

Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com



E-ISSN: 2278-4136 P-ISSN: 2349-8234 Impact Factor (RJIF): 6.35 www.phytojournal.com

JPP 2025; 14(4): 555-559 Received: 11-05-2025 Accepted: 13-06-2025

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A comprehensive review on the pharmacological effect of *Cassia fistula* L.

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DOI: https://www.doi.org/10.22271/phyto.2025.v14.i4h.15517

Abstract

Cassia fistula, that is termed as the golden shower tree also and this serves as a medicinally significant tree that is used in conventional practices of medicine such as Ayurveda, Unani and Siddha [AYUSH]. The origin of the tree is Indian subcontinent and Southeast Asia, every part of this plant including the bark, leaves, flowers, fruit pulp, and seeds has been utilized to treat a wide range of diseases like gastrointestinal disturbances, skin disorders, diabetes and liver conditions. These traditional claims have been given very strong evidence by modern pharmacological studies. The plant is rich in different bioactive compounds that include flavonoids, anthraquinones, tannins, saponins, and phenolics, which validate strong antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and hepatoprotective properties. The extracts of different parts of the plant have proved to be effective in vitro and in vivo experiments, indicating their potential of therapeutic uses. The antioxidant ability assists in fighting oxidative stress whereas the antimicrobial and anti-inflammatory effects indicate its great potential in the treatment of infectious and inflammatory diseases. In addition, C. fistula has hypoglycemic and hepatoprotective properties that present it as a good candidate in the management of metabolic disorders. The current review seeks to provide a comprehensive synthesis of available literature on the pharmacological properties of C. fistula and its therapeutic potential, their mechanisms of action and perspectives related to the use of the plant in the development of medicines based on natural products.

Keywords: Cassia fistula, pharmacological action, Medicinal plants, Traditional medicine, Bioactive compounds

Introduction

Golden shower tree is also found as Cassia or Amaltas which is a member of the family Caesalpiniaceae and usually it is called "Indian Laburnum". The tree is immensely used in Ayurvedic system of medicine in various functions. This deciduous species often occurs in mixed monsoon forests in many parts of India, often to an altitude of 1,300 meters in the outer Himalayas. Its medicinal attributes are extensively recorded; it is recognized for its antifungal, antitussive, anti-inflammatory, and hepatoprotective qualities, utilized to enhance healing of injuries and fight against bacterial infections [1]. The benefits of herbs have been documented in numerous religious scriptures. In Islam, significance of herbs in medical treatment is comprehensively addressed, with Prophet Mohammed (Peace Be Upon Him) endorsing multiple fruits, seeds and plants for treatment of different ailments [2]. Cassia fistula is a deciduous plant that grows up to a moderate size, growing up to 9 meters tall, with its branches spreading outwards. The leaves measure between 20-40 cm in length and are paripinnate, characterized by large, oblong-lanceolate leaflets that end in an acute or acuminate point and are pubescent on the underside, displaying many closely spaced slender main veins. The flowers, which are yellow, grow in long, slender, drooping racemes. The fruits hang down, are cylindrical, nearly straight, and can be dark brown or brownish-black, indehiscent, firm, glossy, and smooth. The seeds are plentiful, smooth, broadly ovate and vary in color from light brown to dark brown [3]. As reported by the World Health Organization (WHO), above 70% of people worldwide depend on conventional medicine to address its essential health requirements. In poorer countries, around 80% of people's fundamental healthcare requirements are met by traditional medicine [4, 5]. Natural medicines and herbal remedies are frequently viewed as having lower toxicity and being devoid of side effects when compared to their syntheti counterparts [6].

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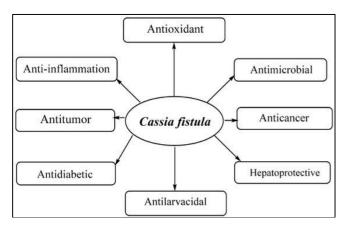
Table 1: Botanical Classification of Amaltas

Kingdom	Plantae	
Subkingdom	Tracheobinota	
Super Division	Spermatophyta	
Division	Mangoliophyta	
Class	Magnoliopsida	
Sub Class	Rosidae	
Order	Fabales	
Family	Fabacae	
Genus	Cassia	
Species	cies fistula	

Table 2: Common vernacular names of *Cassia fistula L.* in various languages and regions

