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Original Article

Ayurveda Section

Hepatoprotective Effects of *Cassia fistula* L.: A Systematic Review of Preclinical Animal Studies

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ABSTRACT

Introduction: *Cassia fistula* Linn., commonly known as the Indian Laburnum or "*Aargwadh*" in Ayurveda, is traditionally valued for its antiseptic and therapeutic properties. Liver diseases, exacerbated by environmental toxins and viral infections, remain a significant global health burden. Medicinal plants, especially those rich in antioxidants, have gained attention for their hepatoprotective potential. Numerous preclinical studies have indicated that *Cassia fistula* exhibits protective effects against liver damage, making it a promising candidate for liver therapy.

Aim: To systematically analyse and synthesise available evidence on the hepatoprotective activity of *Cassia fistula*, evaluating its efficacy across experimental models and identifying its active phytoconstituents.

Materials and Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A comprehensive literature search was carried out using databases including PubMed, Scopus, Web of Science, Ayush, Shodhganga and Google Scholar, employing predefined search terms such as "*Cassia fistula*", "*Aargwadh*", "Hepatoprotective" and "liver injury". Studies were screened based on predefined inclusion and exclusion criteria, focusing on in-vivo, in-vitro and clinical studies assessing hepatoprotective outcomes. The Population (or Patient), Intervention, Comparison, Outcome and Study (PICOS) framework was used to define eligibility criteria. Data were independently extracted by two reviewers and included details on the part of the plant used, type of extract, hepatotoxins employed (e.g., Carbon Tetrachloride (CCl_4), paracetamol, Diethylnitrosamine (DEN)}, biomarkers measured and phytochemicals identified. The SYstematic Review Centre for Laboratory animal Experimentations (SYRCLE's) Risk of Bias tool was used to assess methodological quality of animal studies.

Results: The review included a total of nine studies, demonstrating consistent hepatoprotective effects of *Cassia fistula* across various experimental models of liver injury. Extracts from different plant parts (pods, leaves, bark, fruit pulp) significantly reduced levels of liver enzymes {Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP)}, improved histopathological profiles and enhanced antioxidant defences. Bioactive compounds such as flavonoids, polyphenols, anthraquinones and glycosides were frequently associated with the observed protective effects.

Conclusion: *Cassia fistula* exhibits significant hepatoprotective activity across multiple models of chemically induced liver damage, likely due to its rich phytochemical profile. It holds promise as a complementary herbal therapy for managing liver disorders.

Keywords: *Aargwadh*, Antioxidants, Liver injury, Phytochemicals

INTRODUCTION

Liver disease is a considerable health burden worldwide. Liver diseases are fast being recognised as public health priorities in India. The burden of liver disease in India is significant because it alone contributed to 18.3% of the two million global liver disease-related deaths in 2015 [1]. The environmental pollution that damages liver cells has caused hepatitis to spread widely. In order to reverse this damage, the destroyed cells must gradually be replaced with new ones made of hepatocytes [2]. Because of its innate ability to detoxify and facilitate metabolism, the liver plays a vital function in life. Many intermediate and end products are created as a result of exposure to various endogenous and xenobiotic substances. These compounds have the potential to cause hepatocellular mortality and are the key reasons of liver disease [3,4]. The antioxidant process can counteract oxidative stress and free radicals, which worsen liver damage. The greatest source of these antioxidants that also have hepatoprotective effects is plant extracts [5]. This is one of the causes of the growing number of people worldwide who choose complementary and alternative treatment, especially those who live in wealthy nations. Herbal treatments were the only means of treating and managing a wide range of disorders prior to the development of modern medications. Natural products have long been used to prevent and treat liver illness; in fact, 80% of people on the world still predominantly rely on medicinal plant species and their products when living in large rural areas of poor and undeveloped countries [6].

Cassia fistula Linn [Table/Fig-1] commonly known as the golden shower Indian laburnum is in the legume family, *Fabaceae* and the subfamily *Caesalpiniaceae* which is employed as a medicinal plants which is used in traditional systems of medicines for several disorders since ancient times [7]. *C. fistula* is referred to as *Aargwadha* because it dispels even the possibility of illness and produces stunning golden yellow blossoms that are garlanded, giving it the appearance of the king of trees (*Rajvriksha*) [8]. All parts of the *Cassia fistula* plant are known for their medicinal qualities; they are very notable in the treatment of various illnesses and act as an antioxidant, analgesic, antibacterial, anti-inflammatory, hepatoprotective, carminative, laxative, wound healing, antifungal, antiulcer, antifertility, antipyretic, anti-cancer and anti-tumour agent, among other effects [9,10].

