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REVIEW ARTICLE

Aflatoxin-Induced Neurotoxic Signaling in Animals

Ashiq Ali[1], Kaynaat Akbar[2], Urooj Azmat[2], Sajjad Hussain[3] and Zain ul Abidin[4*]

[1]School of Medical Sciences, Shandong Xiehe University, Jinan 250109, P. R. China; [2]Department of Zoology, Wildlife and Fisheries, University of Agriculture, Faisalabad 38040, Punjab, Pakistan; [3]Directorate General of Research, Livestock & Dairy Development Department Government of Punjab, Lahore Pakistan; [4]Provincial Diagnostic Laboratory, Directorate of Animal Disease Diagnostic, Reporting and Surveillance Livestock & Dairy Development Department, 16-coper road Lahore Pakistan.
*Corresponding author:drzain2063@gmail.com

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A B S T R A C T

Exposure to mycotoxins is a silent and emerging risk to neurological health across the world, especially for vulnerable populations of humans and animals. Aflatoxins (AFTs), produced by fungal contaminants of agricultural commodities are toxic to all the organs of body. The most potent and neurotoxic congener is aflatoxin B1 (AFB1). It has been found that this toxin causes lipid peroxidation, mitochondrial dysfunction, neurotransmitter imbalances, DNA damage, apoptosis and pyroptosis, all of which increase the evidence of disruption of brain homeostasis. Collectively, these neuropathological alterations contribute to a broad spectrum of neurobehavioral disturbances, including heightened emotional dysfunction, depressive manifestations, impaired cognition, deficits in learning and memory retention, and reduced food intake. The neurotoxic effects of AFB1 are mediated through the activation of diverse molecular networks, notably Toll-like receptor signaling (TLR2/TLR4), Akt-dependent pathways, NF-κB and ERK/MAPK cascades, protein kinase C (PKC) signaling, gasdermin D associated pyroptotic mechanisms, and mitochondria-driven apoptotic processes. Phytochemicals, herbal extracts and probiotics are emerging as therapeutic agents with neuroprotective properties against AFB1-induced neuronal injury. Overall, this review offers an overview of the neuropathological mechanisms involved in aflatoxin toxicity and outlines the potential for novel neuroprotective therapeutic approaches.

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INTRODUCTION

Mycotoxins are poisons created by different strains of fungi that have severe impacts on global food safety, public health and agricultural sustainability. Over 500 mycotoxins have been reported, such as fumonisins, aflatoxins, ochratoxins, trichothecenes, tremorgenic toxins, zearalenone, ergot alkaloids, etc. Among these, the most dangerous are the aflatoxins, which are widely distributed and highly toxic (Awuchi*et al.*, 2021; Khatoon *et al.,* 2025). These toxins can be found in food products during cultivation, processing, transportation and storage, and are commonly found in cereals, nuts, edible oils, herbal medicines, tea and water supplies. The formation of cancer, liver or kidney damage, immune system damage, reproductive problems, neurological damage, and other effects have been linked to aflatoxin exposure in animals. Epidemiological studies indicate that populations who consume food containing high levels of aflatoxin, such as peanuts and maize products, suffer from liver cancer (Shekhar*et al.,* 2025).

AFB1 is regarded as biologically active and the most toxic congener within the aflatoxin family because it possesses a unique molecular structure and is very reactive (Khatoon*et al.,* 2024; Ali*et al.,* 2026). Experimental and clinical studies have shown that this toxin is able to cross the blood brain barrier and deposits in brain tissues, causing significant neurological and behavioral effects (Iori*et al.*, 2024). Exposure to AFB1 is associated with learning and memory deficits, depression-like behavior, loss of appetite, peripheral neurotoxicity and developmental neurotoxicity. The underlying mechanism of AFB1 neurotoxicity is mainly oxidative stress, mitochondrial dysfunction, neuroinflammation, disturbance of neurotransmitters, apoptosis, and immunosuppression (Dai*et al.*, 2024).

In addition, the recent development of artificial intelligence (AI) has opened new avenues for exploring and elucidating the neurotoxicity effects of aflatoxin B1 in veterinary and animal models. AI supported imaging and digital analysis can help to assist in identification and quantification of neuropathological changes such as neuronal damage, oxidative injury, neuroinflammation and structural changes in brain tissues (Choudhary and Sarkar, 2025). Furthermore, machine learning and computational tools can correlate toxicological, transcriptomic, proteomic and imaging information to uncover complex mitochondrial signaling networks involved in AFB1-induced mitochondrial dysfunction, NF κB and MAPK activation, apoptosis and pyroptosis (Choudhary, 2025). The use of AI in conjunction with advanced imaging technology and digital pathology could be beneficial for characterizing and predicting Aflatoxin related neurological injury and for the development of new interventions to prevent such injuries (Choudhary*et al.*, 2025). But there are challenges regarding data quality, model validation, accessibility and reproducibility, and ethical issues that need to be addressed in the effective use of AI in veterinary neurotoxicology.

