



Review Article

ISSN: 2454-5023
J. Ayu. Herb. Med.
2023; 9(3): 128-132
Received: 02-07-2023
Accepted: 04-09-2023
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www.ayurvedjournal.com
DOI: 10.31254/jahm.2023.9306

Understanding Mycotoxins from Ayurvedic Perspectives: A Trans-disciplinary approach

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ABSTRACT

Knowledge of the source/origin of a toxin, its development and toxicity manifestation as well as appropriate remedial measures is an integral part of any health system. Mycotoxins are chemical toxins produced by fungi with diverse toxic effects depending on their chemical structure. Modern science recognizes mycotoxins as food contaminants and recommends regulatory limits (max permissible limit), due to the impossibility in avoiding the mycotoxin occurrence completely and for the complications in treating the resulting toxicities. This brings traditional systems of medicine such as ayurveda into the limelight to address the global mycotoxin problem. In this regard, there is paucity of literature available describing the mycotoxins from ayurvedic perspectives. Thus, the current article is focused on the transdisciplinary understand of the mycotoxins and its toxic effects, especially comparing modern medicine with ayurveda. While, modern medicine considers mycotoxins as chemical toxins with molecular mechanism involving receptor or chemical binding, ayurveda considers a holistic approach. In addition to considering its effects on cellular level, ayurveda aligns to recognize the toxin for its effects on the system at tissue and organism level, holistically. From this perspective, ayurveda classifies mycotoxins as both incompatible food (virudha ahara) and visha (toxin). To understand the pathogenesis, ayurveda analyses the systemic effects in terms of effect on "the basic body composition - doshas (humors) and dhaatus (tissues) and the impact on toxin/metabolic waste elimination". Finally, after considering the overall effect ayurveda arrives at the treatment to provide both symptomatic treatment and reinstate the doshas/dhaatus to restore the health status, holistically.

Keywords: Ayurveda, Chemical toxins, Mycotoxins.

INTRODUCTION

Mycotoxins are commonly found as contaminants of human food and animal feed with global public health concern (1), attributed for several food poisoning outbreaks involving deaths in both humans and animals until recent decades (citing human deaths in Kenya, death of dogs in USA, ruminant deaths in Europe) (2–4). These mycotoxins are secondary fungal metabolites, being increasingly identified as responsible for several health issues in humans and animals from cancer, kidney failure to critical subclinical manifestation with serious deleterious effects like immune suppression, stunted growth, etc (5,6). Rapid population explosion that increased the pressure on global food production system over recent decades has also been accompanied with increased contamination of food/feed with mycotoxins (7). High moisture/ humidity with adequate temperature, and availability of oxygen under improper storage conditions are responsible for the accumulation of mycotoxins in food from farm to fork (1). To-make-things-worse, the amount of mycotoxins in food commodities is expected to increase significantly in the near future resulting from climate change (8). The management of mycotoxin contamination and their toxicity is going through a critical phase, due to rapid increase in number of mycotoxins of public health concern totalling atleast 400 to date (9). The unavailability of ideal/suitable preventive measures and treatment options of mycotoxin contamination and their toxic effects in conventional medical practices is further complicated by the diversity of mycotoxins (production, chemical and toxic-effect) (10) with serious adverse impact on the environment, animal and human health. But the conventional modern medicine approach to mitigating the adverse effect of mycotoxin has been mostly limited to setting up of maximum permissible limits (MPL) (11). But these regulations have failed to prevent the occurrence of mycotoxins in feed, as Food Administration Organization (FAO) a leading international food safety/security body, itself recognizes that mycotoxin occurrence in food is unavoidable and unpredictable (12). Further, to-date, no specific therapies for mycotoxins are available in modern medicine, thus increasing the necessity to identify and/or employ natural, alternative and/or complimentary approaches such as ayurveda to address the global mycotoxin problem. However, to date, no specific literature is available that describes the mycotoxins from ayurvedic perspectives. The current article is an effort to understand the mycotoxins through ayurvedic principles. It explains the different categories through which mycotoxins could be classified and further describes the mechanism for their toxicities.

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Finally the article covers the ayurvedic treatment measure for mycotoxin.

SCOPE OF THIS ARTICLE: WHY A LINEAR COMPARISON OF MYCOTOXINS BETWEEN AYURVEDA AND MODERN MEDICINE IS NOT FEASIBLE?

