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ONCOLOGICAL MANIFESTATIONS OF VISHA (POISON): BRIDGING AYURVEDIC TOXICOLOGY WITH MODERN CANCER BIOLOGY

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ABSTRACT

Background: Cancer is a multifactorial disease influenced by environmental, chemical, biological and psychological factors. While modern oncology recognizes chronic exposure to carcinogens as a major contributor to tumor development, Ayurveda describes a comparable concept through *Dushi Visha*, a latent form of cumulative toxicity that gradually impairs physiological functions and predisposes the body to chronic diseases. **Objective**: This review aims to correlate the Ayurvedic concept of '*Visha*', particularly '*Dushi Visha*' with contemporary cancer biology by examining the role of environmental toxins, heavy metals, toxic phytochemicals, psychological stress and animal venoms in carcinogenesis and cancer therapy. **Methods**: A comprehensive narrative review was conducted by critically analyzing published scientific literature on environmental carcinogens, heavy metals, venom-derived bioactive compounds, toxic phytochemicals, psychological stress and chemotherapy-associated toxicities.

Ayurvedic concepts of *Visha* were integrated with current molecular oncology findings to identify conceptual and mechanistic correlations. **Results**: Chronic exposure to environmental pollutants, heavy metals, industrial chemicals, toxic phytochemicals and persistent psychological stress promotes carcinogenesis through oxidative stress, DNA damage, epigenetic alterations, chronic inflammation, angiogenesis, immune dysregulation and genomic instability. These mechanisms closely parallel the Ayurvedic pathogenesis of '*Dushi Visha*', characterized by *Agnimandya*, *Dhatu Dushti*, *Oja Kshaya* and progressive disease development. Conversely, certain biological poisons, including snake, bee and scorpion venoms, contain highly selective peptides with promising anticancer activities by inducing apoptosis, inhibiting angiogenesis and suppressing tumor invasion and metastasis. **Conclusion**: The Ayurvedic concept of '*Dushi Visha*' provides a valuable theoretical framework for understanding chronic toxic exposure and its contribution to cancer development. Integrating Ayurvedic toxicology with modern molecular oncology may offer novel insights into cancer prevention, early diagnosis and the development of innovative therapeutic strategies. Further multidisciplinary research is required to validate these conceptual correlations and facilitate their clinical translation.

1. INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide. Despite remarkable advances in molecular oncology, immunotherapy and targeted therapies, the global burden of cancer continues to rise. Environmental exposure, occupational hazards, dietary toxins and chronic inflammatory conditions are now recognized as major contributors to cancer development. Environmental pollutants such as asbestos, benzene, arsenic, dioxins and airborne particulate matter are established human carcinogens and contribute significantly to cancer incidence.

The review on environmental pollution emphasizes that pollutants originate from industrial emissions, vehicle exhaust, tobacco smoke, agricultural chemicals, indoor combustion and contaminated food and water. Long-term exposure to these toxic agents has been associated with lung, bladder, liver, colorectal, breast and hematological malignancies through mechanisms including oxidative stress, DNA methylation and chronic inflammation.

Ayurveda recognized the harmful effects of toxic substances thousands of years ago under the concept of *Visha*.[1] Classical Ayurvedic texts Acharya Vagbhata says about two types of visha, krithrima (garavisha) and akrithrima (sthavara and jangama).[2] *Dushi Visha*, a unique

concept describing latent, cumulative toxicity that remains in the body for prolonged periods.[3] Unlike acute poisoning, *Dushi Visha* gradually impairs *Agni*, contaminates *Dhatus*, diminishes *Ojas* and predisposes tissues to chronic diseases.

Interestingly, this concept closely resembles chronic low-dose toxic exposure recognized in modern toxicology. Persistent exposure to environmental pollutants, heavy metals, pesticides, industrial chemicals and psychological stress results in continuous oxidative injury, immune dysfunction and genomic instability, thereby increasing the risk of malignant transformation. These similarities suggest that *Dushi Visha* may represent an ancient description of cumulative toxic burden and chronic disease pathogenesis.

