



## Natural Occurrence, Toxicity, Health Implication Of Mycotoxin In Fruits And Their Derivative Products: A Comprehensive Examination

Neelam Dhankhar<sup>1</sup>, Jyoti Sinha<sup>2\*</sup>

<sup>1</sup>Professor: Department of Pharmacy, School of Health Sciences, Sushant University, Gurugram;  
E mail: reenadhankhar@gmail.com

<sup>2\*</sup>Professor: Department of Pharmacy, School of Health Sciences, Sushant University, Gurugram;  
E mail: jyoti\_sinha70@yahoo.com

**\*Corresponding Author:** Jyoti Sinha

\*Professor: Department of Pharmacy, School of Health Sciences, Sushant University, Gurugram;  
E mail: jyoti\_sinha70@yahoo.com

### Abstract

Mycotoxins are natural secondary metabolites produced by filamentous fungi and are commonly found in both food and feed. These toxic compounds are primarily generated by fungal species belonging to *Aspergillus*, *Fusarium*, *Penicillium*, and *Alternaria*. The presence of mycotoxins in the food chain raises significant concerns for human health, as these compounds can induce severe toxicity even at low doses. The contamination of fruits with mycotoxins not only poses health hazards but also leads to substantial economic losses, particularly for countries engaged in exporting such food commodities. Among the mycotoxins commonly found in fruits and their processed products are aflatoxins, ochratoxin A, patulin, as well as *Alternaria* toxins such as alternariol, alternariol methyl ether, and altenuene. These mycotoxins are carcinogenic, immunosuppressive, neurotoxic, genotoxic, teratogenic, and also cause some complications like cerebral edema, impaired child growth, balkan endemic nephropathy, etc. The objective of this study is to conduct a comprehensive review on the toxicity of major mycotoxins, their natural presence in fruits, dried fruits, juices, wines, and various processed products. The review also focuses on the available analytical methods for detecting these mycotoxins and discusses the strategies employed for their control and mitigation.

**Keywords:** Food safety, Mycotoxin, *Aspergillus*, *Fusarium*, *Penicillium*, *Alternaria*

### INTRODUCTION

It is well known in this era & in this century that fruit juices are one of the major sources of vitamins (with low calory), minerals which they may serve as antioxidants, and also play a crucial role in preventing numerous ailments and disease like diabetes mellitus, heart diseases, dermatological problems, cancer and even aging in men & women<sup>1</sup> to which their consumption was so high these days both men & woman, elders and children. Mycotoxins are basically natural products having low molecular weight that are created as secondary metabolites by some threadlike-like fungi species, which mostly. There are almost 400 metabolites classified & termed as mycotoxins of which less than or a dozen are found to be very deleterious to human beings when exposed to them through direct intake of such toxins via food kinds of stuff, vegetables, fruits, meat, eggs, and even dust that are contaminated with these toxins<sup>3</sup> etc. These mycotoxins are usually produced by different fungi/molds mainly from *Aspergillus*, *Alternaria* or *Claviceps*, *Fusarium* & *Penicillium* genera respectively<sup>4</sup>. It has been shown that in one study that raw materials usually were found to have tolerated higher contamination levels (excluding the consumable) than the Completed goods, and these fugal metabolites are practical unavoidable contaminants in foods and feeds right from pre/post harvesting depending on the level of care/sanity given during these agricultural processes<sup>5</sup>. And this has also being seen that it occurs as a result of dilution effect (during formulation) with noncontaminated ingredients when preparing the final product likewise the potential reduction in negative effects through processing. Therefore, the concentration of mycotoxin in the final product is expected to be lower than in the raw material. Toxin formation can occur both in the field and during the storage of agricultural commodities, whether in their raw or processed states food<sup>6</sup>. But it is well known that plants typically evolve efficient detoxification system to counteract fungal infections. It has being shown in one study that these mycotoxins are usually released from the food by the process of digestion as a result of administration of food that has been tainted or polluted with harmful substances into the stomach<sup>5</sup>. It was being found that natural acids (e.g., tartaric acids, malic acids, citric acids) found in fruits imparting tartness to fruits inhibit bacterial spoilage by reducing the Ph, thereby creating an environment less conducive to bacterial growth. This pH of fruit can vary among the different species of fruits, to which usually ranges from <2.5 to 5.0 which discourages bacterial growth but well tolerable for many fungal species<sup>7</sup>. The mycotoxins which are deleterious to human being and most commonly found mycotoxin in fruits and their processed products are *aflatoxins*, *ochratoxin A*, *patulin* and *Alternaria* toxins respectively<sup>8</sup>. Currently in this century it has being reported that almost all the developed and most of the developing countries have their own maximum levels (MLs) of mycotoxin being established for certain food commodities and feed are regulated to safeguard both animal and public health as well<sup>7</sup>.

Mycotoxins contamination in fruits caused not only health hazards to the humans but also animal productivity this situation can lead to financial setbacks and economical losses and for the countries involved in exporting such foods or their processed product, which can also affect the international trade as well<sup>5</sup>. These toxins compose of some toxigenic and referring to a chemically diverse assemblage which are grouped together solely because the members can be deleterious & life-threatening present in both human beings and other vertebrates. These mycotoxins are being classified differently based on which cadre the person making the categorizations, as we studied that the clinicians usually classified them based on the organ they affect, seen as neurotoxins, hepatotoxins, immunotoxins, nephrotoxins etc Physicians by the illnesses they cause. e.g., stachybotryotoxicosis, St. Anthony's fire and the study of fungi responsible for their production, such as toxins produced by *Asperquillus* and *penicillium*." Cell biologists categorize them into broad groups, including allergens, carcinogens, teratogens, and mutagens

Organic chemists categorize them according to their chemical structures, such as lactones and coumarins etc. Biochemists also classified these toxic metabolites based on their biosynthetic origins e.g. amino acid-derived, polyketides<sup>2</sup> etc. It is seen that mycotoxicosis arise as a result of intake of those mycotoxins either via animals (indirectly) or directly to human being which requires an immediate medical intervention with an immediate alacrity<sup>9</sup>.

