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Review Paper

Risk ranking and prioritization of Aflatoxin M_1 in milk: a strategic tool for strengthening the national food safety system in Serbia

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ABSTRACT

In Serbia, aflatoxin M1 (AFM1), a carcinogenic metabolite of aflatoxin B1 (AFB1), is a common contaminant in milk and poses a significant food safety risk. Due to climate change, aflatoxin contamination remains a recurring and serious food safety issue, particularly for vulnerable groups, such as children. In this context, key priorities include AFM1 surveillance, public health risk quantification, regulatory assessment, and exposure modelling. These efforts are essential to support science-based decision-making and evidence-informed policy design. This paper proposes a structured, integrated methodology for risk ranking and prioritization of AFM1 in milk, with the aim of strengthening the national food safety system in Serbia. The approach enables systematic identification of high-risk regions, critical contamination periods, and vulnerable population groups. It also facilitates evidence-based monitoring and more efficient allocation of resources. In addition, the proposed methodology supports regulatory alignment with European Union (EU) food safety standards, enhances risk governance, and increases consumer confidence. Ultimately, risk ranking and prioritization are presented as essential tools for improving food safety outcomes, reducing human exposure to chemical hazards, and protecting public health in the dairy sector.

1. Introduction

Aflatoxins are secondary metabolites produced by *Aspergillus* fungi, mainly *A. flavus* and *A. parasiticus*. Among them, aflatoxin B_1 (AFB_1) is the most toxic and is classified as a Group 1 carcinogen by the International Agency for Research on Cancer (*IARC*, 2012). When ingested by dairy cows *via* contaminated feed, AFB_1 is metabolized into aflatoxin M_1 (AFM_1), which is excreted in milk. AFM_1 retains genotoxic and hepatotoxic properties, posing a significant health risk, particularly to vulnerable groups, such as children and pregnant women.

In Serbia, aflatoxin contamination in milk has been a recurring issue since 2012, closely linked to climate change effects, such as rising temperatures and droughts, which promote fungal growth in corn—the primary cattle feed (*Milićević et al.*, 2020). Studies confirm a correlation between climate variability and increased AFB_1 contamination, leading to

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elevated AFM_1 levels in milk, especially during dry seasons (*Milićević et al.*, 2019). Exposure assessments conducted in Serbia (*Milićević et al.*, 2021) indicate that children are particularly at risk from chronic AFM_1 intake. Although concentrations generally remain within national limits, Serbia's maximum residue level (0.25 µg/kg) is significantly higher than the EU standard (0.05 µg/kg), highlighting the need for stricter controls and harmonized food safety policy. Given the way AFM_1 enters the food chain—combined with its thermal resistance and carcinogenicity—it requires a more structured, science-based risk management approach, which is still lacking in Serbia despite prior monitoring efforts.

Risk ranking is a key component of risk assessment, involving scientific evaluation and comparison of hazards based on potential health impact and exposure likelihood. Risk assessors analyze toxicological and exposure data, while risk prioritization, led by risk managers, determines how to act, where to intervene, and how to allocate limited resources effectively (*FAO,* 2020).

This paper presents a science-based methodology for the risk ranking and prioritization of AFM_1 in milk, tailored to the national context of Serbia and aligned with international food safety principles. The proposed framework supports transparent, evidence-driven risk management in dairy production, particularly in response to climate-related contamination challenges. It aims to improve milk safety for all population groups, with a focus on protecting infants, children, and pregnant women. This initiative is grounded in ongoing interdisciplinary research led by national food safety and public health experts and provides a foundation for future decision-support tools in Serbia's dairy sector.

2. Methodology: risk ranking and prioritization of chemical hazards in food

2.1 Risk ranking: what to monitor

Risk ranking is a structured, evidence-based method used to identify which chemical hazards in food present the greatest public health concern (*FAO,* 2020; *Van der Fels-Klerx et al.*, 2015) (Figure 1). It answers the question: "What should we monitor?" by evaluating the severity of health effects (e.g., genotoxicity, carcinogenicity) as well as the probability of exposure, which is primarily influenced by contamination levels, dietary habits, and population vulnerability. This step is especially critical in systems with limited monitoring capacity, as it enables scientific prioritization of hazards for surveillance and control. International bodies, such as the Food and Agriculture Organization (FAO) and the European Food Safety Authority (EFSA), emphasize that ranking should be transparent, reproducible, and rooted in data to support credible decision-making.