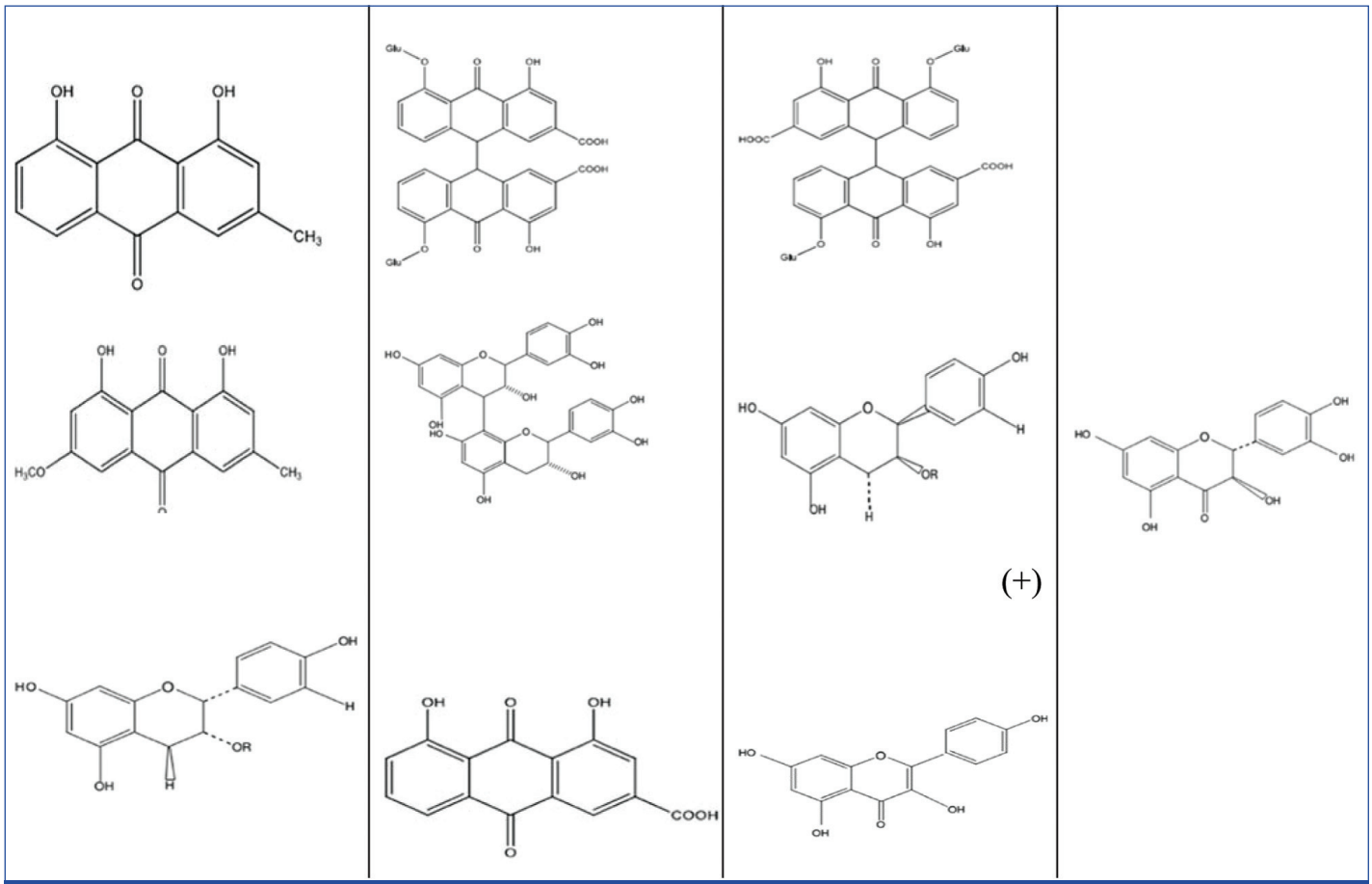
The hepatoprotective activity of *Cassia fistula* has been reported by various studies. Numerous studies support the usefulness of *Cassia fistula* as a natural remedy for hepatic ailments [11-13]. The present systematic review aimed to comprehensively analyse and synthesise the existing literature on the hepatoprotective activities

[Table/Fig-1]: *Cassia fistula* plant parts: plant, flowers and fruit with seeds.

of *Cassia fistula*. The present review focuses on the research on chemically defined molecules, or purified or semi-purified compounds derived from herbs, that have been shown to have hepatoprotective effects in both experimental and clinical settings when used in conjunction with herbal extracts or powdered dry plants to treat particular liver diseases [14,15].

