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Therapeutic Synergy of Picrorhiza kurroa and Piper longum: Mechanistic Perspectives in Hepatoprotection and Liver Disease Management

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ABSTRACT:

Liver disorders such as Drug-Induced Liver Injury (DILI) and Non-Alcoholic Fatty Liver Disease (NAFLD) represent significant global health concerns. Traditional herbal combinations have long been utilized for their multitarget therapeutic actions; however, the complementary hepatoprotective effects of Picrorhiza kurroa and Piper longum remain inadequately explored. This review evaluates the potential synergistic interactions between these two medicinal plants in the management of liver diseases.

P. kurroa exerts hepatoprotective activity primarily through activation of the Nrf2/ARE antioxidant signaling pathway, suppression of NF-κB-mediated inflammation, and inhibition of TGF-β-driven fibrogenesis. Nevertheless, its therapeutic application is constrained by rapid metabolism and limited bioavailability. P. longum, owing to the presence of piperine, functions as a bioavailability enhancer by inhibiting CYP450 enzymes and P-glycoprotein efflux transporters, thereby improving the systemic availability of picrosides. Additionally, P. longum contributes independent antioxidant and anti-inflammatory properties, further supporting hepatoprotection.

Preclinical evidence indicates that the combined administration of these herbs as a botanical formulation provides greater biochemical and histopathological improvement than either herb used individually. Despite encouraging experimental findings, clinical translation remains restricted due to insufficient standardization of formulations and the scarcity of large-scale randomized controlled trials. Future investigations should focus on mechanistic validation through omics-based approaches, advanced nanotechnology-driven delivery systems, and comprehensive clinical evaluation of the synergistic potential of this herbal combination in the prevention and treatment of chronic liver diseases..

Keywords - Picrorhiza kurroa; Piper longum; Hepatoprotection; Synergism; Bioavailability enhancer; Piperine; Picrosides; Oxidative stress; NAFLD; Drug-induced liver injury (DILI)**.**

INTRODUCTION

Liver diseases contribute substantially to global morbidity and mortality, representing a major burden on healthcare systems worldwide. Chronic liver disease and cirrhosis are recognized among the leading causes of death globally. In recent years, Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as the most prevalent hepatic disorder, largely driven by the rising incidence of obesity and metabolic syndrome (1), (2). Additional major etiological factors include viral hepatitis B and C, alcohol-associated liver disease, and drug-induced liver injury (DILI). These conditions continue to pose serious clinical and public health challenges, particularly in developing nations where access to advanced healthcare infrastructure is often limited (3); (4); (5).

Although modern medicine has achieved notable progress, effective hepatoprotective therapies remain limited in many clinical settings. Existing treatment strategies are generally disease-specific and predominantly supportive in nature, offering minimal capability to reverse established hepatocellular injury (6). Furthermore, most synthetic drugs target isolated pathogenic mechanisms such as oxidative stress or inflammation, whereas liver diseases are multifactorial disorders involving interconnected pathways including metabolic imbalance, oxidative stress, inflammatory responses, apoptosis, and fibrosis (7). Long-term pharmacological management is also associated with adverse effects, high treatment costs, and poor patient adherence, thereby increasing interest in plant-based therapies with improved safety profiles and broader therapeutic potential.

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Piper longum (*Pippali*), a well-known medicinal herb in Ayurveda, has traditionally been employed to improve digestion and metabolism. Its principal bioactive constituent, piperine, exhibits potent antioxidant, anti-inflammatory, and immunomodulatory activities. Experimental studies have additionally demonstrated its ability to enhance hepatic antioxidant defenses and reduce lipid peroxidation (8); (9). Similarly, *Picrorhiza kurroa* has a long history of use in traditional medicine systems and is widely recognized for its hepatoprotective properties. The ethnopharmacological relevance of both herbs provides a strong rationale for further investigation into their combined therapeutic potential in liver disorders.

The molecular pathogenesis of hepatobiliary diseases involves several interconnected mechanisms, including oxidative stress, inflammatory cytokine release, mitochondrial dysfunction, apoptosis, and fibrotic signaling pathways (10). Consequently, successful therapeutic interventions require a multitargeted approach capable of modulating these complex pathological processes.

The combination of *Picrorhiza kurroa* and *Piper longum* appears pharmacologically promising because of their complementary and potentially synergistic actions. *P. kurroa* demonstrates significant hepatoprotective activity, while *P. longum* contributes strong antioxidant effects and may enhance the bioavailability of co-administered compounds (11); (12). This concept aligns closely with Ayurvedic principles, where polyherbal formulations are designed not only to augment therapeutic efficacy but also to improve absorption and minimize toxicity.

