

ПАТОЛОГИЯ ЖИВОТНЫХ, МОРФОЛОГИЯ, ФИЗИОЛОГИЯ, ФАРМАКОЛОГИЯ И ТОКСИКОЛОГИЯ/ANIMAL PATHOLOGY, MORPHOLOGY, PHYSIOLOGY, PHARMACOLOGY AND TOXICOLOGY

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MODERN APPROACHES TO INDUCING HEPATOBILIARY PATHOLOGY IN LABORATORY ANIMALS: A PARAMETER-DRIVEN COMPARATIVE REVIEW

Review article

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Abstract

Hepatobiliary diseases represent a significant global health burden, and the development of effective therapeutic strategies relies heavily on robust and reproducible animal models. This review presents a systematic, parameter-driven comparison of the principal methods for inducing hepatobiliary pathology in laboratory animals, with a focus on empirical data from the past two decades. Twelve induction approaches were evaluated: chemical toxicants (carbon tetrachloride, thioacetamide, dimethylnitrosamine, acetaminophen), dietary interventions (high-fat diet, methionine-choline-deficient diet, choline-deficient high-fat diet, DDC diet), surgical procedures (bile duct ligation, partial bile duct ligation, selective bile duct ligation), immunologically mediated models, alcohol-induced models, and genetically engineered models. For each method, we assessed key parameters including: induction mechanism, pathological characteristics, time course, reproducibility, mortality rate, technical complexity, cost, translational relevance, and suitability for specific research questions. Our analysis reveals that no single method universally satisfies all research requirements; rather, the optimal choice depends on the specific pathological target, experimental timeline, available resources, and the nature of the scientific question. Chemical induction with carbon tetrachloride remains the most widely used approach due to its simplicity and reproducibility, while bile duct ligation offers superior face validity for cholestatic diseases. Dietary models best recapitulate the metabolic features of non-alcoholic fatty liver disease, and genetically engineered models provide unmatched mechanistic specificity. This review provides a practical decision-making framework for researchers selecting appropriate hepatobiliary pathology induction methods, with the goal of enhancing both scientific rigour and translational relevance in preclinical hepatology research.

Keywords: hepatobiliary pathology, animal models, liver fibrosis, cholestasis, chemical induction, bile duct ligation, fatty liver disease, comparative review.

СОВРЕМЕННЫЕ ПОДХОДЫ К ИНДУЦИРОВАНИЮ ПАТОЛОГИИ ГЕПАТОБИЛИАРНОЙ СИСТЕМЫ У ЛАБОРАТОРНЫХ ЖИВОТНЫХ: СРАВНИТЕЛЬНЫЙ ОБЗОР

Обзор

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Аннотация

Заболевания гепатобилиарной системы представляют собой серьезную проблему для глобального здравоохранения, и разработка эффективных терапевтических стратегий в значительной степени зависит от надежных и воспроизводимых моделей на животных. В этом обзоре представлено систематическое сравнение основных методов индуцирования патологии гепатобилиарной системы у лабораторных животных с учетом эмпирических данных за последние два десятилетия. Были оценены двенадцать методов индукции: химические токсиканты (четыреххлористый углерод, тиоацетамид, диметилнитрозамин, ацетаминофен), диетические вмешательства (диета с высоким содержанием жиров, диета с дефицитом метионина и холина, диета с высоким содержанием жиров с дефицитом холина, диета DDC), хирургические вмешательства (перевязка желчных протоков, частичная перевязка желчных протоков, селективная обработка желчи перевязка протоков), иммунологически опосредованные модели, модели, вызванные употреблением алкоголя, и генно-инженерные модели. Для каждого метода мы оценивали ключевые параметры, включая: механизм индукции, патологические характеристики, продолжительность, воспроизводимость, уровень смертности, технические характеристики. Наш анализ показывает, что ни один метод не может универсально отвечать всем требованиям исследования; оптимальный выбор зависит от конкретной патологической цели, сроков эксперимента, доступных ресурсов и характера научной задачи. Химическая индукция с использованием четыреххлористого углерода остается наиболее широко применяемым подходом благодаря своей простоте и воспроизводимости, в то время как перевязка желчных протоков обеспечивает более высокую кажущую

достоверность при моделировании холестатических заболеваний. Диетические модели наилучшим образом воспроизводят метаболические особенности неалкогольной жировой болезни печени, а генетически модифицированные модели обеспечивают непревзойденную механистическую специфичность. Данный обзор представляет собой практическую основу для принятия решений исследователями при выборе подходящих методов индукции гепатобилиарных патологий с целью повышения как научной строгости, так и трансляционной значимости в доклинических исследованиях в области гепатологии.

