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Review on Public Health Effects of Aflatoxins in Milk and Milk-Based Foodstuffs of Dairy Cow

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Abstract

Aflatoxins are toxigenic metabolites that are definitely occurring by lethal strains of Aspergillus parasiticus and Aspergillus flavus that commonly dwell and colonize in feed components and various nutritive foodstuffs particularly milk and milk based products. This Review has three main objectives; those are causes of aflatoxin, effects and methods of control in milk and milk products. Drinking of cow milk polluted with aflatoxin may overwhelm immunity and subsidize to stunting in young children, as the young children are not immune-competent during early stage. It has been internationally assessed that aflatoxin is possibly accountable for 30% of the annual cases of liver cancer. Generally, control approaches of aflatoxin can be applied during pre-harvest, cautious management in the time of harvest and postharvest decontamination. Moreover, choosing breed for aflatoxin impervious crop diversities, prevention of aflatoxin production through biological decontamination by microorganisms and their metabolites, rejection of aflatoxin by physical means in addition to inactivation by chemicals are the typical approaches that have been described in different studies. For the reason that cow milk is the most important and principal diet of children, but the risk of exposed to the cancer are more in infants. In addition, according to various investigations it also well thought that young animals are also found to be more vulnerable to aflatoxin than adults. Thus; the contamination of cow milk and milk products by AFM1 should understood as undesirable for young human and animals.

Introduction

Dairy cattle provides valuable source of nutritious food for human particularly as a means of

milk and milk products and they play an important role in supplying human nutrition throughout the world [1] Moreover, they are providing important sources of nutritious diets such as protein, calcium, phosphorus, iodine, riboflavin and vitamins A and B_{12} constituents[2]. However, the quality of dairy products is critical to the dairy industry and the consumers because of the milk production chain particularly in the most developing regions still faces many challenges related to the dairy products quality and safety to meet legislations and the needs of consumers [3].

Besides, food safety and quality control packages for all food substances enclosing animal products are raising issue in several countries predominantly from public health perspective [4]. This incorporates controlling adulterants, obliterating intensities of contaminants, naturally occurring toxins and other constituent that may be able to cause food illness in human. In the direction of sustaining public health and providing safe food for the consumer, milk and milk products need proper and aseptic environments. Producing milk products that are free of contaminants are obligatory for public health safety and satisfactory shelf of the products [3]. Currently, any foodstuff specially milk products that having proper hygiene and reliable quality standards are in the high level of preferences for the consumers. Commonly, health hazards to the consumer relating to dairy products are mostly clustered into chemical, physical and microbiological hazards [5].

From chemical hazards, Aflatoxin is one of the main chronic naturally occurred toxins chemical compounds (Mycotoxins) which are grouped under the potential chemical hazards for both animals and human [6]. According to WHO, [7] stated typically toxic metabolites of fungi pollute food and feedstuff and cause of food-borne illnesses which categorized under chemical hazards. In dairy products among the chemical hazards, Aflatoxin is one of most important frequently exhibited in milk and milk products [1, 8]. They are belongs to the class of mycotoxins and fungal metabolites that are normally formed by Aspergillus species, specifically A. bombycis, A. parasiticus, A. fumigitus A. flavus, A. ochraceoroseus, A. pseudotamari and A. nomius [9]. Among all species A. parasiticus and A. flavus are the most significant moulds in economy of milk and milk products producers because of that it creates entirely aflatoxin G1, G2, B1 and B2 [10].

Morever, Aflatoxins are also can be formed in food and feed resources at low level by Aspergillus *nomius* and *A. tamari* in addition to further developing fungal species [11]. The common Aflatoxins producing fungal spp. *A. parasiticus and A. flavus* is predominantly polluted cereals crop such as peanuts and maize including their by-products and animal feeds [12]. In general, storage problem is the major route for the contamination any food and feed resources by *Aspergillus,* particularly in the period of reductions of soil moisture content and drought stress session [13]

Generally, the framework of ensuring food safety and security has been a most important emphasis of national and international action over the world in the previous centuries [10, 14]. This being the case, the major objective of this review paper is to review the effects of aflatoxin in milk and milk products of dairy cattle with the following specific objectives; to discuss the causes of aflatoxin in milk and milk products, to highlight effects of aflatoxin in milk and milk products on animal and human health and finally to disclose means of controlling the effect of aflatoxin in milk and milk products.

