HEPATOPROTECTIVE AND ANTIOXIDANT ACTIVITY OF THE ALCOHOLIC EXTRACT OF *IPOMOEA TURPETHUM* AGAINST RIFAMPICIN-INDUCED HEPATOTOXICITY IN RATS

Sudheer Kumar.J, Bala Krishna.R.B, Vijay Kumar.G, Ranganayakulu.D.

Abstract

Drug-induced liver injury remains an important clinical and experimental problem because the liver is the principal organ responsible for the metabolism and detoxification of many xenobiotics. Rifampicin, a widely used antitubercular drug, may contribute to hepatotoxicity through metabolic stress, oxidative imbalance, altered membrane integrity, and disturbance of hepatic enzyme systems. Medicinal plants with antioxidant and hepatoprotective properties are therefore of considerable pharmacological interest. *Ipomoea turpethum* Linn., also referred to in current botanical literature as *Operculina turpethum*, has traditionally been used in South Asian medicine for hepatic and gastrointestinal disorders and contains resin glycosides, sterols, coumarins, phenolic compounds, and other secondary metabolites. The aim of this study is to evaluate the hepatoprotective and antioxidant potential of an alcoholic extract of *I. turpethum* against rifampicin-associated hepatic injury and to discuss the biochemical mechanisms that may underlie its protective effects. A literature-based experimental framework was developed with emphasis on serum hepatic biomarkers, lipid peroxidation, reduced glutathione, superoxide dismutase, catalase, and histopathological examination. Previous experimental evidence demonstrates that ethanolic or hydroalcoholic extracts of *O. turpethum* protect against paracetamol-, carbon tetrachloride-, and N-nitrosodimethylamine-induced liver damage [1–3]. These findings support the hypothesis that the plant may reduce drug-associated hepatocellular injury through antioxidant, membrane-stabilizing, and free-radical-scavenging mechanisms. However, direct evidence specifically for rifampicin-induced hepatotoxicity remains more limited than for other experimental hepatotoxins. Further controlled studies are therefore necessary.

Keywords: *Ipomoea turpethum*, *Operculina turpethum*, rifampicin, hepatotoxicity, antioxidant activity, oxidative stress, liver enzymes, medicinal plants.

Introduction

The liver plays a central role in metabolism, detoxification, biotransformation, synthesis of plasma proteins, regulation of energy metabolism, and elimination of xenobiotics. Because many drugs are metabolized in hepatocytes, the liver is particularly vulnerable to chemically induced injury.

Drug-induced liver injury may arise through direct toxicity, formation of reactive metabolites, immune-mediated processes, mitochondrial dysfunction, oxidative stress, or interference with bile transport.

Rifampicin is an important first-line antitubercular agent. Although it is generally effective and well tolerated, hepatotoxicity is a recognized adverse effect, particularly when it is administered together with other hepatotoxic antitubercular drugs.

Rifampicin is a strong inducer of hepatic drug-metabolizing enzymes and can influence the metabolism of other compounds. Experimental and clinical studies indicate that antitubercular drug-associated liver injury involves oxidative stress, changes in hepatic antioxidant defense, lipid peroxidation, and hepatocellular membrane damage [4].

Biochemical indicators commonly used to evaluate hepatocellular injury include alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and bilirubin.

An increase in serum aminotransferase activity often reflects leakage of intracellular enzymes from damaged hepatocytes.

Oxidative stress may also be evaluated through hepatic malondialdehyde or other lipid peroxidation products, together with antioxidant markers such as reduced glutathione, superoxide dismutase, and catalase.

Medicinal plants have long been investigated as potential sources of hepatoprotective agents because many contain phenolic compounds, flavonoids, sterols, and other phytochemicals capable of modulating oxidative processes.

Ipomoea turpethum, commonly referred to as *Operculina turpethum* in pharmacognostic and botanical literature, belongs to the family Convolvulaceae.

The root has traditionally been used in Ayurvedic medicine and has been associated with purgative, anti-inflammatory, antimicrobial, and hepatoprotective properties [5].

Experimental evidence supports its hepatic protective potential.

Suresh Kumar et al. reported that ethanolic root extract of *O. turpethum* reduced serum SGOT, SGPT, alkaline phosphatase, and bilirubin in paracetamol-induced hepatotoxicity in rats [1].

Other studies have demonstrated protective activity in carbon tetrachloride- and N-nitrosodimethylamine-induced hepatic injury [2,3].

The purpose of the present article is to examine the potential hepatoprotective and antioxidant activity of an alcoholic extract of *I. turpethum* in the context of rifampicin-induced hepatic toxicity.

Materials and Methods

This article was prepared as a literature-based experimental analysis using established pharmacological methods commonly employed in hepatoprotective screening.

The proposed experimental framework involves healthy adult Wistar rats maintained under standard laboratory conditions.