Around 1980s in south Asia, soviet army uses these mycotoxins as bioweapons in south-Asian region<sup>10</sup>. It has being shown in one study that some of the metabolites can be even more toxic/deleterious than the parent compounds, "The prevalence of more toxic metabolites over their detoxified counterparts contributes to the species-specific susceptibility to certain mycotoxins"<sup>5</sup>. It has being reported in one study that approximately 25% of global crops may exhibit contamination with mycotoxins and was being revealed that effect 4.5 – 5.0 billion people are supposed to be chronically exposed to these mycotoxins which they resulted in contaminating the food and feeds which can be injurious to health which they can exert various effects including acute toxic, carcinogenic, mutagenic, teratogenic, estrogenic and immunotoxin actions of an individual or a community at large when being exposed via the contaminated food<sup>11</sup>. Poverty is master for all regarding the chronicity of mycotoxins effects to the general community mostly in developing & underdeveloped countries where most of the people in that community consume only the available & affordable foods not the preferable ones<sup>3</sup>.

#### **Occurrence & toxicity of some major mycotoxins via foods, fruits and their byproducts.**

The mycotoxins which are supposed to be deleterious to human being and found mostly in fruits and their processed products are *aflatoxins*, *ochratoxin A*, *patulin* and *Alternaria toxins* respectively. Basically the growth of fungal and subsequent possible mycotoxin contamination depends on intrinsic and extrinsic factors<sup>7</sup>. It has being studied that most at times mycotoxin related health risk, affects the whole population in a certain geographical areas where food manufacturing (right from pre/post-harvesting of such food commodity) lacks hygiene practices<sup>12</sup>. it is very essential to elute the possible factors that are leading to mycotoxin formation at all steps of harvesting, manufacturing, storage and transport, Optimal conditions for crop growth and the prevention of mycotoxin contamination are not consistently attainable in practice. Reports indicate that various environmental stressors, including insect infestation, drought, susceptibility of cultivars, mechanical damage, nutritional deficiencies, and unseasonable variations in temperature, rainfall, or humidity, can contribute to the promotion of mycotoxin production in growing crops. Indeed, modifications in farming practices over recent decades may inadvertently intensify stress on plants, leading to an increased risk of fungal invasion and subsequent mycotoxin contamination as well<sup>7</sup>. It has being shown in many studies that mostly mycotoxins occurs in fruits and their refined products have been patulin (primarily in apples & their processed products like juice of apple) and "ochratoxin A" (most at times in wines) etc. But in terms of cereals crops like maize, these are found to be more prone to mycotoxin contamination compared with rice which was found to be less susceptible to these toxins<sup>13</sup>.

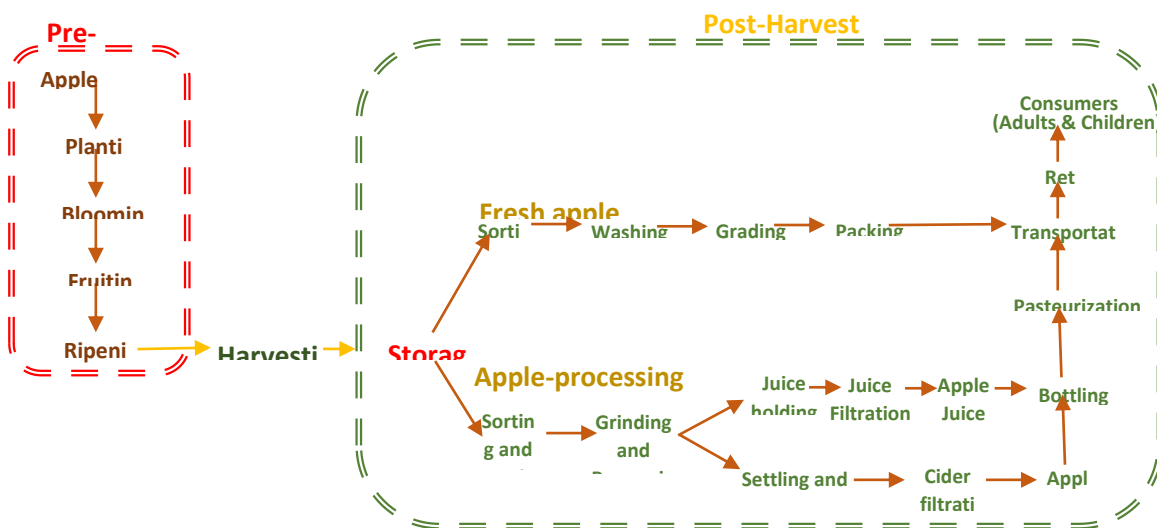
#### **Patulin**

Patulin mycotoxin is popularly known as a polyketide lactone (4-hydroxy-4H-furo{2,3-C} pyran-2{6H}-1) belonging to a class of toxic compound having lower molecular weight 154.12 g/mol with a molecular formula of C<sub>7</sub>H<sub>6</sub>O<sub>4</sub> (as shown structurally in fig.;1). It was found to be stable in aqueous media at around 105–125°C with the melting point 110°C, which is transparent and crystalline in nature<sup>14</sup>. This is basically a poisonous secondary metabolite generated by a range of fungi more specifically by *Penicillium*, *Aspergillus* genera & *Byssochlamys* species<sup>15</sup>. It was being studied previously that the highest temperature for the production of patulin mycotoxins on storage usually ranges between 4 - 25°C<sup>8</sup> to Proven to endure different processing events, including heating and milling<sup>16</sup>. One of the miracle behind these mycotoxin is that it was being reported of having an antibiotic properties<sup>16</sup> and also used around 1940s in for the treatment of common cold<sup>15</sup>. It was scientifically being known and being proven that Human serum among proteins albumin is most plentiful constituent within the circulatory system of a human being which plays an extraordinary vital role physiologically as carrier proteins, which has the capability to attach a diverse range of ligands, including various serum, inorganic ions, fatty acids, and amino acids<sup>15</sup> Etc. By so doing the engagement of any kind of poison with human serum albumin (HSA) definitely directly or indirectly can result in the alteration of nutrients & drugs transport within the human circulatory system as well as distribution into the various organs of the body.

