

## Dietary Exposure Assessment of Aflatoxin From Dried Figs in Turkey

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### ABSTRACT

Aflatoxins are fungi's secondary toxigenic metabolites and known as potent hepatocarcinogen for humans. The purpose of the present study is to assess health risk for Turkish adult population posing by dried fig consumption due to the aflatoxin contamination. In order to make this evaluation total of 23.547 aflatoxin monitoring data of dried figs from the Turkish Ministry of Food, Agriculture and Livestock between the crop years of 2011/2012-2015/2016 in Turkey were used. Intakes were estimated using consumption data and aflatoxin concentrations and expressed using the average Turkish adults' body weight (72.8 kg). Estimated daily exposure was found 0.005 ng/kg bw/day for aflatoxin B<sub>1</sub>, 0.009 for total aflatoxins in a worst case scenario. The calculated margin of exposure (MOE) was higher than the 10.000. Cancer risk in Turkish adult population observed in the range between 0.00017 to 0.00030 cancers per 100,000 people per year. Calculated MOE and population risk according to estimated daily intake revealed that Turkish adult population are not under the toxicological risk through dried fig consumption.

### Keywords:

Aflatoxin, Dietary Intake, Risk Assessment, Exposure Analysis, Dried Figs, Turkey

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### INTRODUCTION

Based on 2017/2018 crop production estimates, dried figs produced mainly by Turkey (58% market share), Iran (13%), USA (7%), Afghanistan (7%) and Greece (6%) for domestic consumption and export trade. Turkey, as the leading country of fig production, exports approximately 90% of their dried fig production and about 75% of the export were carried out with European Union member states [1].

Dried figs are susceptible to aflatoxin (AF) contamination and natural occurrence of AF can be at high levels. Fruit structure, harvesting, drying and storage can affect the occurrence of AF in dried figs as well as its high sugar content. Moreover, due to its fleshy skin -which does not provide any protection- AF contamination can occur easily in it. It is important to note that the natural occurrence of AF in a single fig fruit can reach very high levels, such as 4000 µg/kg, the presence of AF in dried figs is considered a major threat to human health [2].

Fungi belongs to *Aspergillus* genus are the main

producers of AFs. *Aspergillus flavus* is the most common toxigenic species, but different strains produce different amounts of AFs and some produce none. Fungi produce nearly 20 secondary metabolites, among them, food samples contains only four major aflatoxins B<sub>1</sub>, B<sub>2</sub>, G<sub>1</sub> and G<sub>2</sub> naturally [3]. Aflatoxin B<sub>1</sub> (AFB<sub>1</sub>) was found to be a potent hepatocarcinogen according to human, animal and cell and tissue culture studies and International Agency of Research on Cancer was classified both AFB<sub>1</sub> and total AFs (AFTOT) carcinogenic to humans (Group I) [4].

The FAO/WHO Joint Expert Committee on Food Additives (JECFA) in 1987, 1997, 2007 performed an evaluation of this toxin. Due to the genotoxic and carcinogenic properties of aflatoxins, no observed adverse effect level (NOAEL) and a tolerable daily intake (TDI) value have not been specified [5, 6]. Instead, according to epidemiological and toxicological studies, calculated potency estimates for human liver cancer originated AFs exposure [7]. Carcinogenicity of AFs varies in humans having chronic hepatitis B virus infection.

Major toxicological impact of AFs is being responsible for 4.6%-28.2% liver cancer cases throughout the world when hepatitis virus infection positive and negative individuals considered [8]. Similar with JECFA, The European Union Scientific Committee for Food (SCF) also concluded that even very low levels of exposure to AFs (<1 ng kg<sup>-1</sup> bw day<sup>-1</sup>), could promote the liver cancer risk [9]. Therefore ALARA principle is recommended, which means AF contamination levels should be reduced to being as low as reasonably achievable [5].

Regulatory limits for AFs and other mycotoxins expressed for food and feed products in more than 100 countries and AF limits vary widely among countries. The United States Food and Drug Administration (FDA) has accepted a maximum guidance limit for AF in foods at 20 µg/kg AFTOT [10]. Because of high toxicity and carcinogenic properties, legal tolerance levels in the EU and in Turkish legislations are low for AF in dried fruits that are intended for human consumption (AFB<sub>1</sub>:8 µg/kg; AFTOT :10 µg/kg). The Codex Alimentarius Commission has adopted on July 2nd 2012 new maximum limits for AFs in ready to eat dried figs (AFB<sub>1</sub>: 6 µg/kg; AFTOT :10 µg/kg) [11].