Animals would typically be divided into a normal control group, rifampicin-treated hepatotoxic control group, standard hepatoprotective treatment group, and one or more groups receiving alcoholic extract of *I. turpethum*.

A standard hepatoprotective agent such as silymarin may be used as a reference comparator.

The alcoholic extract can be prepared from authenticated root material after cleaning, shade drying, and pulverization.

The powdered plant material may be subjected to extraction using ethanol or a hydroalcoholic solvent, followed by filtration and concentration under reduced pressure.

Previous studies of *O. turpethum* have used ethanolic or hydroalcoholic root extracts successfully in experimental hepatoprotection [1,2].

The exact dose and treatment duration should be selected on the basis of preliminary toxicity assessment and published pharmacological evidence rather than assumed arbitrarily.

The main biochemical parameters for hepatoprotective evaluation include serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, total protein, and albumin.

Antioxidant status may be investigated through hepatic malondialdehyde, reduced glutathione, superoxide dismutase, catalase, and glutathione peroxidase.

Histopathological examination of liver tissue should be used to complement biochemical findings.

All animal experiments should be performed only after approval from the appropriate institutional animal ethics committee and in accordance with relevant animal-welfare guidelines.

Results

The available literature provides substantial indirect support for the hepatoprotective potential of *I. turpethum*.

In paracetamol-induced liver injury, ethanolic root extract of *O. turpethum* reduced elevated SGOT, SGPT, alkaline phosphatase, and total bilirubin values and produced histological evidence of hepatoprotection [1].

The study used an oral ethanolic extract and compared the response with silymarin as a positive control.

This finding is relevant because paracetamol toxicity is strongly associated with reactive metabolite formation, glutathione depletion, and oxidative injury.

A separate study using carbon tetrachloride demonstrated dose-dependent hepatoprotective activity of hydroalcoholic *I. turpethum* root extract.

Treatment reduced SGOT, SGPT, alkaline phosphatase, bilirubin, and cholesterol and improved protein levels, with histopathological findings supporting biochemical protection [2].

Carbon tetrachloride is metabolically activated to highly reactive radicals that initiate lipid peroxidation.

Protection against this model therefore provides additional evidence that antioxidant mechanisms may contribute to the activity of the plant.

Another experimental study evaluated *O. turpethum* against N-nitrosodimethylamine-induced hepatic toxicity.

The root extract attenuated toxic liver injury and associated clastogenic effects in rats [3].

Taken together, these findings indicate that *I. turpethum* may provide hepatic protection across more than one model of chemically induced liver injury.

Histopathological Assessment

Biochemical analysis should be supported by microscopic examination of liver tissue.

Normal liver architecture includes organized hepatic cords, intact hepatocytes, normal sinusoids, and a clear central vein.

Rifampicin-associated toxicity may produce hepatocellular degeneration, inflammatory infiltration, congestion, vacuolar change, and areas of necrosis depending on severity and experimental conditions.

A hepatoprotective effect would be reflected by better preservation of hepatic architecture and reduced cellular degeneration compared with untreated toxic controls.

Histopathology is particularly valuable because serum enzymes show biochemical leakage but do not provide direct information about the structural pattern of injury.

Previous studies of *O. turpethum* against paracetamol and carbon tetrachloride reported histological findings consistent with biochemical hepatoprotection [1,2].

Discussion

The available evidence supports the broader hepatoprotective potential of alcoholic or hydroalcoholic extracts of *I. turpethum*.

Protective activity has been reported in several established models of hepatic injury.

Suresh Kumar et al. demonstrated significant protection against paracetamol-induced hepatotoxicity with an ethanolic root extract [1].

Shah et al. later reported dose-dependent protection against carbon tetrachloride-induced hepatic injury [2].

Another experimental investigation demonstrated protection against N-nitrosodimethylamine-induced toxic liver injury [3].

The fact that protective effects have been observed with different hepatotoxins is important because these agents produce liver injury through different but overlapping biochemical mechanisms.

A common element among several models is oxidative stress.

This suggests that enhancement of antioxidant defense may be one of the central mechanisms of *I. turpethum*.

However, hepatoprotection may not be explained entirely by free-radical scavenging.

The extract may also stabilize cellular membranes, influence inflammatory signaling, improve detoxification, or affect drug-metabolizing enzymes.

These possibilities require direct molecular investigation.

The proposed relevance to rifampicin hepatotoxicity is scientifically plausible because oxidative stress and metabolic disturbance contribute to antitubercular-drug-induced liver injury.

Nevertheless, the evidence base specifically involving rifampicin and *I. turpethum* is weaker than the evidence involving paracetamol, carbon tetrachloride, and N-nitrosodimethylamine.

This distinction is important.

Results from one hepatotoxic model should not automatically be assumed to apply identically to another.

Therefore, a dedicated rifampicin study should directly evaluate serum biomarkers, hepatic antioxidant status, histopathology, dose dependence, and extract standardization.

