



Aflatoxin M1 in Milk: Occurrence and Its Risk Association: A Review

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ABSTRACT

Aflatoxin M1 (AFM1) is the main secondary metabolites of aflatoxin B1 (AFB1) framed in the liver and discharged into milk when people and animals polish off AFB1-polluted food. The persist from feed to milk in dairy cows is affected by different dietary and physiological elements, including taking care of regimens, rate of ingestion, rate of absorption, animal health, hepatic biotransformation limit, and real milk production of the animals. AFM1 exposure might cause both intense and constant toxicity. In humans, AFM1 exposure is related with cancer-causing nature, genotoxicity, mutagenicity, and teratogenicity. In dairy animals, persistent openness to AFs can decrease execution, debilitate liver capability, compromise invulnerable capability, and increment sickness susceptibility. AFM1 openness represents a worry for the worldwide populace, especially for babies and youngsters who drink milk in bounteous amounts and thus, are more powerless to unfavorable impacts. The identification and quantification of AFs represents a critical test in food handling confirmation, since even a low AF concentration is hazardous for people and domesticated animals. Consistent human openness through dietary courses has prompted the burden of most extreme cut off points for AFM1 in milk and dairy products, taking into account that this is a gathering of products with exorbitant premium, particularly for babies and youngsters. Likewise, as per different examinations it is additionally very much felt that youthful animals are additionally observed to be more vulnerable to aflatoxin than grown-ups. Consequently; the defilement of cow milk and milk products by AFM1 ought to be perceived as unfortunate for youthful human and animals. Thus, the point of this paper is to review the occurrence of aflatoxin and its adverse results on animals and human health over the time.

Keywords: Aflatoxin M1, Dairy cattle products, Human health, Milk, Occurrence.

Introduction

Milk and its products are generally consumed by individuals of all age groups, particularly kids and the old as milk is healthfully adjusted and give all fundamental amino acids, and allude to it as "the most incredibly complete normal food". Consequently, the nature of milk should be really great for human utilization. People and animals are more exposed to "biological hazards" from regular poisons that happen in food and feed.

Producing milk products that are liberated from impurities is compulsory for general health safety security and acceptable shelf of the products [1]. At present, any foodstuff particularly milk products that have legitimate cleanliness and dependable quality norms are in an elevated degree of inclination for the purchasers. Normally, health hazards to the consumer connecting with dairy products are for the most part bunched into chemical, physical and microbiological hazards [2]. From chemical hazards, Aflatoxin is one of the fundamental ongoing normally happening poisons chemical compounds (Mycotoxins) which are assembled under the possible compound risks for the two animals and people [3]. As indicated by WHO, [4] expressed ordinarily harmful metabolites of growths dirty food and feedstuff and cause food-borne sicknesses which are classified under chemical hazards.

Aflatoxins (AFs), as secondary metabolites, are essentially produced by three fungi species, *Aspergillus flavus*, *Aspergillus parasiticus*, and *Aspergillus nomius*, these organisms are regular toxins of a few farming commodities, particularly during unfriendly weather patterns, dry spell, and bug harm [5]. Among the AFs delivered by the fungi, AFB1 is the most plentiful and poisonous one. AFB1 might apply immunosuppressive, teratogenic, mutagenic, and cancer-causing impacts, particularly on the liver. Subsequent to ingesting debased feed by milk-producing animals, the AFB1 is used by microsomal cytochrome P450 to deliver AFM1 that can be discharged in the urine and milk [6]. Distinguishable groupings of AFM1 are quantifiable 12-24 h after ingestion, with discharge top in 24-48 h subsequent to consuming profoundly debased feed [7]. AFB1 addresses the most significant level of harmfulness; followed by AFM1, AFG1, AFB2 and AFG2 [8]. AFB1 is considered a most powerful hepatocarcinogen, teratogen and mutagen [9], subsequently, recorded as a group I cancer-causing agent by the International Agency for Research on Cancer [10]. According to the Food and Agriculture Organization (FAO), up to 25% of the world's food crops are significantly contaminated with mycotoxins [11]. It is that 4.5 billion people living in developing countries are chronically exposed to the uncontrolled number of aflatoxins [12]. After the disclosure of aflatoxins, scientists recommended that its buildup could happen in milk and other animal products from the animals that have ingested tainted feedstuff [13]. It is viewed as that the cancer-causing strength of AFM1 is around 2-10% to AFB1 [14]. The mycotoxin contamination of milk and dairy products can happen by aberrant pollution while lactating animals ingest AFB1 tainted feed which will pass to the milk as AFM1, and furthermore by direct pollution when molds can grow in milk (impossible) or on dairy products as deliberate added substances or unintentional defilement. In this way, milk and dairy products are especially susceptible to contamination by AFM1 and are considered to represent specific risks to human health. Accordingly, milk has the best exhibited potential for