Language/Region	Local/Common Name(s)		
Gujarati	Garmala ^[7]		
Bengali	Bundaralati, Soondali, Sonalu [7]		
Hindi	Amaltas, Sonhali [7]		
Punjabi	Kaniyaar, Girdnalee, Amaltaas [7]		
Marathi	Bahava ^[7]		
Kannada	Kakkemara ^[7]		
Telugu	Raelachettu, Aragvadhamu [7]		
Tamil	Shrakkonnai, Irjviruttam [7]		
Urdu	Amaltaas ^[7]		
Sanskrit	Nripadruma [7]		
Odia	Sunaari ^[7]		
Arabic	Khayarsambhar ^[7]		
English	Golden Shower Tree [7]		
French	Douche d'or (translates to "golden shower") [8]		
German	Fistul-kassie [8]		
Malay (Malaysia)	Kayu Raja (meaning "king's tree") [8]		
Sinhalese (Sri	Aehaela-gaha ^[8]		
Lanka)	Achaela-galla		
Thai (Thailand)	Chaiyaphruek [8]		

1.1 Pharmacodynamic Properties of Cassia fistula



2. Traditional Applications

Table 3: Plant parts and their biological activity

Table 5. I failt parts and their biological activity				
Plant parts of Cassia fistula Linn.	Chemical Constituents	Biological Activity	Reference	
Flowers	Flavonoids (quercetin, kaempferol)TanninsGlycosides	- Antioxidant - Antimicrobial - Anti-inflammatory - Antidiabetic	[9]	
Leaves	 Flavonoids (quercetin, kaempferol) Alkaloids Tannins Glycosides 	- Antioxidant - Anti-inflammatory - Antimicrobial - Anticancer	[10]	
Pods	-Anthraquinones (rhein, emodin) - Glycosides	- Laxative - Antioxidant - Antimicrobial	[11]	
Seeds	- Anthraquinones - Flavonoids - Saponins	 Antidiabetic Antimicrobial Antioxidant Anti-inflammatory 	[12]	
Bark	- Flavonoids - Saponins - Tannins	- Antimicrobial - Anti-inflammatory - Antioxidant - Anticancer	[13]	
Roots	- Alkaloids - Flavonoids	- Antioxidant - Hepatoprotective - Anti-inflammatory - Antimicrobial	[14]	

2.1 Seed

It possesses cooling, fever-reducing, laxative, and digestive aid characters. It bears a mildly sweet flavor along with this, it is utilized for preventing constipation ^[15].

2.2 Flower

It is utilized in the management of fever, leprosy, stomach ache, and skin disorders ^[16]. It comprises laxative properties as well as ability to promote wound healing. Its extract is used to relieve gastrointestinal problems ^[17].

2.3 Fruit

It is utilized for managing leprosy, fever, digestive issues, and skin ailments [18].

2.4 Root

It is beneficial for cardiovascular issues, injuries and sores, rheumatic diseases, tuberculosis-related organs, and various skin conditions [19, 20].

2.5 Pulp

It is used to treat blackwater fever, malaria and serves as an antipyretic. This is used for treating rheumatism, biliousness, and liver diseases, and is a suitable laxative for kids and pregnant women [21, 22, 23].

2.6 Leaves

They have the ability to alleviate constipation [16].

3. Pharmacological Activities

3.1 Antioxidant Activity

Antioxidant characteristics of *Cassia fistula* have garnered considerable interest due to its abundant polyphenolic compounds, including flavonoids, tannins, and phenolic acids. These compounds are essential for eliminating oxidative stress and scavenging free radicals, which are linked to the beginning of several diseases, including cancer, heart disease, and aging-related disorders [9]. Antioxidant efficacy of 90% ethanol samples from leaves and 90% methanol samples from

pulp, flowers and stem bark, of *Cassia fistula* demonstrates that stem bark exhibits the highest levels of antioxidant activity, followed by pulp, leaves, and flowers, which correlate well with extract's total polyphenolic content. Therefore, bark of the stem possesses superior anti-oxidant capabilities [33]. The flowers of this plant are significant in addressing skin issues due to their remarkable antioxidant properties. *Cassia fistula* flowers containing methanolic extracts exhibit antioxidant activity through DPPH scavenging, with an evaluated antioxidant activity percentage of around 84%. Additionally, anti-oxidant performance of flower extract in an aqueous environment suggests potential antidiabetic bioactivity [34].

3.2 Laxative Activity

Traditionally, *Cassia fistula* has been used as a natural laxative, particularly the pods of the plant. The laxative property is mainly attributed to the presence of anthraquinones, that stimulate bowel movements by increasing peristalsis (muscle contractions of the intestine) [11]. The infusion of *C. fistula* pods has a significant dosedependent laxative effect, according to a study on *in vitro* effects of *C. fistula* infusion on isolated guinea-pig ileum. [35].