Importantly, there are a number of natural antioxidants and compounds of plant origin, including quercetin, curcumin, gallic acid, dimethyl fumarate, artichoke, pumpkin, *Chelidonium majus* and crocus sativus tea, that have demonstrated promising neuroprotective properties via oxidative stress, inflammation, apoptosis, and mitochondrial damage suppression (Zhang*et al.*, 2015). This review summarizes the mechanisms of action of AFB1-induced neurotoxicity and discusses recent advances in therapeutic strategies to protect against AFB1 toxicity in the brain.

Literature Search Strategy: PubMed, Web of Science, Scopus and Google Scholar were used for a structured literature search to find relevant literature. The literature included in this review was selected based on its relevance to the scientific context, methodological quality, and alignment with the objectives of the review. Articles on significant mechanistic, experimental or clinical information were included, and unrelated, duplicate and non-peer-reviewed publications were excluded. Literature was critically analyzed and the important findings of some relevant studies were summarized and discussed.

AFB1 induced Neurobehavioral Dysfunction and Molecular Neuropathology: Aflatoxin B1 (AFB1) is a highly toxic neurotoxin that can threaten neurological health in humans and animals. Evidence of neurobehavioral abnormalities, neurodegeneration, and neurotransmitter imbalance has been evident through experimentation, and cognitive and emotional dysfunction are outcomes of AFB1 exposure (Owumi*et al.*, 2025a). Murine studies demonstrate that AFB1 exposure induces a spectrum of neurobehavioral and neurodevelopmental abnormalities, including cognitive impairment, reduced locomotion, appetite suppression, memory deficits, and depression-like behavior. Acute and chronic exposures are known to have significant negative effects on cognitive functioning in rodents and aquatic organisms (Subramaniam*et al.*, 2022).

One key feature of AFB1 is its blood–brain barrier (BBB) permeability, allowing it to enter the brain tissues. Both cellular and experimental studies demonstrate marked cytotoxic effects on neurons, astrocytes, microglia, and brain endothelial cells, leading to neuronal degeneration, gliosis, cortical injury and thinning of the hippocampus, vascular congestion, and peripheral nerve injury (Richard*et al.*, 2020). The neurotoxicity of AFB1 is amplified after it is converted by cytochrome P450 enzymes into the more toxic metabolite AFBO (aflatoxin B1-8,9-exo-epoxide).

AFB1 acts as a neurotransmitter system inhibitor, inhibiting acetylcholinesterase, and affects the metabolism of dopamine and serotonin, leading to anxiety, depression, and memory impairment (Ehsanifar*et al.*, 2026). Taken together, these processes oxidative stress, neuroinflammation and neurotransmitter disruption, serve as key cascades of neurotoxicity induced by AFB1 and indicate the critical need for targeted neuroprotective interventions (Altyar*et al.*, 2023). AFB1 induced neurobehavioral dysfunction and molecular neuropathology have been summarized in Fig. 1.

Neurotoxic Molecular Events Induced by Aflatoxin B1 Exposure: Several in vitro models and animal models have revealed that most of the molecular mechanisms involved in aflatoxin B1-induced neurotoxicity are linked with oxidative stress, DNA damage, and inflammatory responses (Selman *et al.,* 2025). Other important mechanisms are release of gasdermin D (GSDMD) mediated pyroptosis, cell cycle arrest, toll-like receptor 2 (TLR2), toll-like receptor 4 (TLR4), protein kinase C (PKC), Akt signaling and mitochondrial apoptotic pathways. The specific sections provide in depth insights to the role of each of the signaling cascades in the neurotoxicity induced by the aflatoxin B1(Dai*et al.*, 2023).

ROS Mediated Neuronal Damage: Among the molecular pathways implicated in AFB1-induced neurotoxicity, oxidative stress is considered a major contributor. It results from an imbalance between the generation of reactive oxygen species including superoxide anions, hydrogen peroxide, hydroxyl radicals, singlet oxygen and the capacity of endogenous antioxidant mechanisms to neutralize them (Shah Alam*et al.*, 2024). But when ROS production is too high, these protective mechanisms are overwhelmed, causing oxidative damage, cell dysfunction, and cell apoptosis. AFB1 exposure is associated with heightened oxidative stress in neural tissues, which plays a pivotal role in mediating its neurotoxic effects (Benkerroum, 2020).