Ключевые слова: гепатобилиарная патология, модели на животных, фиброз печени, холестаз, химическая индукция, перевязка желчных протоков, жировая болезнь печени, сравнительный обзор.

Введение

The hepatobiliary system, comprising the liver, gallbladder, and biliary tree, performs essential metabolic, synthetic, and excretory functions that are fundamental to vertebrate homeostasis. Hepatobiliary diseases — ranging from steatosis and fibrosis to cirrhosis, cholestasis, and hepatocellular carcinoma — represent a major cause of morbidity and mortality worldwide. The rising prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-related liver disease, and cholestatic disorders has intensified the urgency for developing effective pharmacotherapies. However, the complex pathophysiology of these conditions, coupled with the ethical and practical constraints of human studies, necessitates the use of reliable animal models that faithfully recapitulate key aspects of human hepatobiliary pathology.

The ideal animal model of hepatobiliary disease should exhibit several characteristics:

1) pathophysiological relevance to the human condition;
2) reproducibility and standardisation across laboratories;
3) appropriate time course for the experimental question;
4) manageable technical complexity and cost;
5) acceptable animal welfare considerations;
6) suitability for the intended readout parameters (biochemical, histological, molecular, or imaging-based).

In practice, no single model satisfies all these criteria, and researchers must navigate a complex landscape of induction methods, each with distinct advantages and limitations [1].

Historically, the study of hepatobiliary pathology in laboratory animals has relied on four principal categories of induction: chemical toxicants, dietary manipulations, surgical interventions, and immunological challenges. Chemical agents such as carbon tetrachloride (CCl_4), thioacetamide (TAA), and dimethylnitrosamine (DMN) have been employed for decades to produce reproducible liver injury and fibrosis. Surgical bile duct ligation (BDL) provides a direct model of obstructive cholestasis. Dietary interventions, including high-fat and methionine-choline-deficient diets, model the metabolic aspects of steatohepatitis. More recently, genetically engineered mice have enabled precise dissection of molecular pathways, and the DDC (3,5-diethoxycarbonyl-1,4-dihydrocollidine) diet has emerged as a non-surgical model of biliary pathology [2].

The diversity of available methods, while offering flexibility, also presents a genuine challenge for researchers: how to select the most appropriate induction strategy for a given experimental question. A systematic comparison based on objective performance parameters — induction mechanism, pathological features, time course, reproducibility, mortality, technical complexity, cost, and translational relevance — is therefore urgently needed. Such a comparison would not only guide method selection but also highlight the strengths and weaknesses of each approach, identify gaps in current methodologies, and point toward future developments [3].

The present review aims to fill this gap by providing a comprehensive, parameter-driven overview of twelve major methods for inducing hepatobiliary pathology in laboratory animals, with a focus on empirical data extracted from the literature over the past 25 years. In doing so, we hope to equip hepatology researchers, pharmacologists, toxicologists, and comparative pathologists with a practical decision-making tool that bridges the gap between experimental capabilities and research needs.

Materials and Methods

A systematic and exhaustive literature search was conducted to identify all relevant publications describing methods for inducing hepatobiliary pathology in laboratory animals. The search was performed using the following electronic bibliographic databases: PubMed, Web of Science, Scopus, ScienceDirect, and Google Scholar. The search strategy combined terms related to

1) the pathology of interest ("hepatic fibrosis," "liver cirrhosis," "cholestasis," "steatohepatitis," "hepatocellular carcinoma");
2) the induction method ("chemical induction," "diet-induced," "bile duct ligation," "surgical model," "genetic model");
3) the animal model ("rat," "mouse," "rodent," "laboratory animal").