As hazard to public health from AFs are well known, mold growth and mycotoxin production are common concerns for all countries that produce and consume figs. The fig industry in Turkey working together with government agencies have been pro-active in developing programs to improve prevention, detection and analytical methods to minimize AF contamination in dried figs. Estimation of dietary intake of toxins is important for risk analysis. It is also essential to make the necessary regulations for the protection of public health. Risk assessment can be used to quantify the magnitude of exposure, or probability of harmful effect on individuals/populations from chemicals such as mycotoxins. Risk assessments includes four step, which; hazard identification, dose-response analysis, exposure assessment and risk characterization. Risk assessments of AFs have been performed in Africa, China, Taiwan [12], Vietnam [13], Lebanon [14], and public health risk were evaluated calculating the margin of exposure (MOE) values and/or population risk related with consumption of various types of foods. Because Turkey is the leading country for dried fig production, having a risk assessment evaluation of AFs is important.

This study aimed to assess health risks through dietary exposures to AFs with consumption of dried figs among Turkish adult population. Dietary exposure risk assessment was conducted through MOE value and cancer potency factor calculation using the estimated daily intake (EDI).

## MATERIAL AND METHODS

### Aflatoxin Contamination Data

Concentration data were collected and combined from the Turkish Ministry of Food, Agriculture and Livestock between crop years of 2011/2012 and 2015/2016. Results on the concentration of AFB<sub>1</sub> and AFTOT in dried figs was available for a total of 23.547 samples from the mycotoxin monitoring program. Samples were analysed for the presence of AFs with a validated method using an immunoaffinity column clean-up and High Pressure Liquid Chromatography system equipped with fluorescence detection [15] in accredited national control laboratories. Results are expressed in nanograms (ng) per gram weight.

### Estimation of Dried Fig Consumption

Although it is very important to have a detailed consumption survey in order to make accurate AF dietary exposure, Turkey does not have comprehensive national consumption survey, yet. For the present study in order to make the evaluation of AF exposure through dried fig consumption, Turkey's estimated dried figs consumption per capita is taken as 0.5 grams per day [16].

### Calculation of Estimated Dietary Exposure to Afs

Handling of censored data (results below limit of detection) was conducted according to EFSA (2010) for calculation puposes. Prevalence of censored data was between 86.5 and 90.9% during the five year of harvest seasons. The average toxin concentrations were used for the daily intake calculations. During the of average toxin level calculation, not detected samples were considered as 0 for lower bound (LB) estimates and were considered as the limit of detection (LOD) for upper bound (UB) estimates because of censored data percentage was higher than 60% [17]. For the exposure estimates, the average body weight for Turkish adults (72.8 kg) were used according to the National Institute of Statistics [16]. Intake values are expressed in ng per kg body weight per day. The estimated daily intake (EDI) of AFs was calculated as follows:

$$EDI \text{ (ng/kg b.w/day)} = \left[ \text{toxin (ng/g)} \right] \times \left[ \text{consumption (g/day)} \right] / \left[ \text{average b.w. (kg)} \right] \quad (1)$$

### Risk Assessment

There is no threshold value specified for AFs exposures because for the chemicals that cause cancer completely safe level cannot be established. Especially chemicals directly or indirectly act on DNA such as AFB<sub>1</sub> which could start changes leading to cancer. Therefore, the calculated EDI cannot be directly compared with threshold level for AFs.

The JECFA set forth a risk dose of 0.013105 (ng/kg bw/day) for adults in European Countries according to human epidemiological data. Meaning of risk dose is 0.013 increase in the incidence of cancer per year in the general population of 100,000 people exposure of per ng AFs/kg bw/day [6].

Hepatitis also increase the risk of liver cancer in parallel with AFs exposure. Aflatoxin exposure in patients with chronic hepatitis is known to significantly increase the risk of liver cancer. The JECFA also calculated the risk of liver cancer 0.3 and 0.01 cancer/year for 100,000 people/ng AF/kg bw/day for people with hepatitis B surface antigen negative (HBsAg-) and positive (HBsAg+) people, respectively [6].