This review summarizes current evidence regarding the synergistic hepatoprotective effects of *Picrorhiza kurroa* and *Piper longum*, with particular emphasis on the molecular pathways underlying their actions. Relevant in vitro and in vivo studies involving chemically induced hepatotoxicity were critically evaluated, focusing on mechanisms associated with oxidative stress, inflammation, and hepatocellular protection. By integrating traditional Ayurvedic knowledge with contemporary pharmacological research, this review seeks to highlight the therapeutic potential of this herbal combination and identify future directions for its application in liver disease management

Botanical Profile and Phytochemistry

Picrorhiza kurroa

Picrorhiza kurroa (*Kutki*), a member of the Plantaginaceae family, grows in the high-altitude Himalayan regions of India, Nepal, Bhutan, and Tibet (3,000–5,000 m) under cool and moist conditions. Traditionally, it is used as a bitter tonic for liver disorders such as jaundice and hepatitis, as well as fever, asthma, dyspepsia, and inflammatory conditions. In Ayurveda, it is classified as a "*Yakrit-uttejaka*" drug that enhances liver function and bile secretion. Its hepatoprotective activity is mainly attributed to iridoid glycosides collectively known as *Kutki*n (picroside I, picroside II, and kutkoside), along with apocynin and androsin, which possess antioxidant and anti-inflammatory properties that help reduce oxidative stress and inflammatory liver damage. The quality of *P. kurroa* extracts varies with geographical origin, harvesting season, and processing methods. Therefore, standardization is essential and commonly involves physicochemical evaluation, chromatographic fingerprinting, and quantification of marker compounds such as picroside I and kutkoside using HPLC or HPTLC techniques. (13)

Piper longum

Piper longum (*Pippali*), a member of the Piperaceae family, is an aromatic climber distributed across tropical and subtropical regions of India and Southeast Asia. Its dried fruits (long pepper) are widely used in Ayurveda as a digestive stimulant, carminative, immunomodulator, and rejuvenative agent (14). *Pippali* is an important ingredient of formulations such as *Trikatu* and

is known to enhance drug bioavailability and metabolic efficiency, particularly in liver and metabolic disorders (15); (16). The pharmacological activities

of *P. longum* are mainly attributed to piperine, along with other constituents such as piperlongumine, piperlonguminine, related alkaloids, and volatile oils. These compounds exhibit antioxidant, anti-inflammatory, hepatoprotective, and bio-enhancing properties (17); (18). Standardization is commonly carried out using HPLC, GC–MS, LC–MS/MS, and NMR techniques, with piperine serving as the principal chemical marker (19).

Synergistic Phytochemical Interactions

Piperine enhances the bioavailability of drugs and phytoconstituents by inhibiting drug-metabolizing enzymes, increasing intestinal permeability, and suppressing efflux transporters such as P-glycoprotein (20). The combination of *P. kurroa* and *P. longum* is based on synergistic molecular complementarity, where picrosides provide antioxidant, anti-inflammatory, and hepato-regenerative effects, while piperine improves their bioavailability and further modulates oxidative and inflammatory pathways (21). Together, these herbs may produce enhanced hepatoprotective activity by targeting multiple mechanisms of liver injury, potentially improving efficacy while reducing required dosage and toxicity.

Hepatotoxicity: Pathophysiology and Molecular Mechanisms

Drug-induced liver injury (DILI), alcohol-related liver disease, NAFLD, and viral hepatitis are major causes of hepatotoxicity and chronic liver damage. These conditions involve interconnected mechanisms including oxidative stress, inflammation, apoptosis, and fibrosis. Excessive production of reactive oxygen species (ROS) damages cellular membranes through lipid peroxidation, impairs mitochondrial function, and activates inflammatory pathways such as NF-κB, leading to cytokine release and hepatocyte injury. Persistent inflammation and apoptosis further stimulate hepatic stellate cells, promoting extracellular matrix deposition and fibrosis, which may ultimately progress to cirrhosis and hepatocellular carcinoma. Understanding these mechanisms is essential for developing effective multitarget hepatoprotective therapies. (22-26)

Hepatoprotective Mechanisms of *Picrorhiza kurroa*

The hepatoprotective effects of *Picrorhiza kurroa* are attributed to its ability to modulate multiple molecular pathways involved in liver injury. Its major bioactive constituents, particularly iridoid glycosides, exert broad-spectrum hepatoprotective actions through antioxidant, anti-inflammatory, immunomodulatory, and antifibrotic mechanisms. (27).