The primary aim of this article is to focus on the ayurvedic understanding of mycotoxins and not to elaborate the concept of toxicology as per ayurveda. Firstly, the article defines mycotoxins through the concept of agada tantra (toxicology in ayurveda), yet the article is not intended to provide a deeper perspective of agada tantra beyond mycotoxins. The article explains mycotoxins employing all the different ayurvedic perspectives of toxins such as viruddha ahara, aama, visha (toxin) and agada tantra. However, mycotoxins are a diverse group of chemicals with equally varied physiological mechanism of toxicity. The same diversity in mycotoxins makes it not feasible to deliver a linear comparison of mycotoxins between ayurvedic perspectives and modern medicine. There are over 400 mycotoxins currently identified that have a diverse chemical structure. They are classified into a single/common category called mycotoxins only because of their common origin (being produced by fungi - that are over 1,40,000 species currently identified). However based on their chemical structure the effects of mycotoxins on animal/human physiology are elaborately diverse, ranging from effects on reproductive system - estrus cycle defects (ZEA) to liver - hepatotoxicity (AFB1) to kidneys - nephrotoxicity (OTA), etc. This makes it difficult to provide a generalised comparison of the symptoms of mycotoxicosis and some of the visha symptoms (visha lakshanas) in ayurveda. On a biological comparison, this is similar to the poisoning by snake venom, though all snake venom are produced by snakes, the symptoms varies based on the type of the snake such as neurotoxic effects of cobra venom is different from the hemotoxic effects of viper venom. Whereas in pharmacological comparison, taking example of rat-kill agents, though many compounds are classified as rat-kill agents based on commercial usage, but their mechanism of action are different. For example, both warfarin and aldicarb are used as rat-kill, but warfarin is an anti-coagulant and aldicarb is acetyl-choline-esterase-inhibitor and so their symptoms of poisoning as well as treatment are completely different. So they are not pharmacologically classified in same group. Similarly the symptoms of mycotoxicosis and their ayurvedic treatment vary for each mycotoxin. Thus, providing a general comparison of mycotoxin-toxicity symptoms as well as their treatment (visha-chikitsa) to some poison in ayurveda is not the scope of this article. The main focus of this article is thus to identify the mechanistic links in the understanding of mycotoxins and their pathogenic/toxicogenic mechanism from the perspectives as ayurveda and modern medicine, and provide a bridge for the inter-disciplinary understanding.

EPISTEMOLOGY OF AYURVEDA AND AYURVEDIC UNDERSTANDING OF TOXINS

Ayurveda is an ancient medical science that focuses on holistic approach to cure. Literally, ayurveda means "Life force/life span" and "knowledge and practice pertaining to promoting life force and life span". Mechanistically, ayurveda considers body as a composite of seven Dhaatus (tissues) namely, are Rasa (plasma), Rakta (blood), Maamsa (flesh/muscle), Meda (fat tissue), Asthi (bone), Majja (bone

marrow) and Shukra (reproductive system). And health as per ayurveda is state of the body-mind complex that is resultant of the balance in the basic body composition (doshas/humors - Vaata, pitta and kapha) that facilitates proper integrity and functional activity of the dhaatus. Further, to maintain the homeostasis in the body, elimination of metabolites wastes (mala/waste) through the natural orifices (the main channels of elimination) of feces, urine, sweat and breath is also considered important aspect in maintaining health as per Ayurveda. When these excretory channels are blocked leading to accumulation of mala that are unwanted or harmful to the body it results in a wide range of toxic manifestations ranging from headache to death. Any imbalance in these basic body compositions of dhaatus and humors (doshas) is the cause of the disease. Thus any diet or toxin that breaks the integrity of the dhaatus, cause imbalance of the doshas and/or blocks the elimination channels are considered toxic.

TOXICOLOGY IN AYURVEDA AND CLASSIFICATION OF MYCOTOXINS IN AYURVEDA

The branch of ayurveda that deals with toxicology is "Agada Tantra". It is one of the eight main branches of "ashtanga ayurveda" and it deals with visha (toxins/poisons) and its treatment (13). These poisons include toxins from plants, metals, minerals and animal kingdoms, as well as artificial origin. Due to its broad perspective of health and holistic healing approach, ayurveda attributes various properties to toxins and thus classifying toxins in different mechanistic categories that also applies to mycotoxins.