3.3 Antimicrobial Activity

Among the key pharmacological characteristics of *Cassia fistula* is its capability to combat microbial activity. Extracts sourced from different plant parts, such as flowers, seeds, bark, pods, have demonstrated considerable efficacy against a wide range of microorganisms, which include bacteria, fungi, and viruses [24]. The seeds also showed promising antimicrobial properties toward certain bacteria, fungi, and viruses [36]. Additionally, research on flavonoidal glycosides extracted from acetone extract of root further validated its antifungal properties. One yearly report from CCRIMH (Circuit No. 4, Clinical Report, 1970, Trivandrum) indicated that patients with Vipadika and Gajacharma, conditions related to dermatophyte infections, experienced improvement in their lesions and relief from itching with the application of Aragwadha Moola Twak Lepam [37].

3.4 Antidiabetic Activity

Diabetes is a major global health concern, and finding effective natural alternatives for its management is a priority in modern pharmacology. Cassia fistula has shown promising antidiabetic effects in both preclinical and clinical studies [26]. Alloxan-induced diabetic rats were used to test the antidiabetic effects of the Cassia fistula bark's whole alcoholic extract and its ethyl acetate fraction. Ethyl acetate fraction demonstrated major decrease in blood sugar levels compared to alcoholic extract. Its effectiveness has been similar to that of the standard medication glibenclamide. The antidiabetic and hypoglycemic mechanisms of the hydroalcoholic extract of C. fistula Linn in rats were documented. Ethanolic extract of C. fistula Linn stem bark was examined for its antihyperglycemic effects [38]. In 2012, Ali et al. extracted ethyl alcohol from C. fistula bark and conducted an anti-diabetic study. Various doses of ethanolic extract of C. fistula bark were analyzed against standard drugs, and positive outcomes were found. This clarifies the anti-diabetic behavior of C. fistula bark when using the ethanolic extract in distinct dosage amounts [39].

3.5 Hepatoprotective Activity

Liver damage, often caused by toxins, alcohol, and certain medications, is a major health concern worldwide. *Cassia fistula* has demonstrated hepatoprotective effects, making it a useful plant for protecting the liver from various forms of damage ^[27]. Pre-treatment with *C. fistula* demonstrated antioxidant and liver-protective effects in opposition to hepatotoxicity generated by CCl4 ^[40]. The safeguarding impact of *C. fistula* leaves on the liver has been shown to be similar to a standard hepatoprotective agent ^[41].

3.6 Anticancer Activity

One of the main causes of death worldwide is still cancer, making the discovery of effective treatments crucial. *Cassia fistula* has demonstrated significant potential as an anticancer agent. Various research efforts have underscored its ability to hinder development of cancer cells and activate apoptosis (programmed cell death) across several cancer cell lines, including breast, liver, and colon ^[28]. Duraipandiyan *et al.* conducted a study on the adenocarcinoma cell line observed in the human colon, specifically COLO 320 D, to evaluate anti-cancer efficacy of rhein, which was extracted and detoxed from *Cassia spp.* as an anthraquinone. Such findings revealed that rhein exhibited cytotoxic effects at a concentration of 200 µg/ml, with increased cytotoxicity observed with prolonged incubation, showing 80.25% cytotoxicity after 72 hours.

Rhein inhibited cell proliferation through a mechanism that seems to directly involve mitogen activated protein (MAP) kinase pathway. A concentration of 1µ/ml rhein particularly reduced cell proliferation, accompanied by activation of the MAP kinase pathway. Rhein possesses an innate ability to prevent DNA damage utilizing anti-Rhein lysinate that inhibits growth of breast cancer cells. Additionally, an alternate study was conducted to evaluate the anti-cancer effects of fruit extracts from C. fistula on cell lines associated with breast and human cervical cancer. The outcomes pointed out that pulp and seed effectively concealed 2 cancer cell lines while up-regulating p53 and Bax genes, down-regulating Bcl-2 gene, and enhancing the activities of caspase-3, 7, and 10, along with nine other enzymes. Additionally, according to Alfatlawi et al., rhein reduced proliferation of malignant cell lines, such as breast adenocarcinoma (MCF-7), human cervical cancer (SiHa), and hepatocellular carcinoma (HepG2), in a dose-dependent way [42].

