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The Role of Curcumin in Reducing Antituberculosis Drug-Induced Hepatotoxicity: A Literature Review

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Abstract

Antituberculosis drug-associated liver injury may interrupt tuberculosis treatment. This structured narrative review examines curcumin as a potential hepatoprotective adjunct while distinguishing mechanistic findings from evidence of clinical benefit. Four focal publications were identified in the documented literature review: one retrospective observational study of Curcuma-tablet use and three secondary reviews. Two underlying experimental reports were additionally traced to clarify the mechanisms discussed in those reviews; they were not counted as independently screened publications. Preclinical findings suggest modulation of oxidative stress and apoptosis, protoporphyrin IX and ferrochelatase, and SIRT1/PGC-1α/NRF1 signaling. A retrospective study involving 60 patients reported lower mean AST, ALT, and bilirubin values associated with a Curcuma preparation, but its design and incompletely characterized formulation do not establish a curcumin-specific treatment effect. Interpretation is limited by overlapping reviews, preclinical evidence, and sparse human data. Curcumin remains a research candidate rather than an established intervention for antituberculosis drug-induced hepatotoxicity. Controlled clinical studies are needed to determine efficacy, dosage, formulation, safety, and potential drug interactions.

Keywords

antituberculosis drugs, curcumin, drug-induced liver injury, hepatoprotection, narrative review, tuberculosis.

1. Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major public-health concern, including in Indonesia (Nasution et al., 2025). Effective treatment commonly requires combinations of first-line antituberculosis drugs (ATDs), particularly isoniazid, rifampicin, pyrazinamide, and ethambutol. While these regimens are central to TB control, drug-induced liver

injury can complicate treatment and necessitate clinical monitoring, temporary interruption, or modification of the regimen (Soedarsono & Riadi, 2020; Tostmann et al., 2008).

Among first-line agents, isoniazid, rifampicin, and pyrazinamide are particularly relevant to hepatotoxicity. The proposed mechanisms include reactive drug metabolites, disturbed redox homeostasis, mitochondrial dysfunction, inflammatory signaling, and alterations in hepatic metabolic pathways (Ezhilarasan, 2023; Yew et al., 2018; Zhuang et al., 2022).. Previous reports describe a wide hepatotoxicity incidence range of 2%–28%, reflecting differences in diagnostic definitions, treatment populations, and risk factors rather than one universally applicable risk estimate (Tostmann et al., 2008). Preventing clinically important liver injury while preserving effective TB therapy is consequently an important research objective.

Curcumin is a polyphenolic constituent of turmeric (Curcuma longa) that has been investigated for antioxidant, anti-inflammatory, immunomodulatory, and hepatoprotective actions. Studies summarized by Barua & Buragohain (2021) and Fu et al. (2023) connect these activities with molecular pathways relevant to isoniazid- and rifampicin-associated liver injury. However, findings from purified curcumin, turmeric extracts, and commercial Curcuma tablets cannot automatically be treated as equivalent: preparations may differ in composition, bioavailability, and administered dose. Nor can preclinical improvements in biochemical markers be assumed to prevent clinically significant liver injury in humans.

Four publications form the focal evidence base of this review, including a hospital-based observational study reporting changes in biochemical liver-injury indicators (Sari et al., 2025). This article examines (a) molecular mechanisms reported for curcumin, (b) the scope and limitations of the available human evidence, and (c) unanswered questions that must be addressed before curcumin can be considered an evidence-based adjunct to standard TB treatment.

2. Research Methods

Design, Information Sources, and Scope

This study is a structured narrative literature review, not a systematic review or meta-analysis. The documented source-selection process identifies PubMed, Scopus, and Google Scholar as the information sources and lists combinations of the terms “curcumin,” “tuberculosis,” “anti-tuberculosis drugs,” “drug-induced liver injury,” “hepatotoxicity,” and “hepatoprotective.” The review focuses on liver injury associated with first-line ATDs and on curcumin as a potential protective intervention or the subject of mechanistic reviews. No pooled treatment effects or clinical hepatotoxicity incidence estimates were calculated.

