EXPERIMENTAL ANIMAL MODELS USED IN LIVER DISEASES

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Relevance: Liver diseases are among the leading causes of mortality worldwide. Animal models play a crucial role in the preclinical stage for the development and evaluation of hepatoprotective drugs. Liver disorders such as hepatitis, steatosis, fibrosis, and cirrhosis pose significant social and economic challenges globally. According to the World Health

carcinoma. In such circumstances, the development of hepatoprotective therapies becomes an urgent issue, and reliable experimental model systems are essential for evaluating drug efficacy.

Objective of the study: This abstract analyzes the mechanisms of various experimental models, their clinical relevance, evaluation criteria, and modern innovative approaches.

Methods and methodology: Modern scientific literature was reviewed during the preparation of this abstract. Data was collected from databases such as PubMed, Scopus, Google Scholar, and Elsevier.

Results:CCl_4(Carbon tetrachloride): Causes hepatocyte damage through free radicals, leading to necrosis. Advantages of this model include high reproducibility and reliability in modeling fibrosis and cirrhosis. CCl_4 generates free radicals in hepatocytes, damaging cell membranes and stimulating collagen production. Fibrosis develops within a short period (typically 4–8 weeks). Widely used in scientific literature with well-established methodology.*Limitations:* The mechanism does not fully match human hepatotoxicity. CCl_4 vapors are toxic and require safety precautions. It can also harm other tissues (kidneys, lungs). Sensitivity may vary between animals.

Paracetamol(APAP-acetaminophen): Useful for studying drug-induced hepatotoxicity (closely mimics clinical conditions). Like in humans, toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI) is formed in the liver. Allows assessment of effective antidote therapies (e.g., N-acetylcysteine).*Limitations:* The toxic dose range is narrow—slight overdose may be fatal for animals. It models only acute liver injury, not chronic conditions. The activity index changes rapidly, making the timing of analysis critical.

Thioacetamide(TAA): Long-term administration reliably models chronic fibrosis and cirrhosis. Accurately mimics clinical features such as portal fibrosis, nodule formation, and neovascularization. Mechanistically different from the CCl_4 model—induces fibrosis via hepatotoxicity. *Limitations:* Less commonly used, and the methodology is more complex. May cause concurrent kidney damage due to hepatotoxicity. Hypoxia and significant weight loss may lead to stress in animals.

Paracetamol+Ethanol Combined Model: APAP is safe at normal doses but converts to the toxic metabolite NAPQI at high doses. Ethanol induces CYP2E1, increasing NAPQI formation. It also weakens the glutathione detoxification system, making the liver more vulnerable to NAPQI. This combination leads to oxidative stress, mitochondrial dysfunction, and necrosis. *Advantages:* Highly clinically relevant. Accurately models drug–alcohol toxicity seen in humans. Enables realistic evaluation of hepatoprotective and antidote therapies (e.g., N-acetylcysteine).

Conclusion: Each model has its own biological advantages and limitations, and should be selected based on the specific research objective. For instance, while the CCl_4 model is simple and reproducible, it has high overall toxicity. The paracetamol model closely mimics clinical scenarios

and allows precise assessment of cytotoxicity. The ethanol model is useful in modeling chronic alcoholic liver diseases, but requires extended duration and may be influenced by individual animal sensitivity. Combined models (e.g., paracetamol + ethanol) allow for deeper study of complex pathogenesis.