Phytochemistry of different parts of *cassia fistula* [Table/Fig-2]:

1. **Leaves:** Leaves of *Cassia fistula* contains chrysophanol [Table/Fig-2], anthraquinones , free rhein and its glycosides-sennosides A and B, physcion, tannin, chrysophanol, volatile oils, epiafzelechin, (-) epiafzelechin-3-Oglucoside, bioflavonoids, tri flavonoids and other phenolic acids [12],
2. **Flowers:** Flowers of *Cassia fistula* have been found to contain ceryl alcohol, kaempferol, bianthraquinone glycoside A fistulin Alkaloids, rhein, Aurantiamide acetate, heptacosanoic acids, seven biflavonoids and two triflavonoids together with (-)-epiafzelechin (-)epicatechin a hentriacontanoic, triacontanoic, Nonacosanoic and Gibberellic acid [13,14].
3. **Bark:** Bark of the plant has been found to contain two flavonol glycosides, Leucocyanidin, Fistucacidin,-pentahydroxyflavon), Lupeol and OXyanthraquinone ß-sitosterol, Dihydro Xyanthraquinone and hexacosanol [14].
4. **Pods:** Pulp of the pod is rich with anthraquinone glycosides. Fistulic acid is obtained from the alcoholic extract, formic acid, oxalic acid, butyric acid, lavone-3 Catechins barbaloin, aloin contain 5 nonatetracontanone, 2-hentriacontanone [13,14],
5. **Fruits:** Fruit pulp is the rich source of carbohydrates and proteins, phenylalanine, tryptophan, aspartic and glutamic acids have been isolated from fruit pulp; (-) epifzelechin , (+) catechin , Glycosides-Sennosides A and B, volatile oil (essential oils), Chrysophanol and waxy derivative - 3 -methylanthraquinone a 1,8-dihydroxy-3-anthraquinolone derivative, Rhein, tannin, ceryl alcohol [11,15].
6. **Roots:** The roots of the plant contain Oxyanthraquinone and phlobaphenes, 7-methylphyscion, tannins and betulinic acid, ß-sitosterol, Trhamnetin-3-O-gentiobioside [15,16].
7. **Heartwood:** According to reports, the Heartwood contains 3, 4, 7,8and4' pentahydroxyflavan, fistucacidin, 3-dihydroxyflavan-3, 4-diol and an optically inactive leucoanthocyanidin-5 [13].
8. **Pulp:** The fruit pulp contains Rhein, a major anthraquinone derivatives, other phytochemicals associated with the pod is 2,4-dihydrobenzaldehyde, isoscopoletin, vanillic acid, ziganein, rhein methyl ester and isovanillin.
9. **Seeds:** *Cassia fistula* seeds contain bioactive constituents including fatty acids such as linoleic, oleic, palmitic and stearic acids, along with glycerides. Seed proteins such as albumins and globulins have also been reported. In addition, minor phenolic and chromone derivatives including substituted furfural and chromone compounds have been identified [17,18],



[Table/Fig-2]: Chemical structure of some chemical compounds of *Cassia fistula* Linn.
The present review aimed to systematically analyse and synthesise available evidence on the hepatoprotective activity of *Cassia fistula*, evaluating its efficacy across experimental models and identifying its active phytoconstituents.

MATERIALS AND METHODS

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, Scopus, ScienceDirect, Web of Science, Google Scholar, Excerpta Medica dataBASE (EMBASE), the Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) Research Portal and the Cochrane Library. The search was restricted to preclinical animal studies evaluating the hepatoprotective activity of *Cassia fistula* Linn [Table/Fig-3]. All identified records were exported and screened systematically according to predefined inclusion and exclusion criteria. Duplicate records were removed and titles and abstracts were screened for relevance. All databases were searched from their inception until September 2025. Standard PICOS guidelines were followed [Table/Fig-4].

