)^[13]. The high synergistic effect was found on administrating the combination of arsenic trioxide (As) and IFN (alpha-interferon) in Adult T-cell Leukemia (ATL) derived cell lines and control cell lines, resulting in the inhibition of proliferation and DNA synthesis, modification of the cell cycle phases, and induction of apoptosis^[14]. As_2O_3 inhibited dose-dependent proliferation of myeloid and lymphoid culture cell lines but showed different effects on viability of these cell where it could inhibit leukemia and lymphoma cell proliferation by

induction of cell apoptosis or by cell cycle arrest^[15]. The effects of As₂O₃ on the growth and gene expression of cells in HCE16/3 cell line (HPV16 DNA-immortalized human cervical epithelial cells) model showed selective inhibition of expression of viral oncogene suggesting As₂O₃ an agent for treating HPV-associated

tumours^[16]. On treating the oesophageal carcinoma using human EC8712 cell line, As₂O₃ showed inhibition of growth and survival of tumour cells by induction of apoptosis at a half dose effect (ED₅₀) of concentration 1/microM^[17].

Table 1. Formulations indicated in Arbuda (mentioned in Rasayoga Sagar)

Formulations	Parada (Mercury)	Gandhaka (Sulphur)	Abhraka (Mica)	Swarna Makshika (Chalcopyrite)	Hartala (Orpiment)	Manahshila (Realgar)	Swarna (Gold)	Rajata (Silver)	Loha (Iron)	Tamra (Copper)	Tutha (Blue Vitriol)	Naga (Lead)	Shilajatu (Black Bitumen)	Manāura (Rusted Iron)	Vanga (Tin)	Pittala (Brass)	Kaanshya (Bronze)	Kharpar (Calomel)	Kasis (Green Vitriol)	Nagasindoor (Lead Sulphide)
Amavatari Rasa	+	+	-	-	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	-
Chandra-Prabha Vati(Ii)	-	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-
Dinardha Rasa	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemadri Rasa	+	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Kanakagiri Rasa (Ii)	+	+	+	-	-	-	+	-	+	-	-	+	-	-	-	-	-	-	-	-
Kamakala Vati	-	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-
Laxminarayana Rasa (Iii)	+	+	+	-	-	+	+	+	+	-	-	+	-	-	+	-	-	-	-	-
Lavanga Paka	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-
Manikya Rasayanama (Ii)	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
Mohadrivajra Pata Rasa	+	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-
Nityanada Rasa	+	+	-	-	+	-	-	-	+	+	+	-	-	-	+	-	+	-	-	-
Nripatti Vallabha Rasa	+	+	+	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-
Someshwara Rasa (I)	+	+	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
Talkeshwara Rasa (Xv)	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Traymbak Abhrakam	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tryushnadi Vati	-	-	+	-	+	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-
Yogaottama Vati	-	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-

3.3 Realgar

Manahshila (Realgar, Arsenic disulphide) is one of the three important arsenical compounds used in Ayurveda as a therapeutic agent. Purified Manahshila is used in several formulations of Ayurveda. The important therapeutic areas of Manahshila use include skin diseases, respiratory diseases, certain ailments of eyes and psychological disorders. The transdermal delivery of realgar nanoparticles in mouse melanoma skin cancer models and in mouse melanoma cancer

cell lines (B16) induces apoptosis and prevents tumor growth via transdermal delivery along with suppression of B16 cell proliferation in a dose-dependent manner after exposed to different concentrations of As₄S₄^[18]. Nanorealgar suspension in SiHa cell line showed induction of apoptosis in a dose-dependent manner with significant increase in cytochrome c release and activation of caspase-3 and caspase-9 but not caspase-8^[19]. There is a size dependent cytotoxic effect of realgar particles on the human umbilical vein endothelial cell line (ECV-304) where the

particles of diameters 100 nm and 150 nm were found capable to induce the apoptosis in the endothelial cells^[20]. The anti-tumor effect of realgar on transplanted ovarian SKOV3 carcinoma cells in nude mice showed anti-tumour effect through inducing apoptosis, blocking angiogenesis, inhibiting DNA synthesis and prolonged survival of mice^[21]. The bioleaching solution of realgar by *Acidithiobacillus ferrooxidans* was studied for antitumor experiments in hepatic cancer in HepG2 cells (in vitro) and H22 cells transplanted in mice (in vivo) and it showed higher selective affinity to tumor tissues than arsenic trioxide at an LD50 value (6.63mg/kg)^[22].