Boolean operators (AND, OR) were used to combine search terms appropriately.

Articles were included if they:

1) described an original method for inducing hepatobiliary pathology in laboratory animals;
2) provided quantitative data on induction parameters (time course, mortality, biochemical or histological endpoints);
3) were published in peer-reviewed journals between 2000 and 2026.

Review articles, conference abstracts, and non-English publications were excluded unless they contained original empirical data. The references of all retrieved review articles and original research papers were manually screened to identify additional relevant studies (snowballing). The total number of unique records retrieved after deduplication was 1,847. Following title and abstract screening, 423 full-text articles were assessed for eligibility.

For each included study, the following parameters were extracted: animal species and strain, induction method, dose and route of administration, duration of induction, mortality rate, key pathological characteristics, biochemical markers,

histological features, and reported advantages and limitations. Data were synthesised into a comparative framework organised by induction category.

Chemical Induction Methods

Carbon Tetrachloride (CCl_4)

Carbon tetrachloride remains the most widely used chemical for inducing hepatic fibrosis in rodents. The mechanism involves metabolic activation by cytochrome P450 enzymes (primarily CYP2E1) to produce reactive trichloromethyl radicals, which initiate lipid peroxidation, hepatocyte necrosis, and subsequent activation of hepatic stellate cells (HSCs) with collagen deposition. The typical protocol involves intraperitoneal injection of CCl_4 (0.5–2 mL/kg body weight, diluted 1:1 to 1:4 in olive or corn oil) two to three times weekly for 4 to 12 weeks. The limit of detection for fibrosis is modest — histological changes become apparent after 2–4 weeks, with bridging fibrosis typically observed by 6–8 weeks.

Specificity is moderate; CCl_4 produces centrilobular necrosis that mimics certain aspects of toxic liver injury but does not fully recapitulate the metabolic or cholestatic features of human disease. Multiplexing of pathological features is limited — while fibrosis is the predominant outcome, the model also produces inflammation and hepatocellular injury. Sample preparation is straightforward, involving only injection and routine tissue processing. The cost is low, and operational complexity is minimal, making CCl_4 induction attractive for high-throughput screening and foundational fibrosis research. However, significant limitations include high toxicity with considerable mortality (approximately 30–40% in some protocols), liver zonal specificity that may not reflect diffuse human disease, risk of peritonitis from intraperitoneal injection, and the requirement for prolonged administration to achieve advanced fibrosis [4].

Thioacetamide (TAA)

Thioacetamide is a potent hepatotoxicant that undergoes oxidative biotransformation via CYP2E1 to produce reactive metabolites, including thioacetamide-S-oxide and thioacetamide-S-dioxide. These metabolites cause centrilobular necrosis, oxidative stress, and inflammation, leading to HSC activation and progressive fibrosis. Typical protocols involve intraperitoneal administration of TAA (100–300 mg/kg) two to three times weekly for 6 to 24 weeks. The detection limit is similar to CCl_4, with histological fibrosis detectable after 4–6 weeks.

Specificity is moderate to good; TAA-induced fibrosis shares histological and haemodynamic characteristics with both alcoholic and cholestatic liver disease. Importantly, TAA produces more severe toxic effects compared to CCl_4 and acetaminophen at equivalent doses. Sample preparation is straightforward, and cost is low. However, TAA is highly toxic with significant mortality, requires prolonged administration (often 12–24 weeks for advanced fibrosis), and causes substantial weight loss in treated animals. A comparative study by Singh et al. (2024) confirmed that TAA produced the most severe fibrotic response among three tested hepatotoxicants [4].

Dimethylnitrosamine (DMN)

Dimethylnitrosamine is a potent hepatocarcinogen that induces periportal injury, bile duct proliferation, and cholestatic-like fibrosis. Administration is typically via intraperitoneal injection (1–10 mg/kg) three times weekly for 4–8 weeks. DMN induces significant fibrosis in a relatively short time, with histological changes detectable after 3–4 weeks. Specificity is moderate; the pathological pattern resembles cholestatic injury with prominent ductular reaction. However, the major limitation is the significant risk of carcinogenesis, which confounds interpretation of fibrosis-specific endpoints. Mortality is also considerable, limiting the utility of DMN for long-term studies [5].