It was being studied that PAT usually shows its sign & manifestation when apples start to exhibit "brown rot" characteristics which is presently recognized to occur globally in apples and apple-derived products<sup>16</sup>. PAT has been consistently identified in apple products made from externally healthy apples with internal rot (which cannot easily be

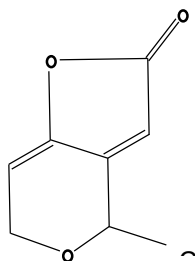
detected by simple physical screening) which are not omitted before pressing for the collection of the juice<sup>17</sup>. Patulin mycotoxin was found to demonstrate its toxic effects by interacting with thiol groups in the cellular system<sup>16</sup>. It has been studied in one study that an acute symptoms of exposure to patulin (most especially via consumption) may include edema, intestinal inflammation, vomiting, agitation, convulsions, ulceration while the Long-term health impacts of patulin might involve; Genotoxicity, immune toxicity, and neurotoxicity have been observed in rodents during clinical trials.<sup>41</sup> However, the effects on humans are not yet fully understood.<sup>18</sup> It has been revealed that exposure to this mycotoxin (PAT) via fruit and vegetables or other foods can easily lead to so many complications will arise like immune suppression, gastrointestinal inflammation, ulcers, bleeding, hepatotoxicity, neurotoxicity, Renal toxicity, immunotoxicity, carcinogenicity (with an inadequate evidence of carcinogenicity in humans)<sup>19</sup>, embryotoxicity & teratogenic effects<sup>16</sup>. It has been reported in one study that children of younger age are at greater risk of intoxication because of their low body weight, specific dietary pattern, higher metabolic rate & poor ability to detoxify hazardous xenobiotics<sup>17</sup>.

Different countries have different limitation of patulin in various fruits and fruit products in respect to the countries and its regulations<sup>14</sup>. Certain nations, including Canada, China, and the USA, have established their respective maximum allowable levels of patulin in apple-based products, ranging from 25 to 50 µg/kg. Moreover, in accordance with Commission Regulation (EC) No. 1881/2006, the European Union (EU) has set specific maximum levels for patulin in various products, such as 50 µg/kg in fruit juices, 10 µg/kg in foods intended for infants and young children, and 25 µg/kg in solid apple products.<sup>20</sup> The Joint Expert Committee for Food Additives has set a maximum tolerable daily intake of 0.4 µg/kg per body weight. Additionally, the Codex Alimentarius has established the maximum allowable level of patulin in fruits and juices, with a limitation set at 50 µg/kg.<sup>21</sup> It was being reported in one study that the amount of patulin found in mango is higher than that found in orange sample<sup>14</sup>.



**Fig.1:** Flowchart Showing an apple from orchard to up to industrial processing, storage & transportation for sales.

Although many studies have been carried out showing how patulin is densely contaminating apple and apple products<sup>17</sup>.



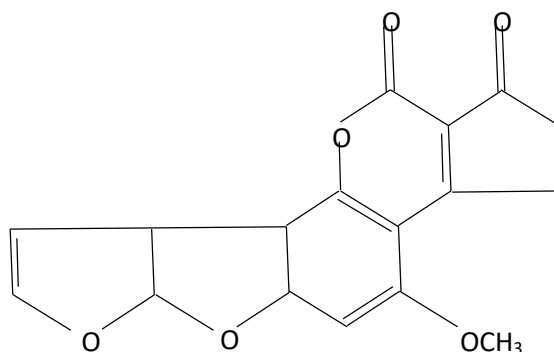
**Fig.2:** Showing the chemical structure of patulin (mycotoxin)

Due to high chances of patulin contamination right from pre/post harvesting process (As shown in fig.1), It has been observed that temperature, atmospheric composition, and moisture levels are often regarded as critical factors for the appropriate storage of apples, to which less temperature is basically used for the commercial storage of this fruit in order to target the decrease in the growth of *P. expansum*<sup>22</sup>. In a particular study, it has been found that detoxification procedures not only lower toxin levels to safe thresholds but also prevent any reduction in the nutritional and palatability content of treated fruits or their processed products. Historically, strategies employed to decrease patulin contamination in apple products included both physical and chemical methods. In another study, it was reported that implementing practices such

as summer pruning (conducted in July and August), hand thinning, and bark mulching had a positive impact on the productivity and/or storability of early-season apples, specifically the "Katja" variety, as well as several other organically grown apple cultivars (e.g., "Dayton," "Delorina," "Santana," "Sultanat," and "Zarya Alatau" in Sweden)<sup>23</sup>. Some of the mulching practices like cornstalk treatment as an example, It was also discovered to significantly enhance the firmness of apples from the Loess Plateau in China. This improvement in firmness may prove beneficial in reducing the incidence of diseases and patulin contaminations<sup>24</sup>. In a study conducted on pear fruit, it was recommended that when a lesion reaches a diameter of 5 mm, both the lesion and the surrounding 20 mm should be removed. Similarly, if a pear exhibits a lesion with a diameter of 10 mm, the recommendation is to remove the lesion along with the surrounding 30 mm; for 20 mm lesions, it is advised to remove not only the lesion itself but also the surrounding 40 mm of tissue. If the diameter of lesion is greater than 30 mm, it was being suggested that the entire pear should not be used completely<sup>25</sup>. The main ways of reducing or eliminating patulin contamination in fruits (e.g., apple and apple products) implementing proper management in orchards and procedures after harvest will surely help to a better control of the *P. expansum* spread, lowering the level of patulin contaminations within the final products. It has also being suggested in one study that the use of fungicide & The use of insecticides for plant treatment, maintaining sanitation quality, removing decayed tissue from fruits, thorough washing (utilizing either the hot water method or alternative approaches) before processing, effective sorting, and adopting sound packaging practices have been identified as measures that can significantly decrease levels of contamination<sup>18</sup>.