3.7 Neuroprotective Activity

In fact, recent studies have been carried out to identify the protective influence of *C. fistula* on the nervous system with particular interest in its ability to safeguard against neurological diseases such as Parkinson's and Alzheimer's disease ^[29]. Moreover, the neuroprotective effects of a methanol extract of *C. fistula* roots were demonstrated due to its capacity to inhibit acetylcholinesterase (AChE), which is deemed a potential target in the management of neurodegenerative disorders such as Alzheimer's disease ^[43]. This was done by determining the neuroprotective effect of *C. fistula* on the generation of polyQ40 aggregates that have been linked to Huntington disease and other protein-related disorders ^[44].

3.8 Anti-obesity Activity

Among the chronic diseases, the risk factor of which obesity is one of the most significant, there are type 2 diabetes, cardiovascular diseases, and certain types of cancer. The impacts of *C. fistula* on obesity have been researched particularly in its potential to reduce body weight and fat storage [30]. The efficiency of the *C. fistula* extract in modulating lipid metabolism and exhibiting antioxidant activity has illuminated the possible mechanisms behind the recorded results, which have associated the decrease of the LDL with the enhanced hepatic LDL receptor binding facilitated by its polyphenolic extracts ^[45]. Moreover, the increase in the HDL levels could be associated with the increased activity of the lecithin-cholesterol acyltransferase that contributes to the reverse cholesterol transport and endothelium protection ^[46]. Hepatoprotective effects of *C. fistula* were demonstrated through the decrease in levels of AST and ALT, which is explained by the presence of antioxidants in it ^[45].

3.9 Antiparasitic Activity

Research has indicated that *Cassia fistula* extracts have been found to be active against protozoan parasites such as Plasmodium falciparum (causative agent of malaria) and Entamoeba histolytica (parasite causing amoebiasis) [31]. In the guide of antileishmanial activity, a fractionation procedure of the dichloromethane extract of the fruits of C. fistula (Leguminosae) leads to the identification of a bioactive isoflavone biochanin A by spectroscopic means [47]. The active concentration (EC50) of the compound against *Leishmania* (L.) chagasi promastigotes was 18.96µg/mL. The cytotoxicity of this compound against peritoneal macrophages resulted in an EC50 value of 42.58µg/mL. Along with it, an EC50 value of 18.32microg/mL, biochanin A demonstrated anti-Trypanosoma-cruzi activity, making it 2.4 times more beneficial than benznidazole [48].

3.10 Immunomodulatory Activity

Recent research has also highlighted the immunomodulatory effects of *Cassia fistula*, which can help modulate the immune system to improve responses to infections and diseases ^[32]. The triterpene present in C. fistula is lupeol. Lupeol is a naturally occurring triterpene from the lupine family that can be found in several plants [50]. Recent studies have indicated that lupeol notably high potential for wound healing in a mouse model featuring dead space wounds ^[51]. It was observed that lupeol inhibits various immune responses, including the phagocytic activity of macrophages and the cytokine production mediated by CD4+ T helper cells. The administration of lupeol resulted in a reduction of CD4+ T cell counts and levels of the cytokines IL-2, IFN-γ (Th1), and IL-4 (Th2) ^[51, 52, 53].

4. Conclusion

C. fistula Linn., often described as "Indian Laburnum" or "Golden Shower," is a valuable and adaptable medicinal plant that is commonly utilized in traditional medicinal practices throughout India and other areas. Numerous bioactive substances found in this plant's flowers, leaves, pods, seeds, bark, and roots contribute to its wide range of pharmacological properties. These characteristics include immunomodulatory, hepatoprotective, antioxidative, antimicrobial, anti-inflammatory, antidiabetic,

neuroprotective, anticancer, anti-obesity, and antiparasitic effects.

The plant's rich composition of flavonoids, tannins, anthraquinones, and glycosides is responsible for these therapeutic effects. *Cassia fistula* demonstrates promise in addressing various health issues, supported by encouraging

findings in both preclinical and clinical research, including gastrointestinal and metabolic disorders, as well as chronic illnesses such as cancer and neurodegenerative diseases. Its traditional uses, including as a laxative, antipyretic, and treatment for skin diseases, are well-supported by modern research, confirming its efficacy and safety.

Moreover, the plant's minimal side effects compared to synthetic drugs make it a valuable candidate for future pharmacological applications. As scientific exploration continues, *Cassia fistula* may offer innovative solutions for various health challenges, reinforcing its place in both traditional and modern medicinal practices.

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