Recent scientific investigations have further expanded this concept by demonstrating that not all poisons exert harmful effects. Animal venoms contain highly selective peptides capable of targeting cancer hallmarks such as uncontrolled proliferation, angiogenesis, invasion, metastasis and resistance to apoptosis. Several venom-derived compounds have therefore emerged as promising leads for anticancer drug discovery.

Similarly, medicinal plants have long been regarded as valuable sources of anticancer agents. However, scientific evidence also indicates that certain naturally occurring phytochemicals possess carcinogenic or tumor-promoting properties, emphasizing that natural origin alone does not guarantee safety.

Psychological stress represents another important but often overlooked form of toxic exposure. Chronic activation of neuroendocrine pathways stimulates β-adrenergic signaling, enhances inflammatory mediators, promotes angiogenesis, suppresses immune surveillance and facilitates tumor progression and metastasis.

Therefore, poison should not be viewed merely as an acute lethal agent but rather as a broad spectrum of biological, chemical, environmental, and psychological factors capable of initiating or promoting carcinogenesis. An integrated understanding of these diverse toxic influences is essential for advancing both preventive oncology and personalized medicine.

2. AIM AND OBJECTIVES

The present review aims to

1. Describe the Ayurvedic concept of *Visha* in relation to cancer biology.

2. Summarize current evidence regarding environmental, chemical, biological and psychological poisons involved in carcinogenesis.
3. Explain the molecular mechanisms responsible for poison-induced oncogenesis.
4. Highlight the therapeutic potential of venom-derived anticancer compounds.
5. Correlate the Ayurvedic concept of *Dushi Visha* with modern molecular oncology.

3. METHODOLOGY

This review was prepared by critically analyzing classical Ayurvedic literature along with published review articles and contemporary scientific literature focusing on the relationship between various forms of poisons and cancer development. Classical Ayurvedic texts, including the *Charaka Samhita*, *Sushruta Samhita and Ashtanga Hridaya* literature, were reviewed to understand the concepts of *Visha*, particularly *Dushi Visha* and their pathological implications. Modern literature included studies on environmental carcinogens, animal venoms, toxic phytochemicals, psychological stress, natural anticancer products and chemotherapy-associated toxicities. The collected evidence was synthesized to correlate the Ayurvedic concepts of *Visha*, especially *Dushi Visha*, with contemporary molecular oncology and the mechanisms of carcinogenesis.

Ayurvedic Concept of *Visha* and Cancer

Ayurveda considers *Visha* as a substance capable of disturbing normal physiological functions and ultimately destroying life if not neutralized. Depending upon its origin, *Visha* is classified into four major categories.

Table 1: Classification of *Visha* and Possible Oncological Correlation.

Ayurvedic Classification	Source	Modern Correlation
Sthavara Visha	Plant & mineral poisons	Heavy metals, toxic phytochemicals, mycotoxins
Jangama Visha	Animal poisons	Snake venom, bee venom, scorpion venom
Gara Visha	Artificial mixtures	Industrial chemicals, pesticides, food contaminants
Dushi Visha	Chronic latent poison	Chronic toxin exposure, persistent inflammation, carcinogenesis

Among these, *Dushi Visha* is particularly important in relation to oncology. Classical Ayurvedic literature describes *Dushi Visha* as a poison that remains dormant within the body for prolonged periods. It gradually contaminates the *Dhatus*, weakens *Agni*, reduces *Ojas*, and produces chronic diseases.

Modern toxicology recognizes an almost identical phenomenon where repeated low-dose exposure to environmental toxins gradually causes oxidative stress, DNA damage, immune suppression and chronic inflammation that finally culminate in malignancy.

Thus, *Dushi Visha* may be interpreted as the Ayurvedic counterpart of chronic cumulative toxic exposure.

Environmental Poisons as Carcinogens[4]

Environmental pollution has emerged as one of the most significant causes of preventable cancers worldwide. Pollutants originate from industries, automobiles, tobacco smoke, agricultural activities, contaminated food, polluted water, indoor combustion and occupational exposure.