Experimental studies have demonstrated that AFB1 causes significant cell toxicity and increased ROS production in neuronal and glial cells such as neuroblastoma cells (IMR-32), astrocytes and microglia. Overexpression of nicotinamide adenine dinucleotide phosphate oxidase 2 (NOX2), a key enzyme in the generation of ROS in the nervous system, is one such contributor to this oxidative damage (Braga*et al.*, 2023). NOX2 has been implicated in neuronal damage, oxidation and neuropathic pain, and thus has a central role in the neurotoxicity of AFB1. Sustained AFB1 exposure undermines neuronal antioxidant capacity through the depletion of critical antioxidant enzymes and

glutathione reserves, accompanied by increased MDA production. This disruption of redox balance amplifies oxidative damage and heightens neuronal vulnerability to injury (Baruaet *al.*, 2019).

Among the endogenous antioxidant defense systems, the Nrf2/HO-1 pathway serves as a pivotal safeguard against oxidative injury and has emerged as a promising target for combating AFB1 neurotoxicity. Notably, AFB1-induced suppression of OXR1 expression compromises cellular antioxidant defenses, enhancing oxidative stress and accelerating neuronal degeneration (Kanget *al.*, 2026). RNS (Reactive nitrogen species) and NO (nitric oxide) are other important factors involved in AFB1-induced neurotoxicity. After AFB1 exposure, the production of RNS has been observed in the cerebrum, cerebellum, astrocytes, and microglial cells, as well as activation of the NF-κB/iNOS/NO signaling pathway (Chenet *al.*, 2025). Aberrant NF-κB signaling induces iNOS-mediated overproduction of nitric oxide, a key event that promotes neuroinflammation, neuronal dysfunction, and DNA injury. Importantly, dimethyl fumarate confers neuroprotection against AFB1-induced toxicity by attenuating iNOS expression and restraining excessive NO generation, thereby preserving neuronal integrity (Adedaraet *al.*, 2021). Fig. 2 provides a schematic overview of the molecular pathways through which AFB1 induces oxidative stress and inflammatory signaling in neural cells.

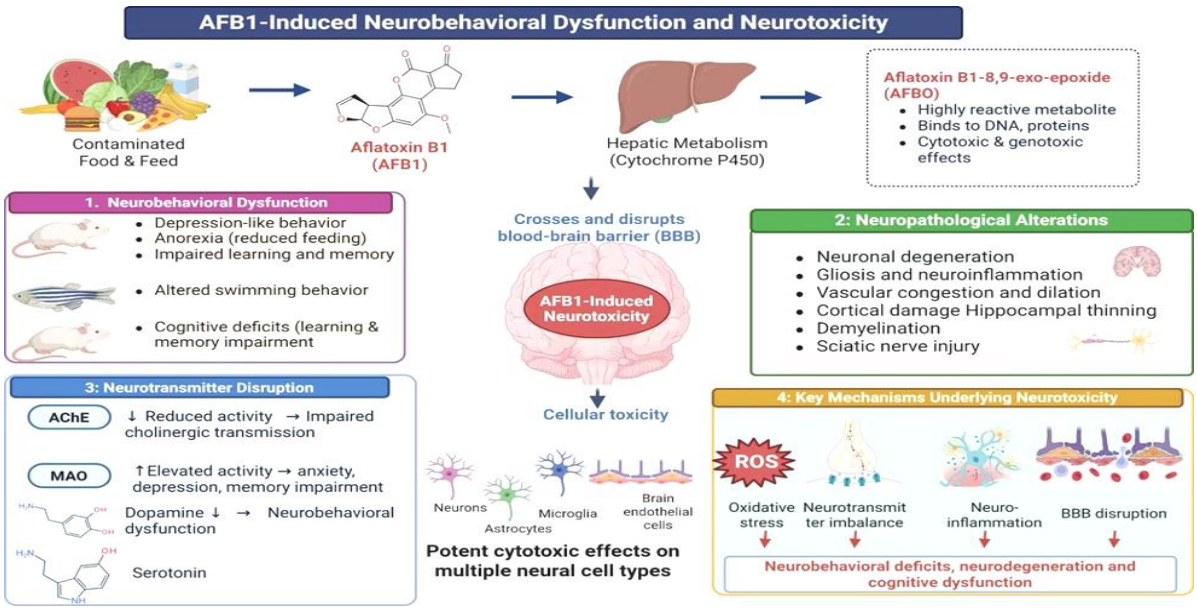


Fig. 1: Neurobehavioral and molecular events of the neurotoxicity of aflatoxin B1. After liver activation, AFB1 damages the blood-brain barrier, resulting in neuroinflammation, neurotransmitter imbalance, and neuronal cell death. These pathological changes eventually lead to neurodegeneration, cognitive impairments and behavioral changes in experimental systems (Biorender.com).