If the calculated MOE is below 10.000 which is equivalent to 170 ng/kg bw/day AFs, there is public health risk due to the AFs contaminated food consumption [5].

Evaluation of MOE and population health risk which were calculated based on estimated daily intake level was conducted. The risk of liver cancer for the Turkish population was evaluated according to the EDI results and average potency factor calculated using the chronic hepatitis prevalence. WHO classified Turkey as intermediate in terms of endemicity for hepatitis B (2-8%). Prevalence of chronic hepatitis B infection was reported between 4.0% and 5.0%. Similar with these data, Mehmet et al., [18] reported that the prevalence of HBsAg(+) as 8.2% and 6.2% in the rural and urban areas of Southeastern of Turkey, respectively. In order to point out worst case scenario, prevalence rate of 8% is used for calculation of average potency. Average potency and population risk were calculated using the formulas below.

$$\begin{aligned} \text{Population risk} &= \text{Exposure} \times \text{average potency} \\ \text{Average potency} &= 0.3 \times 0.08 + 0.01 \times 0.92 = 0.033 \end{aligned} \quad (2)$$

## RESULTS AND DISCUSSION

Limit of detection (LOD) and limit of quantification (LOQ) for AFB<sub>1</sub> and AFTOT was 0.067, 0.2 and 0.17, 0.5 ng/g, respectively. Table 1 shows concentration data of AF contaminated dried figs in Turkey from 2011-2012 to 2015-2016 harvest seasons. The concentrations of AFB<sub>1</sub> and AFTOT varied from 0.20 to 431.43 ng/g and from 0.51 to 477.90 ng/g, respectively.

There are several studies available in literature with regard the natural occurrence of AFs in dried figs. It can be seen from the Table 2, AF contamination is a problem mainly in Turkey because it is the major producer. Aflatoxin contamination data from the Turkey in accordance with our contamination results express that AF contamination in dried figs can be menace Turkish population and risk assessment is a vital necessity.

**Table 1.** Summary of annual AF contamination (ng/g) of dried figs.

Year	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016
No. of Samples	4116	4644	5041	4677	5069
No. of Positive Samples (%)	403 (9.79%)	627 (13.50%)	550 (10.91%)	426 (9.11%)	504 (9.94%)
Mean AFB <sub>1</sub> of positive samples (ng/g)	5.94	5.39	6.56	4.84	5.08
Mean AFTOT of positive samples (ng/g)	10.93	8.08	9.79	8.32	6.79
Mean AFB <sub>1</sub> - LB* (ng/g)	0.58	0.73	0.72	0.44	0.51
Mean AFB <sub>1</sub> - UB* (ng/g)	0.64	0.79	0.78	0.50	0.57
Mean AFTOT - LB (ng/g)	1.07	1.09	1.07	0.76	0.68
Mean AFTOT - UB (ng/g)	1.22	1.24	1.22	0.91	0.83
AFB <sub>1</sub> Range (ng/g)	0.2-183.00	0.2-254.40	0.2-431.43	0.2-88.04	0.2-381.30
AFTOT Range (ng/g)	0.51-374.10	0.51-415.19	0.50-477.90	0.51-264.00	0.51-403.90

\* LB (lower bound): results under LOD reported as 0, UB (upper bound): results under LOD reported as LOD.

**Table 2.** Summary of natural occurrence of AFTOTs in dried figs in literature.

Positive sample/ Total Sample (%)	Range of AFTOTs (ng/g)	Country	Reference
26/33	0.22-83.4	Algeria	[19]
4/14	LOD*-11.10	Pakistan	[20]
13/22	0.3-7.0	Iran	[21]
16/130	0.1-28.2	Turkey	[22]
219/104 (47.5%) (for export)	ND*-267.48	Turkey	[23]
2461/580 (23.6%) (from local store)	ND-278.04	Turkey	[23]
11/115	0.1-763.2	Turkey	[24]
313/2643	0.2-162.76	Turkey	[25]
1575/4917	0.2-259.46	Turkey	[25]

\*LOD: Limit of Detection, ND: Not Determined

In order to reveal the worst scenario, the estimated daily intake was calculated by using the data from harvest year with the highest contamination of AF. The highest daily exposure may occurred during 2012/2013 harvest season due to the highest AF contamination (Table 1). Based on highest AF levels in the analyzed dried fig samples and using an average body weight of 72.8 kg, estimated daily intake was determined 0.005 (LB), 0.005 (UB) ng/g bw/day for AFB<sub>1</sub> and 0.008 (LB), 0.009 (UB) ng/g bw/day for AFTOT.