Ayurveda has a unique concept of toxin/poison classification. In addition to dealing with medical aspects (yoga, meditation, pranayama), medicines and avoiding visha for healthy living, ayurveda emphasizes the importance of ahara (food) for the overall wellbeing of a person/animal. In particular ayurveda asserts that ahara is responsible for both arogya (health) and vyadhi (disease). The difference between proper health and ill-health being based on the difference between wholesome ahara and unwholesome ahara (viruddha ahara) (14). With contamination of food being the major route of mycotoxicosis, understanding mycotoxins from incompatible food (Viruddha ahara) perspective is a basic approach through Ayurvedic toxicology.

However, in addition to incompatible food, the ayurvedic concept of toxicology encompasses a much broader elaboration such as Visha (toxin) and upavisha that involves poisoning through ingestion, inhalation and dermal toxicity. Ayurveda as per Agada-Tantra categorises poisons/toxins into "akritrimavisha (natural poison) and kriterimavisha/Garavisha (unnatural or chemically prepared poison)" (15,16). Akritrima visha is again sub-divided into jangama visha (animal origin) and sthāvara visha (plant origin) (16). Thus mycotoxins fall under the "jangama" category of ayurvedic toxin classification.

Further, mycotoxins could also be categorised as "Malina Ahara" that indicates food which is contaminated with unwholesome ingredients or the food which has become putrefied (17). Malina ahara has been found to have impact on the mental health as per Charaka Samhita (17).

AYURVEDIC MECHANISM OF TOXICITY WITH CORRELATION TO MYCOTOXINS

According to Ayurveda, the health is state of the body-mind complex that is resultant of the balance in the basic body composition (doshas/humors - Vaata, pitta and kapha) and dhaatus. Any imbalance in these basic body compositions is the cause of the disease and any diet or toxin that disturbs the balance among the body's elemental composition is called as Viruddha Ahara or Visha, respectively.

Virrudha ahar

Any food is said to be Virrudha ahar (incompatible diet), when the type of food restricts proper growth and nutrition of the tissue (17). The concept of Viruddha ahara further explains in depth various factors (totalling 18), that makes food incompatible to the body. These include improper cooking methods, improper combination, inadequate quantity, wrong portion size, wrong time of food consumption, to name a few (17). Among the 18 types, Mycotoxins could be categorised into several classes of Viruddha ahara, such as Satmya Viruddha (Consumption of those substances which are unwholesome) or Sampad Viruddha (Consumption of those substances which are not having their proper qualities, for example - intake of substance those are not mature, over matured or putrefied) (18). Further, mycotoxins could also be dosha viruddha (utilization of compounds, diets and regimen having similar qualities with dosha, but at variance with the habit of the individual) (14). Howe

ver, the diverse modes of action of mycotoxins and their several target organs owing to the varied chemical structure of mycotoxins necessitates further detailed investigations by ayurvedic community for much appropriate categorization of mycotoxins (18).

It is further explained that virudha ahara when consumed may lead to mal absorption and mal-metabolism generating harmful metabolites (Aama) leading to tissue or cellular damage resulting in many serious disease process (17). Indeed, mycotoxins have shown to have deleterious effects on cellular level such as oxidative stress mechanism (19), energy depletion and apoptosis (20) to name a few, substantiating its categorization with Viruddha ahara.

Visha

Visha (poison/toxin) as per ayurvedic texts is a substance that produces ill-health in the body and fear/unhappiness in the minds, after exposure by affecting the "OJA" (the ultimate and subtle humor of the body that protects from the external harmful aetiology) (21). Overall Visha causes life threatening conditions. Vishes are described to have gunas (properties) that are responsible for their toxic effects. But ayurvedic texts differ in their concept as far as numbers of gunas are concerned. However, Acharya Charaka, considered as a pillar for Ayurveda, describes 10 Visha gunas that includes, ruksha, anirdeshya rasa, ushna, laghu, sukshma, tikshna, aashu, vishad, vyavayi and vikasi,. These gunas and their effects are explained in table 1 (21).

A visha (toxin), having all the 10 properties/gunas to its maximum extent, is called as mahavisha, while those having these gunas to a smaller extent are termed as upavishas (16,23). Based on this concepts, mycotoxins that are reported in several acute deaths incidents with seriously/dangerous effects even in small doses including the likes of aflatoxins B, ergot alkaloids could be termed as Visha and mycotoxins

like Zearalenone which have toxic effects without mortality in low doses could be termed Upavisha.