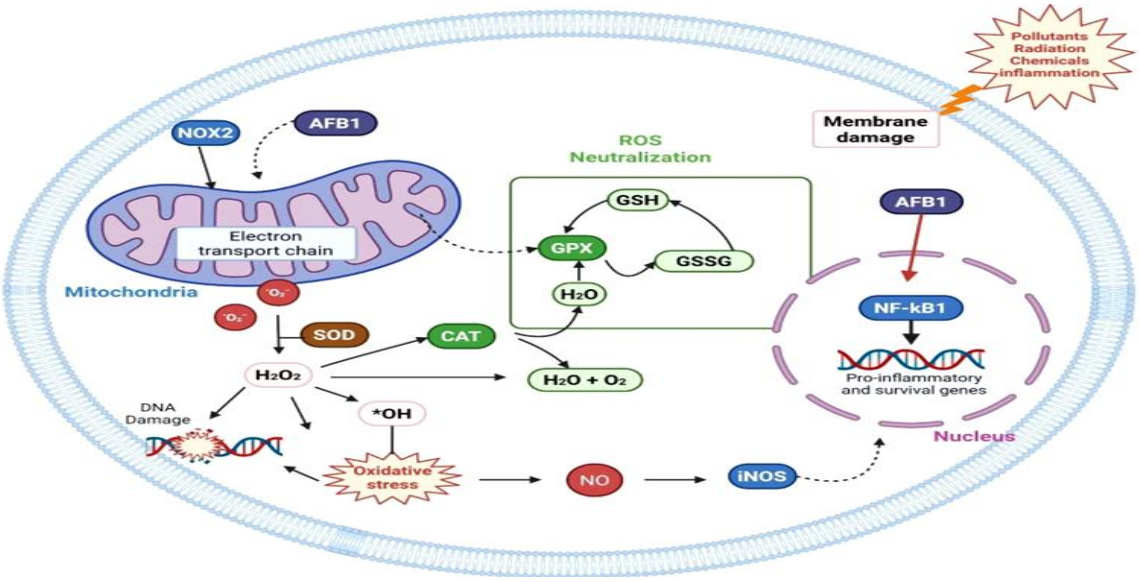


Fig. 2: Proposed mechanism of aflatoxin B1 (AFB1)-induced oxidative stress and inflammatory signaling in neural cells. AFB1 increase the ROS production through mitochondrial damage and the activation of NOX2, which cause lipid peroxidation, DNA damage and cellular injury. An additional activation of NF-κB and iNOS pathways further exacerbates oxidative stress and neuroinflammatory responses (Biorender.com).

Cumulative evidence supports a central role for oxidative and nitrosative stress in AFB1-induced neurotoxicity, characterized by excessive ROS/RNS accumulation, heightened NOX2 activity, activation of NF-κB-dependent inflammatory signaling, and compromised antioxidant defenses. These molecular alterations synergistically drive neuroinflammation, oxidative injury, and progressive neuronal degeneration (García-Esparza*et al.*, 2025). Thus, antioxidant supplementation and specific inhibition of NOX2 and NF-κB/iNOS signaling pathways could be considered as therapeutic targets in the prevention of oxidative stress mediated neurodegeneration resulting from AFB1 exposure (Elgohary*et al.*, 2022).

The mechanisms of neuroinflammation and pyroptosis: Increasing evidence identifies AFB1 as a key inducer of neuroinflammatory and neurodegenerative pathology. By activating multiple inflammatory and immune signaling cascades, AFB1 promotes the accumulation of immune cells such as neutrophils and macrophages within neural tissues, thereby amplifying inflammatory responses in the central nervous system and contributing to neuronal injury (Huang*et al.*, 2020). Among the cellular targets of AFB1 neurotoxicity, astrocytes and microglia are especially susceptible due to their critical roles in maintaining brain homeostasis and neuronal integrity. Long-term AFB1 exposure markedly enhances GFAP expression within the cerebral cortex and hippocampus, signifying reactive astrogliosis and the establishment of chronic neurodegenerative pathology *et al.*, 2025).

Experimental research also indicates that low-dose AFB1 greatly upregulates the expression of inflammatory mediators like TNF-α, IL-10, NF-κB, IL-1β and IL-6 in astrocytes and microglial cells (Park*et al.*, 2020). Activated microglia act as key mediators of AFB1-induced neural injury, with co-culture experiments revealing significantly greater neuronal cytotoxicity in the presence of microglia than in isolated neuronal cultures. Collectively, these observations suggest that glial activation not only contributes directly to neuronal damage but also amplifies the inflammatory milieu associated with AFB1 neurotoxicity (Zhou*et al.*, 2026).