Literature Review

The Main Aflatoxin in Milk and Milk-Based Foodstuffs of Dairy Cattle

Aflatoxins are toxigenic metabolites that are certainly happening by lethal strains of Aspergillus parasiticus and A. flavus that frequently dwell and colonize feed components and various nutritive foodstuffs in addition to principal crops such as corn, groundnuts, rice and maize [15,16]. The four major naturally produced aflatoxins in milk foodstuffs of dairy animals are known as G1, G2, B1 and B2 [10]. Where letter “B” talk about the blue fluorescent color whereas “G” substituted for green fluorescent that are formed on thin layer chromatography

plates in Ultraviolet light, though the subscript numbers 1 & 2 specify main and small mixtures [10, 16]. The occurrence of aflatoxin B1 (AFB1) in milk is usually after ingested, then secrete enzyme and hydroxylated in order to form aflatoxin M1 (AFM1) that is secreted and concealed in the milk and its product [17, 18]. According to International Agency for Research on Cancer WHO, [19] aflatoxin B1 and aflatoxin M1 are categorized in type I cancer-causing agent. However, among both Aflatoxins (AFM1 and AFB1), aflatoxin B1 is the most serious one, since it is extremely oncogenic and producing liver cancer in humans in addition to its establishing power in most foods and feeds [20]. Probably this indicates that different dairy foodstuffs may enclose contaminants that pose hazard to public health, predominantly for youngsters who devour the dairy products [16] Moreover, immunosuppression and growth impairment can be caused in both animals and humans through frequent acquaintance of aflatoxin [18, 21].

Causes of Aflatoxin in Milk and Milk-Based Foodstuffs

Aflatoxins are mainly caused by mycotoxins that introduced in milk and milk-based foodstuffs. The aflatoxin B1 is naturally occurring in feed by means of various metabolites including AFM1 that are hydroxylated copies of AFB1, through bio-transformation in mammary glands excreted in milk, which is causative agent for liver cancer [6]. The principal sources of alfatoxin for cattle and human are frequent exposure and consumption of groundnuts and maize due to greater susceptibility and high degree of contamination of both feedstuffs for aflatoxin throughout the world [22]. Also, Wu and Khlangwiset, [10] suggested that peanuts and Maize are the chief sources of dairy animal and human acquaintance to aflatoxin. For the reason that, existences of aflatoxin contaminated animal feeds can biologically be produces aflatoxin in milk. So this phenomenon is the most worrying delinquent through time in all over the world, as the most important cow milk is principally precious while feeding are contaminated everywhere in the world [23]. As Nyaga, [24] reported, milk is highly contaminated with aflatoxins in and around Addis Ababa milk shed. Moreover, totally dairy cow feeds exceeded 5 mg/kg of AFB1 can be produce the over conventional standard perimeter of 0.05 mg/L aflatoxins in the milk. The result as well indicates that the major sources of aflatoxin in and around peri-urban areas of Addis Ababa dairy value chain is pollution of noug cake that is extensively used as dairy cattle feed AFB1.

Aflatoxins in Food Products From Contaminated Animal Feed

According to Elzupir & Elhussein, [25] investigation of different feeds shown that brewer's waterless yeast, wheat bran and maize grain had comparatively low levels of aflatoxin contamination, however noug cakes maize and groundnuts are extremely contaminated with aflatoxin B1. Besides, dairy cows that have consumed aflatoxin B_1 contaminated feed are secreted aflatoxin M_1 in the milk [26]. There was adequate and necessary association among AFB1 and AFM1, as presence of enormous amount of AFB1 in feed results in high contamination of milk by AFM1. After ingesting of AFB1 contaminated feeds, AFM1 is excreted within twelve hours of consumption [27]. Additionally as Dawit et al. [28] founds, there was a reasonable link between level of AFB1contamination in feed ingested by animal and aflatoxin M_1 in milk. As authors found transference of aflatoxin from animal feeds to milk and milk products are within an average of approximately 1%.