the presentation of aflatoxin buildups in the human eating diet [15]. AFM1 can cause serious human illness, particularly primary liver cancer, DNA damage and intense poisonousness and cancer-causing nature contrasted with the parent particle AFB1, AFM1 openness to kids particularly babies, is of specific worry, as they have possibly higher weakness and responsiveness than grown-ups and their ability for biotransformation of cancer-causing agents is more slow than grown-ups [16]. A few researchers led on the event of AFM1 in milk however right now need to zero in on the improvement of an effective and delicate technique for the assurance of AFM1 in milk and milk products. Different physical, chemical and biological techniques are utilized for the inactivation and alleviation of AFB1 and AFM1 from milk and milk products [17]. The significant target of this review paper is to review and survey the impacts of aflatoxin in milk and milk products of dairy cows to talk about the reasons for aflatoxin in milk and milk products, to figure out the effects of aflatoxin in milk and milk products on animal and human health.

Indirect Contamination

The presence of mycotoxins in milk and milk products results essentially because of circuitous pollution and once in a while direct contamination. The dairy animal seating feeds or fodder contaminated with AFB1 discharge AFM1 in their milk [8]. *Aspergillus flavus* and *A. parasiticus* are pervasive organisms, have a liking for oily seeds as a development source e.g. peanut meal, maize and cottonseed meal. These funguses colonize the plants or yields in fields of tropical and subtropical environment regions yet they can likewise colonize products in post-collect handling and stockpiling. Aflatoxin creation happens at temperature between 20°C to 30°C and this higher breaking point is additionally the ideal one for aflatoxin production in the feeds of dairy animals. *Aspergillus parasiticus* prefers a soil environment climate and is more normal on peanuts while *A. flavus* is adjusted to an aeronautical climate is more tracked down on dry natural product, cotton and corn. Aflatoxin production unequivocally relates to the moisture content of feeds and ecological condition especially temperature and water pressure. The Cropping frameworks assumes a significant part in aflatoxin production e.g., monoculture and the work of half breeds that are unacceptable for the development region, with a low protection from insect attack, ideal elements for aflatoxin production. The Elements that are complement of water pressure, as unsatisfactory cultivating thickness and timing, sandy soil, deficient pest control and over the top nitrogenous fertilization, increment aflatoxin gathering in the plants. Gathering time and states of drying and stockpiling can assume a similarly significant part in aflatoxin production. A drying interaction is more vital to control contagious movement during capacity feed ought to be safeguarded with the moisture of 13% or less. It is crucial to keep a low and uniform grain moisture level since sporadic moisture of the mass, emphasized with a combination of various parts, favors contagious improvement in the mass [26]. In any case, weather conditions changes in the previous ten years could represent a justification behind AF-related issues on the world regions with temperate environments [18].

Direct Contamination

Direct pollution of dairy products with mycotoxins results because of contagious development utilized for aging or unexpected parasitic development. Molds that are purposefully developed on cheese are cheese starter cultures, for example, *Penicillium* sp. on French Roquefort and Camembert cheeses; under specific circumstances (defilement of starter cultures with toxigenic strains or ecological tainting) these growths can create mycotoxins. One more conceivable pollution of dairy products is the inadvertent event of mould on products, albeit great assembling practices will frequently keep dairy items from getting sullied [19].

Toxicity of AFM1

AFM1 can cause intense and chronic the two kinds of poisonousness, by direct ingestion of tainted milk or dairy products and AFB1 digestion in the liver [20]. Late reports featured the event of AFM1 in plants, produced by *Aspergillus spp.* through an alternate biosynthetic example not including AFB1, or potentially by insect pest's digestion from AFB1 [21, 22]. In people, exposure to AFM1 happens principally through the utilization of milk [23]. Intense hepatotoxicity of AFM1 was at first seen in ducklings fed with AFM1-polluted milk [24]. From that point forward, concentrates on in various animal species affirmed the hepatotoxicity of AFM1 and its cancer-causing impact, despite the fact that lower by around one significant degree when contrasted with AFB1 [23].