Antioxidant Activity

Picrorhiza kurroa exerts significant antioxidant activity through free radical scavenging and enhancement of endogenous antioxidant defenses. Picrosides and related phenolic compounds neutralize reactive oxygen and nitrogen species, thereby reducing oxidative damage to lipids, proteins, and DNA in hepatocytes (28); (29). Experimental studies have demonstrated increased levels of antioxidant enzymes such as SOD, CAT, GPx, and GSH following *P. kurroa* administration, helping maintain cellular redox balance and reduce lipid peroxidation (30); (31). Its antioxidant effects are further mediated through activation of the Nrf2 pathway and protection of mitochondrial integrity, ultimately reducing ROS generation and hepatocyte apoptosis (32)-(35).

Anti-inflammatory Effects

Picrorhiza kurroa exerts anti-inflammatory effects primarily through inhibition of the NF-κB signaling pathway, thereby suppressing the expression of pro-inflammatory mediators involved in liver injury (36)-(38). It also significantly reduces levels of inflammatory cytokines such as TNF-α, IL-6, and IL-1β, helping prevent immune-mediated hepatocellular damage (39); (40). Additionally, *P. kurroa* inhibits COX-2 and iNOS expression, reducing the production of nitric oxide and prostaglandins associated with oxidative stress and hepatic inflammation (41); (42)

Membrane Stabilization and Cellular Protection

Picrorhiza kurroa protects hepatocyte membranes from oxidative damage caused by lipid peroxidation, thereby preserving cellular structure and function (43); (44). It also supports bile acid homeostasis by promoting bile acid metabolism and secretion, which helps protect against cholestatic injury and supports hepatic detoxification processes (45).

Immunomodulatory and Anti-fibrotic effects:

Picrorhiza kurroa modulates immune responses by regulating T-cell and B-cell activity, thereby reducing immune-mediated hepatocellular damage associated with chronic liver diseases (46); (47); (48). It also regulates Kupffer cell activation by decreasing pro-inflammatory cytokine and reactive oxygen species production while promoting an anti-inflammatory phenotype (49); (50-51). Additionally, *P. kurroa* exhibits anti-fibrotic activity through inhibition of the TGF-β signaling pathway, thereby suppressing profibrotic gene expression and collagen deposition in the liver.

Hepatoprotective Mechanisms of *Piper longum*

Bioavailability Enhancement

Piperine enhances the oral bioavailability of drugs and phytoconstituents by increasing intestinal absorption and reducing hepatic metabolism, thereby improving plasma concentration and half-life of co-administered compounds (52). It inhibits P-glycoprotein (P-gp), reducing drug efflux and increasing intracellular accumulation of hepatoprotective agents (53). Piperine also modulates CYP450 enzymes, including CYP3A4 and CYP2E1, thereby reducing reactive metabolite formation and oxidative stress associated with hepatotoxicity (54).

Antioxidant and Free Radical Scavenging

P. longum exerts hepatoprotective effects through multiple antioxidant mechanisms, including direct scavenging of reactive oxygen species (ROS) such as superoxide anions, hydroxyl radicals, and hydrogen peroxide. Piperine and related alkaloids reduce oxidative liver damage by neutralizing free radicals. It also enhances endogenous antioxidant defenses by increasing superoxide dismutase, catalase, glutathione peroxidase, and reduced glutathione levels, thereby restoring redox balance. Additionally, *P. longum* inhibits lipid peroxidation and malondialdehyde formation, preserving hepatocyte membrane integrity and preventing liver injury (5559).

Anti-inflammatory Actions Inflammatory mediator suppression

P. longum exhibits significant anti-inflammatory activity by suppressing pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β through inhibition of the NF-κB signaling pathway, thereby reducing hepatic inflammation and slowing liver damage progression. It also decreases leukocyte infiltration by downregulating adhesion molecules and chemokines, limiting immune-mediated secondary tissue injury and promoting restoration of liver architecture (60-62).

Hepatocyte Regeneration

P. longum promotes liver regeneration by stimulating hepatocyte proliferation through enhancement of hepatic energy status and modulation of growth factor pathways. It also increases DNA and protein synthesis in hepatocytes by improving nutrient absorption and metabolic efficiency, thereby supporting repair of damaged liver tissue and restoration of normal hepatic function following toxic injury (63,64).