The available search records do not specify when each database was searched, the complete database-specific search strings, the number of records identified or screened, deduplication totals, or a record-by-record exclusion log. These details cannot be reconstructed from the four publications ultimately included. Consequently, this review does not present a PRISMA flow diagram, claim exhaustive retrieval, or imply that a prospective protocol was registered. Its scope is limited to the documented databases, search concepts, and selected publications.

Eligibility and Study Selection

The documented eligibility criteria included English- or Indonesian-language publications, generally from the preceding decade, with exceptions for relevant foundational sources. Eligible work examined curcumin, curcumin-containing preparations, or related formulations in relation to liver

injury associated with isoniazid, rifampicin, pyrazinamide, or their combinations. Outcomes of interest included liver enzymes (ALT, AST, ALP, and GGT), bilirubin, oxidative-stress markers (including SOD, GSH, and malondialdehyde), inflammatory or apoptotic mediators (including TNF-α, IL-6, and caspase-3), and hepatic histopathology. Full-text access and sufficient methodological reporting were relevant to the assessment.

The reported exclusion criteria concerned duplicate records, publications without relevant hepatotoxicity outcomes, studies of unrelated causes of liver injury, and combination interventions in which the contribution of curcumin could not be distinguished. The four focal publications were Sari et al. (2025), Barua and Buragohain (2021), Al Ikhsan (2024), and Fu et al. (2023). Because the historical screening log is unavailable, the completeness of this selection relative to all potentially eligible studies cannot be verified.

Evidence Classification and Source Tracing

These four focal publications are not four independent intervention studies. Sari et al. (2025) reported a retrospective, non-experimental observational investigation of Curcuma-tablet exposure and biochemical outcomes in patients receiving ATDs. Barua and Buragohain (2021), Al Ikhsan (2024), and Fu et al. (2023) are secondary reviews that may discuss overlapping animal and cellular experiments. Their findings were therefore synthesized qualitatively and were not counted as independent demonstrations of curcumin efficacy.

To improve attribution of the mechanisms discussed in the secondary literature, two underlying primary studies were traced to their published records: He et al. (2017), addressing protoporphyrin IX (PPIX) and ferrochelatase (FECH), and Li et al. (2022), addressing the SIRT1/PGC-1α/NRF1 pathway. Table 2 presents these reports separately from the four focal publications. Source tracing does not constitute an additional systematic database search and does not increase the original focal-publication count.

Synthesis and Assessment Limitations

The synthesis was organized by evidence type and biological pathway, with attention to the identity of the intervention, experimental model or population, measured outcomes, and limits to inference. No standardized risk-of-bias instrument, independent dual screening, meta-analysis, or formal certainty-of-evidence grading was applied. Findings are thus interpreted as preliminary and hypothesis-supporting, not as demonstrated clinical benefits. The principal limitations include a small documented focal corpus, overlap among secondary reviews, heterogeneity between purified curcumin and Curcuma preparations, reliance on preclinical data, and incomplete exposure information in the observational patient study.

3. Results and Discussion

Profile of the Four Focal Publications

The focal evidence base comprises one observational patient study and three narrative reviews. Table 1 distinguishes their study designs, populations or interventions, reported findings, and interpretive limitations. Agreement among secondary reviews may reflect shared primary sources rather than independent replication.

Table 1. Focal publications and evidentiary limitations

Source and evidence type	Focus, population, and findings	Interpretive limits
Sari et al. (2025) Retrospective observational study	60 pulmonary TB patient records; Curcuma tablets during ATD therapy. Mean AST: 57.03 → 50.82 U/L; ALT: 47.95 → 43.67 U/L; total bilirubin: 2.63 → 1.53 mg/dL; reported $p < .05$.	Not randomized; preparation, curcumin content, dose, exposure period, and contemporaneous comparator not adequately established for causal inference.
Barua & Buragohain (2021) Narrative review	Reviews antimycobacterial and proposed hepatoprotective effects, including PPIX/FECH, oxidative stress, and immunomodulation.	Secondary evidence; may overlap with other reviews; no direct evidence of improved TB clinical outcomes.
Al Ikhsan (2024) Narrative review	Reviews curcumin and ATD-associated injury, particularly PPIX regulation and oxidative-stress mechanisms.	No independent intervention sample; animal/cell mechanisms cannot establish clinical benefit.
Fu et al. (2023) Broader narrative review	Surveys nutrition-related interventions, including curcumin-related Bax/caspase-3, redox, and signaling findings and separate chitosan results.	Multiple agents and models; chitosan findings must not be attributed to curcumin; underlying evidence can overlap.