There is proof found for an in-vivo cancer-causing impact of AFM1 and AFB1 in rat models and in-vitro in murine and human liver microsomes [25]. The restricted capacity to use AFM1 into the DNA-receptive epoxide may in this way represent the decreased degree of DNA damage and pre-neoplastic lesions when contrasted with AFB1. The mutagenic impacts of AFM1 found during in-vitro examinations on *Salmonella typhimurium* strains [26], a comparative genotoxic impact saw in *Drosophila melanogaster* with AFB1 in-vivo investigations, which show the conceivable unfriendly impacts in mammalian cells in vivo [27]. At first, AFM1 was ordered as a group 2B human carcinogen by IARC [28]. Further research and review permit us to rename of AFM1 as a group 1 human cancer-causing agent [10]. AFB1 should be changed over into its responsive epoxide to tie protein and apply acute harmful impacts, yet this interaction doesn't appear to be essential to the cytotoxicity of AFM1. AFM1 direct cytotoxicity was revealed in refined human digestive enterocytes-Caco-2 and cytotoxicity brings about intracellular reactive oxygen species (ROS) generation [29]. AFM1 might cross the placental obstruction from the pregnant mother and accordingly influence the baby by presenting the infant to aflatoxin risk. The presence of aflatoxins in human cord sera found at birth and in serum obtained immediately after birth from the mother [30], uncovers the exchange of aflatoxin by the fetoplacental route, which might be of biological importance. The presence of AFM1 in milk and milk product is an overall worry for people as even modest quantities of AFM1 are significant for shoppers, particularly kids who are generally susceptible to the unfriendly impacts of aflatoxins [30]. The small kids who are weaned on cow's milk at an early

age; utilization of milk tainted with AFM1 might decrease the improvement of their immune capability and make them more susceptible to different diseases [25].

Satisfactory Limits of Aflatoxin in Milk and Milk Products

At present, the acceptable degrees of aflatoxins in milk and milk-based products are different based with respect to different variables. Reasons like the economic status of the nations and meteorological circumstances are the most impacting factors in allowing levels of aflatoxin [31]. A few countries are confirmed and set satisfactory degrees of aflatoxins in milk and milk products to diminish and control destructive properties of the aflatoxin. For example, in the US, Food and Drug Organization (FDA) has permitted a general amount of 0.5 g/kg or 50 ng/l in milk and 20 ng/g in dairy cows feed [32]. In Europe, the acceptable amount is 0.005 mg/kg AFM1 in milk foodstuffs of dairy cows provided for small kids [33]. Also, the decided degrees of AFM1 in milk and milk-based have been set in various parts of the world as in Table 1, 2 and 3.

Table-1 presence of AFM1 in raw and processed animal milk samples in Europe [33]

| Country | Quantity | Food |
|------------|------------------------|-----------------|
| Brazil | 150–1020 ng/kg [34] | UHT milk |
| Chile | 0.015 µg/kg [35] | Raw milk |
| Costa Rica | 0.042–154 ng/mL [36] | Raw milk |
| Ecuador | 0.023–0.751 µg/kg [37] | Raw milk |
| Italy | 0.009–0.015 µg/kg [38] | Raw milk |
| Mexico | 0.021–18.5 µg/kg [39] | Raw milk |
| Spain | 0.05–0.50 µg/L [40] | Commercial milk |

Table-2 presence of AFM1 in raw and processed animal milk samples in Asia [33]

| Country | Quantity | Food |
|------------|------------------------|------------------|
| Bangladesh | 22.79–1489.28 ng/kg | Raw milk |
| | 18.11–672.18 ng/kg | Pasteurized milk |
| | 25.07–48.95 ng/kg [41] | UHT milk |
| China | 0.022–0.049 µg/kg [42] | Raw milk |
| India | 0.013–0.396 µg/L [43] | Raw milk |
| Iran | 0.005–0.098 µg/kg | UHT milk |
| | 0.005–0.120 µg/kg [44] | Pasteurized milk |
| Pakistan | 0.187–0.346 µg/L [45] | Raw milk |
| | | Processed milk |

