An overview of effective detoxification methods for aflatoxin-contaminated pistachio

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Abstract

Introduction: Aflatoxins are a group of fungal secondary metabolites generally produced by *Aspergillus flavus* and *A. Parasiticus.* The Aflatoxin contamination especially occurs during processing stages in dried fruits, after harvesting. Aflatoxin contamination of Iranian pistachios has caused an export reduction in the last years. Aflatoxins contribute to replacing thymidine with guanine at the codon 249 of *P53* (tumor suppressor gene) in the human genome; this mutation in the DNA could cause liver cancer.

Materials and Methods: Methods to manage the reduction of aflatoxin contamination has great importance; the most effective treatments, including chemical (ozone and citric acid) and physical (UV-C and gamma radiation), are reviewed in this paper

Results: In ozone (O3) treatments in which the sensitivity of aflatoxin B_1 and G_1 is more than aflatoxin B_2 and G_2, under UV-C radiation, the degradation of aflatoxin B_2 and G_2 to is higher than aflatoxin B_1 and G_1. Acidic and alkaline substances also are utilized to eliminate aflatoxins in some products.

Conclusion: Use of acids along with other detoxification methods such as ozone, UV- C radiation, and …, will be more effective to degrade aflatoxins in pistachio nuts.

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1. Introduction

Mycotoxins are natural toxins, caused by fungal activity on agricultural and food products that could make acute and chronic diseases in humans and animals. Aflatoxins (AFs) the secondary metabolite that generally produced by *Aspergillus flavus* and *A. parasiticus* are among the most well-known mycotoxins with carcinogenic, mutagenic, and teratogenic effect. AFs could contaminate most crops, such as cereal and nuts. The investigations on *A. flavus* and *A. parasiticus* have led to identifying an approximately 75 kb DNA cluster consisting of two specific transcriptional regulators (*aflR* and *aflS*) and at least 30 co-regulated downstream metabolic genes in the AFs biosynthetic pathway (Fig 1) [1- 4]. The maximum acceptable levels for AFB_1 and total AFs in pistachio nuts in Iran are 8 and 10 µg/kg, respectively [5]. Pistachio tree (*Pistacia vera* L.) is cultivated in many parts of the world under different climatic conditions, especially in subtropical and temperate regions due to its high nutrient kernels. Pistachio is one of the most important export products in Iran, and there are many reports about contamination of pistachio crops with AFs, as a major global problem, which has led to a decrease in the export value of this strategic product. Also, the consumption of contaminated pistachios is considered a significant mutagenic factor for humans; aflatoxin B_1 (AFB1) is the most toxic in connection with hepatocellular carcinoma (HCC) [6], this is partly due to the integration of AFB_1 and hepatitis B (HBV) [7]. The carcinogenicity of aflatoxin B is 30 times higher than in children with hepatitis B. The fungus spores can be found almost everywhere, and with minimal living conditions, they could germinate, grow, and be active [8]. This fungal growth and AFs production in nuts, especially pistachio, occurs at various stages, including pre-harvest, during harvest, post-harvest, and during processing stages in warehouses and shopping centers [9]. Thus far, 18 types of AFs have been found as the most important in terms of toxicity, some of which include AFB_1> AFG_1> AFB_2> AFG_2> AFM_1. At the end of AFB, the furan ring forms a penatne ring structure, and also the other ring is a hexagonal lactone at the end of AFG; these furan and lactone have an important role in determining the biological activity of the group of potent mycotoxins (Fig. 2), It has been found that AFB_1 by cytochrome P_{450} to 8, 9 epoxides B_1 these two factors resulted in a replacement of thymidine with guanine, and therefore, transforming AGG[1] to AGT[2] at codon 249 of the *P53* gene that is a tumor suppressor gene, causes a DNA mutation and result in cancer in the (Fig 3) [10]. Therefore, it is extremely significant for agricultural products to be free from fungal toxins. On the other hand, some appropriate and efficient methods for the elimination or reduction of AFs in contaminated crops should be considered. In this review, according to previous scientific research conducted for the detoxification of AFs, the authors attempt to bring together all aflatoxin detoxification methods that not only are efficient but also have the least negative impact on product quality, individually, and in combination.