Table 1: Represents various Gunas/properties of Visha/Toxin and their effects (13,16,22)

	Visha Guna	Effects of the Visha guna
1.	<i>Ruksh Guna (dryness)</i>	<i>Vitiates Vaat Prakopa</i>
2.	<i>Anirdeshya Rasa Guna (unidentifiable taste)</i>	<i>Vitiates Kapha Prakopa</i>
3.	<i>Ushna Guna (hotness)</i>	<i>Vitiates Pitta Prakopa</i>
4.	<i>Laghu Guna ((lightness)</i>	<i>Responsible for Dushchikitsya</i>
5.	<i>Sukshma Guna (fineness)</i>	<i>Responsible for sharer Avayay Pravesha</i>
6.	<i>Tikshna Guna (sharpness)</i>	<i>Vitiates Sarva Dosha Prakop</i>
7.	<i>Aashu (fast acting)</i>	Shighra
8.	<i>Vishada (clearing)</i>	Asaktagatidosha
9.	<i>Vyavayi (spreading)</i>	Vyapnoti kevalam deham
10.	<i>Vikasi (opening channels)</i>	<i>Pranaghna</i>

Mechanism of toxicity

Every virudha ahara or visha guna, has got some action on dosha, dhatu and mala. For example, visha with sukshma guna helps penetrate the subtle srotas (layers) of the body, resulting in vitiation of rakta dhatu (blood). On-the-other-hand, "Laghu guna" of visha explains its bio distribution in the body. A visha with laghu Guna moves fast from one place to another (anavasthitatva) in the body (16). Vikasi guna breaks the bonding between various dhatus (like skin, blood, bone, etc) and brings about looseness in the dhatus (dhatushaithilya) and resulting in their improper function (16). In this way, visha leads to vitiation of all the three humors (doshas), leading to its toxic effects that further gets complicated to treat.

Potency of a visha depends on the dominancy of its possessing property/guna. For instance the domination of ruksha guna will lead to the vitiation of vata, domination of sukshma guna lead to vitiation of rakta dhatu as compared to others, while domination of tikshna guna will lead to the impairment three marmas of the body i.e. shira, hridaya and basti and may lead to murchha, sanyasa and other symptoms of marmaghata (16).

While as of today, we do not have a specific effect of mycotoxins in terms of their effects on the three Dosha systems as per ayurveda. Further investigation in this direction shall be needed for gaining deeper understanding of ayurvedic toxic modes of action for mycotoxins, to have relevant comprehension of mycotoxins from ayurvedic perspective. This could help us take appropriate strategies for ayurvedic treatment and promote dietary rules and regulations in human and animal population, specially related to food safety.

PATHOGENESIS (SAMPRAPATI) AND CLINICAL FEATURE OF MICROBIAL FOOD POISONING IN AYURVEDA AND ALLOPATHY

As Per modern medicine food poisoning (of Microbial aetiology) may be divided into two groups. Firstly, infection Type- resulting from ingestions of viable microbes, which multiply in the gastrointestinal tract producing infections as, (ex: Salmonella spp, E. coli spp, etc). Secondly, toxin type- results from ingestion of food containing toxins produced by micro-organisms (ex: mycotoxins, botulinum toxin, etc). Food borne illnesses (including mycotoxins) are presented typically with gastrointestinal symptoms such as vomiting, diarrhea, abdominal pain, hepatotoxicity or nephrotoxicity etc. In addition, non-specific symptoms & neurologic symptoms may occur (24).

However, as per ayurveda, jeevanu (microbes) and their toxins vitiates different dhatus and/or doshas and then causes irritation, inflammation in those tissues starting from annavaha srotas and purishvah srotas (gastro intestinal tract) commonly manifested as vomiting, diarrhoeas, abdominal cramps, colic pain and including fever (24), similar to the signs noted in allopathy. Various ayurvedic scholars, mention that Visjanya Abhisang (exotoxin) contamination of food, termed as food poisoning (Anna Visaj Atisar), when it reaches the amasaya (stomach) gives rise to vomiting, burning sensation, atisar (loose motion), abdominal distention, shivering and a derangement of the sense-organs and even Syncope (24). Others have argued that putrefied food have shown to vitate raja and tama property of mind further leading the person into delirium, coma, unconsciousness or some nervous/memory disorders (17). With new and new research showing nervous effects of mycotoxins with multiple mechanisms of cellular damage (19), categorization of mycotoxins as virudha ahara could also be relevant in gaining Ayurvedic understanding of mycotoxicosis. Further, depending on the dhaatus and doshas affected, the clinical manifestation varies for each and every mycotoxins and their doses (24).