Table-3 presence of AFM1 in raw and processed animal milk samples in Africa [33]

| Country | Quantity | Food |
|----------|------------------------|-----------------|
| Algeria | 95.59–557.22 ng/L [46] | Raw milk |
| Congo | 4.8–26.11 ng/kg [47] | Raw milk |
| Egypt | 0.18–0.41 µg/L [48] | Raw milk |
| Ethiopia | 0.031–5.16 µg/L [49] | Raw milk |
| Kenya | 290.3–500 ng/kg [50] | Commercial milk |
| Malawi | 0.42–1.02 µg/L [51] | Raw milk |
| Sudan | 0.05–0.1 µg/kg [52] | Raw milk |

Negative Impacts of Aflatoxin on Animals Farm Health

In dairy animals, the destructiveness of aflatoxins has an intense and persistent syndrome; likewise, it shows generally dissimilar properties in various individual animals in light of weakness to aflatoxins. Impacts of aflatoxins on animal health rely upon age, species, sustenance, and sex as well as resistance status. In animals, intense poison levels are brought about by taking care of the unnecessary sum aflatoxins, while the persistent poison levels are started by ingesting of less amount, this sort of aflatoxicosis is the justification for liver weakness by disease, GIT injury, decrease in craving for food, rate of reproduction, development, production and body weight [53]. As Denli & Perez, [54] announced clinical indications of intense aflatoxicosis include anorexia, discouragement, ailment, deficiency of weight, bleeding from GIT, liver harm and aspiratory oedema. Too diminished feed consumption, milk production and development rate are the essential side effect of chronic aflatoxin exterminating. Besides, a lactating cow don't open to aflatoxin contaminated feeds since it decays the element of milk and milk-based products and even can cause the death of lactating dairy cow might follow within 60 minutes/days mainly in acute aflatoxin toxicity [53, 54, 55].

Negative Effects of Aflatoxin on Human Health

The Presence of Mycotoxins especially AFM1 in milk and dairy items can make serious medical issues in people. As International Agency for Research on Cancer order, AFB1 and AFM1 are named class 1 and 2B are potential cuts loose for human cancer-causing agents, correspondingly [56]. Thusly, as dairy products are broadly consumed off by youngsters and babies as well as grown-ups, the event of aflatoxins in milk and milk products their significant passageways in milk based foodstuffs has a serious experiencing on human prosperity. For the most part, the significant impacts of aflatoxin on human health are remembers its belongings for the nervous system (abnormal behaviour and depression), decreased sperm count and increment infertility, low birth weight and diminished rate of development in babies and youngsters. Utilization of con ended milk with AFM1 especially by adolescents pulverize their illness obstruction system and sponsors unfortunate development in light of the fact that in many countries young people are not drunk cow's milk thus their resistance is less capable at their baby stage [57]. Besides, as per WHO, [4] revealed, potentially aflatoxin is responsible and assume part in up to 30% of the instances of liver disease globally consistently. Along these lines, as people are impacted by aflatoxins, liver cancer growth is continued as well as showing jaundice eye sclera.

Control and Prevention Strategies for Aflatoxin Impacts

To limit chances related with undeniable exposure to aflatoxins, guideline and observing measures should be upheld by in-field (pre-harvest) and capacity (post-collect) mediations which might be applied to limit aflatoxin defilement. AFM1 is discharged in milk of dairy cows

following ingestion and digestion of AFB1 tainted feed. Pollution of milk may, subsequently, be diminished either straightforwardly, by diminishing AFB1 content of defiled milk, or by implication, by diminishing AFB1 tainting in feed of dairy cows [25]. As mentioned by Yousof and Zubeir [52] in case of reducing AFB1 to level zero the milk could promote it as organic food.

Indirect Techniques for Aflatoxin Decrease in Animals Feed

Thus, indirect controlling of dairy cows feed cleanliness is the potential in diminishing aflatoxin tainting [58, 59]. Stringently diminishing method for aflatoxin defilement over crop production, conventional and modern capacity of animals feed as well as animals feed industrial facilities are mandatory to accomplish the goal, worth and prosperity concerns [59]. Moreover, compelling approaches to diminishing the tainting can be acquired through legitimate putting away of yields which embraces keeping crops on dry and clean sides, keeping crops from wetness, high temperature, irritations and practice of fungicidal medications [60]. Extra central method of administrative and diminishing aflatoxin contamination is severe perception of sterile circumstances in regular and present day levels processing plants and animals feed storerooms [59]. Checking development of organism and arrangement of aflatoxin in old-style ranches and stockpiles are very basic [58, 61]. Level aflatoxin in milk can likewise be impacted via occasional circumstance, for example occasions of aflatoxin is more noteworthy in winter and autumn contrasted with summer and spring because of unavailability of new feeds and ranchers utilize ware housed scrounges in this negative season [33, 62]. Thus, it is key to progress inappropriate storeroom and moisture states of domesticated animals feed storage.

