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Computational Prediction of Mycotoxin-Protein Interactions: A Veterinary Perspective

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INTRODUCTION & AIM

Mycotoxins are naturally occurring toxic metabolites produced by fungi that contaminate animal feed, posing significant risks to livestock health and food safety. The molecular interactions of these toxins with key proteins are critical for elucidating toxicity mechanisms and developing preventive strategies. This study explores the application of computational methods, particularly molecular docking and molecular dynamics (MD) simulations, to predict and validate interactions between major mycotoxins and biologically relevant target proteins in food-producing animals.

Molecular docking was first employed to estimate the binding affinity and interaction profiles of representative mycotoxins, including aflatoxin B1 and ochratoxin A, with proteins directly implicated in toxin transport, metabolism, and bioavailability. These included **bovine serum albumin (BSA)**, a primary carrier protein mediating systemic distribution; **porcine organic anion transporter 1 (OAT1)**, which facilitates renal elimination; and **cytochrome P450 enzymes** responsible for metabolic activation. The resulting complexes were subsequently evaluated using MD simulations to assess the stability, flexibility, and dynamic behaviour of the ligand–protein interactions under physiological conditions. Parameters including root-mean-square deviation (RMSD), root-mean-square fluctuation (RMSF), hydrogen bond occupancy, and molecular mechanics Poisson–Boltzmann surface area (MM-PBSA) energy calculations were analysed to validate binding stability and interaction persistence over time.

METHOD

Molecular Docking:
Representative mycotoxins (aflatoxin B1 and ochratoxin A) were docked to three biologically relevant proteins implicated in toxin transport and metabolism: bovine serum albumin (BSA), porcine organic anion transporter 1 (OAT1), and cytochrome P450 enzymes. Docking was performed using AutoDock Vina to estimate binding affinities and predict interaction residues.

Molecular Dynamics (MD) Simulations:
The most favourable docking poses were subjected to 100 ns MD simulations in explicit solvent using GROMACS. Analyses included RMSD, RMSF, hydrogen bond occupancy, and MM-PBSA free energy calculations to assess the stability and persistence of interactions under near-physiological conditions.

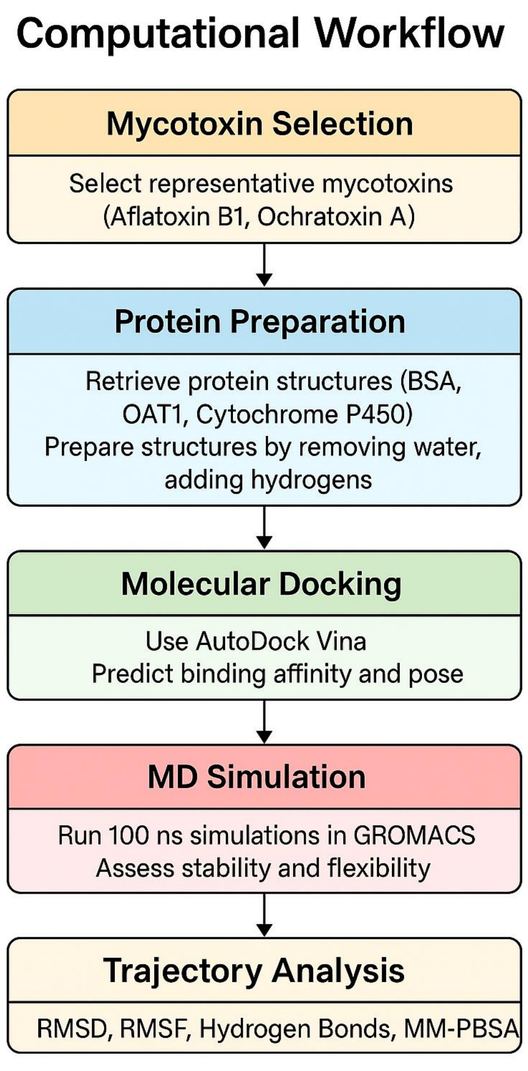

Figure 1. Computational workflow combining molecular docking and molecular dynamics simulations to investigate mycotoxin–protein interactions.