Databases	Search terms
PUBMED	("*Cassia fistula*"[All Fields]) AND ("Hepatoprotective"[All Fields] OR "Hepatoprotection"[All Fields] OR "Liver injury"[All Fields] OR "Liver damage"[All Fields] OR "Hepatotoxicity"[All Fields] OR "CCl_4"[All Fields] OR "Carbon tetrachloride"[All Fields] OR "Preclinical"[All Fields] OR "Animal study"[All Fields] OR "Experimental study"[All Fields] OR "Antioxidant"[All Fields] OR "Oxidative stress"[All Fields] OR "Liver"[All Fields])
Scopus	TITLE-ABS-KEY("*Cassia fistula*" AND Hepatoprotective) OR TITLE-ABS-KEY("*Cassia fistula*" AND "Liver injury") OR TITLE-ABS-KEY("*Cassia fistula*" AND "Animal study") OR TITLE-ABS-KEY("*Cassia fistula*" AND "CCl_4-induced hepatotoxicity") OR TITLE-ABS-KEY("*Cassia fistula*" AND "Pre-clinical Studies") OR TITLE-ABS-KEY("*Cassia fistula*" AND Antioxidant AND Liver)
Web of Science	TS=("*Cassia fistula*" AND Hepatoprotective) OR TS=("*Cassia fistula*" AND "Liver injury") OR TS=("*Cassia fistula*" AND "Animal study") OR TS=("*Cassia fistula*" AND "CCl_4-induced hepatotoxicity") OR TS=("*Cassia fistula*" AND "Pre-clinical Studies") OR TS=("*Cassia fistula*" AND Antioxidant AND Liver)
Science direct	"*Cassia fistula*" AND Hepatoprotective "*Cassia fistula*" AND "Liver injury" "*Cassia fistula*" AND "Animal study" "*Cassia fistula*" AND "CCl_4-induced hepatotoxicity" "*Cassia fistula*" AND "Pre-clinical Studies" "*Cassia fistula*" AND Antioxidant AND Liver
Google Scholar	"*Cassia fistula*" AND Hepatoprotective "*Cassia fistula*" AND "Liver injury" "*Cassia fistula*" AND "Animal study" "*Cassia fistula*" AND "CCl_4-induced hepatotoxicity" "*Cassia fistula*" AND "Pre-clinical Studies" "*Cassia fistula*" AND Antioxidant AND Liver
Embase	('*Cassia fistula*':ti,ab AND 'Hepatoprotective':ti,ab) OR ('*Cassia fistula*':ti,ab AND 'Liver injury':ti,ab) OR ('*Cassia fistula*':ti,ab AND 'Animal study':ti,ab) OR ('*Cassia fistula*':ti,ab AND 'CCl_4-induced hepatotoxicity':ti,ab) OR ('*Cassia fistula*':ti,ab AND 'Pre-clinical Studies':ti,ab) OR ('*Cassia fistula*':ti,ab AND 'Antioxidant':ti,ab AND 'Liver':ti,ab)
Ayush Portal	*Cassia fistula* hepatoprotective *Cassia fistula* liver injury *Cassia fistula* animal study *Cassia fistula* CCl_4 hepatotoxicity *Cassia fistula* pre-clinical studies *Cassia fistula* antioxidant liver
SHODHGANGA	*Cassia fistula* hepatoprotective *Cassia fistula* liver injury *Cassia fistula* animal study *Cassia fistula* CCl_4 hepatotoxicity *Cassia fistula* preclinical studies *Cassia fistula* antioxidant liver

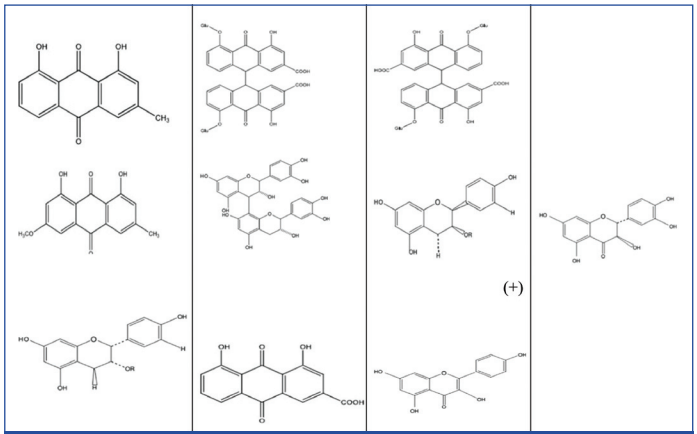
[Table/Fig-3]: Search yield for identification of preclinical studies on *Cassia fistula* Linn. in different databases.