Aflatoxins in Milk Based Foodstuffs from Contaminated Dairy Cow

Mycotoxin M1 and M2 is derivative of milk aflatoxins, that are heat impervious and hydroxylated metabolites created by lactating cow that were consuming feeds contaminated by aflatoxin [26, 29]. As various authors indicated, the consumed AFB1 is metabolized into AFM1 while AFB2 is metabolized into AFM2 in dairy cattle, with assessed transformation percentage of 1-3 among AFB1 and AFM1 [30].

Moreover, the most important metabolite that excreted by various animals in milk is aflatoxin M1 [26]. AFM1 is formed through bioconversion in mammary

glands of dairy cattle by oxidative reactions catalyzed in liver CYP enzyme mechanism, which is principal to hydroxylation in the terminal furan ring of the parental molecule AFM1 represents the 95% of AFs detected in milk. Other metabolites, such as Q1 (AFQ1), aflatoxicol (AFL), M2 (AFM2), and M4 (AFM4) are distinguished in small quantities and then deliberated of less importance for human wellbeing.

Occurrences and Effects of Aflatoxin in Milk and its By-Products

Aflatoxin has critically various occurrences degree, effects, concentration and character depends on prevalent substrate, nature of mould and weather conditions [10, 26]. Aspergillus parasiticus formulate whole aflatoxin type (AFG1, AFG2, AFB1 and AFB2) on corn whereas A. flavus produces primarily aflatoxin B1and B2 on corn. Among the feed used for milk production there are three main feedstuffs; peanuts, cottonseed and corn have great character to be attacked by Aspergillus species throughout growing, yield and loading or storing [10]. Generally, colonization arises and assisted through storage especially in the case of small grains and soybean. The formation of Aflatoxin can be promoted by high moisture content, poor storage surroundings, kernel damage, temperature, nonexistence of ventilation [31]. Moreover as the production of milk and milk based foodstuffs needs various processes, the impacts of handling and storage process has great potential on the dissemination and stability of Alfatoxin M1. Due to that relatively the occurrence of Alfatoxin in milk is higher when comparing with occurrence of Alfatoxin in the other milk products such as cheese, yogurt, butter, butter milk, cream, and skim milk because of some mechanical, chemical and biological processes are performed depending on the types of the products [32].

As many authors suggested incidence of aflatoxin in cheese may due to several potential reasons. The primary reason for occurrence AFM1 in the raw milk is the import of leftover of AFB1 from polluted feeds of animal to milk. The second one is production of AFB1, AFB2, AFG1, and AFG2 by molds that propagate on cheese although the minute amount of CHO does not create suitable environment and substrate. The 3rd one is the consumptions cheese made from milk powder contaminated with aflatoxin M_1. However, several authors reported that increases in AFM1 concentration in cheese as a function of cheese variety machineries to be recycled to process it, and the quantity of water removed in the course of manufacture [17]. As Barbiroli et al. [33] stated, particular influences can be occurred by high temperature, renneting, pH, and duration of pressing can exaggerated the volume of water removed and increase the amount of AFM1 in the cheese.

Effects of Aflatoxin

Aflatoxicosis is illness initiated by the feeding of the metabolites of mold (aflatoxins) that formed by certain species of Aspergillus parasitisus and Aspergillus flavus. Among all aflatoxin, AFB1 is a strong cancer mediator through raising the actual protein necessity of dairy cow.

Aflatoxin Effects on Animal Health

In dairy animals, the harmfulness aflatoxins have an acute and chronic syndrome; also it shows relatively disparate properties on different individual animals based on vulnerability to aflatoxins. Effects aflatoxins on animal health are depend on age, species, nutrition, and sex as well as immunity status. In animals, acute toxicities caused by feeding of excessive amount of aflatoxins, whereas the chronic toxicities are initiated by ingesting of less quantity, this type of aflatoxicosis are the reason for liver impairment by cancer, GIT injury, reduction in desire for food, rate of reproduction, growth, production and body weight [18]. As Denli & Pérez, [34] reported clinical signs of acute aflatoxicosis involves anorexia, depression, malady, loss of weight, bleeding from GIT, liver damage and pulmonary edema. As well decreased feed intake, milk production and growth rate are the principal symptom of chronic aflatoxin exterminating. Furthermore, lactating cow do not exposed to alfatoxin polluted feeds since it deteriorate the feature of milk and milk based products and even can cause death of lactating dairy cow may follow within 60 minutes/days mainly in acute aflatoxin toxicity [16, 18, 34].