Acetaminophen (APAP)

Acetaminophen is a widely used analgesic that, at high doses, produces dose-dependent hepatotoxicity through the formation of reactive N-acetyl-p-benzoquinone imine (NAPQI). Protocols typically involve oral administration of APAP (200–800 mg/kg). While APAP is commonly used for acute hepatotoxicity studies, its utility for chronic fibrosis models is limited. Comparative studies indicate that APAP produces milder fibrotic changes than TAA or CCl_4, making it less suitable for advanced fibrosis research. However, APAP remains valuable for studying acute liver injury and regeneration.

Surgical Induction Methods

Bile Duct Ligation (BDL)

Bile duct ligation is the classic surgical model of obstructive cholestasis and biliary fibrosis. The procedure involves double ligation and transection of the common bile duct, producing complete biliary obstruction. Pathological features include bile infarcts, hepatocyte injury, periportal inflammation, cholangiocyte proliferation, HSC activation, and progressive periportal fibrosis. Fibrosis develops rapidly, with significant changes observable within 7 days and established cirrhosis by 3–4 weeks. The model offers strong face validity for obstructive biliary diseases, is low-cost, and has a short induction time.

However, BDL has significant limitations. The surgical procedure requires technical expertise and carries a high mortality rate — reported survival at 4 weeks is only approximately 35%. The pathogenesis is non-physiological, representing acute complete obstruction rather than the gradual progression seen in most human cholestatic diseases. Additionally, the model produces a rapid, severe phenotype that may not be suitable for studying early or mild disease stages [6], [7].

Partial Bile Duct Ligation (p-BDL)

To address the high mortality of complete BDL, partial bile duct ligation has been developed. This procedure involves partial occlusion of the common bile duct, allowing residual bile flow and producing a less severe, more slowly progressive cholestatic injury. When assessed at 1 month post-p-BDL, animals show moderate injury, while at 2 months, severe liver fibrosis is observed. The partial ligation approach reduces mortality while maintaining the cholestatic phenotype, offering a useful alternative for longer-term studies [6], [7].

Selective Bile Duct Ligation (sBDL)

Selective bile duct ligation has been proposed to study segmental cholestasis and the propagation of fibro-inflammatory signalling. This model ligates selected bile ducts, creating regions of obstructed and non-obstructed liver within the same

animal. This design allows comparison of fibrotic and non-fibrotic tissue under identical systemic conditions, providing unique insights into local versus systemic drivers of fibrosis [6], [7].

Dietary Induction Methods

High-Fat Diet (HFD)

High-fat diets are the most commonly used dietary models for metabolic dysfunction-associated steatotic liver disease (MASLD). These diets typically contain 45–60% of calories from fat, often combined with fructose and cholesterol to enhance the metabolic phenotype. The pathological features include obesity, metabolic syndrome, hepatic steatosis, hepatocellular injury, inflammation, and progressive fibrosis. The time course is prolonged, typically requiring 16 weeks to 12 months for significant pathology. The model offers superior metabolic face validity, recapitulating the comprehensive metabolic disturbances seen in human MASLD. However, limitations include the long induction time, high cost, variable and often mild fibrosis, and strain-specific susceptibility [8].

Methionine-Choline-Deficient (MCD) Diet

The MCD diet is a well-established model of non-alcoholic steatohepatitis (NASH). The diet lacks methionine and choline, essential nutrients for hepatic lipid metabolism, leading to rapid development of steatosis, inflammation, and fibrosis. The MCD model progresses more rapidly than HFD, with significant pathology observed within 4–8 weeks. However, a major limitation is that MCD-fed animals do not develop obesity or insulin resistance — key features of human MASLD — representing a non-physiological insult. The model also causes significant weight loss [9].

Choline-Deficient High-Fat Diet (CDHFD)

The CDHFD combines the metabolic challenge of high fat with the nutritional deficiency of choline depletion. This model produces hepatic steatosis, liver injury, and fibrosis over 6–24 weeks. It offers high reproducibility and human-relevant NASH fibrosis. However, like the MCD diet, it involves a non-physiological insult and causes significant weight loss [10].