3.4 Copper

Tamra (Copper) *Bhasma* one of the metallic preparations in Ayurveda is useful in the treatment of *Udara* (ascitis), *Pandu* (anemia), *Svasa* (bronchial asthma), and *Amlapitta* (hyperacidity), etc^[23]. *Tamra* is attributed with *Ashtamahadoshas* (eight blemishes) hence proper *Shodhana* (purification measures) played key role in preparation of *Tamrabhasma*^[24].

In vitro anticancer efficacy of the bare copper nano-particles (CNP), CuSO₄, and copper-loaded chitosan nanoparticles (CuCNPs) were studied in MG-63 osteosarcoma cancer cells, showed concentration-dependent cytotoxic effect by CuSO₄ and CuCNPs. There was superior anticancer effect of CuCNP due to the generation of higher mitochondrial ROS level compared to control^[25]. Copper oxide nanoparticles synthesised using the extract of *Acalypha indica* were evaluated for its cytotoxic potential against MCF-7 breast cancer cell lines, showed the activity at IC₅₀ value of 56.16 µg/ml with the size of nanoparticles ranged from 26 to 30 nm^[26]. Copper oxide nanoparticles (CuONPs) induce autophagy in human breast cancer cell line (MCF7) in a time and dose-dependent manner, suggesting employing a combination of CuONPs along with the autophagy inhibitor to induce apoptosis in breast cancer cells^[27]. *Ficus religiosa* leaf extract was employed to formulate copper oxide nanoparticles and studied for its anticancer potential in human A549 lung cancer cells showed apoptotic effect by the generation of reactive oxygen species (ROS) involving the disruption of mitochondrial membrane potential in the cells^[28]. CuONPs in the concentration ranging from 2 to 50 µg/ml were found to induce cytotoxicity in human hepatocellular carcinoma HepG2 cells in dose-dependent manner, also suggesting mitochondrial-mediated pathway involved in apoptosis^[29].

3.5 Silver

Rajatabhasma or incinerated silver is widely used in ayurvedicherbo-mineral preparations, used along with different

Anupanas (adjuvant) in several diseases. It stokes agni and improve appetite, it augments longevity and intelligence^[30].

A series of silver (I) complexes were synthesised and studied for its cytotoxic activity against B16 (murine melanoma) and 10T1/2 (murine fibroblasts) cells showed low toxicity to non-cancerous 10T1/2 cells and two of the complexes showed greater cytotoxicity against B16 cells^[31]. The gold (I) imidazolium metal complexes and their silver precursors were evaluated against NCI-H460 lung cancer cells along with cisplatin showed similar anticancer efficacy^[32]. Biogenically synthesised silver nanoparticles using *Sesbania grandiflora* leaf extract studied for its *in vitro* cytotoxic effect against human breast cancer (MCF-7) cells showed an immediate induction of cellular damage in terms of loss of cell membrane integrity, oxidative stress and apoptosis suggesting it as a biogenic anti-cancerous agent^[33]. Silver nanoparticles using the aqueous extract of *Origanum vulgare* (Oregano) were characterized and evaluated against human lung cancer A549 cell line showed direct dose-response relationship and a minimum of 100 g/ml of silver nanoparticles found well enough to induce 50% of cell mortality^[34]. Synthesised AgNPs using culture supernatant of *Bacillus funiculus* were studied against MDA-MB-231 breast cancer cells at various concentrations (5 to 25 µg/mL) for 24 hours showed dose-dependent cytotoxicity by nuclear fragmentation concluding it as a potential alternative agent for human breast cancer therapy^[35].