Figure 1. Contaminated maize with aflatoxin

Table 1. Association among high level AFM1 in milk and level of AFB in feed composed from the dairy farm of some towns of Ethiopia.

Municipality	**Feed samples used for milk production**	**AFB (mg/kg)**	**AFM (mg/L)**
Addis Ababa	Mixture of noug seed cake, wheat bran and sweet pea hull	72	2.92
Debre Zeit	Mixture of noug seed cake and wheat bran	405	4.98
	Mixture of sweet pea grain and maize	30	
	Mixture of noug seed cake, wheat bran and maize grain	274	2.16
Sendafa	Mixture of sweet pea hull and wheat bran	14	2.93
Sululta	Mixture of noug seed cake, heat bran and maize grain	300	4.79
	Mixture of calcium, noug seed cake, wheat bran and maize grain	17	1.23

Sources: Dawit et al. [28]

Aflatoxin Effect on Human Health

Presence Mycotoxins particularly AFM1 in milk and dairy products can create severe health problems on human. As International Agency for Research on Cancer classification, AFB1 and AFM1 are classified as class 1 and 2B are possible carouses for human carcinogens, correspondingly [19]. Consequently, as dairy products are extensively consumed by children and infants as well as adults, the occurrence of aflatoxins in in milk and milk products particularly their substantial entrances in milk based foodstuffs has a severe suffering on human wellbeing.

Generally the major effects of aflatoxin on human health are includes affects the nervous system (abnormal behavior and depression), reduced sperm count and increase infertility, low birth weight and reduces the rate of growth in infants and children. Consumption of con taminated milk with AFM1 particularly by the youngsters devastate their disease resistance mechanism and subsidize to poor growth because of in most countries youngsters are not consumed cow's milk and so there immunity is less competent at their infant stage [22]. Moreover, according to WHO, [7] reported, possibly aflatoxin is accountable and play role in up to 30% of the cases of liver cancer internationally in every year. Subsequently as human affected by aflatoxins, liver cancer is followed in addition to manifesting of jaundice eye sclera (figure 2).

Acceptable Levels of Aflatoxin in Milk and Milk Products

Currently, the acceptable levels of aflatoxins in milk and milk based products are different based on various factors. Reasons like economic status of the countries and meteorological situations are the most influencing factors in permitting levels of aflatoxin [32]. Several countries are certified and set the acceptable levels of aflatoxins in milk and milk products to reduce and control harmful properties of the aflatoxin. For instance in US, Food and Drug Administration (FDA) has allowed overall quantity of 0 .5 g/kg or 50 ng/l in milk and 20 ng/g in dairy cattle feed [35]. In Europe, the acceptable amount is 0.005 mg/kg AFM1 in milk foodstuffs of dairy cattle provided for young children [36]. Moreover, the determined levels of AFM1 in milk and milk based products in different regions of the world are demonstrated in (table 2)

Economic Impacts of Aflatoxin

Food safety problems generate massive problem on the country's budget such as expenditures to outbreak surveys and food recalls, national supervisions from enlarged therapeutic payments, absenteeism from work and school due to food born disease, loss of consumer confidence in the foodstuffs, improved burdens on previously imposed and unwell subsidized healthcare structures [37].

Moreover along with economic loss and financial expenditures to public health, farmer and livestock husbandry manufacturing, fatalities attributable to aflatoxin pollution of foods involves expenditures to treatment of food intoxication and medication cost. As per Boutrif [37] reports, yearly, around 20% of the foods manufactured in the world are infected by mycotoxins; of which aflatoxins have a superior portion compared to others. Occurrence of dairy cattle infection and cancer, decrease in milk production and productivity as well as declining of immune system in dairy cows are particular illustrations of charges to milk based foodstuffs as well as dairy cattle production. Bearing in mind such like enormous economic damages and public health safety, inhibition and frustration of the aflatoxin in food products of animal origin and dairy cow feed is critical [38].