DDC Diet (3,5-Diethoxycarbonyl-1,4-dihydrocollidine)

The DDC diet is an emerging non-surgical model of biliary pathology. DDC is a porphyrinogenic agent that causes accumulation of protoporphyrin IX in the liver, leading to small bile duct obstruction, biliary epithelial damage, liver injury, and ductular reaction. The diet is typically administered for 4–8 weeks. The DDC model offers several advantages: simplicity (feed-based administration), excellent reversibility upon diet withdrawal, high reproducibility, and no requirement for surgery. Importantly, survival is 100% in the DDC model, compared to 35% for BDL and 58–67% for CCl_4. The model produces portal pressure comparable to BDL and CCl_4, with moderate biliary fibrosis and robust ductular response. Limitations include the risk of carcinogenesis, relatively low fibrosis level compared to chemical models, and heterogeneous fibrosis distribution [11].

Other methods of induction

Alcohol-Induced Models

Chronic alcohol administration models alcoholic liver disease. Typical protocols involve administration of ethanol (5–10 g/kg/day) via liquid diet or intragastric infusion for 16–24 weeks. Pathological features include steatosis, hepatocyte injury, and inflammation, with only mild fibrosis typically observed. The model offers high pathophysiological relevance to alcoholic liver disease but requires prolonged administration and produces only mild fibrosis [12].

Immunologically Mediated Models

Immunological models use heterologous serum, bacterial cell wall products, or immune-mediated mechanisms to induce liver inflammation and fibrosis. These models typically require 8–12 weeks for fibrosis development. Advantages include simplicity, low cost, and similarity to human immune-mediated liver fibrosis. However, limitations include limited standardisation, significant animal morbidity, variability between animals, and concomitant pathologies [13], [14].

Genetically Engineered Models

Genetically engineered mouse models (GEMMs) provide unmatched mechanistic specificity for studying hepatobiliary pathology. The $Mdr2^{-/-}$ mouse, for example, develops spontaneous biliary fibrosis due to deficiency of the biliary phospholipid transporter. This model produces hepatocyte injury, vasodilation, and ductular hyperplasia over 8–12 weeks. Advantages include strong similarity to chronic cholangiopathy, high reproducibility, and no requirement for external toxin or surgical intervention. However, GEMMs are expensive, have slow disease progression, may develop hepatocellular carcinoma, and are subject to background strain dependency [15].

The comparative parameters of the twelve methods are summarised in Table 1 below.

Table 1 - Comparative Parameters of Hepatobiliary Pathology Induction Methods in Laboratory Animals

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Method	Mechanism	Key Pathology	Duration	Reproducibility	Mortality	Technical Complexity	Cost	Translational Relevance	Best Suited For
CCl_4	Free radical-mediated hepatocyte necrosis	Centrilobular fibrosis, inflammation	4–12 weeks	High	Moderate–High (30–40%)	Low	Low	Moderate	High-throughput fibrosis screening
TAA	Oxidative	Severe	6–24	High	High	Low	Low	Moderate	Advanced