These inflammatory responses are mediated, in part, by NF-κB signaling. AFB1 exposure results in increase in level of phosphorylated NF-κB in neural tissues, which in turn results in an increased transcription of pro-inflammatory cytokines and chemokines (Ramhøj*et al.*, 2016). This response is exacerbated by oxidative stress, via activation of the iNOS/NO pathway, which leads to excessive NO production and neuronal damage. The antioxidant supplements like N-acetylcysteine (NAC) have also been found to be protective, since they downmodulate the activity of NF-κB and dampen oxidative stress induced inflammation (Sakai*et al.*, 2023).

Emerging evidence identifies NLRP3 inflammasome signaling and gasdermin D-driven pyroptosis as key mediators of AFB1-associated neural injury. Through the induction of NLRP3, ASC, caspase-1, and gasdermin D expression in microglial cells, AFB1 and aflatoxin M1 activate inflammatory cascades that facilitate IL-1β and IL-18 maturation, ultimately driving neuroinflammation and pyroptotic neuronal damage (Su *et al.*, 2023). Pharmacological inhibition of gasdermin-D using dimethyl fumarate significantly decreases inflammation, nitric oxide levels and neuronal injury, making it an interesting therapeutic target. The exact connection between oxidative stress and gasdermin D–dependent pathways, however, is not completely understood and needs to be further studied (Wu*et al.*, 2024). Cellular and molecular pathways involved in aflatoxin B1 (AFB1)-induced neuroinflammation and neurotoxicity have been explained in Fig. 3.

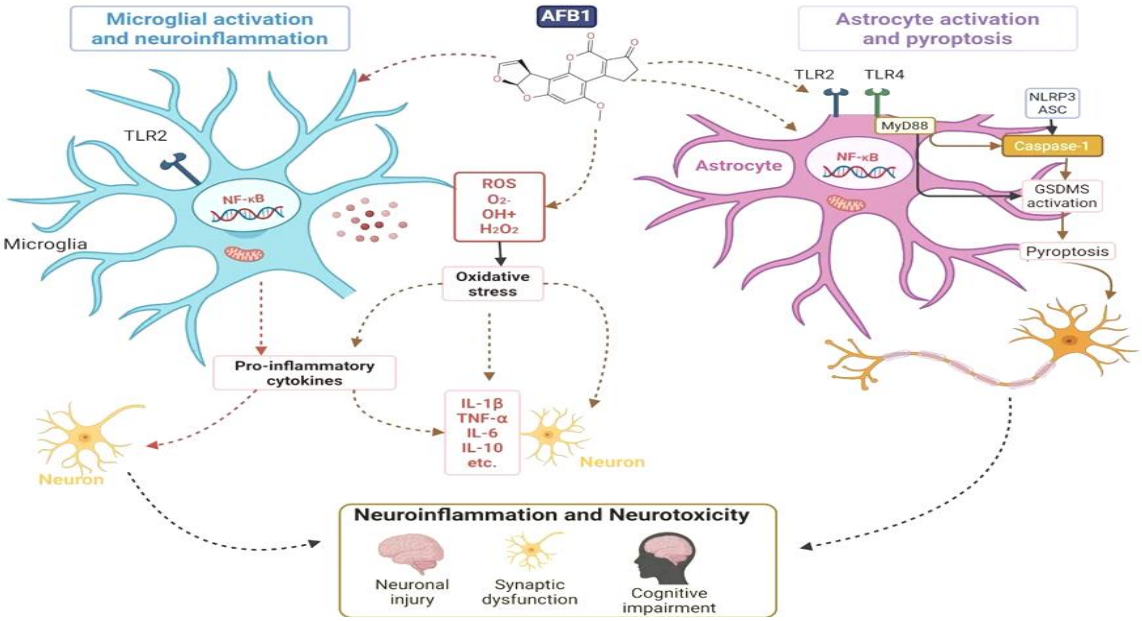


Fig. 3: Cellular and molecular pathways involved in aflatoxin B1 (AFB1)-induced neuroinflammation and neurotoxicity. AFB1 triggers microglial and astrocytic signaling via TLR2/TLR4, NF-κB, and NLRP3 inflammasome pathways, resulting in oxidative stress, pro-inflammatory cytokine production and pyroptosis mediated by GSDMD. All these inflammatory responses contribute to neuronal damage, synaptic dysfunction and cognitive impairment (Biorender.com).