[1] Arginine

[2] Serine

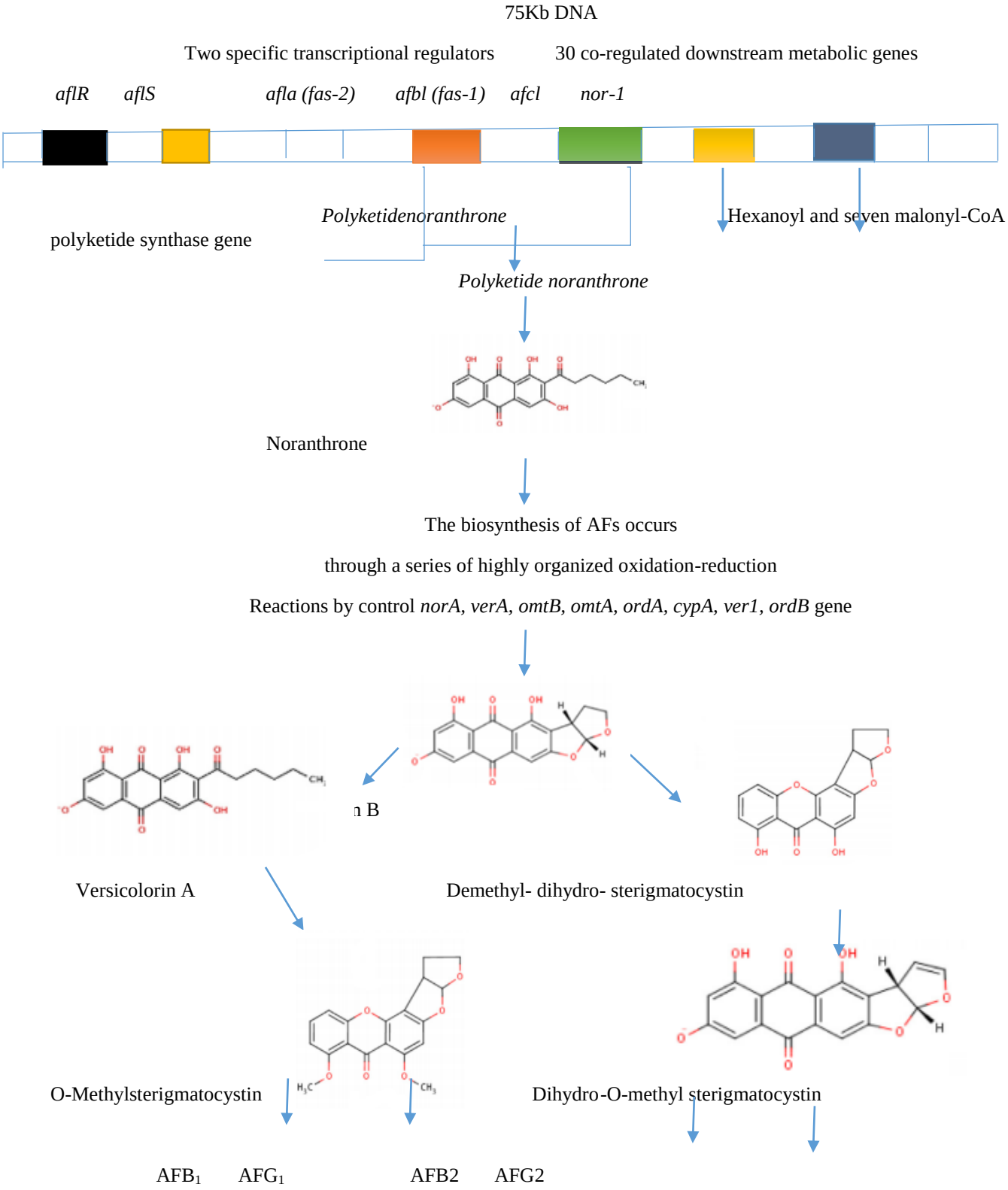

Fig. 1 Genes involved in the biosynthesis of AFs [3,2]