Component	Description
Population (P)	Preclinical experimental animals (rats, mice, chicks) with chemically induced liver injury
Intervention (I)	*Cassia fistula* Linn. extracts (aqueous, ethanolic, methanolic, hydroalcoholic) from various plant parts
Comparator (C)	Disease/toxin-treated control groups, untreated controls, or standard hepatoprotective drugs (e.g., silymarin)
Outcomes (O)	Liver enzymes (ALT, AST, ALP, bilirubin), oxidative stress markers (MDA, GSH, SOD, CAT) and histopathology
Study Design (S)	In-vivo preclinical experimental studies published in English

[Table/Fig-4]: PICOS criteria for study selection.
MDA:Malondialdehyde; GSH: Glutathione SOD: Superoxide Dismutase; CAT:Catalase

The present systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [19] [Table/Fig-5]. The review protocol was not registered in International Prospective Register of Systematic Reviews (PROSPERO) as this study is based solely on published literature and classical Ayurvedic textual sources and does not involve interventional clinical trials or patient-level outcomes.

Articles such as editorials, narrative reviews, conference abstracts without full text and studies not assessing hepatoprotective activity of *Cassia fistula* were excluded. Additionally, studies lacking appropriate control groups, employing different interventions, or not reporting relevant biochemical or histopathological outcomes were considered methodologically unsuitable and excluded. Data extraction was performed independently by two reviewers using a predesigned data extraction form covering model, plant part, extract, dosage, hepatotoxin, biomarkers, antioxidant status, histopathology and key findings. Qualitative synthesis was performed. Discrepancies were resolved through discussion or consultation with a third reviewer.



[Table/Fig-5]: The PRISMA flow diagram.

Risk of Bias (RoB) assessment was done using SYRCLE tool, a specialised risk of bias assessment framework for animal intervention studies, adapted from the Cochrane tool to address features unique to laboratory animal research. It evaluates 10 specific entries across six main bias categories to appraise preclinical study quality [20].

RESULTS

A total of nine preclinical studies published between 1999 and 2025 were included in this systematic review [11,21-28]. The hepatoprotective activity of *Cassia fistula* Linn. was evaluated using different plant parts and extract types across these studies. Leaves were examined in two studies using n-heptane and ethanolic extracts, both showing significant hepatoprotective and antioxidant activity. Fruit and fruit pulp were assessed in three studies employing aqueous and hydroalcoholic extracts, with consistent dose-dependent protection against paracetamol, CCl_4 and bromobenzene-induced hepatotoxicity. Seeds were evaluated in one study using methanolic extracts, which demonstrated both hepatoprotective and nephroprotective effects. Bark, flower and fruit pulp extracts were comprehensively studied in one investigation, with bark extract showing the highest phenolic content and strongest radical scavenging activity, alongside significant improvements in liver function enzymes and antioxidant status. Roots were examined in one study where

ethanolic root extract provided hepatoprotection comparable to silymarin. A recent study on ethanolic fruit extract highlighted molecular docking evidence, showing (+)-Catechin binding to Keap-1 and activating the NRF2 pathway, thereby promoting hepatocyte protection and regeneration. Most studies employed Carbon Tetrachloride (CCl_4)-induced hepatotoxicity as the experimental model due to its well-established oxidative damage mechanism, while other hepatotoxins included diethyl nitrosamine, paracetamol, bromobenzene and acetaminophen. Silymarin was frequently used as a standard comparator, serving as a reference hepatoprotective agent. Across studies, *Cassia fistula* extracts consistently improved biochemical markers such as ALT, AST, ALP and bilirubin, enhanced antioxidant enzyme activity including SOD and CAT and reduced lipid peroxidation, with histological evidence confirming hepatoprotection.

The methodological quality and risk of bias in the included animal studies were assessed specifically designed for preclinical animal studies [Table/Fig-6] [11,21-28].

S. No.	Author (Year)	Random sequence generation	Allocation concealment	Blinding (performance)	Incomplete outcome data	Selective reporting	Other bias	Overall risk
1	Bhakta T et al., (1999) [21]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
2	Pradeep K (2005) [22]	L (Low)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
3	Das S et al., (2008) [23]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
4	Wasu S and Muley B (2009) [24]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
5	Sharma DK et al., [25]	L (Low)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
6	Ahirwar DK et al., [26]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
7	Kalantari H et al., (2011) [27]	L (Low)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
8	Dawada S et al., (2012) [11]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High
9	Faysal Ahmeda BM et al., [28]	U (Unclear)	U (Unclear)	H (High)	L (Low)	L (Low)	U (Unclear)	High

[Table/Fig-6]: Risk of Bias Assessment (SYRCLE Tool) [11,21-28].