TREATMENT OF MYCOTOXINS IN AYURVEDA

Treatment of toxicity is known as Viśacikitsā and Garacikitsā, as per Agada Tantra of Ayurveda (18). Knowledge of the source/origin of a toxin, its development and toxicity manifestation as well as appropriate remedial measures are an integral part of any health system. Since disease in ayurveda is imbalance in the basic body composition (doshas/humors and tissues/dhaatus), therefore, the basic principle of treatment from ayurvedic perspective, is to restore the balance of the doshas, re-stabilize the integrity of dhaatus and/or to open up the elimination channels (whereby the wastes are eliminated), paving way for the normalization of the functions of the body.

The first and fundamental aspect against food poisoning is prevention. Classical textbooks of Ayurveda, dedicates specific chapters exclusively for food safety known as "annarakṣā" (15), this explains the concepts of prevention of food contamination at the first place. This is similar to the conventional modern medicine where in food safety regulatory agencies set maximum permissible limits for mycotoxin in food and feed above which mycotoxin should not exist in food and feed (EFSA, US FDA).

For treatment of food toxicity, ayurveda follows the principle of restoring the balance of doshas and dhaatus, through the concept of samanya-vishesha siddhanta. Here, a drug (anti-toxin) or diet (anti-virusha-ahara) having opposite properties as that of the disease should be used for its treatment (16). In this approach, we notice both the

principles of antedotes and symptomatic therapy. For the management of visha, the drug or formulation used must be of the opposite guna to that of visha (16), this approach is similar to use of antedotes. Further ayurveda promotes use of drugs similar to the guna of oja/ jivaniya gana (life supporting), for the treatment of visha. Since Oja gets vitiated due to visha-prayoga, ayurveda believes that Oja should be brought back to its normalcy. This concept could be similar to use of symptomatic treatment to bring the homeostasis.

As summarised by other authors, samhitha grantha of Acharya Charaka mentioned that diseases caused by intake of Viruddha Aahar (that applies to Mycotoxins) (18) can be treated by following therapies:

- Prevention of exposure to mycotoxins
- Vaman Karma (Medicated Emesis)
- Virechana (Purgation)
- Administration of antedotes (Administration of substances which are of converse qualities)
- Taking prophylactic measures

Similarly, treatment of visha/toxin from microbes (that could be applied to mycotoxins) has been explained earlier (24)

- Removal of the causative factor - Aparakshana
- Interruption in the nature of causative factor – Prakriti Vighata. This is similar to symptomatic treatment. For example if kapha is aggravated then drugs that reduce kapha humor is given.
- Escaping of causative factor - Nidaana Parivarjana.

These concepts are similar to modern medicine.

Emesis and purgation could be suited for immediate treatment with known consumption history such as in acute poisoning (18). But for mycotoxins, for which low dose chronic exposure is in general an actual/common exposure scenario the treatments such as antedotes could be more suitable.

CONCLUSION

The medical recognition/consideration and classification of toxins and their approach to treatment of toxic effects is what differs between modern medicine and traditional medicine. Ayurveda is an ancient system of medicine with concrete principles of medicines and toxins. While a modern medicine is still facing several challenges in prevention and treatment of mycotoxin-toxicities (mycotoxicosis), ayurveda is a definitive alternative and/or complementary medical system with holistic approach for mycotoxicosis. Despite the current article providing insights into the ayurvedic understanding of mycotoxins, further detailed investigations by ayurvedic community for gaining deeper understanding of mycotoxin toxic modes of action might be necessary, to have relevant comprehension of mycotoxins from ayurvedic perspective. This could help us take appropriate strategies for ayurvedic treatment and promote dietary rules and regulations in human and animal population, specially related to food safety.

Disclosure

The author reports no conflicts of interest in this work and the research is self-funded.

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HOW TO CITE THIS ARTICLE

Prathap Kumar K, Balakrishna Nair MN, Punniyamurthy N, Subrahmanya K. Understanding Mycotoxins from Ayurvedic Perspectives: A Trans-disciplinary approach. *J Ayu Herb Med* 2023;9(3):128-132. DOI: 10.31254/jahm.2023.9306

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