5.5 Detoxification Support

P. longum supports hepatic detoxification by modulating Phase I and Phase II detoxifying enzymes, thereby enhancing xenobiotic metabolism and safe elimination of toxic by-products. It also improves glutathione metabolism by increasing intracellular glutathione levels, which strengthens conjugative detoxification reactions and protects hepatocytes against oxidative and electrophilic damage. These actions contribute to its role as a hepatoprotective metabolic enhancer and adjunct in liver disorder management (65-67).

5.6 In Vitro Studies

In vitro studies using human hepatocellular carcinoma (HepG2) cells and primary rat and human hepatocytes have shown that *P. kurroa* extracts and isolated compounds exert cytoprotective effects against chemically induced oxidative damage by restoring hepatocyte viability and membrane integrity. Similarly, alkaloids such as piperine from *P. longum* protect hepatocytes from reactive oxygen species (ROS)-mediated oxidative injury (68).

In vivo Animal Models

In experimental models of liver injury, -and *P. longum* have demonstrated significant hepatoprotective effects. In CCl_4-induced hepatotoxicity, both herbs reduced oxidative stress, lipid peroxidation, inflammatory markers, and hepatocellular damage while enhancing antioxidant enzyme activity. In paracetamol-induced liver injury, *P. kurroa* restored glutathione levels, normalized liver enzymes, reduced necrosis, and inhibited CYP2E1-mediated toxic metabolite formation. In alcohol-induced liver damage, both herbs decreased oxidative stress, inflammatory cytokines, hepatic fat accumulation, and progression to steatohepatitis. In bile duct ligation models, *P. kurroa* improved bile flow and reduced fibrosis, while piperine enhanced antioxidant and anti-inflammatory protection. In NAFLD/NASH models, *P. kurroa* improved oxidative stress and steatosis, whereas *P. longum* enhanced insulin sensitivity and antioxidant status, collectively slowing disease progression (69-72).

Synergistic Studies

Combined formulation evaluations

Preclinical research has demonstrated that combining *P. kurroa* and *P. longum* is more effective in protecting the liver than using either extract alone, evidenced by a greater ability to normalize liver enzymes, improve antioxidant levels and histological recovery, when studies were conducted on laboratory models of liver damage induced by toxins (73).

Pharmacokinetic interactions

Pharmacokinetic studies have shown that piperine enhances the oral bioavailability of picrosides by preventing their breakdown through metabolism and by effluxing them back into the intestines and liver. By doing so, there is an increase in the amount of picrosides available to the body over time and how long they will last in the body (74).

Enhanced therapeutic outcomes

When combined, *P. kurroa* and *P. longum* show a synergistic effect resulting in the following enhanced therapeutic results, such as decrease in oxidative stress, reduction of inflammation, increased regeneration of hepatocytes, and decreased production of scar tissue (fibrosis). Therefore, the rationale for developing multi-targeted herbal formulations is validated through these findings, and should be studied in clinical trials (75).

Clinical Evidence and Human Studies

Evidence for the use of *P. kurroa* (*Kutki*) for treating infections has been studied on humans but limited to poor quality data primarily derived from an older clinical setting, including studies and clinical reports that

were conducted prior to the introduction of the Controlled Trials Registry (CHARA). Studies conducted on men and women infected with hepatitis via virus, conducted between 2006 and 2023, found improvement in sympto-biochemistry following treatment with *Kutki* formulations. However, most of these studies do not conform to current reporting standards used by the CLASS (Clinical Trials and Study Reporting). Many have used small sample sizes and have insufficient sample size and study length, to see the effect of *Kutki* on patients diagnosed with hepatitis. A recent clinical report comparing Picroliv (a standardized fraction of *P. kurroa*) for acute viral hepatitis (14 patients studied) indicated symptomatic and biochemical improvement in patients treated with Picroliv (100 mg bid x 4 weeks). A separate clinical report studied the adjunct benefit of routine use of *Kutki* supplements by patients taking lipid-lowering medications (statins), evaluated for the potential for reducing the adverse effects associated with taking statins based on measuring levels of transaminases and bilirubin. The findings reported in this clinical evaluation provide some evidence for the safety and efficacy of using *Kutki* supplements for this indication, but cannot be viewed as isolated use of *Kutki* only (76).