The review article on environmental pollution reports that several environmental chemicals have already been classified as human carcinogens, including:

- Asbestos
- Benzene
- Arsenic
- Inorganic arsenic compounds
- Dioxins
- Exhaust gases
- Polycyclic aromatic hydrocarbons (PAHs)
- Airborne particulate matter

These pollutants contaminate air, water, soil and food chains, resulting in prolonged human exposure.

Table 2: Important Environmental Poisons and Associated Cancers.

Poison	Major Source	Associated Cancer
Asbestos	Construction materials	Mesothelioma, Lung cancer
Benzene	Petroleum industry	Leukemia
Arsenic	Drinking water	Skin, Lung, Bladder cancer
Dioxins	Industrial waste	Soft tissue sarcoma, Lymphoma
PAHs	Tobacco smoke, combustion	Lung cancer
Air pollution	Vehicle exhaust	Lung, Bladder cancer

Long-term exposure to these agents induces oxidative stress, chronic inflammation, DNA methylation, chromosomal instability and impaired DNA repair mechanisms, thereby promoting malignant transformation.

Heavy Metals and Carcinogenesis[5,6]

Heavy metals represent one of the most important categories of chronic poisons implicated in cancer development.

A. Arsenic

Arsenic contamination of drinking water affects millions of individuals worldwide. Chronic exposure has been associated with:Skin cancer, Lung cancer, Bladder cancer and Liver cancer. Mechanistically, arsenic induces:

- Reactive oxygen species (ROS)
- DNA strand breaks
- DNA methylation abnormalities
- Impaired DNA repair
- Chronic inflammation

These events progressively increase genomic instability and tumor formation.

B. Cadmium

Cadmium is widely used in batteries, pigments, electroplating, and fertilizers. Long-term exposure has been associated with: Breast cancer, Prostate cancer and Lung cancer.

Cadmium promotes carcinogenesis by:

- Estrogen receptor activation
- Oxidative stress
- Mitochondrial dysfunction
- Apoptosis resistance

C. Chromium (Hexavalent)

Occupational exposure occurs in: Leather industries, Welding and Electroplating. Associated cancers include: Lung carcinoma and Nasal carcinoma.

Mechanism:

- ROS generation
- DNA cross-linking
- Gene mutations

D. Nickel

Nickel compounds are classified as human carcinogens. Associated cancers: Lung cancer and Nasal carcinoma.

Mechanism:

- Epigenetic modification
- Histone alteration
- Hypoxia signaling activation

E. Lead

Although weaker than arsenic, chronic lead exposure has been associated with:

- Kidney tumors
- Brain tumors
- Hematological malignancies

Table 3: Molecular Mechanisms of Heavy Metal-Induced Carcinogenesis.

Heavy Metal	Major Molecular Target	Outcome
Arsenic	ROS, DNA methylation	Skin, Lung, Bladder cancer
Cadmium	Estrogen receptor, ROS	Breast, Prostate cancer
Chromium VI	DNA damage	Lung carcinoma
Nickel	Epigenetic alterations	Lung carcinoma
Lead	Oxidative stress	Renal malignancy

Heavy metal toxicity closely resembles the Ayurvedic description of *Dushi Visha*, where repeated exposure to low doses of poison gradually accumulates in tissues. This cumulative toxicity results in:

- *Agnimandya*
- *Dhatu Dushti*
- *Rakta Dushti*
- *Oja Kshaya*
- *Granthi* formation
- *Arbuda* (tumor)

Thus, the molecular events recognized in modern oncology—oxidative stress, DNA injury, chronic inflammation, and immune dysfunction—can be conceptually correlated with the Ayurvedic pathogenesis of *Dushi Visha*.

Psychological Stress as a Biological Visha

Ayurveda describes prolonged emotional disturbances such as *Chinta* (anxiety), *Shoka* (grief), *Bhaya* (fear) and *Krodha* (anger) as factors capable of disturbing *Dosha* equilibrium, weakening *Agni*, impairing *Ojas* and predisposing the body to chronic diseases.[7] Although classical Ayurvedic texts do not explicitly classify psychological stress as *Visha*, its cumulative harmful effects closely resemble the concept of *Dushi Visha*, where persistent noxious influences gradually impair physiological functions.