**Table 3.** AF dietary exposure assessment\* and risk characterization.

	Mean Exposure (ng/kg bw/day)	MOE <sup>b</sup>	Risk <sup>c</sup>
AFB <sub>1</sub>	(LB) <sup>a</sup> 0.005	34.000	0.00017
	(UB) <sup>a</sup> 0.005	34.000	0.00017
AFTOT	(LB) 0.008	21.250	0.00027
	(UB) 0.009	18.889	0.00030

\* Calculated using 2012/2013 harvest season data

<sup>b</sup> MOE=BMDL<sub>10</sub>/Dietary exposure, BMDL<sub>10</sub>= 170 ng/kg bw/day

<sup>c</sup> Risk, liver cancer cases/100.000 population/year

Dietary intake of AFs through dried fig consumption in Turkey does not pose a potential public health risk with regard to MOE, because calculated MOE was higher than 10.000. Based on the average exposure of AFB<sub>1</sub> and AFTOT associated with an average risk of excessive liver cancer of 0.0002-0.0003 cases / 100,000 individual for a year. It can be seen from the risk factor AF exposure through dried figs is not a problem alone. But it should be remember that people are exposed to AF contamination from various types of food in which the most important one is cereals for Turkish consumers. Table 4 summarises estimates of dietary aflatoxin exposure from other countries.

**Table 4.** Summary of AF exposure assessment studies in literature.

Food Product	Mean intake of AFB <sub>1</sub> (ng/kg bw/day)	Mean intake of AFTOT (ng/kg bw/day)	Potential Risk	Country	Reference
Hazelnut	0.014 (LB) 0.016 (UB)	0.018 (LB) 0.023 (UB)	-	Turkey	[22]
Dried fig	0.003 (LB) 0.003 (UB)	0.004 (LB) 0.005 (UB)	-	Turkey	[22]
Dried fig (from local store)	-	1.27	-	Turkey	[23]
Dried fig (for export)	-	0.2	-	Turkey	[23]
Various types of foods (cereals, pizza, pulses, nuts etc.)	0.63 (LB) 0.66 (UB)	-	0.0527-0.0545 cases / 100,000 persons / year	Lebanon	[14]
Mullberry, Date, Fig, Apricot	0.04 0.12 0.04 0.06	-	4250 1417 4250 2833 (MOE) 1.2 0.3	Iran	[21]
Rice and maize	17.7 4.0	-	Cancers / 100,000 pop. / year 0.0007-0.2713 cancers / 100,000 pop. / year	Vietnam	[13]
Peanut and peanut products	-	0.03 (UB)	-	Taiwan	[12]
Muthokoi, maize kernel, maize meal	-	27 292 59	-	Kenya	[26]

The average exposure estimates to AFB<sub>1</sub> and AFTOT as revealed in this study were similar with those reported in Kabak [22] and much lower than estimates from other countries. These differences are appropriate because the methods and models used to evaluate dietary exposure, the LOD/LOQ of the analytical technique, handling of the censored data may differ. Also it must be noted that risk assessment from single type of food can be a limitation because AF effect should be evaluated cumulative.

All calculations in this publication are based on the assumption that the entire population consumes dried figs. On the other hand, in the Turkey nutrition and health research 2010 conducted by Ministry of Health, it is expres-

sed that 60.5 % of individuals of Turkish population stated that they do not consume dried fruits daily [27]. While the toxicological risk assessment is carried out, it is not taken into consideration how much the population consumes in the calculations. In this publication, the worst case scenario was tried to be presented.

## CONCLUSION

Although AFs are present in dried figs consumed by Turkish populations, there is no toxicological risk for consumers in Turkey. Estimates of dietary AF exposure are consistent with estimates in other developed countries. However it must be noted that AF exposure may come from consumption of various types of foods. That is why exposure estimation should be conducted through total diet study which will provide cumulative exposure assessments. In order to provide a precise risk assessment, especially consumption data and exposure data are required. Unfortunately national food consumption data which includes dried figs are not available in Turkey, yet. There is an urgent need for comprehensive national food consumption survey for further studies in order to make a more precise health risk estimation for Turkish population arising from the exposure of AFs.

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