Table 1: Clinical Evidence on *Picrorhiza kurroa* and *Piper longum* in Human Studies

Plant / Compound	**Study type & population**	**Formulation / Standardization**	**Dose & duration**	**Key outcomes**	**Major limitations**
Picrorhiza kurroa (*Kutki*)	Clinical study in **acute viral hepatitis** patients	**Picroliv** (standardized iridoid glycoside fraction)	100 mg twice daily, 4 weeks	Improvement in clinical symptoms and reduction in serum bilirubin and transaminases	Small sample size, short duration, older study design, limited mechanistic biomarkers
Picrorhiza kurroa	Clinical evaluation in patients on **long-term statin therapy**	*Kutki*-based Ayurvedic preparation (polyherbal context)	Variable; formulation-dependent	Protection against statin-associated elevation of liver enzymes	Not a *Kutki*-only intervention; lack of randomization and blinding
Picrorhiza kurroa	Observational/experience-based reports in hepatic disorders	Crude or semi-standardized extracts	Not uniformly reported	Symptomatic relief in jaundice and chronic liver complaints	Heterogeneous preparations; absence of modern trial endpoints
Piper longum /	**Human pharmacokinetic study** in healthy volunteers	Piperine-containing	100–200 mg	Demonstrated systemic	Not disease-specific; not

Piperine		herbal	(single/sho	exposure and	focused on
		formulation	rt-term	PK feasibility	liver
			dosing)	of piperine	endpoints
Piperine	Randomized trials in	Curcuminoids	Product-	Reduction/tre	Effects not
(adjunct)	**metabolic/inflammatory**	+ piperine	specific	nds in ALT	attributable
	conditions (liver enzymes	combinations	dosing	and AST;	solely to
	as secondary outcomes)			improved	piperine
				inflammatory	
Piper longum	Traditional/ethnopharmacol ogical human use	Whole fruit powder or formulations	Variable	Markers Reported digestive and metabolic benefits supporting liver health	Lacks controlled clinical validation

Comparative Analysis with Standard Hepatoprotective Agents

Compared with standard hepatoprotective agents, *P. kurroa* and *P. longum* demonstrate broader multi-target hepatoprotective actions. Unlike silymarin, whose efficacy is limited by poor bioavailability, *P. kurroa* exhibits comparable or superior antioxidant and anti-inflammatory effects, while piperine from *P. longum* enhances bioavailability of co-administered agents. In contrast to N-acetylcysteine (NAC), which is mainly effective in acute paracetamol toxicity, *P. kurroa* modulates inflammatory, apoptotic, and fibrogenic pathways in addition to replenishing glutathione. Compared with ursodeoxycholic acid (UDCA), which is primarily useful in cholestatic disorders, *P. kurroa* and *P. longum* offer wider benefits through antioxidant, anti-inflammatory, detoxifying, antifibrotic, and hepatocyte regenerative effects. These herbs may therefore serve as promising complementary or alternative hepatoprotective agents, although further well-designed clinical studies are required to establish their efficacy and safety (77-81).

Pharmacokinetics and Bioavailability

Picrosides from *P. kurroa* exhibit moderate oral bioavailability due to limited intestinal permeability and extensive first-pass metabolism, whereas piperine from *P. longum* is highly lipophilic and rapidly absorbed. Both compounds preferentially accumulate in the liver, supporting their hepatoprotective activity. Picrosides undergo hydrolysis, oxidation, and conjugation before biliary and renal excretion, while piperine is metabolized mainly by CYP2C9 and CYP3A4. Piperine acts as a natural bioenhancer by inhibiting CYP3A4, UDP-glucuronosyltransferases, and P-glycoprotein, thereby reducing first-pass metabolism, increasing intracellular retention, enhancing hepatic absorption, and prolonging systemic availability of picrosides. Co-administration also increases hepatic tissue concentrations of phytochemicals, supporting synergistic therapeutic effects, although potential herb-drug interactions must be considered clinically (82-90).

Safety, Toxicology, and Adverse Effects

Available toxicological and pharmacokinetic evidence suggests that *P. kurroa* and *P. longum* are generally safe within therapeutic ranges, with animal and human studies showing favourable safety profiles and high LD_{50} values for piperine. Genotoxicity and mutagenicity studies have largely demonstrated low risk at recommended doses, although long-term carcinogenicity data remain limited. Piperine's inhibition of CYP450 enzymes and P-glycoprotein contributes to its bio-enhancing effects but may also increase the risk of herb–drug interactions, particularly in patients on multiple medications. Safety during pregnancy and lactation remains inadequately studied, and high doses of piperine may exert uterine stimulatory effects; therefore, use during these periods is not recommended without medical supervision. Overall, both herbs appear relatively safe for short- to medium-term hepatoprotective use, though standardized formulations, toxicological profiling, and long-term clinical studies are still needed (91-95).