Modern oncology also recognizes chronic psychological stress as an important modifier of cancer biology. According to the uploaded review, sustained activation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS) increases the secretion of cortisol, norepinephrine and epinephrine. These stress mediators activate β-adrenergic signaling pathways that promote tumor cell proliferation, angiogenesis, epithelial–mesenchymal transition (EMT), immune suppression and metastasis. Chronic stress has also been associated with DNA damage, degradation of tumor suppressor p53 and activation of oncogenic pathways including STAT-3, CREB.[8]

Table 4: Biological Effects of Chronic Stress in Cancer.

Stress Mediator	Major Molecular Target	Oncological Effect
Cortisol	Immune suppression	Reduced antitumor immunity
Norepinephrine	β-adrenergic receptors	Tumor proliferation
Epinephrine	PKA–CREB pathway	Angiogenesis and metastasis
Chronic inflammation	NF-κB activation	Tumor progression
Persistent stress	DNA damage and p53 dysregulation	Genomic instability

From an Ayurvedic perspective, these chronic neuroendocrine alterations may be interpreted as a biological form of *Dushi Visha*, producing gradual *Dhatu Dushti* and increasing susceptibility to *Arbuda*.

Toxic Phytochemicals and Carcinogenesis[9,10,11]

Medicinal plants are invaluable therapeutic resources; however, the uploaded review emphasizes that not every natural phytochemical is inherently safe. Several naturally occurring compounds have been identified as potential carcinogens or tumor promoters when consumed under specific conditions or in excessive amounts.

Examples discussed in the review include

- *Capsaicin (controversial role; both chemopreventive and tumor-promoting evidence)*

- *Aristolochic acids*
- *Pyrrolizidine alkaloids*
- *Safrole*
- *Certain phytoestrogens*
- *Bracken* fern constituents

These compounds may induce DNA adduct formation, oxidative stress, chronic inflammation, or mutagenesis, thereby contributing to carcinogenesis. The review also cautions that many herbal supplements are used without adequate toxicological evaluation and should not automatically be considered safe simply because of their natural origin.

Table 5: Toxic Phytochemicals Associated with Cancer Risk.

Phytochemical	Major Source	Proposed Effect
Aristolochic acid	Aristolochia species	DNA adduct formation, urothelial cancer
Pyrrolizidine alkaloids	Several medicinal herbs	Hepatotoxicity, carcinogenesis
Safrole	Sassafras oil	Liver carcinogenesis

Animal Venoms: From Poison to Precision Oncology

One of the most fascinating aspects of modern toxicology is the transformation of venom-derived toxins into potential anticancer therapeutics. The uploaded review explains that animal venoms contain highly selective peptides capable of interfering with several hallmarks of cancer, including proliferation, angiogenesis, invasion, migration and resistance to apoptosis.

Snake Venom

Snake venom contains biologically active molecules such as:

- Disintegrins[12]
- Phospholipase A_2 (PLA_2)[13]
- L-amino acid oxidase[14]
- Metalloproteinases[15]
- Cytotoxins[16]

These molecules inhibit tumor cell adhesion, suppress angiogenesis, induce apoptosis and reduce metastatic potential. For example, disintegrins interfere with integrin-mediated cell adhesion, while certain venom proteins inhibit vascular endothelial growth factor (VEGF)-mediated neovascularization.

Bee Venom[17]

Bee venom contains **melittin**, which has demonstrated anticancer activity by:

- Inducing mitochondrial apoptosis
- Inhibiting inflammatory MAPK signaling
- Suppressing VEGF-mediated angiogenesis

Melittin has shown activity against gastric, lung, and osteosarcoma cell lines in experimental studies.

Scorpion Venom[18]

Scorpion venom contains **chlorotoxin**, a peptide that selectively binds tumor-associated molecules such as matrix metalloproteinase-2 (MMP-2). This reduces tumor cell migration and invasion and has been investigated particularly in brain and pancreatic cancers.

Table 6: Venom-Derived Anticancer Compounds.