TLR signaling contributes significantly to AFB1-induced neuroinflammation, with low-dose AFB1 exposure upregulating TLR2, TLR4, and MyD88 expression in glial cells and subsequently activating NF-κB-mediated inflammatory pathways (Elangovan*et al.*, 2025). Overall, oxidative stress, glial activation, NF-κB signaling, NLRP3 inflammasome activation, and pyroptosis emerge as the principal mechanisms underlying AFB1-induced neurotoxicity. The results highlight the need to devise specific anti-inflammatory and neuroprotective measures to mitigate neurological insults resulting from chronic exposure to aflatoxin (Liao*et al.*, 2024).

DNA Damage, Mitochondrial Dysfunction, and Cell Death: Mitochondria are the main organelles where the cell generates energy, have roles in calcium homeostasis and are important in cell survival. Neural tissues are especially important in relation to mitochondrial integrity since neurons are highly energy demanding and require a lot of energy to properly function (Wang, *et al.*, 2025). There is growing evidence that mitochondrial dysfunction is a key mechanism of neurotoxicity induced by AFB1. Elevated levels of ROS and RNS generated in response to AFB1 exposure contribute to profound mitochondrial dysfunction, leading to diminished ATP synthesis and progressive loss of neuronal viability *et al.*, 2024).

AFB1 profoundly disrupts mitochondrial function by impairing membrane potential and inhibiting respiratory complexes I–V, ultimately reducing ATP production and compromising cellular energy metabolism (Moloi*et al.*, 2024). These results are consistent with those seen in endothelial cell models of the blood–brain barrier, suggesting that AFB1 directly impairs mitochondrial bioenergetics in neural cells. In addition, exposure to AFB1 significantly raises the level of calcium accumulation in mitochondria, which leads to mitochondrial overload, increasing the neuronal injury (Ye*et al.*, 2025).

In addition to impairing mitochondrial function, AFB1 influences mitochondria-dependent apoptosis by modulating Bax and Bcl-2 expression. Experimental studies have shown that AFB1 and aflatoxin M1 induce apoptosis in neuronal and microglial cells with a significant rise in the ratio of Bax/Bcl-2. Chronic exposure to AFB1 has also caused ultrastructural damage to mitochondria of peripheral nerves, such as swelling and degeneration (Jalili*et al.*, 2024). Notably, antioxidant treatment using N-acetylcysteine (NAC) dramatically decreases the level of oxidative stress, normalizes the Bax/Bcl-2 ratio and rescues neurons from cell death, demonstrating the strong link between oxidative stress and mitochondrial-mediated apoptosis.

In addition to causing mitochondrial dysfunction, AFB1 directly damages neuronal DNA and destabilizes genomic integrity. This is evidenced by increased DNA strand breaks and γH2AX formation, coupled with the downregulation of critical DNA repair genes such as PARP1, BRCA2, and RAD51, which exacerbates genomic damage (Alshamrani*et al.*, 2023). In addition to promoting DNA damage, AFB1 interferes with cell-cycle progression by modulating the expression of CDKN1A, CDKN2A, and CDKN2D. The involvement of oxidative stress is supported by findings that reducing ROS levels mitigates AFB1-induced cell-cycle arrest (Ma *et al.*, 2021).

AFB1 exposure triggers pronounced apoptotic cell death by activating caspase-3, caspase-8, and caspase-9 in a dose and time-dependent manner, leading to progressive neuronal injury and loss. Animal studies also show that chronic administration of AFB1 causes dose-dependent apoptosis in the spinal cord (Chałaśkiewicz*et al.*, 2025). Several intracellular signaling pathways have been involved in this apoptotic response, such as ERK/MAPK, Akt, and p53 signaling pathways. AFB1 inhibits the Akt signaling pathway and its downstream effectors and stimulates the ERK/MAPK pathway to induce neuronal apoptosis. Interestingly, the role of p53 signaling is different in various types of neural cells, indicating cell-specific mechanisms of AFB1-induced toxicity. Further pharmacological evidence of ERK/MAPK signaling in AFB1-induced neurodegeneration was provided by partial reduction in neuronal cell death upon ERK/MAPK inhibition (Chen*et al.*, 2016). Molecular mechanisms underlying aflatoxin B1 (AFB1)-induced neuronal apoptosis and cell cycle arrest have been depicted in Fig. 4.