Formulation Development and Standardization

Effective therapeutic use of *P. kurroa* and *P. longum* requires optimized formulation and delivery strategies to ensure efficacy, safety, and standardization. Hydroalcoholic extraction is commonly employed for recovering picrosides from *P. kurroa*, while ethanolic, hydroalcoholic, and supercritical fluid extraction methods are used for isolating piperine and related alkaloids from *P. longum*. Optimization of extraction parameters improves yield and consistency of bioactive compounds. Novel delivery systems such as polymeric nanoparticles, solid lipid

nanoparticles, liposomes, and phytosomes enhance solubility, stability, bioavailability, controlled release, and hepatic targeting. Co-encapsulation of constituents from both plants may further improve synergistic hepatoprotective effects and therapeutic efficiency while reducing the required dose of active compounds (96,97).

Regulatory Perspectives and Market Status

Successful integration of *P. kurroa* and *P. longum* into mainstream healthcare requires overcoming regulatory and quality-control challenges. While *P. kurroa* is recognized as an Ayurvedic medicine in India, *P. longum* is mainly marketed as a dietary supplement in Western countries, limiting therapeutic claims. Variability in product standardization and regulatory frameworks across countries affects clinical acceptance and confidence. Therefore, establishing standardized formulations, quality assurance measures, and harmonized international regulatory guidelines is essential for wider clinical adoption of these hepatoprotective agents.

Future Research Directions

Although *Picrorhiza kurroa* and *Piper longum* possess well-recognized hepatoprotective potential supported by traditional use and preclinical evidence, further validation through molecular characterization and robust clinical trials is required for their development as evidence-based therapeutics. Future research should focus on identification of novel bioactive compounds using metabolomics, elucidation of mechanisms through multi-omics approaches, and well-designed multicentric randomized clinical studies. Integration of preclinical and clinical findings, along with advanced delivery systems such as nanomedicine, may further enhance their bioavailability, therapeutic efficacy, and potential role in personalized hepatoprotective therapy.

CONCLUSION

Substantial evidence supports the synergistic hepatoprotective potential of *Picrorhiza kurroa* and *Piper longum*. *P. kurroa* primarily reduces oxidative stress and inflammation, while *P. longum* enhances the bioavailability and therapeutic efficacy of co-administered compounds. Preclinical studies and emerging clinical evidence suggest potential benefits in liver disorders such as Non-Alcoholic Fatty Liver Disease (NAFLD) and Drug-Induced Liver Injury (DILI). However, limited randomized clinical trials and inadequate long-term safety data currently restrict broader clinical acceptance. Further research involving robust clinical studies, omics-based approaches, and advanced drug-delivery systems is required to establish their therapeutic applicability in liver disease management.

Abbreviations

Abbreviation	Full Term
ADME	Absorption, Distribution, Metabolism, and Excretion
ALT	Alanine Aminotransferase
ARE	Antioxidant Response Element
AST	Aspartate Aminotransferase
CAT	Catalase
CCl_4	Carbon Tetrachloride
COX-2	Cyclooxygenase-2
CYP450	Cytochrome P450
DILI	Drug-Induced Liver Injury
ECM	Extracellular Matrix
GPx	Glutathione Peroxidase
GSH	Reduced Glutathione
HCC	Hepatocellular Carcinoma
HSCs	Hepatic Stellate Cells
IL-1β	Interleukin-1 beta
IL-6	Interleukin-6
iNOS	Inducible Nitric Oxide Synthase
LD50	Lethal Dose, 50%
NAC	N-acetylcysteine
NAFLD	Non-Alcoholic Fatty Liver Disease
NASH	Non-Alcoholic Steatohepatitis

NF-κB	Nuclear Factor kappa-light-chain-enhancer of activated B cells
Nrf2	Nuclear Factor Erythroid 2–Related Factor 2
P-gp	P-glycoprotein
PK	Pharmacokinetics
ROS	Reactive Oxygen Species
SOD	Superoxide Dismutase

TGF-β	Transforming Growth Factor-beta
TNF-α	Tumor Necrosis Factor-alpha
UDCA	Ursodeoxycholic Acid

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