



Reproductive Toxicity of Aflatoxins: A Brief Report with Implications for Public Health Policy

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Abstract

Context: Aflatoxins (AFs) are toxic metabolites produced by *Aspergillus* species and pose a serious threat to human and animal health. Exposure to AFs may lead to reproductive disorders and reduced fertility.

Objectives: This health policy brief highlights the potential reproductive health risks associated with chronic AF exposure and emphasizes the need for continuous monitoring of food quality and storage conditions to reduce contamination.

Evidence Acquisition: This health policy brief synthesizes evidence from our previously published studies and other relevant literature to assess the effects of AF exposure on fertility in in vitro and in vivo models. Evidence was identified from several databases.

Results: Aflatoxin B₁ (AFB₁) and aflatoxin G₁ (AFG₁) disrupt spermatogenesis by interfering with genes involved in cell-cycle progression, including cyclins. They also induce the expression of apoptosis-related genes in vivo, activate the intrinsic apoptotic pathway, and exert cytotoxicity in TM3 mouse Leydig cells.

Conclusions: AFs may affect fundamental molecular mechanisms involved in spermatogenesis, potentially reducing fertility. Reducing chronic exposure through improved food storage and monitoring is important for protecting reproductive health.

Keywords: Aflatoxin, Spermatogenesis, Reproductive Toxicology, Health Policy

1. Background

Aflatoxins (AFs) are toxic metabolites produced by certain *Aspergillus* species and are commonly found in foods such as peanuts, corn, nuts, oilseeds, cereals, dried fruits, milk, dairy products, and animal feed (1). Studies in animal models have shown that aflatoxin exposure can induce reproductive toxicity, resulting in testicular damage, altered estrous cycles, and reduced fertility (2, 3). AFs can cause testicular tissue atrophy by disrupting molecular pathways involved in spermatogenesis, thereby reducing fertility (4).

Our recent study investigating the association between aflatoxin B₁ (AFB₁) and the intrinsic and extrinsic pathways of apoptosis in TM3 cells confirmed that AF exposure

suppresses TM3 cell viability, triggers apoptotic pathways, and ultimately damages male reproductive cells (5).

Reducing aflatoxin exposure is important for protecting reproductive health through proper food storage, improved agricultural practices, and routine food monitoring. This health policy brief highlights the potential reproductive risks of chronic aflatoxin exposure and emphasizes the need for continuous food-safety surveillance.

2. Objectives

This health policy brief highlights that the chronic consumption of AFs poses a serious threat to reproductive health. Evidence was synthesized from our previously published studies and the relevant literature to summarize

the reproductive toxicity of AFs and discuss their public health implications. Continuous monitoring of food quality and storage conditions is essential to minimize aflatoxin contamination in food products.

3. Methods

This health policy brief synthesized evidence from previously published studies on the reproductive health effects of AFB₁ and aflatoxin G₁ (AFG₁) in vivo and in vitro. The primary emphasis was on original studies reporting the molecular and histopathological effects of AFs on the reproductive system. Relevant evidence was identified through searches of Google Scholar, ScienceDirect, Scopus, and PubMed. The retrieved studies were critically reviewed, and findings were narratively synthesized according to AF type, experimental model, exposure conditions, and reported molecular and histopathological outcomes.

4. Results

In an animal study, 24 albino mice were exposed to AFG₁ at a daily dose of 20 µg/kg body weight via intraperitoneal (i.p.) injection for 35 days. AFG₁ significantly altered Cyclin D₁, p21, and ERα expression ($P < 0.05$) and increased the proportion of seminiferous tubules with negative TDI, RI, and SPI values, suggesting disruption of testicular cell-cycle regulation and spermatogenesis (3).

Another animal study reported that AFG₁ exposure (20 µg/kg for 28 days) increased MDA and NO levels and decreased SOD levels in mouse testicular tissue, accompanied by intercellular edema and seminiferous tubular atrophy (4).

In another animal study, mice were exposed to AFB₁ at a daily dose of 20 µg/kg body weight via intraperitoneal (i.p.) administration for 7, 14, and 21 days. AFB₁ reduced Cyclin D₁, CDK4, and ERα expression and increased p21 and p53 expression in mouse testicular tissue ($P < 0.05$), suggesting cell-cycle dysregulation and activation of p53-associated apoptotic signaling (2).

A recent review by Jalili et al. (1) highlighted oxidative stress, DNA damage, cell-cycle dysregulation, and apoptosis as potential mechanisms underlying AFB₁-induced reproductive toxicity. Finally, an in vitro study in TM3 cells exposed to 3.6 µM AFB₁ for 24 h showed increased caspase-3 and caspase-9 levels, indicating activation of apoptotic pathways (5). The main molecular and reproductive effects of AFB₁ and AFG₁ reported in these studies are summarized in Figure 1.

5. Discussion

AF exposure through contaminated food is a public health concern. Preclinical evidence indicates that AFs may disrupt spermatogenesis through altered cell-cycle regulation, estrogen signaling, apoptosis, and oxidative stress (1), although their effects on human fertility remain uncertain. Zamir-Nasta et al. (3) reported that AFG₁ exposure in albino mice increased Cyclin D₁ and p21 expression and reduced ERα expression, with alterations in TDI, RI, and SPI.

Another study by Zamir-Nasta et al. (4) indicated that AFG₁-related changes in Cyclin D₁, SOD, MDA, and NO were associated with testicular damage, tubular atrophy, and intercellular edema. Zamir-Nasta et al. (2) showed that AFB₁ reduced Cyclin D₁, CDK4, and ERα expression and increased p21 and p53 expression, suggesting p53-associated apoptotic signaling.

