Mouse precision-cut liver and kidney slices: an optimized ex vivo model for acute toxicity testing

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Abstract

As excretion organs, the kidneys and liver are exposed to high concentrations of potentially toxic substances. While animal models remain the gold standard for organ-specific toxicity testing, alternative ex vivo approaches are essential to align with the 3R principles (refinement, reduction, replacement). Precision-cut tissue slices (PCTS) retain native tissue architecture, cellular heterogeneity, the interplay of different cell types, and metabolic capacity, offering a promising link between in vitro and in vivo models. Here, we aimed to establish an optimized protocol for preparing and culturing precision-cut kidney and liver slices (PCKS and PCLS) from mice for use in substance-oriented toxicological tests. Key parameters - including slice thickness, media composition, oxygenation, glucose levels, and incubation time - were refined to maintain tissue viability and metabolic function. Five known toxins - acetaminophen, cyclosporin A, cisplatin, arsenic trioxide, and aristolochic acid I - were tested. While PCKS showed comparable sensitivity to established kidney cell lines, PCLS achieved IC50 values closely matching in vivo toxicity data. High reproducibility across different experimenters was achieved, highlighting the robustness of the model. In conclusion, this ex vivo system provides a valuable, reproducible, and ethically approved platform for acute nephrotoxicity and hepatotoxicity testing, supporting preclinical drug screening and potentially reducing reliance on animal experiments.