DISCUSSION

In the present systematic review, a total of 206 articles were initially identified through a computer-based literature search using databases such as PubMed, Scopus and Web of Science. After applying predefined inclusion and exclusion criteria and screening for relevance, nine preclinical studies investigating the hepatoprotective activity of *Cassia fistula* Linn. were included [11,21-28]. These studies evaluated different plant parts including leaves, fruit pulp, bark, flowers, roots and seeds, using various extract types to assess hepatoprotective outcomes. The selection and reporting of studies were conducted in accordance with the PRISMA 2020 guidelines [19].

Cassia fistula Linn., known in Ayurveda as "*Aargwadh*/Amaltas" ("disease killer"), is a highly valued medicinal plant with multiple therapeutic applications. Different parts of the plant including leaves, pods, seeds, flowers, roots and fruit pulp possess bioactive compounds responsible for its medicinal properties. Phytochemical studies indicate the presence of anthraquinones, flavonoids, flavan-3-ol derivatives, steroids, carbonyl compounds, phlobatannins, reducing sugars, alkaloids and terpenoids. Anthraquinone glycosides such as physcion, chrysophanol and rhein are found in higher concentrations in mature leaves and lower amounts in pods [21,22,25]. These phytoconstituents contribute to its hepatoprotective, antioxidant and anti-inflammatory activities.

The hepatoprotective activity of *Cassia fistula* Linn. was evaluated using different plant parts and extract types across the included preclinical studies. Leaves were examined in two studies using n-heptane and ethanolic extracts, both showing significant hepatoprotective and antioxidant activity [21,22]. Fruit and fruit pulp were assessed in three studies employing aqueous and hydroalcoholic extracts, with consistent dose-dependent protection against paracetamol, CCl_4 and bromobenzene-induced hepatotoxicity [23,26,27]. Seeds were evaluated in one study using methanolic extracts, which demonstrated both hepatoprotective and nephroprotective effects [24]. Bark, flower and fruit pulp extracts were comprehensively studied in one investigation, with bark extract showing the highest phenolic content and strongest radical scavenging activity, alongside significant improvements in liver function enzymes and antioxidant status [25]. Roots were examined in one study where ethanolic root extract provided hepatoprotection comparable to silymarin [11]. A recent study on ethanolic fruit extract highlighted molecular docking evidence, showing (+)-Catechin binding to Keap-1 and activating the Nuclear Factor Erythroid 2-Related Factor 2 (NRF2) pathway, thereby promoting hepatocyte protection and regeneration [28].

Most studies employed CCl_4-induced hepatotoxicity as the experimental model due to its well-characterised mechanism of oxidative liver damage and lipid peroxidation [11,21,22,24,26]. Other hepatotoxins included diethyl nitrosamine [25], paracetamol [23], bromobenzene [27] and acetaminophen [28]. In addition, hepatotoxicity models involving Isoniazid and Rifampicin (INH + RIF), widely used antitubercular drugs that produce oxidative stress-mediated liver injury, have been cited in related preclinical hepatotoxicity studies [29-31]. Silymarin was frequently used as a standard comparator, serving as a reference hepatoprotective agent [11,25,26]. Comparative findings demonstrated that *Cassia fistula* extracts exhibited hepatoprotective activity comparable to silymarin, with leaves, bark, fruit pulp and flower extracts consistently restoring liver enzyme levels, bilirubin and histopathological features. These results reinforce the traditional use of the plant in Ayurvedic and Siddha medicine and highlight its potential as a source of hepatoprotective agents.

The included studies were evaluated using an adapted SYRCLE risk-of-bias tool for preclinical studies [20]. Most studies exhibited a high-risk of bias in domains such as blinding and allocation concealment, primarily due to incomplete reporting. Future animal studies should aim for rigorous methodology, standardised extract preparation and transparent reporting to strengthen the evidence base for the hepatoprotective potential of *Cassia fistula* Linn.

CONCLUSION(S)

The present systematic review highlights the hepatoprotective potential of *Cassia fistula* Linn. Across all included preclinical studies, various plant parts including leaves, pods, seeds, flowers, roots and fruit pulp demonstrated protective effects against multiple hepatotoxins (CCl_4, paracetamol, DEN, bromobenzene, INH + RIF). The findings consistently indicate restoration of liver enzymes, bilirubin and histopathological architecture, providing strong preclinical evidence for developing *Cassia fistula*-based hepatoprotective agents.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 22, 2025
- Manual Googling: Jul 09, 2026
- iThenticate Software: Jul 11, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

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