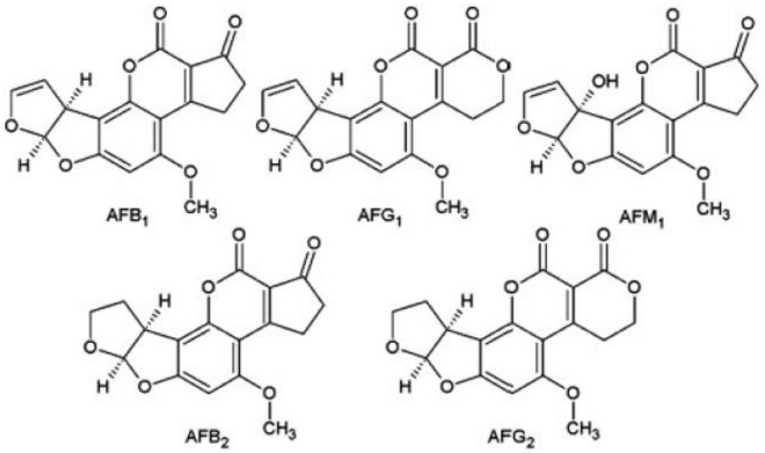

Fig. 2 Chemical structure of aflatoxin B_1, B_2, G_1, G_2, and M_1 [11]

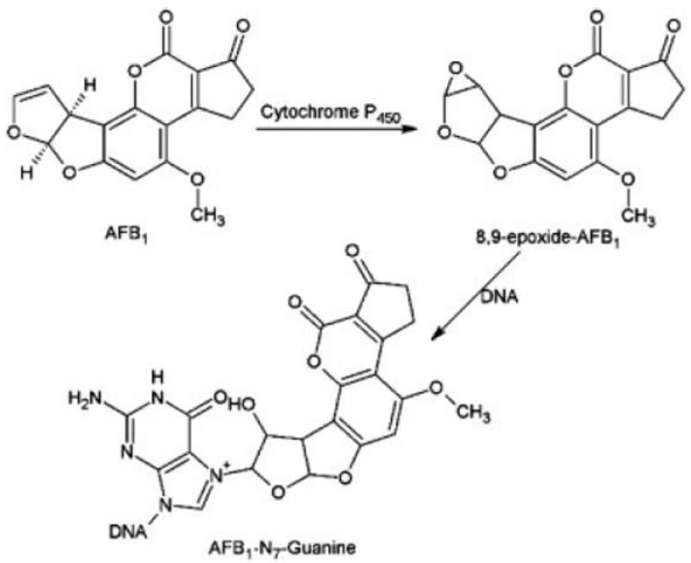

Fig. 3 AFB_1 by cytochrome P450 to 8, 9 epoxides to be converted; The epoxide caused by Thymidine in N7 guanine switch open and the DNA mutation [11]

Physical effective methods in detoxification of aflatoxin

Some physical methods have been advantageous for the reduction of potent mycotoxins, including AFs. Currently, gamma-ray, UV radiation, and the ozone are considered effective methods to detoxify AFs contaminated products, such as nuts.

1-Gamma-ray

Due to the methods for harvesting and transporting fruits, vegetables, and herbs, the risk of additional contamination is high. Microbial purity is an important aspect of healthy products, and gamma-rays can be used to achieve that. Gamma-ray ionization is considered an effective physical method to preserve food from insects, rodents, inhibition of germination, delay ripening, pasteurization, and sterilization [12]. It also is used for prolonging the shelf life of horticultural products [13]. Thus, the usage of cobalt 60 (CO_{60}) with radiation dosages 0.3, 0.75, and 0.9 KGy could control germs and insects in peanut samples at room temperature (from 30 days to 2 months). Some food (peanuts and shelled pistachios, rice, corn) and feed (barley, bran, corn), artificially inoculated by *Aspergillus* sp. have been examined for the efficiency of gamma radiation, reducing fungal growth and degrading AFs. The utilized gamma radiation doses are determined as 6/4 to 10 Kgy; the highest percentage of degradation is observed as 58.6, 68.6, 84.8, 81.1, and 78.8 % for shelled peanuts, pistachios kernels, pistachio shells, corn, and rice, respectively. Further, the percentage of degradation for feed barley, corn, and bran are obtained as 90, 84, and 83, respectively, by radiation dose 10 KGy [14]. Moreover, gamma irradiation by doses of 1, 1.5, 3, 5, and 7 KGy in the infected cashew nuts is applied; also, some physicochemical properties (color, acid value, Hexanal content, fatty acids, volatile compounds) and sensory characteristics (color, texture, and flavor) are evaluated. The analysis has illustrated that, based on mentioned characteristics; radiation by 3 KGy is the best gamma irradiation dose [15]. Also, gamma radiation by doses 0-15 KGy in the contaminated peanut samples proved that the maximum reduction (23.9 %) is reachable in the dose 15 KGy [16]. Furthermore, gamma-rays are used to reduce mycotoxins, such as ochratoxin A (OTA) and aflatoxin B_1, B_2, G_1, and G_2, in black pepper in the range of doses between 0-60 Kgy, reducing mycotoxin concentrations between 10 to 100 ng. g^{-1}; the best result is obtained in 60 KGy treatment. The reduction rate is 52, 43, 24, 40, and 36 % for OTA, AFB_1, AFB_2, AFG_1, and AFG_2, respectively [17]. In addition, the application of the gamma radiation in two different treatments ranged from 1-5, and 1-10 KGy in the case of millet flour decreases the OTA (74%); however, the vitamin A content is considerably decreased (88%) in the dose of 10 KGy. In contrast, 1 KGy radiation notices an important loss of vitamin A of about 88.6% [18]. All doses reduced the fungal infection *A. niger*, *A. flavus*, *Fusarium* spp., *Penicillium* spp., and *Rhizopus* spp; samples are irradiated compared to the control; however, the total number of bacteria is between 106 -105 in all samples at the designated time [18]. To control contamination, food and medicinal plants products can be disinfected using gamma radiation which has effectively reduced the concentrations of aflatoxin (Table 1).