Although Cyclin D₁ showed opposite changes following AFG₁ and AFB₁ exposure, both increased and decreased expression may disrupt cell-cycle regulation and spermatogenesis. Jalili et al. (5) further showed that AFB₁ activated intrinsic apoptosis in TM3 cells. These findings provide biological plausibility for aflatoxin-associated reproductive toxicity but do not establish direct effects on human fertility.

Regarding human evidence, Francis et al. (6) detected AFs more frequently in semen from infertile men than in fertile controls. Similarly, Suhail et al. (7) reported significantly higher seminal AFB₁ levels in infertile Iraqi men than in fertile controls. However, these observational findings do not establish causality.

AF contamination is an important food-safety concern, particularly in cereals, maize, and nuts. National surveillance and food-safety standards may help reduce dietary AF exposure, although their effects on reproductive health remain uncertain (8,9).

5.1. Limitations

The evidence is predominantly derived from animal and in vitro studies. Species differences, experimental conditions, and exposure doses may limit translation to humans. Further epidemiological studies are needed to clarify the relationship between chronic AF exposure and male reproductive health.

5.2. Conclusions

Monitoring high-risk foods, including cereals, maize, and nuts, through routine food-safety surveillance is warranted as a precautionary measure. Available evidence suggests a potential association between AF exposure and adverse male reproductive outcomes, but its impact on human fertility remains uncertain. Improved food storage

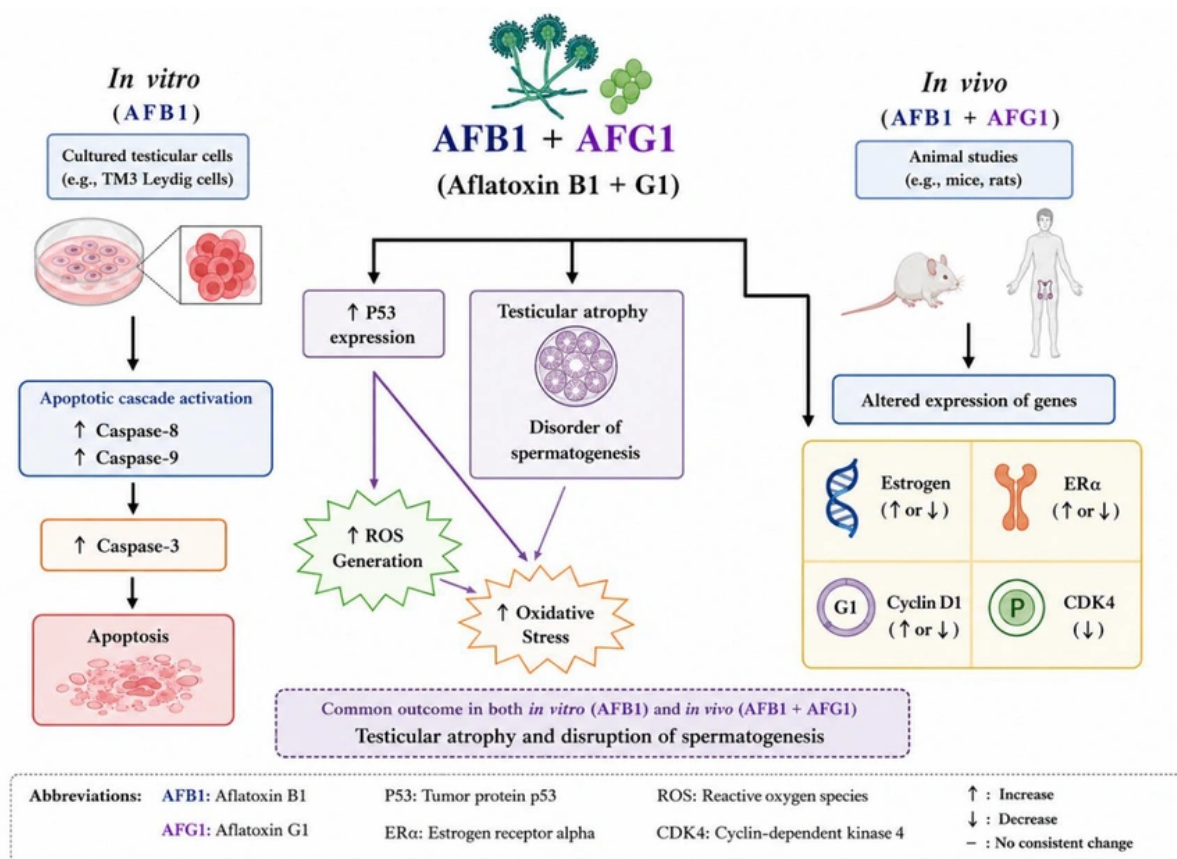


Figure 1. Schematic representation of the effects of AFB1 and AFG1 on testicular cells in vitro and in vivo. In vivo exposure altered the expression of estrogen, ERα, Cyclin D1, and CDK4, while in vitro exposure increased caspase production and activated the apoptotic cascade. Both exposures to AFB1 and AFG1 were associated with testicular atrophy, disrupted spermatogenesis, increased p53 expression, oxidative stress, and reactive oxygen species generation.

and routine monitoring of high-risk foods are practical measures that may help reduce chronic AF exposure and protect reproductive health. These are precautionary policy proposals, and further human studies are needed to clarify reproductive risks.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

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