3.6 Gold

Gold *bhasma* are widely used as therapeutic agent in Ayurvedic formulations. It is beneficial to heart, augments strength, memory, intelligence and complexion, detoxifies the toxic metabolites and said to possess *Rasayana* properties^[36]. There has been an emerging interest in drug discovery strategies where natural products and traditional medicines are re-emerging as attractive option and hence one can see the renewed interests in agents like *Swarnabhasma*^[37]. In modern medicine, gold nanoparticles plays significant role in drug delivery system as they are found to be capable of encapsulating active drugs and targeting. A completely novel technology using colloidal gold nanoparticles has been demonstrated in the field of particle-based tumor-targeted drug delivery^[38]. Methotrexate (MTX), a chemotherapeutic agent, conjugated with gold nanoparticles showed cytotoxic effect on number of tumour cell lines compared to same dose of free MTX, along with suppression of tumour growth mouse ascites model of Lewis lung carcinoma (LL2)^[39]. The AuNPs synthesized from aqueous chlorauric acid solution were assessed for cytotoxicity in MRC-5 human fetal lung fibroblast cell lines, showed oxidative DNA damage along with inhibition of

cellular proliferation^[40]. Ultra small gold nanoparticles (AuNPs) coated with Tiopronin (2 to 15nm), evaluated in monolayer breast cancer cells, a MCF-7 tumor spheroid model, and *in vivo* tumor tissue in mice showed higher levels of accumulation in tumours and high degree of penetration behaviour^[41].

4. DISCUSSION

Bhasmas are the multi-elemental drugs. Bajaj and Vohora (2000) have reported that *Swarnabhasma* consists of 46.9% gold and 0.15ppm mercury. Goel and Sairam (2002) have reported that *Tamrabhasma* contains copper oxide between 44.45 to 66.13%, ferric oxide less than 6.03%, and less than 2.75% sulphur^[42]. XANES- and EXAFS- based analysis of Hg-based Nano-drug *Rasasindura*, carried out in Bhabha Atomic research centre, revealed composition of Single phase α -HgS nanoparticles (size~20 nm), free of HgO or organic molecules, and better controlled structural parameters (size dispersion, coordination configuration^[43]). There are number of analytical modern tools and techniques to study the particle size of engineered metallic nanoparticles using SEM, XRD, TEM, EDAX etc. technologies, which are also adopted to investigate various Ayurvedic *Bhasma*. Analysis of *Swarnamakshika bhasma* using SEM (Scattering Electron Microscopy) shows particles size of 1 to 2 μm ^[44]. Transmission Electron Microscopy(TEM) analysis of nanoparticulate fraction of *Jasada Bhasma* particles shows the appearance of 15–25 nm particles in the sample, and size of the particles present in un-fractionated part of *Yashada Bhasma* was 0.85–1.35 μm with the mean size 1.2 μm in Dynamic Light Scattering (DLS) analysis^[45]. Sieve analysis of *lauhabhasma* indicates that 30 % (by mass) of the particles were smaller than 45 μm with the sub-sieve size distribution ranged between 1.7 and 10.4 μm , whereas in SEM analysis reported irregular shaped aggregates of nano-dimensional particles (~ 28 nm)^[46]. The size of gold crystallites in *Swarnabhasma* using XRD analysis lie in the range 23 to 37 nm with average particle size be 57 nm with globular morphology^[47]. XRD analysis of *Vangabhasma* shows particle size of 12 to 53 nm^[48].

Thus, from the above evidences and studies carried out by the scholars at various platforms, it provides a strong inference that Ayurvedic *Bhasma* are nearer to nano-crystalline materials and can play a strong role in the emerging era of nano-medicine and can serve as an excellent tool for the development of nano-medicine, to be an efficient therapeutic cure in dreadful disease like cancer.

Gold nanoparticles in *Swarna Bhasma* at 27 ± 3 nm size have been found effective in symptoms of arthritis and at 4 nm

size helped in increased apoptosis in B-chronic lymphocytic leukemia^[49]. The size and shape of nanomedicine is directly proportional to their activity in desired field. The number and type of *puta* in traditional incineration process is responsible for the pharmacological activity of the *Bhasma*.

In Ayurveda system of medicine a holistic approach towards ailments is adopted. On reviewing the publications, the methodology adopted by the various Ayurvedic physician in relation to cancer management and scientific studies published in various journals can be enumerated and is as follows.

In 1960, treatment of Hodgkin's Lymphoma patient with bone metastasis were successfully treated with an Ayurvedic preparation called *Valipani* developed by Vaidya Chandra Prakash, which consists processed mercury, sulphur, iron, *harad* (*Terminalia chebula*) along with *bhilava* (*Semecarpus anacardium*), *amla* (*Embllica officinalis*), *ginger* (*Zingiber officinale*) and honey, which was primarily given to the patient to strengthen the bone marrow function^[50].