### **Aflatoxin**

These are found to be highly toxic, mutagenic, teratogenic & also carcinogenic metabolites which are basically Di furanocoumarin derivatives produced by a polyketide pathway by the fungi of genus *Aspergillus*<sup>2</sup>, specifically by species of *A. Parasiticus*, *A. Flavus* & *A. Nomius*<sup>26</sup>. Basically just like some of the mycotoxin, excessive drought conditions, temperatures and also elevated insect presence can lead to preharvest contamination of plant product by the aflatoxin<sup>26</sup>. This mycotoxin (aflatoxin) was first isolated and discovered after an outbreak of a certain disease (in turkey) of unknown etiology around 1960 in England, that leads to the lost/death of more than 100,000 turkey poults<sup>2</sup>. And because the cause is unknown that's why it was labelled as "Turkey X affliction" But subsequently the disease induced as a result of exposure of human being or animals to this mycotoxin of aflatoxin was termed as "aflatoxicosis"<sup>2</sup>. It has being shown in some research studies that most at times the most vulnerable to foodborne hazards because of high amount of exposure to a diet per kilogram of body weight and variations in physiological processes are mostly the children compared to adults<sup>27</sup>. This mycotoxin can simultaneously be detected along with other kind of some mycotoxin using the modern HPLC-MS/MS technique or methods which helps in rapid detection of many mycotoxins in a certain specific food or feed product sample within a stipulated time<sup>28</sup>. There are many different types of aflatoxins, but the main ones that usually found to contaminate the feed & foodstuffs are the aflatoxin B1, B2, G1 & G2. To which AFB1 is almost toxic and highly occurring aflatoxin compared with the remaining types of aflatoxins (as its chemical structure being shown in fig.;3)<sup>29</sup>, although aflatoxin M1 (AFM1) was usually found to be the most highly occurring toxin that was found to be the most toxic contaminant in dietary products like milk<sup>30</sup>, although there is no any tangible evidence of AFM1 presence in a fresh breast milk of a human breastfeeding mother<sup>31</sup>, and one study reports that there has being found a significant amount/quantity of AFM1 mycotoxin in both fluid milk and powder milk, cheese and even yoghurt<sup>26</sup>.



**FIG. 3:** Showing chemical structure of aflatoxin B1

Special emphasis is typically placed on cereals, particularly cereal-based baby food, and infant formulas, with a designated maximum tolerable limit of 1µg/kg for the cumulative aflatoxin content, according to a specific study.<sup>32</sup> But one study clearly revealed that peanuts and its derivatives have high incidence of being the main source of aflatoxin (basically the AFB1, AFB2, AFG1 & AFG2) to which AFB1 is the major highly occurring and nearly all toxicogenic form of aflatoxin<sup>33</sup>. Many research agencies reported and talk about also on some mycotoxin along with their set limitation in feed and foodstuffs, moreover The International Agency for Research on Cancer classified AFB1 & mixtures of total aflatoxins into group 1: "Carcinogenic for humans". Aflatoxin can lead to hepatocellular carcinoma & also aflatoxicosis to which it

can bring about loss of life or death in humans<sup>28</sup>. Increased risk of liver cancer along with stunted child development<sup>34</sup>, and an immunosuppressant are been documented in individuals who are revealed to these aflatoxins (most especially AFB1)<sup>35</sup>. Apart from presence of aflatoxin in some cereals, legumes, dietary products etc. it has also reported being found in egg, oily seeds, meat as well as meat products<sup>27</sup>. It has been postulated in one study that the acute lethal dose for adults is estimated to be around 10 to 20 mg of aflatoxins<sup>2</sup>. It has been shown in one study that in the case of children, children in weaning status of age 1-3yrs (receiving both breast milk and solid foods) are found to be less exposed than the one that are fully weaned children who are more labile to get exposed to these mycotoxin due to high chances of them ingesting some of the food (maize, fruits, dietary products etc.) & feed products that they may be contaminated with these toxins<sup>35</sup>. Some of the aflatoxin symptoms of exposure could include; Abdominal pain, Alveolar injury, bile duct hyperplasia, bile duct metaplasia, brain injury, cancer, carbohydrate metabolism impaired, decreased catecholamine levels, centrilobular coagulative necrosis, cerebral edema, convulsions, corrhachia, cough, dark urine, death, diarrhea, degeneration of heart muscle due to accumulation of fat, degeneration of the liver due to accumulation of fat, infiltration of heart due to fat, fatty infiltrations kidney, fatty infiltrations of liver, fever, hematemesis, depleted hepatic glycogen stores, hepatocellular carcinoma, high blood sugar, hypoglycemia, immunosuppression, impaired child development, impaired child health, impaired nutritional intake, respiratory distress, teratogen<sup>36</sup>.

### Ochratoxin

This is a colorless crystalline compound with a molecular weight (403.8g/mol)<sup>37</sup> that was found to be blue fluorescence under UV light & having found to be weakly acidic to which it can be detected using liquid Chromatography (LC) with Fluorescence Detection (FLD) following a cleanup procedure involving Solid Phase Extraction (SPE) with an IAC<sup>38</sup>. Basically, Ochratoxins are of different types, but our main concern is the "ochratoxin A", this was found to be a phenylalanine- dihydroisocoumarin derivative, It was discovered that this is a derivative of phenylalanine-dihydroisocoumarin, which exhibited notable stability under both temperature and hydrolysis conditions (as shown structurally in figure 4)<sup>39</sup>. These type of mycotoxin was initially discovered (from *Aspergillus Ochraceus*) in the year in 1965, during an extensive screening of fungal metabolites explicitly designed to uncover new mycotoxins.<sup>2</sup> These toxin were basically found to be a metabolite from many variety of *Aspergillus* like; *Aspergillus glaucus*, *Aspergillus niger*, *Aspergillus melleus*, *Aspergillus alliaceus*, *Aspergillus carbonarius*, *Aspergillus auricomus*<sup>40</sup>. It has been reported in one study that "*A. carbonarius* acts as a saprophyte, with the penetration of grape berries occurring preferentially after damage caused by various agents, including insects, heavy rainfall, storms, or other fungal infections (such as powdery mildew)".<sup>41</sup> Ochratoxin A (OTA) exhibits resistance within the range of applied thermal processing conditions but is partially destroyed during fermentation processes.<sup>42</sup>

As being reported in one study, the longer the juice extraction process/time (20 to 120mins) the lower the level or percentage of OTA presence in the final juice product<sup>43</sup>. The contamination of this toxin has being reported to be one of the contaminant of barley & stored cereals<sup>44</sup>, also some fruits like grapes or fruit juices like wines to which mostly occurring most in subtropical regions & temperate climate<sup>45</sup>. Moreover the contamination of foods with OTA in cool climates (8–37 °C) is usually caused by *P. verrucosum*, whereas the occurrence of OTA in foods in warmer and tropical climates is most at times associated with *A. ochraceus*<sup>7</sup>. One study also reported that significant contamination of ochratoxin also being found on beer, coffee, pork meat, and also cocoa products as well<sup>39</sup>. Ochratoxin is very deleterious to humans health to which the kidney is the primary target (which can lead to Chronic kidney disease)<sup>46</sup>, and it is somehow toxic as that of aflatoxin being discussed earlier<sup>44</sup>.