To accomplish successful avoidance and control of aflatoxins, it is necessary to industriously notice assorted procedures of production and capacity condition, controlling moisture content and changing intensity through ventilation strategies, and utilizing uncontaminated materials to preparing animals feed [63]. To keep away from mould improvement and repress development of the molds in the early occurrences of tainting, organisms, chemicals, ionizing rays, and permeable material can be utilized [64]. According to Dakovic *et al.* [65] indication, extraordinary methodology of diminishing aflatoxin pollution in contaminated animal feed is utilizing aflatoxin absorbents. Throughout utilizing absorbents, aflatoxin existing in animal feed forestalls poisonous responses in animal's body as well as from retention into gastrointestinal system by restricting to absorbents Huwig *et al.* [66]. Moreover, counteraction of aflatoxins by substance compounds includes a progression of organic acids like ascorbic, propionic, acetic acid, and benzoic, organic acid salts, for example, potassium sorbate, calcium propionate, fluid or solid copper sulfate as well as different microorganisms, for example, *Lactobacillus brevis* and *Lactobacillus pentose's* is an elective way to deal with diminishing aflatoxin in animals feed [67].

Direct Techniques for Aflatoxin Decrease in Milk

Utilization of aflatoxins in dirtied feed for dairy cattle commonly prompts the production of debased milk with aflatoxins. The utilization of natural techniques, chemical and polluted absorbents are likewise useful for direct decrease of aflatoxin in milk and its product. Using of toxin absorbents is one of the chief direct methods of decreasing the amount of aflatoxin in milk as absorbent topsoil such as vermiculite; bentonite, active carbon and hydrated sodium calcium aluminosilicate (HSCAS) have been recognized as absorbent complexes for captivating different contaminants in aqueous atmospheres [30]. Also, hydrogen peroxide is the best chemical compound for decreasing aflatoxin and can be utilized for putting away milk based foodstuffs [69]. Use of joined chemicals substances, for example, lactoperoxidase, riboflavin and hydrogen peroxide notwithstanding heat treatment is smarter to accomplish adequate results in lessening aflatoxin in milk. Also, the use of potassium sulfite for neutralizing AFM1 in milk is well known [68, 69]. Organic method for lessening aflatoxin is simplest and modest methodology thus it is interesting than other strategy. At present, different examinations are being led on detecting active microorganisms [68]. For example, a few authors have demonstrated in their exploration that Gram- negative bacterium which is known as *Flavobacterium aurantiacum*, has been utilized for diminishing production of aflatoxin in milk. This organism has exceptional ability to convert poisonous elements of aflatoxin that exist in milk to innocuous components [67].

Conclusion

Aflatoxin is one of the fundamental persistent normally happening chemical compounds (Mycotoxins) which are gathered under the likely substance dangers for the both animals and human. Regularly are two ways of pollution of milk and milk based foodstuffs by aflatoxin. Both direct contamination of milk and milk products by mould, or indirectly way poisons pass to milk with ingestion of feeds dirtied with Aflatoxin. Aflatoxin M1 is asserted to be a justification for positive sterilization worries in milk and milk based foodstuffs of dairy cows. Presence of AFM1 in human milk is of extraordinary worry as it can cause serious dangers to mother, fetus and baby also. To forestall a general wellbeing risk, ordinary occasional overview of milk is an unquestionable a must. Additionally, scientific proof is likewise expected for the unsafe impacts coming about because of ongoing exposure to low degrees of AFM1. Good agricultural practices, different heat treatment and dietary intercessions by aflatoxin covers, can decrease however not totally wipe out the pollution of milk with AFM1. These sterilization strategies can be executed as a part of counteraction and control of food sanitation and quality confirmation to decrease the public health hazards, be that as it may, further research ought to be led for improvement of successful disinfecting processes.

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