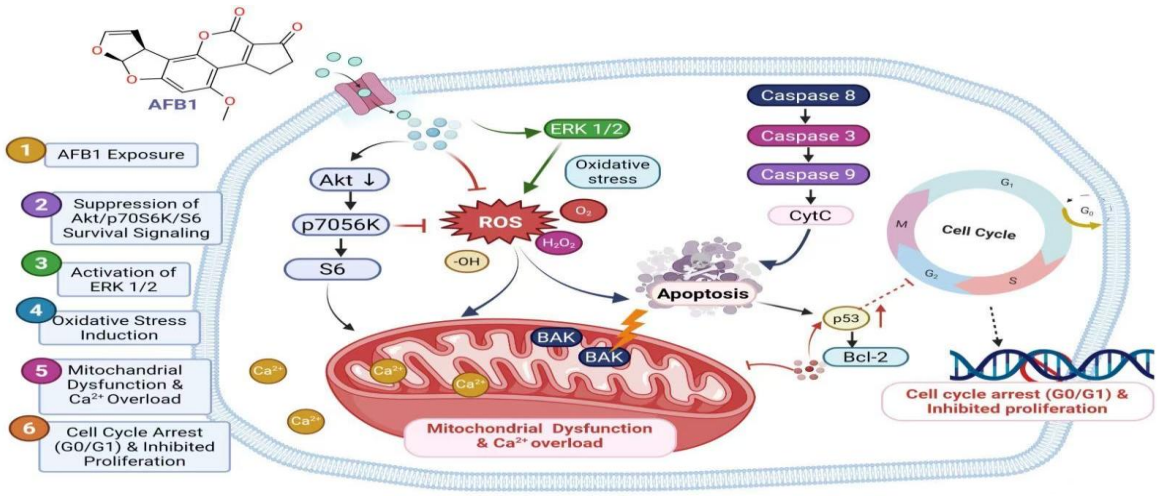


Fig. 4: Mechanisms of AFB1-induced neuronal apoptosis and cell-cycle arrest. AFB1 disrupts cellular homeostasis through oxidative stress, mitochondrial dysfunction, calcium dysregulation, inhibition of Akt/p70S6K signaling, and activation of ERK1/2 and caspase pathways, leading to apoptosis, G0/G1 arrest, and reduced cell proliferation (Biorender.com).

Taken together, the available data identify mitochondrial impairment, oxidative stress, DNA damage, cell-cycle arrest, and apoptosis as key mechanisms underlying AFB1-induced neurotoxicity (Abia*et al.*, 2025). All of these increased ROS production, mitochondrial calcium overload, diminished ATP production, and dysregulation of ERK/MAPK and Akt pathways play a role in neuronal injury and neurodegeneration. The results point to the significance of therapeutic intervention for antioxidant and mitochondria targeting in reducing AFB1 induced neurological damage (Adedara*et al.*, 2023).

Aflatoxin B1 induced neurotoxicity via activation of PKC: The protein kinase C (PKC) signaling pathway has been linked to neurotoxicity brought about by Aflatoxin B1. Single oral acute exposure of AFB1 results in marked enhancement in the PKC activity within the cerebral cortex of rats after 48 hours. Other than receptor desensitization, PKC has been implicated in several other physiological processes such as: modulation of cellular development, learning, and memory; immune system function; and regulation of membrane structure (Souto*et al.*, 2018).

Newly Discovered Neuroprotective Drugs for Aflatoxin B1 induced Neuronal Injury: Natural antioxidants, including quercetin, curcumin, gallic acid, and dimethyl fumarate, together with herbal extracts and probiotic strains such as *Bifidobacterium* and *Lactobacillus*, have been shown to effectively attenuate AFB1-induced neurobehavioral impairments and neurotoxicity (Dai*et al.*, 2022). The protective mechanisms are primarily through decreased oxidative stress, inflammatory modulation, and inhibition of the apoptotic and pyroptotic cell death pathways. The following sections give a general overview of the current literature on these promising neuroprotective drugs (Karvandi*et al.*, 2023).

Functional Antioxidant Compounds: AFB1 neurotoxicity is primarily driven by excessive ROS production, which induces mitochondrial dysfunction and activates apoptotic and pyroptotic pathways via NLRP3 inflammasome activation and GSDMD upregulation. Agents such as NAC and dimethyl fumarate may therefore provide therapeutic benefits by attenuating oxidative stress and suppressing pyroptotic signaling (Song*et al.*, 2024). Studies have shown that quercetin mitigates anxiety-like behavior and confers significant neuroprotection in mice chronically exposed to AFB1. These benefits are associated with reduced MDA accumulation and enhanced antioxidant defenses, including increased SOD, CAT, and GSH levels in brain tissue (Gugliandolo*et al.*, 2020). In addition, quercetin significantly reduced TNF-α and IL-1β levels, highlighting its ability to protect against AFB1-induced neurotoxicity through the suppression of oxidative and inflammatory damage (Sallam*et al.*, 2022).