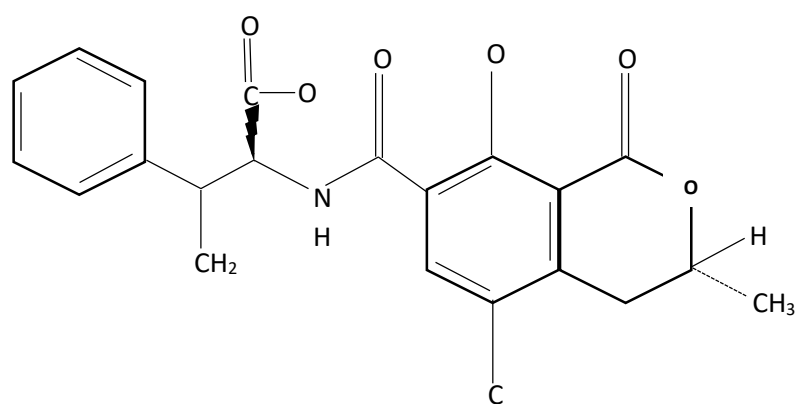


FIG. 4: Ochratoxin A

A study performed earlier shows that OTA is an immune suppressant, carcinogen (classified by IARC), potent teratogen as well as hepatotoxic<sup>47</sup>. In some years ago there have being a report of one study that there is a wide spread of a disease called "endemic balkan nephropathy" that is often associated with OTA toxicity<sup>48</sup>. The most major factors that often

affect the OTA contamination level could include the geographical location, climate conditions, type & cultivar of fruit, production year, pre/post-harvest treatments, and the use of pesticides, superficial fruit damage surface as a result of bruising of the fruit during the process of harvest or transportation and likewise the storage condition to which this fruit & their processed products are being kept<sup>45</sup>. Each of every single country has their own regulation along with maximum limit of OTA set to be tolerable on food & feed, fruits or their processed products to which they are being contaminated with such mycotoxin. The induced toxicity of ochratoxin A (OTA) is intricate and cumbersome due to the unclear understanding of its mechanism of action.<sup>49</sup>But studies have reported some of the symptoms of ochratoxin exposure which may include; Anemia, anorexia, apoptosis, carcinogenic, copper colored skin, decreased hemoglobin, decreased lymphocytes, endemic nephropathy (to which females are more sensitive), fatigue, headache, increased apoptotic phagocytes, elevated clotting time, heightened eosinophils, increased leukocytes, heightened neutrophils, and escalated levels of reactive oxygen radicals, Elevated clotting time, heightened eosinophils, increased leukocytes, heightened neutrophils, and escalated levels of reactive oxygen radicals), inhibition of protein synthesis, inhibits phenylalanine hydroxylase, intermittent hematuria, lassitude, nephrotoxic<sup>50</sup>, neurotoxin, reduced phagocytosis, suppresses the immune system, teratogenic, trinary tract tumors, yellow palms<sup>36</sup>. And It has being reported that females are more sensitive to this toxicity than males<sup>51</sup>. Other mycotoxin found in food and feed products which are less toxic (as compared with the mycotoxins being discussed above) could include; Zearalenone, Fumonisin, Trichothecenes Alternariol etc.

### Analysis of mycotoxins

As Hippocrates (460 – 377 BC) famously stated, 'Let food be your medicine, and medicine be your food', and yet nowadays many contaminants seem to be making the food unhealthy and toxic. And therefore, analysis of such food commodities that are contaminated with such toxins is mandatory in order to make the food healthy and be our medicine for healthy living. So, for the analysis and determination of mycotoxin levels in samples of food, many steps are involved which could include; sampling, homogenization, Extraction, followed by cleanup, and ultimately detection and quantitation. Which is diagrammatically shown below in figure-5.

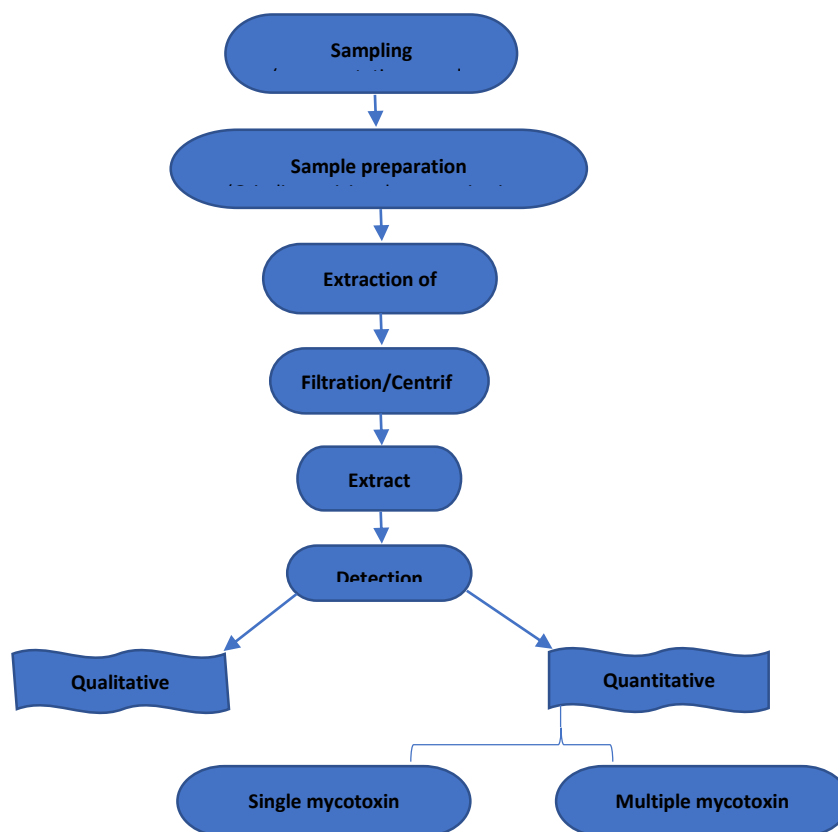


FIG. 5: Diagram showing some common steps involved in mycotoxins analysis in food commodities.