Venom Source	Bioactive Component	Principal Anticancer Action
Snake	Disintegrins	Inhibition of cell adhesion and angiogenesis
Snake	L-amino acid oxidase	Apoptosis induction
Bee	Melittin	Mitochondrial apoptosis, anti-inflammatory activity
Scorpion	Chlorotoxin	Reduced migration and invasion
Wasp	Polybia-MPI	Selective membrane disruption in tumor cells

Molecular Mechanisms of Poison-Induced Carcinogenesis

Despite the diversity of toxic agents, several common molecular pathways are consistently implicated in cancer development.

Oxidative Stress

Many environmental toxins and heavy metals increase intracellular reactive oxygen species (ROS), resulting in lipid peroxidation, protein oxidation, mitochondrial dysfunction and DNA damage.

DNA Damage and Genomic Instability

Persistent toxic exposure promotes:

- DNA strand breaks
- Chromosomal instability

- DNA methylation abnormalities
- Defective DNA repair

These changes facilitate oncogenic mutations and malignant transformation.

Chronic Inflammation

Environmental pollutants and chronic stress activate inflammatory signaling pathways, particularly NF-κB, leading to sustained cytokine production and tumor-promoting inflammation.

Angiogenesis

Tumor growth requires neovascularization. Several carcinogenic processes stimulate VEGF, enabling tumors to establish an adequate blood supply.

Epithelial–Mesenchymal Transition (EMT)

Stress hormones and inflammatory mediators promote EMT, allowing cancer cells to acquire invasive and metastatic properties.

Table 7: Major Molecular Events in Poison-Induced Cancer.

Molecular Event	Biological Consequence
ROS generation	Oxidative damage
DNA mutation	Oncogene activation
p53 dysfunction	Loss of tumor suppression
NF-κB activation	Chronic inflammation
VEGF overexpression	Angiogenesis
EMT activation	Metastasis
Immune suppression	Tumor immune escape

Ayurvedic Management of Dushi Visha[19]

Ayurveda advocates a systematic approach for the management of *Dushi Visha* aimed at eliminating accumulated toxins, restoring physiological homeostasis, and preventing chronic tissue damage. According to the classical texts, patients suffering from *Dushi Visha* should initially undergo Swedana (sudation therapy), followed by Vamana or Virechana Karma, depending upon the predominance of the involved Doshas, to achieve Kaya Shodhana (systemic purification). After successful purification, Agadapana (administration of anti-toxic formulations) is recommended, particularly Dushi Vishari Agada, to neutralize the residual toxic effects and restore normal body functions.

The classical formulation Dushi Vishari Agada consists of Pippali (*Piper longum*), Dhyamaka (*Cymbopogon martinii*), Jatamamsi (*Nardostachys jatamansi*), Lodhra (*Symplocos racemosa*), Ela (*Elettaria cardamomum*), Suvarchika (*Tribulus terrestris*), Kutannata (*Oroxylum indicum*), Natam (*Valeriana wallichii*), Kustha (*Saussurea lappa*), Yashtimadhu (*Glycyrrhiza glabra*), Chandana (*Santalum album*), and Gairika (Red ochre). These ingredients are traditionally described to possess Vishaghna (anti-toxic), Shothahara (anti-inflammatory), Rasayana (rejuvenative), and antioxidant properties.

From an oncological perspective, the Ayurvedic management of *Dushi Visha* may help reduce the cumulative toxic burden, chronic inflammation, oxidative stress, and immune dysregulation that are conceptually linked to carcinogenesis. Therefore, appropriate management of *Dushi Visha* has the potential to alleviate the oncological manifestations associated with chronic toxic exposure and may serve as a supportive strategy in integrative oncology. However, these correlations remain conceptual and require further experimental and clinical validation before definitive therapeutic conclusions can be drawn.

DISCUSSION

Cancer is no longer considered merely a genetic disease but a multifactorial disorder resulting from complex interactions among environmental exposures, genetic susceptibility, chronic inflammation, immune dysregulation, and metabolic disturbances. The uploaded review articles consistently indicate that prolonged exposure to environmental pollutants, heavy metals, toxic phytochemicals, psychological stress and industrial chemicals contributes significantly to cancer initiation and progression through oxidative stress, DNA damage, chronic inflammation, angiogenesis and immune suppression.