Table 1. The effects of gamma-rays in reducing aflatoxin content

Type of radiation	Dose (KGY)	Product	Best result	Reduction in AFs%	Quality characteristics	Reference
Gamma	6.4 and 10	Peanut	10 KGY	58.6	-	[14]
		Pistachio skin		68.8		
		Pistachio Hull		84.6		
		Corn		81.1		
		Rice		78.8		
		Feed barley		90		
		Bran		84		
		Corn		83		
Gamma	1, 1.5, 3, 5 and 7	Cashew nuts	3 KGY	-	Physicochemical and sensory characteristics remain unchanged compared to the control	[15]
Gamma	0-15	Peanut	15 KGY	23.90	-	[16]
Gamma	0-60	Black pepper	60 KGY	52 OTA	-	[17]
				43 AFB_1		
				24 AFB_2		
				40 AFG_1		
				36AFG_2		
Gamma	1-10	Millet flour	10 KGY	74 OTA	Vitamin A 88% significant reduction	[19]
			1 KGY		An important loss of vitamin A of about 88.6%	

2-Aflatoxin destruction with ultraviolet

Ultraviolet radiation (UV) is a non-thermal technology widely used in the food industry for decontamination. UV-C is a type of ultraviolet radiation with a wavelength of 265 nm. Application of radiation for 15, 30, and 45 minutes, after 12 weeks of storage at 10 and 16 % humidity levels in products: almonds, peanuts, walnuts, pistachios, the complete elimination of AFG2 after 15 minutes' exposure to UVC occurred in all samples. While AFG1 in almonds and pistachios samples was destroyed only in 45 minutes, the maximum reduction of AFB_1 of about 96.5 percent in almonds and pistachios was revealed [20]. Peanuts at radiation with a wavelength of 254 nm of irradiation distance between 15 and 30 cm of 0-12 hours were contaminated. The maximum reduction of aflatoxin in both distances after 10 hours of radiation exposure was found. Reduce aflatoxin content in a distance of 15 cm 99.1% (from350 ppb to 9 ppb); the fungus content was less than 10 colonies unite gram. However, quality parameters, including nutritional values and physicochemical parameters (fat, protein and carbohydrate contents, acid, peroxide, and saponification values) of peanut were unchanged compared to the control. The use of UV lamps with a power of 36 W at a wavelength of 365 nm and intensity of 6.4 mW / m^2 for 5, 10, 20, and 40 minutes in contaminated peanut oil with AFB_1 (96.51 ppb) were observed after 10 minutes of exposure, reduced AFB_1 (from 96.51 ppb to 23.7 µg), which is about 86.08 % [21].

These rays can effectively control *A. flavus* and *A. parasiticus*, that cause decreases the AFs (Fig. 4). Several studies show that the wavelength, intensity, time of radiation exposure, moisture content of the food, the type of AFs, pH, and thickness of irradiated material, significantly affect detoxification AFs, whereas types of UV rays, especially UV-C on AFB_2 and AFG_2 groups, are effective (table 2) [21].