Note. ATD = antituberculosis drug; AST = aspartate aminotransferase; ALT = alanine aminotransferase; PPIX = protoporphyrin IX; FECH = ferrochelatase. Numerical outcomes and patient count reported for Sari et al. (2025) are taken from the cited publication. The reviews are secondary sources; no pooled treatment effect is calculated.

Human Evidence: Interpretation of Curcuma-Tablet Findings

Sari et al. (2025) examined medical records of pulmonary TB patients treated at Pasar Rebo Hospital, East Jakarta, between January and December 2024. The authors described a non-experimental analytical design, a cross-sectional approach, and retrospective data collection. Their report included 60 patient records and presented mean AST levels of 57.03 and 50.82 U/L, mean ALT levels of 47.95 and 43.67 U/L, and mean total bilirubin levels of 2.63 and 1.53 mg/dL at the compared measurements. Statistically significant differences were reported ($p < .05$).

These findings do not constitute evidence from a randomized or controlled clinical trial. The product was described as a Curcuma tablet containing temulawak (*Curcuma xanthorrhiza*) extract, not as a quantified dose of purified curcumin. The report does not establish the curcumin content, standardized product composition, or a contemporaneous untreated comparison group. The duration of exposure and potential co-interventions are also insufficiently detailed for a compound-specific causal inference. Changes in liver markers could reflect the stage of TB treatment, baseline liver function, other medications, nutritional status, or clinical management. A statistically significant change in biomarkers alone does not demonstrate prevention of clinically adjudicated drug-induced liver injury.

Accordingly, the clinical report offers an observational association involving a Curcuma product and selected liver-function markers, not an estimate of the causal effect of purified curcumin. Its findings should remain separate from experiments involving well-characterized curcumin. The evidence reviewed here does not establish reductions in TB mortality, treatment failure, or the incidence of clinically adjudicated drug-induced liver injury.

3.3. Mechanistic Evidence from Experimental Studies

Two primary experimental studies, identified through the secondary reviews, provide more direct support for the proposed mechanisms (Table 2). Their results support biological plausibility in nonhuman systems but cannot establish the clinical effectiveness or appropriate dosage of curcumin in patients receiving multidrug TB treatment.

Table 2. Primary experimental evidence traced from secondary reviews

Primary study and model	Reported curcumin-related findings	Limit to inference
He et al. (2017) Hepatocyte and mouse isoniazid–rifampicin models	Reduced PPIX accumulation and increased FECH expression. Fu et al. (2023) summarize a 200 mg/kg mouse experiment with ALT approximately 25% and AST approximately 16% lower.	Experimental dose and outcomes; not a basis for human dosage or clinical efficacy claims.
Li et al. (2022) Cell and animal isoniazid-injury models	Improvement in oxidative-stress and injury markers associated with SIRT1/PGC-1α/NRF1 upregulation. Fu et al. (2023) describe 100 mg/kg curcumin in a 28-day rat experiment.	Preclinical mechanistic evidence; no direct extrapolation to multidrug TB therapy in patients.

Note. Curcumin exposures of 200 mg/kg and 100 mg/kg are experimental animal doses described by Fu et al. (2023) when discussing He et al. (2017) and Li et al. (2022). They must not be interpreted as dosing recommendations for humans.

Protoporphyrin IX and Ferrochelatase

The PPIX–FECH pathway offers a mechanistically specific explanation for part of the liver injury observed in experimental models. FECH catalyzes the final step in heme formation by incorporating iron into PPIX. He et al. (2017) reported that isoniazid–rifampicin exposure was associated with PPIX accumulation and altered FECH regulation in cultured hepatocytes and mouse liver. In these models, curcumin reduced PPIX accumulation and increased FECH expression, alongside attenuation of measured injury markers. These observations should not be generalized to all turmeric preparations or to patients without further clinical evidence.