### METHODOLOGY

The papers/journals used in this review study were searched manually and were being selected based on the following key points; Mycotoxin, Aspergillus, Alternaria, Claviceps, Fusarium, Penicillium, A.Parasiticus, A.Flavus & A.Nomius, Byssochlamys species, patulin, ochratoxin, aflatoxin, zearalenone, fumonisin, Trichothecenes, occurrence, toxicity, teratogenicity, hepatogenic, carcinogenic, neurotoxin, immunotoxin, nephrotoxin, stachybotryotoxicosis, Balkan endemic

nephropathy, polyketide lactone, difuranocoumarin derivatives, Codex Alimentarius, food and feed contaminants, fruits contaminant, fruit juice contaminants, exposure, health implication, turkey X disease, pre/post-harvest exposure. The scientific data base used were Science direct, PubMed, Google scholar, Scopus etc. where about 100plus research work related to this subject topic were put into study and only 50plus were found to be most relevant and usable for the review of the subjected topic of interest as the title being given.

### IMPLICATIONS AND CONCLUDING REMARKS ON MYCOTOXIN

It is now clearly known that food contaminants most especially the various type of mycotoxin are the most challenging aspect globally that affect not only the people being exposed to it within the nation but also affect the economy of that particular nation as well. The health implication of some of this contaminant (mycotoxin) is shown in table-1.

**Table 1.** Health implication of some common mycotoxin that are toxic to human

Mycotoxin	Health implication	Reference
Patulin	Genotoxic, immunosuppressive, neurotoxic, hepatotoxic. etc.	12, 52, 53
Aflatoxin	Cerebral edema, immunosuppressive, impaired child growth	27, 53
Ochratoxin	Carcinogenic, nephrotoxic, urinary tract tumor, teratogenic	47, 54, 51
Fumonisin	Immunosuppressive, hepatotoxic, carcinogenic, nephrotoxic	55
Deoxynivalenol	Toxicosis, reproductive effect, diarrhea etc.	1, 9
Zearalenone	Hormonal imbalance, reproductive effect etc.	56, 31, 3
Trichothecenes	Hepatotoxic, genotoxic, immunosuppressive	3, 44, 53, 1

In the past patulin was initially being discovered as an antibiotic that is used against Gram-positive likewise the Gram-negative bacteria, but later on, this molecule was found to be toxic/deleterious to human health. Although the remaining mycotoxin there is less report or study being performed that shows their important in reviving human physiological functions rather than their toxic effect on human physiology as being shown in table-1 above. In addition, some of the regulation & tolerable limit of this mycotoxin across in some countries across the world can be slightly heightened in the tables below;

**Table 2.** Showing limits of different aflatoxin in some Asian countries.

Country	Aflatoxin types	Maximum limit (ppb)	Food and feed contaminated	Refs.
Japan	B1	10	Rice	57
	B1	5	Other grains	44
Hong Kong	All	20	Peanut & peanut products	44
	All	15	Other foods	58
India	B1	30	All food	44
	B1	120	Feed (peanut meal)	59
China	B1	20	Maize, peanut	44
	B1, M1	0	Infant foods	60
S - Korea	B1	10	Grains, cereals, dried fruits, streamed rice.	44
	B1	0.1	Baby foods	44
	B2,G1,G2	15	Streamed rice, baby foods, grains, dried fruits.	44
Sri Lanka	M1	0.5	Raw milks and milks before processing	44
	All	30	All	44
Thailand	M1	1	Infant foods	44
	All	20	All	44

**Table 3.** Showing limit of ochratoxin laid in some countries

Country	Maximum limit (ppb)	Food and feed contaminated	Refs.
Singapore	2.5	Roasted coffee beans, raw coffee beans, Cereal	61
Taiwan	5	Rice and wheat products	62
Indonesia	20	Spices	44
S - Korea	10	Instant coffee and raisins, coffee beans, and roasted coffee	44

**Table 4.** limit of patulin laid in some countries around the globe.

Country	Maximum limit ( $\mu\text{g kg}^{-1}$ )	Food/Food products contaminated	Refs.
China	50	Apple, Pear fruit, Mango, Orange, Fruit juices, grapes	45
Austria	50	Fruit juice	59
Russia	50	Canned/potted/bottled fruits & berries & canned vegetables	59

Czech & Slovak republic	20	Infants foods	59
Romania	20	Children food	1
South africa	50	All foods	59
	30	All foods and feed stuff	59
	50	All foods	63

## CONCLUSION

Mycotoxins pose a significant threat to human health, potentially causing severe and irreversible damage, including the risk of cancer, particularly in developing nations worldwide. The risk of mycotoxin contamination is a crucial concern that currently has a significant impact on global food safety and the quality control of food and feed commodities. Although once food and feed has been contaminated with this mycotoxin, there is nothing to do to completely eliminate such toxin on the contaminated food, feed, fruit or their processed products. Therefore, lot of measures and precautions has to be taken to avoid mycotoxin occurrence in food chain (which include the pre/post-harvest of such cultivated food and their processed products) which is the primary objective necessitates an understanding of both the sources and the pathways of contamination. Developing methods (appropriate investigative criteria & reliable laboratory tests), which are more rapid, sensitive, selective, precise as well as inexpensive (in the field of research), affordable & accessible can significantly contribute to reducing the prevalence of mycotoxins.

Our review data's basically point out the significance of enhancing food safety concerning mycotoxin contamination and their health implication to the society. Collaboration of governmental authorities between academia and industries is crucially needed to control mycotoxin production in the field., inhibition of growth of toxigenic molds in food & feed, and also improved detection techniques. Moreover, some strategies that will help in alleviating the chances of mycotoxin contamination or even eliminate the mycotoxin on the foods and their processed products could include; Preventing mycotoxin contamination during both the pre-harvest and post-harvest periods, detoxification of mycotoxins present in foods and inhibition of mycotoxin absorption into the GIT. Postharvest contamination can be mitigated by controlling factors such as moisture, temperature, and addressing microbiological, insect, and animal pests accordingly.