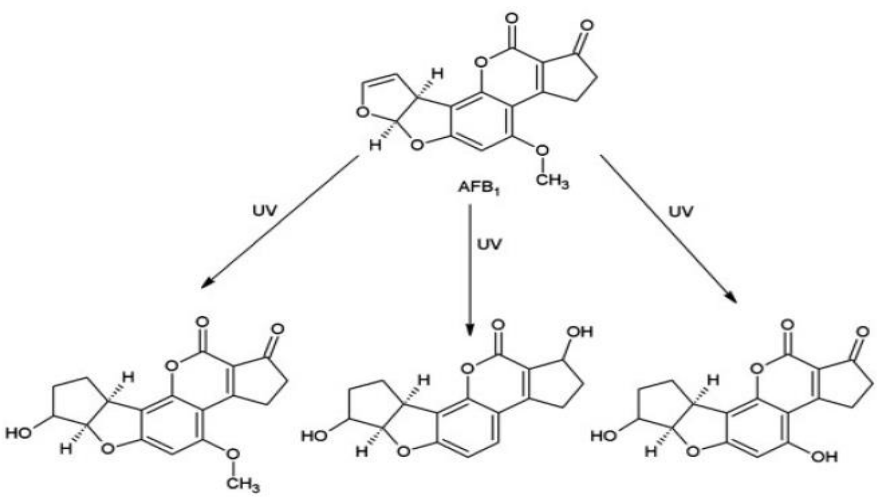

Fig. 4 The composition of the optical degradation of AFB_1 (22)

Table 2. Effect UV-C radiation in reducing aflatoxin-contaminated products as a physical method

Type of radiation	Wavelength (nm)	Dose	Time	Irradiation distance (cm)	Temperature	Relative humidity%	Product	Reduction in aflatoxin%	Reduce aflatoxin total %	Reference
UV-C	265	-	15 30 45 minute	-	Room temperature	10, 16	Peanuts and dried fruits (walnuts and pistachios, Destruction 96/5% of aflatoxin B1 percent almonds and pistachios	Complete elimination of aflatoxin G_1, G_2 Almonds and pistachios	-	(20)
UV-C	254	0-648 Kj/m^2	2-12 watch	15	Room temperature	-	Peanut	-	99/1%	(23)
		0-432 Kj/m^2		30					97/4%	

UV	365	6/4 mw/cm^2	5 10 20 40 minute	-	Room temperature	-	Peanut	86/6% AFB_1	-	(21)

Chemical methods to reduce aflatoxin

1-Ozonation

Ozone is a powerful oxidant material with high reactivity with unsaturated double bonds and carbon (C = C) [22]. Using AFB1 labeled products of degradation showed that after 15 seconds. Products are derived from AFB1, 3- ketones, organic acids, and volatile compounds or mineral products (e.g., CO_2, O_2, and H_2O), respectively. These non-toxic or less toxic compounds were destroyed or altered in some parts of the structure are produced (Fig. 5)[23]. AFs degradation compounds were identified by (UPLC–Q-TOF MS) than A (C17H10O7 with mass (m/z) for [M+H] + 327.05003), B (C17H22O9 to m/z for [M+H] + 371.1346), C (C6H12O7 to m/z for [M+H]+ 317.0660), D (C16H16O6 to m/z for [M+H] + 305.1028), E (C17H14O8 to m/z for [M+H] + 347.0763), F (C16H14O7 to m/z for [M+H] + 319.0816) Products compounds in resulting from the ozonation of the first track on the mechanism of oxidative Craig and four of the second track based on the oxidative and electrophilic reaction of ozone (Fig. 6). Reduce the toxicity of AFB1 and also the mechanism of the destruction or disappearance of the double bond at the end of the eruption or from the lactone ring on the benzene ring. To further investigate the toxicity of products resulting from ozonation was performed on mice. The results showed that the toxicity of these products was much lower than AFB1 and no toxic effects were observed on animals in this process [24]. Ozone at concentrations of 5, 7.5, and 9 mg/l for 140 and 420 minutes with a relative humidity of 70 % in almonds, pistachios, and peanuts showed that 9 mg/l ozone concentrations in 420 minutes' decrease AFB1 (23%) and total AFs (24%), While studying the quality of free fatty acids, peroxide value, pH and Sensory analysis showed no difference between the samples ozone disinfection in comparison to the control treatment [25]. If they showed ozone whit Concentration 20 ppb for 5 minutes, ppb 40 for 10 minutes, and 50 ppb for 5 minutes in peanuts, Application 40 ppb ozone for 10 minutes to showed about 70-80 % reduce aflatoxin total and AFB1 [26]. The ozone at a concentration of 13 and 21 mg / l for 0, 24, 45, 72, and 98 hours with 95precent humidity showed that the concentration of 21 mg / L ozone for 98 hours decreased and 30 % of AFB1 (20%) and total AFs (30%) in samples treated with the ozone respectively [27]. While ozone in the cornflour with a concentration of 15, 30, 45 and 75 mg / l for 0, 5, 15, 30 and 60 minutes was performed with 75% humidity, 75 mg / L of ozone in 60 minutes the cause degradation AFB1 (77.29%) and total AFs from 53/06% to 12/08% (28). Ozone at a concentration of 3, 5.4, 6, and 5.7 mg / l for 30 minutes with 5% water content in peanuts showed that concentrations 6 and 5.7 mg / L of ozone destroy AFB1