Barua and Buragohain (2021) and Al Ikhsan (2024) discuss this pathway in their secondary reviews. Their agreement may reflect the same underlying experimental evidence and should not be presented as independent replication. The clinical relevance of PPIX modulation during routine multidrug TB therapy, including human dose–response relationships, remains uncertain.

Oxidative Stress, Inflammation, and Cell Survival

Oxidative stress and disrupted redox signaling are implicated in liver injury associated with first-line ATDs (Ezhilarasan, 2023; Yew et al., 2018; Fu et al., 2023) summarize preclinical work in which curcumin affected reactive oxygen species, antioxidant defenses, and apoptosis-related proteins such as Bax and caspase-3. Li et al. (2022) linked curcumin-associated protection to activation of the SIRT1/PGC-1α/NRF1 pathway in cellular and animal models of isoniazid-induced injury. Reported anti-inflammatory actions, including modulation of cytokines and related enzymes, offer additional mechanistic hypotheses (Wahyudi et al., 2025).

Fu et al. (2023) also review nutritional compounds other than curcumin. In particular, they describe a separate experiment using chitosan (100 mg/kg) and reporting outcomes involving ALP, ALT, and AST. These results are attributable to chitosan, not curcumin. The curcumin-specific experimental observations discussed in this article are traced to He et al. (2017) and Li et al. (2022). Chitosan is mentioned solely to distinguish the interventions and is excluded from curcumin-specific evidence.

Critical Appraisal and Clinical Translation

Three issues constrain interpretation. First, the evidence hierarchy is uneven: three of the four focal publications are potentially overlapping secondary reviews, and the only human investigation is

retrospective and concerns a Curcuma-containing preparation. Mechanistic evidence is predominantly preclinical. Second, favorable changes in biomarkers (including ALT, AST, bilirubin, oxidative-stress indicators, and histopathology) do not substitute for clinically meaningful endpoints, such as prespecified drug-induced liver injury, treatment interruption, adverse events, or TB outcomes. Third, purified curcumin, turmeric, temulawak extracts, and bioavailability-enhanced formulations are distinct exposures and should not be treated as interchangeable.

Curcumin faces formulation challenges, particularly limited oral bioavailability. The reviewed human report does not provide a sufficient basis for inferring a therapeutic curcumin dose or schedule during ATD treatment. Potential pharmacokinetic and pharmacodynamic interactions with antituberculosis medicines require direct study; a presumed favorable safety profile for a natural product does not establish its safety during multidrug treatment. The evidence does not support substituting curcumin for standard TB medicines, modifying prescribed regimens, or recommending its routine adjunctive use.

Future research should examine chemically characterized curcumin formulations with explicit dosing, prospective comparison groups, and adequate follow-up. Studies should measure concomitant medicines and hepatotoxicity risk factors and incorporate both biochemical measures and clinically meaningful liver-injury outcomes. Independent replication is essential because several secondary reviews rely on overlapping preclinical evidence.

4. Conclusion

Curcumin remains a plausible hepatoprotective research candidate for liver injury associated with first-line ATDs. Experimental studies identify potential mechanisms involving reduced PPIX accumulation and increased FECH expression, attenuation of oxidative stress and apoptosis, and SIRT1/PGC-1α/NRF1 signaling. A retrospective observational study involving 60 pulmonary TB patient records reported favorable changes in AST, ALT, and bilirubin after exposure to Curcuma tablets. However, differences in formulation, limited exposure detail, and the nonrandomized design prevent attribution of these changes specifically to curcumin or confirmation of clinical efficacy.

The four-publication narrative synthesis is limited by its small documented corpus, overlap among secondary reviews, and incomplete historical search records. Curcumin should therefore be considered a candidate for further investigation, not an established hepatoprotective therapy. Controlled clinical studies are required to establish meaningful benefit, reproducible formulations, appropriate dosing, safety, and potential interactions with standard TB treatment.

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Ethics and Consent : This study employed a structured narrative review of previously published scientific literature. No new human participants were recruited, and no identifiable patient-level data were collected. Participant informed consent was therefore not applicable to the review itself.

Data Availability : The evidence supporting this review is derived from previously published studies identified in the reference list. The characteristics of the four focal publications and two traced experimental studies are summarized in the manuscript. Additional literature-selection and analytical records may be obtained from the corresponding author, subject to their availability.

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