Another important consideration is plant identity.

The name *Ipomoea turpethum* has appeared frequently in older medicinal literature, whereas the plant is widely treated as *Operculina turpethum* in modern pharmacognostic literature.

Researchers should therefore provide a voucher specimen and authenticated botanical identification to avoid taxonomic confusion.

Standardization of the extract is equally necessary.

Alcoholic extracts contain many compounds, and their relative concentrations can change according to plant origin, harvesting season, root age, solvent concentration, extraction time, and storage.

Chromatographic fingerprinting should therefore accompany pharmacological evaluation.

Without chemical standardization, reproducibility between laboratories may be poor.

Limitations

The principal limitation of this article is that it is based on published evidence and an experimental framework rather than newly generated animal data.

Most direct hepatoprotective evidence for *I. turpethum* involves paracetamol, carbon tetrachloride, or N-nitrosodimethylamine rather than rifampicin alone.

The precise active compounds responsible for hepatoprotection have also not been definitively established.

Crude alcoholic extracts contain multiple phytochemicals that may act synergistically.

Furthermore, results in animal hepatotoxicity models cannot automatically be translated into clinical efficacy in humans.

Future studies should use standardized extracts, appropriate dose-response designs, validated oxidative-stress biomarkers, and pharmacokinetic investigation.

Conclusion

The alcoholic extract of *Ipomoea turpethum*/*Operculina turpethum* represents a promising source of hepatoprotective and antioxidant phytochemicals.

Previous experimental studies have demonstrated protective effects against paracetamol-, carbon tetrachloride-, and N-nitrosodimethylamine-induced hepatic injury.

These effects were associated with improvement in serum hepatic biomarkers and preservation of liver structure [1–3].

The probable mechanisms include reduction of lipid peroxidation, preservation of reduced glutathione, maintenance of antioxidant enzymes, stabilization of hepatocyte membranes, and possible modulation of inflammatory or metabolic processes.

These mechanisms provide a reasonable biochemical basis for evaluating the extract against rifampicin-induced hepatotoxicity.

However, specific evidence for the rifampicin model requires further controlled experimental confirmation.

Future research should include standardized phytochemical characterization, multiple extract doses, comparison with an established hepatoprotective agent such as silymarin, measurement of ALT, AST, ALP, bilirubin, GSH, SOD, catalase, and MDA, together with detailed histopathological evaluation.

The plant should therefore currently be regarded as a promising experimental hepatoprotective agent rather than an established clinical treatment for drug-induced liver injury.

References

1. Suresh Kumar SV, Sujatha C, Syamala J, Nagasudha B, Mishra SH. Protective effect of root extract of *Operculina turpethum* Linn. against paracetamol-induced hepatotoxicity in rats. *Indian Journal of Pharmaceutical Sciences*. 2006;68(1):32–35. doi:10.4103/0250-474X.22960.
2. Shah VV, Shah VK, Patel KN, Sheth NR, Patel MM. Improvement on the carbon tetrachloride inducing hepatotoxicity in rats using *Ipomoea turpethum* root. *Research Journal of Pharmacognosy and Phytochemistry*. 2017;9(4):231–234. doi:10.5958/0975-4385.2017.00043.7.

3. Ahmad R, Ahmad N, Naqvi AA, et al. *Operculina turpethum* attenuates N-nitrosodimethylamine-induced toxic liver injury and clastogenicity in rats. *Chemico-Biological Interactions*. 2009;181(2):145–153. doi:10.1016/j.cbi.2009.06.021.

4. Ramappa V, Aithal GP. Hepatotoxicity related to anti-tuberculosis drugs: Mechanisms and management. *Journal of Clinical and Experimental Hepatology*. 2013;3(1):37–49.

5. Kohli KR, Nipanikar SU, Kadbhane KP. A comprehensive review on *Operculina turpethum* as a medicinal plant species: Bioactive components and pharmacological properties. *Journal of Traditional and Complementary Medicine*. 2017.

6. Kaplowitz N. Drug-induced liver injury. *Clinical Infectious Diseases*. 2004;38(Suppl 2):S44–S48.

7. Jaeschke H, McGill MR, Ramachandran A. Oxidant stress, mitochondria, and cell death mechanisms in drug-induced liver injury. *Expert Opinion on Drug Metabolism & Toxicology*. 2012;8(9):1095–1106.

8. Halliwell B, Gutteridge JMC. *Free Radicals in Biology and Medicine*. 5th ed. Oxford University Press; 2015.

9. Recknagel RO, Glende EA, Dolak JA, Waller RL. Mechanisms of carbon tetrachloride toxicity. *Pharmacology & Therapeutics*. 1989;43(1):139–154.

10. Wellington K, Jarvis B. Silymarin: A review of its clinical properties in the management of hepatic disorders. *BioDrugs*. 2001.