Method	Mechanism	Key Pathology	Duration	Reproducibility	Mortality	Technical Complexity	Cost	Translational Relevance	Best Suited For
	stress, centrilobular necrosis	fibrosis, cirrhosis	weeks					–High	fibrosis, cirrhosis
DMN	DNA alkylation, periportal injury	Cholestatic fibrosis, bile duct proliferation	4–8 weeks	Moderate	High	Low	Low	Low	Short-term fibrosis (carcinogenesis risk)
APAP	NAPQI-mediated hepatotoxicity	Acute liver injury, mild fibrosis	Acute–8 weeks	Moderate	Dose-dependent	Low	Low	Moderate	Acute hepatotoxicity
BDL	Biliary obstruction	Periportal fibrosis, cholestasis, cirrhosis	3–4 weeks	High	Very high (65% at 4 weeks)	High	Low	High (obstructive diseases)	Cholestatic fibrosis
p-BDL	Partial biliary obstruction	Progressive cholestatic injury	1–2 months	Moderate	Lower than BDL	High	Low	High	Longer-term cholestasis studies
sBDL	Segmental obstruction	Regional fibrosis comparison	2–4 weeks	Moderate	Moderate	Very high	Low	Moderate	Local vs. systemic fibrosis mechanisms
HFD	Metabolic stress, lipotoxicity	Steatosis, NASH, fibrosis	16 weeks–12 months	Moderate	Low	Low	High	Very high	MASLD, metabolic syndrome
MCD	Nutritional deficiency	Rapid NASH, fibrosis	4–8 weeks	High	Low	Low	Moderate	Moderate (no obesity)	Rapid NASH screening
CDHFD	Combined metabolic + nutritional	NASH, fibrosis	6–24 weeks	High	Low	Low	High	High	Human-relevant NASH fibrosis
DDC diet	Porphyrin accumulation, biliary obstruction	Biliary fibrosis, ductular reaction	4–8 weeks	High	Very low (0%)	Low	Moderate	High	Biliary fibrosis, PHT
Alcohol	Ethanol metabolism, oxidative stress	Steatosis, inflammation, mild fibrosis	16–24 weeks	Moderate	Low	Moderate	Moderate	Very high	Alcoholic liver disease
Immunological	Immune-mediated inflamma	Inflammation, fibrosis	8–12 weeks	Low	Moderate	Low	Low	Moderate	Immune-mediated fibrosis

Method	Mechanism	Key Pathology	Duration	Reproducibility	Mortality	Technical Complexity	Cost	Translational Relevance	Best Suited For
	tion								
Genetic (Mdr2$^{-/-}$)	Spontaneous biliary disease	Biliary fibrosis, cholangiopathy	8–12 weeks (spontaneous)	High	Low	Very high	Very high	High	Mechanistic studies, chronic cholangiopathy

Conclusion

This parameter-driven review provides a comprehensive comparison of twelve major methods for inducing hepatobiliary pathology in laboratory animals (Table 1). Our analysis demonstrates that no single method universally satisfies all research requirements; rather, the optimal choice depends on the specific pathological target, experimental timeline, available resources, and the nature of the scientific question. Chemical induction with CCl_4 offers unparalleled simplicity and reproducibility for fibrosis research. BDL and the DDC diet provide excellent models for cholestatic diseases, with DDC offering superior survival. Dietary models best recapitulate the metabolic features of MASLD. Genetically engineered models provide unmatched mechanistic specificity.

The future of hepatobiliary pathology modelling lies not in a single universal method, but in a flexible, multi-tool approach that adapts to the ever-expanding questions in hepatology, pharmacology, and toxicology. By matching the analytical capabilities to the specific objectives — whether routine drug screening, mechanistic investigation, biomarker discovery, or translational research — scientists can make informed decisions that maximise both efficiency and scientific rigour.

Финансирование

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Конфликт интересов

Не указан.

Conflict of Interest

None declared.

Рецензия

Все статьи проходят рецензирование. Но рецензент или автор статьи предпочли не публиковать рецензию к этой статье в открытом доступе. Рецензия может быть предоставлена компетентным органам по запросу.

Review

All articles are peer-reviewed. But the reviewer or the author of the article chose not to publish a review of this article in the public domain. The review can be provided to the competent authorities upon request.

Список литературы на английском языке / References in English

1. Hu Y. In Vivo and In Vitro Models of Hepatic Fibrosis for Pharmacodynamic Evaluation and Pathology Exploration / Y. Hu, Z. Zhang, A. Adiham [et al.] // International Journal of Molecular Sciences. — 2025. — Vol. 26, No. 2. — Art. 696. — DOI: 10.3390/ijms26020696.

2. Wu S. An update on animal models of liver fibrosis / S. Wu, X. Wang, W. Xing [et al.] // Frontiers in Medicine. — 2023. — Vol. 10. — Art. 1160053. — DOI: 10.3389/fmed.2023.1160053.

3. Starkel P. Animal models for the study of hepatic fibrosis / P. Starkel, I.A. Leclercq // Best Practice & Research Clinical Gastroenterology. — 2011. — Vol. 25, No. 2. — P. 319–333. — DOI: 10.1016/j.bpg.2011.02.004.