In 1980s, a new metal based formulation called *Navjeevan* was prepared and it was consisting of processed and detoxified silver, mercury, sulphur and arsenic trioxide in 1:1:1:1 ratio along with some Ayurvedic herbs like *Nirvishi* (*Delphinium denudatum*) and ground with rose (*Rosa rubiginosa*), sandalwood (*Santalum album*), *Gajwan* (*Onosma bracteatum*), and *Latakasturi* (*Hibiscus abelmoschus*) and it was administered along with Ayurvedic medicines *Kamdudha Rasa*, *Kehruba Pishti* and *Leucas aspeca* root and found to be effective in the treatment of myeloma and lymphoma. *Navjeevan* is aimed to restore the homeostasis thus reversing the proliferation of neoplastic cells in bone marrow^[51].

In one of the study which was aimed to detect the effect of *Swarna Bhasma* (SB) on solid malignancies. A total of 43 patients were included in this study received SB (50mg/kg/day), were followed up monthly for 1 year, then 6 monthly for 5 years. Seventeen patients showed response. In the rectal cancer group around 70% (i.e, 7 out of 10 patients) showed best response out of all solid malignancies. There were around nearly 41.02% patients who showed survival for 1 year after treatment, but after 5 years it was reduced to 15.38%^[52].

A novel Herbomineral preparation Las01 containing a number of herbs and different types of inorganic minerals such as mercury which has been extensively purified through 75 steps as per *Kupipakva Rasayana* technique, which was said to be an anticancer drug in the form of *bhasma*. This herbomineral drug was standardized and its anti-cancerous effects were studied in

the human cell lines, the MCF-7 and HeLa cancer cell lines, which was studied further for its acute and sub-chronic toxicity study. Cytotoxic effects were evaluated on cell line using MTT and LDH methods, respectively and it was found that inhibited proliferation of both MCF-7 and HeLa cervical cancer cells was in a dose-dependent manner. It was observed that there was decrease in the viability of cancer cells when the concentration was increased (10 to 500 mg/L). There was no significant change in total WBC count, haemoglobin content, and biochemical parameters in animals treated upto 40-fold doses for a period of 14 days. Subchronic administration of these drugs did not produce any toxic effect. The preparation Las01 was also found to be devoid of toxicity both in animals as well as in human subjects^[53].

On scrutinizing the available literature on Cancer published in various journals and collating the formulations described in classical literature, it can be inferred that Ayurveda can be a promising tool in the management of life-threatening diseases including cancer. Nanoparticles of Arsenicals, Copper, Silver, Gold etc. has been utilized by various scholars for their anticancer activities. Similarly, in *Arbudahara Yogas* (formulations), *Bhasma* of these metal and minerals are mentioned as major or minor ingredients. These formulations are compiled and tabulated, which can provide a strong database for further researches in the area of cancer management. However, Proper Pre-clinical and Clinical trials along with suitable toxicity and safety data is required for generating evidences, so that these formulations can be utilized as line of treatment in Cancer.

CONCLUSION

In the past, metal-based compounds were widely used in the treatment of disease conditions, but the lack of clear distinction between the therapeutic and toxic doses was a major challenge. In recent times, there has been an upsurge of activities relying on the structural information, aimed at improving and developing other forms of metal-based compounds. However, the classical Ayurvedic *Bhasmas*, has distinct mechanism of action from conventional anti-cancer agents. In line with this, many more metal-based compounds can be utilized or building the entire new compound with enhanced safety and cytotoxic profile. on Thus, from the above evidences and studies carried out by the scholars at various platforms, it provides a strong inference that Ayurvedic *Bhasma* are nearer to nano-crystalline materials and can play a strong role in the emerging era of nano-medicine and can serve as an excellent tool for the development of nano-medicine, to be an efficient therapeutic cure in dreadful disease like cancer. However, because of increased emphasis on the clinical relevance of metal-based complexes, a few of these drugs

are currently on clinical trial and many more are awaiting ethical approval to join the trial. Lack of publication among practicing physicians is also a matter of great concern.

CONFLICT OF INTEREST The authors declare no conflict of interest.

CONTRIBUTORS Dr. Anu contributed to literature review and draft preparation. Dr. Pramod, Dr. Galib and Dr. Prajapati contributed to the conceptualization of topic, analysis and finalisation of the draft.

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