(65.8%) and AFs (65.9). Experimental treatments 2, 5, and 8precent at a concentration of 6 mg / L ozone for 30 minutes AFs reduction of about 70-80% moisture at three levels. Treatment times of 10, 20, 30, and 60, and 120 minutes at a concentration of 6 mg /l with 5 percent humidity was obtained degradation AFs (60-64%). The oxidative indexes (polyphenols, resveratrol, acid value, peroxide value) between treated and untreated samples were non-significant [24]. Studies show that using ozone as a chemical method to effectively AFs contaminated products to be degradation (Table 3).

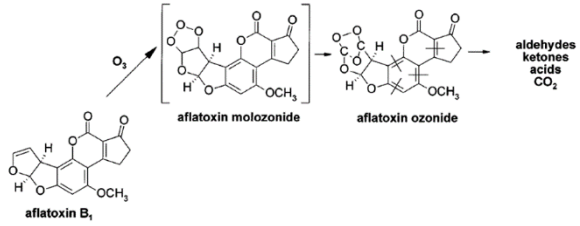

Fig. 5 Pathway destruction of ozone AFB_1 and its compounds [25]

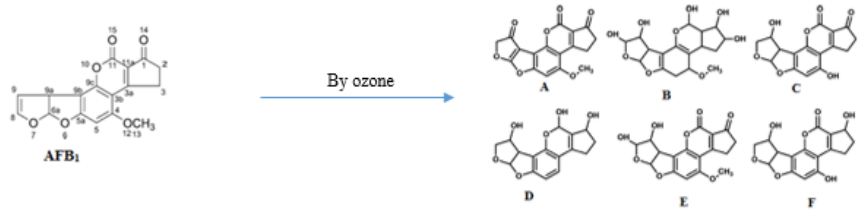

Fig. 6 The composition of the destruction ofAFB_1 by ozone [26]

Table 3. Effect of ozone on reducing AFs products as a chemical method

Gas use	Concentration	Time	Temperature° C	Relative humidity %	Product	Best result	reduction in aflatoxin B_1 %	Reduce aflatoxin total %	Quality characteristics	Reference
Ozone gas (O_3)	5, 7/5 and 9 (mg/l)	140,420 minute	20	70	Pistachio kernel, peanut	9 mg/l O_3 for 420 minute	23	24	There was no difference between the treated samples compared to control.	[27]
Ozone gas	20, 40, 50 ppb	0, 24, 45, 72, 98 h	Room temperature	-	peanut	40 ppb for 10 minute	70-80	70-80	-	[28]
Ozone gas	13 and 21 (mg/l)	-	Room temperature	95	peanut	21 mg/l for 98 h	20	30	-	[29]
Ozone gas	15, 30, 45 and 75 (mg/l)	0, 5,15, 30, 60 minute	Room temperature	75	corn flour	75 mg/l for 60 minute	77/29	From 53/60 decrease to 12/08	-	[26]
Ozone gas	3, 4/5, 6, 7/5 (mg/l)	30 minute	Room temperature	5	peanut	6, 7/5 mg/l	65/9	65/8	Minor changes were observed between treated and	[30]

Humidity (white 6 mg/l ozone)	2, 5, 8%	30 minute -				In all three levels of moisture	60-64	60-64%	control samples	
Time (white 6 mg/l ozone)	10, 20, 30, 60, 120 minute					30 minute	60-64	64		