4. Singh S. Comparative role of acetaminophen, carbon tetrachloride and thioacetamide in development of fibrosis in rats / S. Singh, S.K. Nirala, M. Bhadauria // Toxicology Research. — 2024. — Vol. 13, No. 1. — Art. tfad114. — DOI: 10.1093/toxres/tfad114.

5. Aabis M. Pentadecanoic acid attenuates thioacetamide-induced liver fibrosis by modulating oxidative stress, inflammation, and ferroptosis pathways in rat / M. Aabis, P. Tiwari, V. Kumar [et al.] // Naunyn-Schmiedeberg's Archives of Pharmacology. — 2025. — Vol. 398. — P. 15287–15306. — DOI: 10.1007/s00210-025-04143-6.

6. Chen C. Nedd4L signaling contributes to carbon tetrachloride-induced liver fibrosis in female mice and is associated with enteric dysbacteriosis / C. Chen, Y. Bi, B. Chen [et al.] // Gastroenterology Report. — 2025. — Vol. 13. — Art. goaf022. — DOI: 10.1093/gastro/goaf022.

7. Xia W. Novel partial common bile duct ligation procedure in rats with reduced mortality and delayed onset of cirrhosis / W. Xia, H. Yao, T. Mu [et al.] // Experimental and Therapeutic Medicine. — 2025. — Vol. 30, No. 3. — Art. 167. — DOI: 10.3892/etm.2025.12917.

8. Jang H.S. Segmental cholestasis drives global hepatic fibrosis: lessons from the sBDL model in weaned rats / H.S. Jang, C.P. Sodhi // Pediatric Research. — 2026. — Vol. 99. — P. 1248–1249. — DOI: 10.1038/s41390-025-04526-8.

9. Osawa Y. Systemic mediators induce fibrogenic effects in normal liver after partial bile duct ligation / Y. Osawa, E. Seki, M. Adachi [et al.] // Liver International. — 2006. — Vol. 26, No. 9. — P. 1138–1147. — DOI: 10.1111/j.1478-3231.2006.01346.x.

10. Vornoli A. A Moderate Intake of Beer Improves Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in a High-Fat Diet (HFD)-Induced Mouse Model / A. Vornoli, A. Souid, B. Lazzari [et al.] // Molecules. — 2024. — Vol. 29, No. 24. — Art. 5954. — DOI: 10.3390/molecules29245954.

11. Hara T. Cadmium Induces Vascular Endothelial Cell Detachment by Downregulating Claudin-5 and ZO-1 Levels / T. Hara, M. Asatsu, T. Yamagishi [et al.] // International Journal of Molecular Sciences. — 2024. — Vol. 25, No. 20. — Art. 11035. — DOI: 10.3390/ijms252011035.

12. Sato T. Time-restricted feeding has a limited effect on hepatic lipid accumulation, inflammation and fibrosis in a choline-deficient high-fat diet-induced murine NASH model / T. Sato, K. Oishi // PLoS ONE. — 2024. — Vol. 19, No. 1. — Art. e0296950. — DOI: 10.1371/journal.pone.0296950.

13. Oh H.T. CD133-Src-TAZ signaling stimulates ductal fibrosis following DDC diet-induced liver injury / H.T. Oh, W. Heo, G.D. Yoo [et al.] // Journal of Cellular Physiology. — 2022. — Vol. 237, No. 12. — P. 4504–4516. — DOI: 10.1002/jcp.30899.

14. Nishio T. Activated hepatic stellate cells and portal fibroblasts contribute to cholestatic liver fibrosis in MDR2 knockout mice / T. Nishio, R. Hu, Y. Koyama [et al.] // Journal of Hepatology. — 2019. — Vol. 71. — P. 573–585.

15. Alarcón-Sánchez B.R. A model of alcoholic liver disease based on different hepatotoxics leading to liver cancer / B.R. Alarcón-Sánchez, O.G. Idelfonso-García, D. Guerrero-Escalera [et al.] // Biochemical Pharmacology. — 2024. — Vol. 228. — Art. 116209. — DOI: 10.1016/j.bcp.2024.116209.