Control and Prevention Methods of Aflatoxin Effects

Aflatoxicosis or contamination of milk based products by aflatoxin can only be prevented by feeding aflatoxin free rations to dairy animal which can be enhanced through preventing fungal growth in feed and good agricultural practice in dairy production farm and processing scheme. So preventing contamination of aflatoxin needs continues plus systematic scrutiny and analysis platform [39].

Generally, to reduce the threat of animal and human exposure to aflatoxins requires multidisciplinary

Figure 2. Jaundiced eye sclera of human (source: Gong et al. [22

Table 2. Maximum standard levels of aflatoxin M1 in milk and milk based foodstuffs in different countries

Country	**Acceptable Level (ng/l)**	**Variety of products**
Australia	20	Milk
European Union	50	Milk
Germany	50	Milk
Sweden	50	Liquid milk products
USA	50	Milk
France	30	Youngsters' milk< 3 years
	50	Adult's milk
Turkey	50	Milk and milk products
	250	Cheese
Switzerland	50	Milk and milk products
	250	Cheese

Source: [16].

and universal methodology due to the complex nature of aflatoxin contamination ways of milk and milk products. For that reason, it requires increasing of public perception on aflatoxins and applying scrutiny provision beside the whole dairy products. Commonly, elimination of aflatoxin requires both direct and indirect reduction approaches of aflatoxin in milk and dairy cow feed [36].

Indirect Methods of Aflatoxin Reduction in Livestock Feed

Using of aflatoxins polluted feed for dairy cattle are typically leads to the production of contaminated milk with aflatoxins. Hence, indirect controlling of dairy cattle feed hygiene is potential in decreasing aflatoxin contamination [39, 40]. Strictly decreasing means of aflatoxin contamination in the course of crop production, traditional and industrial storage of livestock feed as well as livestock feed factories are obligatory to attain the objective, value and wellbeing concerns [40]. Furthermore, effective ways of decreasing the contamination can be gained through proper storing of crops which embraces keeping crops on dry and clean sides, keeping crops from wetness, high temperature, pests and practice of fungicidal drugs [10]. Additional central way of regulatory and decreasing aflatoxin pollution is strict observation of hygienic conditions in conventional and modern levels factories and livestock feed storerooms [40]. Monitoring growth of fungus and formation of aflatoxin in old-style farms and storages are extremely imperative [38, 39]. Level aflatoxin in milk can also be influenced by seasonal situation, for instance occurrences of aflatoxin is greater in winter and autumn compared to summer and spring due to inaccessibility of fresh feeds and farmers use warehoused forages in this unfavorable time of year [31, 36]. So, it is indispensable to advance improper storeroom and moisture conditions of livestock feed storage.

To achieve effective prevention and control of aflatoxins, persistent and vigilant observation of diverse techniques of production and storage condition, controlling moisture content and adjustment of heat through ventilation methods, use of uncontaminated materials aided for preparing livestock feed are compulsory [41]. In order to avoid mold development and inhibit growth of the molds in the early occurrences of contamination, microbes, chemicals, ionizing rays and absorbent material can be used [42]. According to Dakovic´ et al. [43] indication, outstanding approach of decreasing aflatoxin contamination in infected animal feed is using of aflatoxin absorbents. In the course of using absorbents, aflatoxins existing in animal feed prevents from toxic reactions in livestock body as well as from absorption into digestive tract by binding to absorbents Huwig et al. [44].

In addition, prevention of aflatoxins by chemical compounds involves series organic acids like sorbic, propionic, acetic acids and benzoic, organic acid slats such as potassium sorbate, calcium propionate, liquid or solid copper sulfate as well as diverse microbes such as lactobacillus brevis and lactobacillus pentose's is alternative approach of decreasing aflatoxin in animals feed [45].

Direct Methods of Aflatoxin Reduction in Milk

The use of biological methods, chemical and contaminant absorbents are also helpful for direct reduction of aflatoxin in milk and its product [46]. Using of toxin absorbents is one of the chief direct methods of decreasing amount of aflatoxin in milk as absorbent top soil 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 [17].