2.2 Risk prioritization—how and where to act

Risk prioritization builds on ranking to address the next essential question: "How and where should action be taken?" It translates scientific insights into management strategies, integrating additional practical considerations, primarily public and political sensitivity, economic and trade impact, and feasibility of implementation (infrastructure, technology, logistics) (*FAO,* 2020; *Van der Fels-Klerx et al.*, 2015). The result is a ranked list of actionable interventions, adapted to national circumstances. While based on scientific risk assessments, prioritization also reflects stakeholder values, regulatory feasibility, and capacity for mitigation, making it the bridge between risk assessment and practical food safety management.

2.3 Methodological approaches: top-down vs bottom-up

2.3.1 Top-down—based on public health outcomes

The top-down approach uses population-level health metrics to prioritize risks (*FAO,* 2020). These metrics include disease burden indicators (Disability-Adjusted Life Years (DALYs) and Quality-Adjusted Life Years (QALY), epidemiological data on incidence, mortality, and disease attribution, and global frameworks, such as WHO's Foodborne Disease Burden Epidemiology Reference Group (FERG) methodology. This approach is typically applied to well-characterized hazards and is commonly employed by public health agencies to inform high-level policy decisions, for instance, assessing the attributable risk of AFM_1 in hepatocellular carcinoma incidence.

2.3.2 Bottom-up—based on hazard and exposure

When health outcome data are limited, as is commonly observed in developing countries, the bottom-up approach provides an alternative by focusing on:

- Exposure Context, e.g., consumption patterns and contaminated food items (such as milk and maize-based feed), measured levels of AFM_1, and exposure routes and vulnerable groups (children, infants).
- Hazard Characteristics, e.g., identity and toxicological profile of AFM_1 (Group 1 carcinogen), and threshold values, such as the lower bound of the benchmark dose ($BMDL_{10}$) and the margin of exposure (MOE) for risk estimation.
- Contextual Considerations, e.g., socio-economic capacity, technical infrastructure, and feasibility of intervention (*FAO,* 2020).

This method is especially relevant for AFM_1 in Serbia, where public health data may be limited, but contamination monitoring and exposure modelling can inform effective, evidence-based interventions (*Milićević et al.*, 2021; *Udovicki et al.*, 2023).

2.3.3 Methodological tools used in bottom-up risk ranking

The bottom-up approach combines scientific data with context-driven analysis using quantitative, semi-quantitative, and qualitative tools (*Van der Fels-Klerx et al.*, 2018). Quantitative tools like the MOE and hazard quotient (HQ) assess health risks by comparing estimated human exposure to toxicological benchmarks. For genotoxic carcinogens such as AFM_1, MOE below 10,000 or HQ above 1 indicate a public health concern. When data availability is limited, semi-quantitative tools are commonly used. Although they retain certain quantitative aspects, their evaluations are less robust than those produced by qualitative tools. Among others, these include scoring method, in which numerical weights are assigned to factors, such as prevalence, severity or exposure; risk matrices which map severity against likelihood; and Multi-Criteria Decision Analysis (MCDA) which integrates scientific, social, and economic dimensions to support balanced, transparent decision-making.

Qualitative tools are generally used when both resources and available data are severely limited, making it the most basic assessment approach. These tools include drafting decision trees and flowcharts designed to classify hazards into risk categories. The advancement of risk assessment methodologies can be enhanced through integration with EFSA-developed databases and tools. These include OpenFoodTox, which provides toxicological profiles of food and feed; DietEx tool, which estimates dietary exposure; or RACE, a tool that provides an assessment of acute and chronic exposure in different populations.

2.4 Risk ranking and prioritization: focus on the dairy chain

When determining the risk from aflatoxin exposure, multiple factors specific to the dairy chain have to be considered. Firstly, AFB_1 has a rapid biotransfer and carry-over, meaning that AFM_1 will appear in milk within 24 hours of AFB_1 ingestion from contaminated feed. Secondly, AFM_1 is heat-stable, meaning it persists through pasteurization and other processing methods, remaining in final dairy products. Furthermore, special attention should be paid to exposure in infants and children, as they consume more milk relative to their body size.