2-Alkaline and acidic compounds

Alkaline and acidic compounds help the detoxification process due to hydrolysis and lactone rings eruption to be AFs. The composition of the destruction of AFs opening (sodium hydroxide and hydrogen peroxide) gets to usually establishes 8,9 epoxides from AFs, which can cause mutagenesis on the DNA, by using the acidic compounds such as citric acid, AFB1 converts to AFB2a, which is less toxic compound (Fig. 7) [31]. So to reduce AFs in dried figs with changes in pH by citric acid, sodium hydroxide between 3.1, 3.53 and 8.6, 10 at Temperature 5, 7.5, and 9 ° C was adjusting for 1 or 2 hours. The reduction of AFB1 (12%) and AFB2 (11%) in pH = 6 and reduction AFB2 (100%) at PH = 10, respectively [32]. Using citric acid is 1 normal use for 15 minutes at room temperature to reduce AFB1 and total AFs for rice to be less than the standard specified of standard aflatoxin Europe and Iran [33]. In another study, 6 and 18 hours of immersion soybeans the organic acids (citric acid, lactic acid, succinic acid, and tartaric acid), 1 normal (1N) at room temperature, to decrease aflatoxin total 94.1, 92.7, 62.0, and 95.1 % respectively, in case of heating process at a temperature of 100 ° C and 150° C caused reduced 41.9 and 81.2 % AFs. However, treatment cooking for 90 minutes reduces aflatoxin total (97/9%) [34]. In addition, a combination of lemon juice (5% citric acid) and citric acid was studied on pistachio; thus, after treatment with 30 ml of distilled water, 30 ml lemon juice, and 6 g of citric acid after 4 days of storage at room temperature, the temperature was 120 ° C for one hour of roasting, reduction of AFB_1 (93.1%) [35]. So alkaline compounds such as sodium hydroxide compare to acid compounds, such as citric acid, have a greater degradation effect on AFs. Lactic acid is another effective acid to reduce AFs, which is produced by lactic acid bacteria [36]. The decrease in mold growth and AFs production may be caused by competition for nutrients between bacterial cells and fungi. The binding of AFs most likely depends on environmental conditions. The dead bacteria cells possess consistently better binding abilities for AFB1 than living cells [37,38].

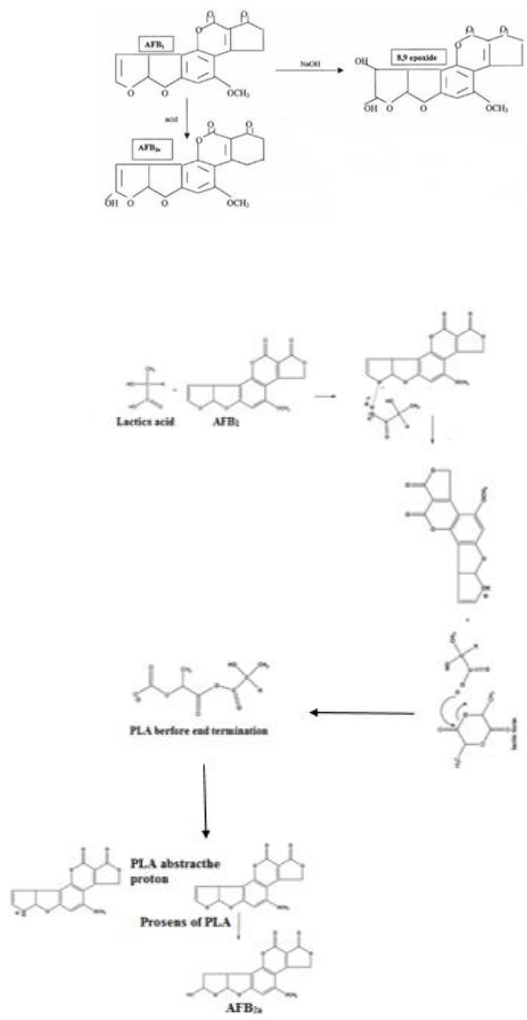

Fig. 7 Pathway destruction of AFB_1 by alkali and acid compounds [37, 31]

Table 4. The effect of alkali and acid compounds to reduce aflatoxin as a chemical method