Besides, hydrogen peroxide is the most effective chemical compounds reduced aflatoxin and used for storing of milk based foodstuffs [47]. Application of combined chemicals such as lactoperoxidase, riboflavin and hydrogen peroxide in addition to heat treatment is better to attain sufficient outcomes in reducing aflatoxin in milk. Also, use of potassium sulfite for neutralizing AFM1 in milk is well known [46, 47].

Biological means of reducing aflatoxin is easiest and cheap approach and so it is interesting than other method. Currently, various investigations are conducted on detecting active microbes [46]. For instance, as Line et

al., [48] indicated in their research, gram negative bacterium which is known as Flavobacterium aurantiacum, has been used for decreasing production of aflatoxin in milk. This microbe has special ability, as it converts toxic ingredients of aflatoxin that exist in milk to harmless ingredients.

Conclusion and Recommendations

Aflatoxin is one of the main chronic naturally occurred toxin chemical compounds (Mycotoxins) which are grouped under the potential chemical hazards for both animals and human. Normally there are two ways of contamination of milk and milk based foodstuffs by aflatoxin. Both direct pollution of milk and its product with mold, or indirectly toxins pass to milk with ingestion of feeds polluted with Aflatoxin. Aflatoxin M1 is testified to be a reason for positive sanitation concerns in milk and milk based foodstuffs of dairy cattle. Aflatoxins are extremely toxic to dairy cattle and general community by causing serious impairments on human wellbeing and reducing production efficiency of cattle. Currently the incidence of AFM1in dairy cow milk and milk based products are extensive due to lack of proper controlled scheme in dairy value chain and due to inadequate efforts are made in maintaining squat amount of AFB1in the feeds of lactating cows. Many authors reported that, there is greater amount of AFM1 are appear in winter seasons than spring, the reason being in winter's typically lactating cows are feeding with multiple feeds and so absorption of AFB1 rises, which in turn amplifies the meditation of AFM1 in produced milk. This is due to temperature and moisture matters are undesirably affecting the occurrence of AFB1 in feeds. Food safety problems (particularly milk and milk products) produce a massive burden on the country's economy such as costs to administrations due to amplified medical costs, food recalls and outbreak examinations.

Depending on the above conclusion the next opinions are forwarded as recommendations:

Awareness creation for dairy farmers, dairy animal feed producers as well as for consumer are very important to minimize and eliminate effects of Aflatoxicosis.

It is essential to keep and adjust continuously presence of AFM1contamination in milk and milk products of dairy cattle industry by accurate and reliable systematic methods and checking regularly AFB1 contamination of dairy animal feeds.

Moisture content and storage conditions of dairy animals feed should be kept and regulated at its proper level.

Efforts should be made in attempt to provide further and wide scientific information on human health hazards related to low-level long term Aflatoxins exposure and to standardize the already existing regulatory limits for Aflatoxins.

Policymakers and developmental organizations should be disseminating evidence around virtuous pastoral and storing system as well as other conventional risk decrease actions.

Abbreviations

AFB1: Aflatoxin B1; AFB2: Aflatoxin B2; AFG1: Aflatoxin G1; AFG2: Aflatoxin G2; AFM1: Aflatoxin M1; EC: European Commission; EFSA: European Food Safety Authority; EFTA: European Free Trade Association; EU: European Union; FAO: Food And Agriculture Organization Of The United Nations; FAPAS: Food Analysis Performance Assessment Scheme; HSCAS: Hydrated Sodium Calcium Alumino Silicate; ILRI: International Livestock Research Institute; WHO: World Health Organization

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This review article doesn't included Animal or human investigation.

Conflicts of Interest

The authors declare that they have no conflict of interest regarding the publication of this paper

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Sadik Zakir was the principal Author, who directed and prepared the original review paper. Sufian Abdo and Mukarim Abdurahman were participated in preparation of the final version of the manuscript. Suresh Kumar participated as supervisor and assisted in preparing and proof reading of manuscript. All Authors have read and approved the final version of manuscript and agreeing for publication.

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