## REFERENCE

- Pallarés, N., Carballo, D., Ferrer, E., Fernández-Franzón, M. & Berrada, H. Mycotoxin dietary exposure assessment through fruit juices consumption in children and adult population. *Toxins (Basel)*. **11**, 1–12 (2019).
- Bennett, J. W. & Moore, G. G. Mycotoxins. *Encycl. Microbiol.* **16**, 267–273 (2019).
- Omotayo, O. P., Omotayo, A. O., Mwanza, M. & Babalola, O. O. Prevalence of mycotoxins and their consequences on human health. *Toxicol. Res.* **35**, 1–7 (2019).
- Berthiller, F. *et al.* Masked mycotoxins: A review. *Mol. Nutr. Food Res.* **57**, 165–186 (2013).
- Dellaflora, L. & Dall'Asta, C. Forthcoming challenges in mycotoxins toxicology research for safer food-a need for multi-omics approach. *Toxins (Basel)*. **9**, (2017).
- Karlovsky, P. *et al.* Impact of food processing and detoxification treatments on mycotoxin contamination. *Mycotoxin Res.* **32**, 179–205 (2016).
- Fernández-Cruz, M. L., Mansilla, M. L. & Tadeo, J. L. Mycotoxins in fruits and their processed products: Analysis, occurrence and health implications. *J. Adv. Res.* **1**, 113–122 (2010).
- Moss, M. O. Fungi, quality and safety issues in fresh fruits and vegetables. *J. Appl. Microbiol.* **104**, 1239–1243 (2008).
- Van Egmond, H. P., Schothorst, R. C. & Jonker, M. A. Regulations relating to mycotoxins in food : PPPPerspectives in a global and European context. *Anal. Bioanal. Chem.* **389**, 147–157 (2007).
- Pitschmann, V. Overall view of chemical and biochemical weapons. *Toxins (Basel)*. **6**, 1761–1784 (2014).
- Blanco, I. Current Research and Future Perspectives. *Blanco's Overv. Alpha-1 Antitrypsin Defic.* 207–225 (2017) doi:10.1016/b978-0-12-809530-0.00015-5.
- Saleh, I. & Goktepe, I. Health risk assessment of Patulin intake through apples and apple-based foods sold in Qatar. *Heliyon* **5**, e02754 (2019).
- Chulze, S. N. Strategies to reduce mycotoxin levels in maize during storage: A review. *Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment* (2010) doi:10.1080/19440040903573032.
- Hussain, S. *et al.* Patulin mycotoxin in mango and orange fruits, juices, pulps, and jams marketed in Pakistan. *Toxins (Basel)*. **12**, 1–10 (2020).
- Yuqin, L. *et al.* Investigation of the interaction between patulin and human serum albumin by a spectroscopic method, atomic force microscopy, and molecular modeling. *Biomed Res. Int.* **2014**, (2014).
- Pal, S., Singh, N. & Ansari, K. M. Toxicological effects of patulin mycotoxin on the mammalian system: An overview. *Toxicol. Res. (Camb)*. **6**, 764–771 (2017).
- Zhong, L., Carere, J., Lu, Z., Lu, F. & Zhou, T. Patulin in apples and apple-based food products: The burdens and the mitigation strategies. *Toxins (Basel)*. **10**, 1–30 (2018).



18. Azizi, I. G. & Rouhi, S. Determination of patulin in fruit juices and compote of apple and pear. *Toxin Rev.* **32**, 39–42 (2013).
19. Evaluation of certain food additives and contaminants. *World Health Organization technical report series* vol. 859 1–54 (1995).
20. ► B COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. 1–34 (2012).
21. WHO/FAO. Codex general standard for contaminants and toxins in food and feed. *Codex Stand.* **193**, 1–48 (1995).
22. Morales, H., Marín, S., Centelles, X., Ramos, A. J. & Sanchis, V. Cold and ambient deck storage prior to processing as a critical control point for patulin accumulation. *Int. J. Food Microbiol.* (2007) doi:10.1016/j.ijfoodmicro.2007.01.004.
23. Tahir, I. I. & Nybom, H. Tailoring organic apples by cultivar selection, production system, and post-harvest treatment to improve quality and storage life. *HortScience* (2013) doi:10.21273/hortsci.48.1.92.
24. Chen, Y. *et al.* Mulching practices altered soil bacterial community structure and improved orchard productivity and apple quality after five growing seasons. *Sci. Hortic. (Amsterdam)*. (2014) doi:10.1016/j.scienta.2014.04.010.
25. WEI, D. mei *et al.* Penicillium and patulin distribution in pears contaminated with *Penicillium expansum*. Determination of patulin in pears by UHPLC-MS/MS. *J. Integr. Agric.* **16**, 1645–1651 (2017).
26. Jager, A. V., Tedesco, M. P., Souto, P. C. M. C. & Oliveira, C. A. F. Assessment of aflatoxin intake in São Paulo, Brazil. *Food Control* **33**, 87–92 (2013).
27. Huong, B. T. M. *et al.* Total dietary intake and health risks associated with exposure to aflatoxin B1, ochratoxin A and fumonisins of children in Lao Cai Province, Vietnam. *Toxins (Basel)*. **11**, 1–18 (2019).
28. Selvaraj, J. N. *et al.* Mycotoxin detection - Recent trends at global level. *J. Integr. Agric.* **14**, 2265–2281 (2015).
29. International Agency for Research on Cancer. International Agency for Research on Cancer Iarc Monographs on the Evaluation of Carcinogenic Risks To Humans. *Iarc Monogr. Eval. Carcinog. Risks To Humans* (2002).
30. Ball, R. W. & Coulombe, R. A. Comparative biotransformation of aflatoxin B1 in mammalian airway epithelium. *Carcinogenesis* (1991) doi:10.1093/carcin/12.2.305.
31. Valitutti, F. *et al.* Assessment of mycotoxin exposure in breastfeeding mothers with celiac disease. *Nutrients* **10**, 1–9 (2018).
32. ANVISA. Formulário de Fitoterápicos da Farmacopeia Brasileira. *Agência Nac. Vigilância Sanitária* (2011).
33. Frisvad, J. C. *et al.* Taxonomy of *Aspergillus* section *Flavi* and their production of aflatoxins, ochratoxins and other mycotoxins. *Stud. Mycol.* **93**, 1–63 (2019).
34. Gong, Y. Y. *et al.* Dietary aflatoxin exposure and impaired growth in young children from Benin and Togo: Cross sectional study. *Br. Med. J.* **325**, 20–21 (2002).
35. Gong, Y. *et al.* Postweaning exposure to aflatoxin results in impaired child growth: A longitudinal study in Benin, West Africa. *Environ. Health Perspect.* **112**, 1334–1338 (2004).
36. Bibliography, W. & Prevention, M. Mycotoxin Sample Medical Concerns From Small Sample of Literature Symptoms of Ochratoxin Mycotoxin Exposure. (2001).
37. Pyo, M. C., Shin, H. S., Jeon, G. Y. & Lee, K. W. Synergistic interaction of ochratoxin A and acrylamide toxins in human kidney and liver cells. *Biol. Pharm. Bull.* **43**, 1346–1355 (2020).
38. Visconti, A., Pascale, M. & Centonze, G. Determination of ochratoxin A in wine and beer by immunoaffinity column cleanup and liquid chromatographic analysis with fluorometric detection: Collaborative study. *J. AOAC Int.* (2001) doi:10.1093/jaoac/84.6.1818.
39. Petzinger, E. & Weidenbach, A. Mycotoxins in the food chain: The role of ochratoxins. in *Livestock Production Science* (2002). doi:10.1016/S0301-6226(02)00124-0.
40. Al-Hazmi, N. A. Determination of Patulin and Ochratoxin A using HPLC in apple juice samples in Saudi Arabia. *Saudi J. Biol. Sci.* (2010) doi:10.1016/j.sjbs.2010.06.006.
41. Mondani, L. *et al.* Pest management and ochratoxin A contamination in grapes: A review. *Toxins (Basel)*. **12**, 1–21 (2020).
42. Soufleros, E. H., Tricard, C. & Bouloumpasi, E. C. Occurrence of ochratoxin A in Greek wines. *J. Sci. Food Agric.* (2003) doi:10.1002/jsfa.1300.
43. Dachery, B., Veras, F. F., Dal Magro, L., Manfroi, V. & Welke, J. E. Exposure risk assessment to ochratoxin A through consumption of juice and wine considering the effect of steam extraction time and vinification stages. *Food Chem. Toxicol.* **109**, 237–244 (2017).
44. Anukul, N., Vangnai, K. & Mahakarnchandkul, W. Significance of regulation limits in mycotoxin contamination in Asia and risk management programs at the national level. *J. Food Drug Anal.* **21**, 227–241 (2013).
45. Oteiza, J. M. *et al.* Influence of production on the presence of patulin and ochratoxin A in fruit juices and wines of Argentina. *LWT - Food Sci. Technol.* **80**, 200–207 (2017).
46. Schulz, M. C., Gekle, M. & Schwerdt, G. Epithelial-fibroblast cross talk aggravates the impact of the nephrotoxin ochratoxin A. *Biochim. Biophys. Acta - Mol. Cell Res.* **1866**, 118528 (2019).
47. Beardall, J. M. & Miller, J. D. Diseases in humans with mycotoxins as possible causes. in *Mycotoxins in Grain: Compounds other than Aflatoxin* (1994).
48. Plestina, R. *et al.* Human exposure to ochratoxin A in areas of Yugoslavia with endemic nephropathy. *J. Environ.*