These observations remarkably parallel the Ayurvedic concept of *Dushi Visha*, which describes a weak but persistent poison that remains dormant within the body and gradually produces disease by contaminating the *Dhatus*. Unlike acute poisoning, *Dushi Visha* manifests slowly, often after repeated exposure to incompatible diet, contaminated food, environmental toxins, or poisonous substances. Classical Ayurvedic texts describe its progression through *Agnimandya*, *Dhatu Dushti*, *Oja Kshaya*, and finally chronic systemic disorders. This conceptual framework aligns closely with the modern understanding of chronic toxic exposure leading to carcinogenesis.

The uploaded review on environmental pollution identifies asbestos, benzene, arsenic, dioxins and airborne pollutants as major environmental carcinogens. These toxic agents induce oxidative stress, DNA methylation abnormalities, and chronic inflammatory responses that eventually culminate in malignant transformation. Such chronic, cumulative exposure is conceptually similar to the Ayurvedic description of latent poison.

Interestingly, the uploaded review on psychological stress demonstrates that prolonged activation of the HPA axis and sympathetic nervous system increases catecholamine release, stimulates β-adrenergic signaling, suppresses antitumor immunity, and promotes metastasis. Although psychological stress is not described as a classical poison in Ayurveda, its long-term detrimental effects resemble the cumulative pathological impact of *Dushi Visha*.

Another important observation emerging from the reviewed literature is the dual nature of poison. While many toxins initiate cancer, certain biological poisons—particularly snake, bee and scorpion venoms—contain highly selective peptides capable of targeting tumor hallmarks. Venom-derived molecules inhibit angiogenesis, induce apoptosis, suppress invasion and interfere with tumor cell adhesion, illustrating that poisonous substances can also serve as valuable therapeutic agents. This scientific evidence strongly resonates with the Ayurvedic principle of '*Viṣasya Viṣamauṣadham*' (poison itself can become medicine when properly processed and administered).

Furthermore, the uploaded review on toxic phytochemicals reminds us that natural origin does not necessarily imply safety. Certain herbal constituents, including aristolochic acids and pyrrolizidine alkaloids, possess carcinogenic potential and therefore require scientific evaluation before therapeutic use. This reinforces the Ayurvedic emphasis on proper purification (Shodhana), dose regulation and rational use of toxic substances.

Future Perspectives

The integration of Ayurvedic toxicology with molecular oncology offers several promising research opportunities:

- Molecular characterization of *Dushi Visha* using biomarkers of oxidative stress and chronic inflammation.
- Experimental evaluation of Ayurvedic detoxification (*Shodhana*) procedures for reducing toxic burden.

- Development of venom-derived peptide therapeutics targeting specific hallmarks of cancer.
- Investigation of Ayurvedic *Rasayana* formulations as adjuncts to reduce treatment-related toxicities.
- Systems biology approaches integrating Ayurvedic concepts with genomics, metabolomics and immunology.

CONCLUSION

The available evidence demonstrates that chronic exposure to environmental pollutants, heavy metals, toxic phytochemicals, industrial chemicals, and prolonged psychological stress contributes significantly to carcinogenesis through oxidative stress, DNA damage, chronic inflammation, angiogenesis, immune dysregulation and genomic instability. Simultaneously, certain biological poisons such as animal venoms possess remarkable anticancer potential by selectively targeting cancer cell proliferation, invasion and angiogenesis.

The Ayurvedic concept of *Dushi Visha* provides a unique theoretical framework for understanding cumulative toxic exposure and its long-term pathological consequences. Although direct equivalence between Ayurvedic concepts and modern molecular mechanisms cannot yet be established, striking conceptual similarities exist regarding chronic toxicity, tissue degeneration, immune dysfunction and tumor development.

Bridging Ayurvedic toxicology with contemporary cancer biology may provide new insights into cancer prevention, early diagnosis and the development of innovative therapeutic strategies. Further multidisciplinary research integrating traditional knowledge with molecular oncology is warranted to validate these correlations and explore their clinical significance.

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