2.4.1 Risk ranking: key inputs and indicators

In order to effectively perform risk ranking of AFM_1, it is essential to integrate several sources of data. Toxicological data must be considered first, notably the classification of AFM_1 as an IARC Group 1 carcinogen and EFSA's $BDML_{10}$ of 4 µg/kg bw/day. Next, the carry-over rate (COR) from feed to milk requires evaluation of multiple variables, including AFB_1 concentration in feedstuffs, the cows' diet composition, lactation stage, and herd productivity metrics. Lastly, exposure assessment in humans should incorporate both milk consumption patterns and monitoring data on AFM_1 levels. Analytically, this translates to applying MOE and HQ methodologies, supplemented by scoring methods that weigh hazard severity against exposure prevalence and population vulnerability.

2.4.2 Prioritization of risk management actions

After hazards are ranked, prioritization focuses on where interventions will have the greatest impact. For AFM_1 in milk, priority actions could include: targeting regions prone to drought and maize contamination; focusing on periods of elevated risk (late summer–winter); identifying high-risk farm profiles (e.g., heavy silage use, poor hygiene); and enhancing monitoring of milk intended for infants or export. Based on the determined focus of priority, recommended measures could include: implementing risk-based seasonal monitoring; training farmers in feed management and mycotoxin control; gradually aligning Serbian MRLs with EU standards to reduce public health risks and enhance trade opportunities.

2.4.3 Case study: Serbia

Following the severe AFM_1 milk contamination crisis in 2013, triggered by extreme weather and widespread maize contamination, several scientific studies have established a rationale for the development of a structured risk ranking and prioritization framework in the Serbian dairy sector. The findings of these studies point to AFM_1 in milk and dairy products as a priority hazard, with confirmed presence not only in fluid milk but also in traditional cheeses from regional markets. This observed high threat highlights the need for broader monitoring (*Milićević et al.*, 2020; *Torović,* 2015; *Torović et al.,* 2021; *Udovicki et al.,* 2018).

Several studies (*Milićević et al.,* 2021; *Torović,* 2015; *Torović et al.,* 2021) emphasize that population-specific co-factors must be incorporated into risk assessments to accurately evaluate the risk of developing diseases. A critical example is the synergistic effect between AFM_1 exposure and Hepatitis B, which significantly exacerbates the risk of hepatocellular carcinoma. Furthermore, some populations, primarily children, must be recognized as vulnerable groups, as they consistently exhibit the highest exposure due to their higher milk intake relative to body weight. This exposure usually exceeds safety thresholds during peak contamination periods, especially in school milk programs (*Milićević et al.,* 2021; *Udovicki et al.,* 2023). Climate change has been identified as a significant factor in crop contamination by mycotoxins. Extreme weather conditions, such as floods and droughts, which have occurred in Serbia in recent years, have led to the promotion of fungal growth and aflatoxin accumulation in feed, further increasing the scientific attention, especially from the perspective of risk analysis (*Milićević et al.,* 2019). These findings provide the scientific foundation for a data-driven, risk-based management system for AFM_1 in Serbia's dairy chain, aligned with international food safety standards.

Figure 1. Conceptual flowchart for managing AFM_1 risk in milk supply chain

3. Conclusion

Risk ranking and prioritization of AFM_1 in milk are essential for enhancing food safety in Serbia's dairy sector. The direct transfer of AFB_1 from contaminated feed to milk, combined with AFM_1's thermal stability and its proven genotoxic and hepatocarcinogenic effects, necessitate a preventive, evidence-based strategy. National data confirm the value of exposure-based models in identifying high-risk groups—especially children—and in guiding timely, targeted interventions. Implementing structured risk assessment frameworks will enable more effective monitoring, optimized resource allocation, and better alignment with EU food safety standards. This, in turn, will contribute to improved public health protection, greater consumer confidence, and enhanced regulatory and export readiness. Rather than functioning as standalone tools, risk ranking and prioritization should be embedded within a broader, integrated strategy to build a resilient and future-oriented national food safety system.

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