- Pathol. Toxicol. Oncol.* (1990).
49. Malir, F., Ostry, V., Pfohl-Leszkwicz, A., Malir, J. & Toman, J. Ochratoxin A: 50 years of research. *Toxins (Basel)*. **8**, 12–15 (2016).
  50. Zhu, L. *et al.* Limited link between oxidative stress and ochratoxin A—Induced renal injury in an acute toxicity rat model. *Toxins (Basel)*. **8**, (2016).
  51. Ćeović, S., Hrabar, A. & Šarić, M. Epidemiology of Balkan endemic nephropathy. *Food Chem. Toxicol.* (1992) doi:10.1016/0278-6915(92)90031-F.
  52. Kujawa, M. Evaluation of Certain Food Additives and Contaminants. WHO Technical Report Series 859. VI and 54 pages, 1 table. World Health Organization, Geneva 1995. Price: 11,- Sw.fr. *Food / Nahrung* (1997) doi:10.1002/food.19970410233.
  53. Alshannaq, A. & Yu, J. H. Occurrence, toxicity, and analysis of major mycotoxins in food. *Int. J. Environ. Res. Public Health* **14**, (2017).
  54. Krogh, P., Hald, B., Plestina, R. & Ceovic, S. Balkan (endemic) nephropathy and foodborn ochratoxin A: preliminary results of a survey of foodstuffs. *Acta Pathol. Microbiol. Scand. - Sect. B Microbiol. Immunol.* (1977) doi:10.1111/j.1699-0463.1977.tb01702.x.
  55. Jian, Q. *et al.* Rapid assessment of the toxicity of fungal compounds using luminescent *Vibrio qinghaiensis* sp. Q67. *Toxins (Basel)*. **9**, (2017).
  56. Kalagatur, N. K., Kamasani, J. R. & Mudili, V. Assessment of detoxification efficacy of irradiation on zearalenone mycotoxin in various fruit juices by response surface methodology and elucidation of its in-vitro toxicity. *Front. Microbiol.* **9**, 1–13 (2018).
  57. Vasanthi, S. & Bhat, R. V. Mycotoxins in foods - Occurrence, health and economic significance and food control measures. *Indian J. Med. Res.* (1998).
  58. Studies, R. A. & Evaluation, C. H. Aflatoxin in foods. *Evaluation* 1–17 (2001).
  59. Mazumder, P. M. & Sasmal, D. Mycotoxins - limits and regulations. *Anc. Sci. Life* **20**, 1–19 (2001).
  60. Chiou, J., Leung, A. H. H., Lee, H. W. & Wong, W. tak. Rapid testing methods for food contaminants and toxicants. *J. Integr. Agric.* **14**, 2243–2264 (2015).
  61. Anukul, N., Vangnai, K. & Mahakarnchandkul, W. Significance of regulation limits in mycotoxin contamination in Asia and risk management programs at the national level. *Journal of Food and Drug Analysis* (2013) doi:10.1016/j.jfda.2013.07.009.
  62. Kuiper-Goodman, T. Risk assessment and risk management of mycotoxins in food. *Mycotoxins Food* 3–31 (2004) doi:10.1533/9781855739086.1.3.
  63. Leggott, N. L. & Shephard, G. S. Patulin in South African commercial apple products. *Food Control* (2001) doi:10.1016/S0956-7135(00)00023-2.