RESULTS & DISCUSSION

Binding Affinity and Interaction Profiles:
Docking revealed high-affinity binding of aflatoxin B1 to BSA (predicted ΔG ≈ –9.3 kcal/mol) and ochratoxin A to OAT1 (ΔG ≈ –8.7 kcal/mol), highlighting their potential for systemic transport and renal accumulation.

Dynamic Stability:
MD simulations confirmed stable complexes with consistent RMSD (<0.25 nm fluctuation) and persistent hydrogen bonding throughout the trajectory, particularly between aflatoxin B1 and BSA.

Energetic Analysis:
MM-PBSA calculations supported favourable binding free energies consistent with docking predictions, validating the computational approach.

Implications:
These findings reinforce the relevance of protein–mycotoxin interactions in toxicokinetics. Characterising these interactions helps explain bioavailability and accumulation in animal tissues, supporting the design of effective mitigation strategies and risk assessment frameworks.

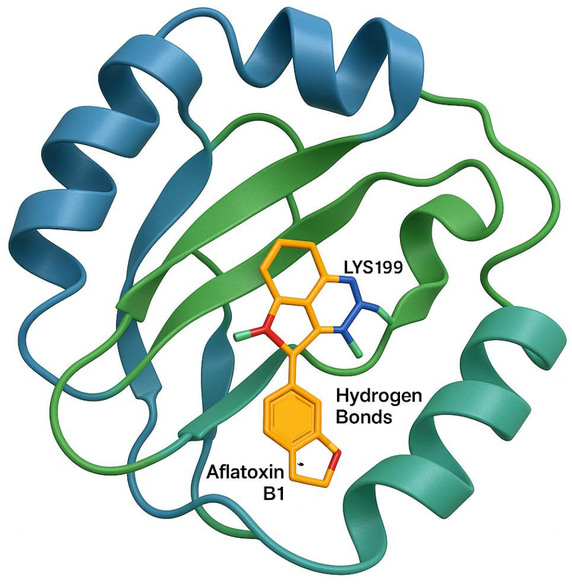

Figure 2: Predicted docking poses of (A) aflatoxin B1 bound to bovine serum albumin and (B) ochratoxin A bound to OAT1, highlighting key interactions relevant to toxin transport and bioavailability.

The predicted binding affinities and interaction patterns are consistent with the known toxicokinetic behaviors of these compounds, including their bioavailability and potential for tissue accumulation. These insights enhance mechanistic understanding of toxin transport, metabolism, and elimination processes critical to animal health and food safety. Furthermore, the combination of docking and MD simulations provides a cost-effective, scalable framework that can complement experimental studies and inform the design of mitigation strategies such as competitive inhibitors or binding agents to reduce mycotoxin bioavailability.

CONCLUSION

The findings underscore the potential of *in silico* approaches in veterinary toxicology for identifying high-risk feed contaminants and elucidating their molecular mechanisms of action through interactions with biologically relevant proteins. This framework not only advances the understanding of mycotoxin toxicity but also supports evidence-based risk assessment, regulatory monitoring, and the rational design of protective feed additives. Importantly, characterising these protein–mycotoxin interactions provides mechanistic insights into toxicokinetics, informs the development of targeted mitigation strategies to reduce mycotoxin exposure in livestock, and contributes to safeguarding public health by limiting the transfer of residues into the human food chain. The integration of computational toxicology into veterinary research aligns with One Health principles, offering scalable tools for protecting animal health and ensuring food safety.

FUTURE WORK

Expand the ligand library to include emerging mycotoxins (e.g., fusariotoxins) for comprehensive risk profiling.

Evaluate additional transporter and detoxification proteins relevant across species.

Integrate quantitative structure–activity relationship (QSAR) modelling to predict novel inhibitors of toxin–protein binding.

Collaborate with experimental toxicology labs to validate computational predictions in vitro and in vivo.

Develop a publicly accessible database of mycotoxin–protein interactions to support regulatory and research communities.