The neurobehavioral deficits, inflammation, apoptosis and oxidative stress in cerebral tissues caused by aflatoxin B1 was found to be significantly reduced by 20 and 40 mg/kg of gallic acid supplementation in a subsequent study. Low-dose (1ppb/1ng/mL) aflatoxin M1 (AFM1) is synergistic with low-molecular-weight whey protein, β-lactoglobulin, in PC12 neuronal cells. This neurotoxicity effect can be overcome or reduced, when taken in combination (Owumi*et al.*, 2025b). The beneficial effects of curcumin against AFB1-associated hepatotoxicity, nephrotoxicity, and immunotoxicity are primarily attributed to Nrf2 activation and NF-κB inhibition, mechanisms that collectively suppress oxidative stress, inflammation, and apoptotic cell death. The results indicate the possibility of using antioxidants as functional food ingredients to reduce the neurotoxicity effects caused by aflatoxins, as small molecule antioxidants (Kozieł*et al.*, 2021).

Plant Derived Neuroprotective Agents: Preclinical evidence highlights the neuroprotective potential of several traditional medicinal plant preparations, including artichoke leaf extract, *Chelidonium majus* ethanolic extract, pumpkin extract, and *Crocus sativus L*. tea, in alleviating aflatoxin B1-induced neuronal damage (Kasem, 2022). In rats, artichoke leaf extract is effective for significantly alleviating neurotoxicity induced by Aflatoxin B1 by boosting antioxidant enzyme activities and re-establishing their metabolic parameters such as lipid profile, elevated plasma glucose and insulin levels. The hepatoprotective activity of artichoke leaf extract against hepatotoxicity caused by AFB1 has been identified in rats mostly through antioxidant activity (Ibrahim*et al.*, 2022). Oral treatment with *Chelidonium majus* ethanolic extract (CMEE) for 28 days has shown a significant decrease in the oxidative stress, apoptosis and, inflammatory response caused by aflatoxin B1, while the level of neurotransmitters, such as acetylcholinesterase activity, dopamine and serotonin, has been restored. Studies indicate that pumpkin extract mitigates AFB1-induced mitochondrial dysfunction through the upregulation of respiratory complex I, IV, and V genes. In parallel, saffron tea improves cognitive performance and attenuates oxidative stress and MAO activity in neural tissues following chronic AFB1 exposure (Rotimi*et al.*, 2018).

To conclude, available evidence suggests that traditional chinese medicine is a potential therapeutic approach to neurotoxicity caused by aflatoxin B1. Numerous molecular targets and pathways are believed to mediate these positive actions including regulation of genes associated with oxidative stress, replenishment of the mitochondrial respiratory chain and regulation of neurotransmitter systems (Yan*et al.*, 2022).

Neuroprotective Role of Probiotics: Gut dysbiosis, characterized by changes in *Bifidobacterium* and *Lactobacillus* populations, has been implicated in the neurobehavioral disturbances observed in AFB1-exposed rats. Probiotic administration of these bacteria alleviates depressive like symptoms induced by aflatoxin exposure (Liew*et al.*, 2019). These probiotics may confer neuroprotection by restoring gut microbial balance, strengthening intestinal barrier function, and reducing AFB1-induced intestinal toxicity. The available evidence underscores the importance of the gut–brain axis in aflatoxin-associated neurotoxicity; however, the underlying molecular pathways require further validation

in rigorously conducted clinical studies (Choi*et al.*, 2025).

Conclusion: Overall, AFB1 poses a serious threat to brain health due to its ability to penetrate the blood–brain barrier and persist in neural tissues. Cognitive and memory impairments, learning deficits, decreased locomotion, anorexia, and depression-like behavioral disturbances reflect its neurotoxic effects. The underlying molecular mechanisms of these pathological processes include interconnected mechanisms of oxidative stress, activation of glia, neuroinflammation, dysbiosis of gut microbiota, neurotransmitter imbalance, mitochondrial dysfunction, apoptotic and pyroptotic cell death. They play a crucial role in these neurotoxic pathways including GSDMD, TLR2/TLR4, Akt, NF-κB, ERK/MAPK, PKC and mitochondrial apoptotic pathways. Interestingly, several therapies have been identified as neuroprotective by regulating these pathways, such as quercetin, curcumin, gallic acid, dimethyl fumarate, extracts from medicinal plants, and probiotics like *Bifidobacterium spp.* and *Lactobacillus spp.* Future research needs to focus on carefully designed experimental and clinical trials, elucidation of the role of gut dysbiosis, and investigation into the connection between aflatoxin exposure and neurodegenerative diseases. The collective evidence underscores the potential for translating mechanistic insights into effective neuroprotective interventions against aflatoxin-induced brain injury.

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