Material used	pH adjust	Thermal processing	Time	Best result	Reduce aflatoxin %	product	Quality characteristics	Reference
Citric acid	Between 3.1-3.5,	5, 7.5, 9 ° C	1-2 h	pH=6	12% AFB_1 11% AFB_2	dried fig	-	[32]
Sodium hydroxide	until the 8.6,10			pH=10	100% AFB_2			
Citric acid (1N)	-	Room temperature	15 minute	-	Aflatoxin B1 and total AFs are determined to be less than the standard reached in Iran and Europe	Soybean	-	[38]
Citric acid, lactic acid, succinic acid, tartaric acid, 1 normal (1N)	-	Room temperature	18 and 6 hours of immersion	18 hours immersion	94.1 % 92.7 % 62.0 % 95.1 %	Soybean	-	[39]
Heat Treatment		100, 150 °C	90 minute	-	41.9 %			

Cooking treatment					81.2 %			
Lemon juice (5% citric acid) and citric acid with two levels of aflatoxin 268 and 383 ng /g	-	Roasting at 120 ° C for one hour	4 days of storage at room temperature 1-hour storage at room temperature	30 ml of distilled water, 30 ml lemon juice, and 6 g of citric acid 30 ml of distilled water, 15 ml lemon juice, and 2/5 g of citric acid	93.1 % AFB_1 49.2 % AFB_1	Pistachios	The apparent change compared to control samples No apparent change compared to control samples	[34]

2. Discussion

Due to the growth of Aspergillus spores with minimal living conditions there is always the possibility of contamination of agricultural and food products to AFs [40-42]. Thus, the legislation in over 75 countries set allowable limits for AFB_1 and total AFs within the concentration range of 1–35 μg kg^{-1} [43][5]. Studies show that there are several ways to reduce AFs in contaminated products, but most of them decrease the quality and nutritional value of the products [44]. The ionization techniques such as gamma-ray addition to destroying the AFs, could eliminate microbial and fungal contamination, as well as could destroy the AFs. Hence, the dose for each product depends on the characteristics of the product and its contamination rate, so the radiation dose for each product should be optimized. In addition, methods of reducing microbial and AFs contamination should not affect the nutritional value and quality of the product. For example, in 3 KGy, the best radiation dose on cashew nuts to destroy AFs with no changes in physicochemical properties (peroxide value, volatile compounds such as aldehydes, ketones, and alcohols increased after irradiation indicating enhanced lipid oxidation) and color parameter. Medicinal plants containing secondary metabolites are also important and used to control of fungal grows from many years ago [45,46]. The UV-C rays are currently used to reduce the microbial contamination of the food and feed. Research showed that UV-C rays could be used to reduce AFs in contaminated products; however, the wavelength, intensity, distance of irradiation, type of AFs are effective in reducing AFs. The degradation products of AFB_1 by UV-C rays are less toxic than AFB_1 (Fig 4). The physicochemical parameters (fat, protein, and carbohydrate contents, acid, peroxide, and saponification values) in peanuts after the destruction of AFs by UV-C rays did not change [23]. The reduction of AFs in food and feed by ozone also was studied; studies show that ozone can reduce AFs in contaminated products without loss of nutritional value and quality of the product (Table 2). The use of ozone at a concentration of 9 mg. L^{-1} for 420 minutes reduces AFs without significant changes in pH, color, moisture content, and free fatty acid values of pistachio kernels and peanuts. Fatty acid compositions of pistachios did not change significantly after the ozonation treatments. No significant changes were found between sweetness, rancidity, flavor, appearance, and overall palatability of ozonized and non-ozonized pistachio kernels when significant changes were observed in the organoleptic properties of ground pistachios, except rancidity, after 5.0 mg. L^{-1} ozone treatment for 140 min. Also, peanut put for 30 min exposure to ozone with concentrations 6, 7.5 mg. L^{-1}, the oxidative index (polyphenols, resveratrol, acid value, peroxide value) between treated and untreated samples were non-significant (Table 3) [47]. The use of alkaline and acid compounds such as sodium hydroxide (NaOH) causes to produce 8, 9 epoxides in AFs which makes mutations (Fig 6), so increasing the pH will raise the mutagenicity of AFs, while citric acid is a weak organic acid converts AFs the less toxic forms (AFB_{2a})(Fig 6). Lactic acid is another acid produced by lactic acid bacteria that could transform AFs to AFB_{2a} (Fig 7) [33].

3. Conclusion

The AFB2 and also AFG2 are more sensitive to UV-C radiation compared to the AFB1and AFG1. In contrast, ozone has more effect on AFB1, and AFG1 compared to AFB2 and

AFG2. Thus, a combination of techniques can be an effective process. Accordingly, using citric acid and then use of UV-C radiation, and ozone to convert AFs to less toxic forms could be more effective.

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