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Cassia Fistula (Bundaralati) Linn: Phytochemical and pharmacological studies: A review

[1] Mohammad Abu Bin Nyeem, [2] Mohammad Sadul Haque, [3] Mohammad Abdul Hoque, [4] Mohammad Manirul Islam, [5] Shafiqul Islam

[1, 2] Assistant Professor, Department of Unani Medicine, Hamdard University Bangladesh, Gazaria, Bangladesh
[3, 4] Department of Pharmacology, Bangladesh Agricultural University, Mymensingh 2202, Bangladesh
[5] Government of Unani & Ayurvedic Medical College, Mirpur, Dhaka, Bangladesh

Abstract
Cassia fistula L. belongs to the family of Caesalpinaceae, commonly known Amaltash, Sonalu or Bundaralati, has been used in different system of medicines since ancient times. Cassia fistula grows throughout in Bangladesh and in many other Asian countries such as India, China, Philippines, Malaysia, Indonesia, and Thailand. The aim of the present study was to provide a comprehensive review on the phytochemical and pharmacological aspects of *Cassia fistula*. It has a rich source of alkaloids, tannins, saponin, flavonoids and anthraquinone glycosides and secondary metabolites especially phenolic compounds. Pharmacological activities include antioxidant, hepatoprotective, wound healing, anti-diabetic, antipyretic, antibacterial and antifungal, anti-inflammatory, antitussive, CNS, leukotriene inhibition, laxative, larvicidal and ovicidal, and hypolipidemic, antifertility, anti-leishmaniatic, anti-ulcer and anti-itching activity.

Keywords: *cassia fistula*, banarlati, amaltash, pharmacological activity

Introduction
Natural therapy always believe more in prevention rather than curing a disease with the help of natural products obtained from natural resources like plants and herbs etc. Among such plants one such example is *Cassia fistula*, which is an Indian Laburnums also popularly known as the golden shower tree in India. It is distributed in various regions including Asia, South Africa, China, West Indies and Brazil [1]. Cassia fistula moderate sized deciduous tree, distributed throughout India. It is 8-15 m to 24 height, with greenish grey smooth bark when young & rough, dark brown when mature. Pod cylindrical & pulpy. Seeds light brown, hard & shiny. Ayurvedic medicine recognizes the seeds as anti-bilious aperitif, carminative and laxative, hard reddish wood, growing up to 40 feet tall [2]. A fruit is cylindrical pod and seeds many in black, sweet pulp separated by transverse partitions. The long pods which are green, when unripe, turn black on ripening after flowers shed [3]. The pods are 40-70 cm long and 2027mm in diameter, straight or slightly curved, smooth but finely striated transversely, the striations appearing as fine fissures. The rounded distal ends bear a small point marking the position of the style. The dorsal suture appears as a single vascular strand and the ventral suture as two closely applied strands. Internally the pod is divided by thin, buff colored, transverse dissepiments at intervals of about 0.5cm. Each compartment contains one seed which is flat, oval, reddish brown with a well-marked raphe. The seed contains a whitish 8mm. long, slightly less in breadth, and 5mm thick [4] endosperm in which the yellowish embryo is embedded [5]. Pulp is dark brown in color, sticky, sweet and mucilaginous, odour characteristic, and somewhat disagreeable [6]. Drug occurs in flat or curved thick pieces; outer surface smooth to rough with warty patches; greenish grey to red; inner surface rough, reddish with parallel Striations; fracture, laminate; odor, sweet and characteristic; taste, astringent [7]. Seeds are broadly ovate.

Vernacular Names:

Bengali	- Bundaralati, Sonalu, Soondali, Sondal
English	- Golden Shower
Guajarati	- Garmala
Hindi	- Sonhali, Amultus
Kannad	- Kakkemara
Marathi	- Bahava
Tamil	- Shrakkonnai, Konai, Irjviruttam
Telegu	- Kondrakayi, Raelachettu, Aragvadhamu
Sanskrit	- Nripadruma
Arab	- Khayarsambhar
Oriya	- Sunaari
Punjabi	- Amaltaas, Kaniyaar, Girdnalee
Urdu	- Amaltus

Cassia fistulas used in different disease conditions. The root is prescribed as a tonic, astringent, febrifuge and strong purgative [8]. The extract of leaves of the plant has been found to reduce mutagenicity in E. coli [9]. The extract of the root bark of the plant with alcohol can be used for back wart fever. Its leaves are laxative and are used externally as emollient, a poultice is used for chilblains, in insect bites, swelling, rheumatism and facial paralysis [10]. Leaves of the plant possess anti- periodic and laxative properties. The leaves are used in jaundice, piles, rheumatism ulcers and also externally skin eruptions, ring worms, eczema. The leaves and bark mixed with oil are applied to pustules, insect bites. The roots of the plant are used in chest pain, joint pain, and migraine and blood dysentery. The extract of the root of the plant has been found to lower the blood sugar level up to 30% [11]. Leaves and flowers of the plant are both purgative like the pulp. Ashes from burnt pods mixed with

little salt are used with honey taking 3- 4 times to relieve cough. Root of the plant is useful in fever, heart diseases, retained excretions and biliousness [12]. Fruits are used as cathartics and in snake bite. Juice of leaves of the plant is used in skin diseases [13-14]. Flowers and pods of the plant are used as purgative, febrifugal, biliousness and astringent. The ethanolic (50%) extract of pods has been found to show anti-fertility activity in female albino rats. The heated pods are applied to swellings on the neck due to cold. The fruits of the plant are reported to be used for asthma [10]. Pulp of the plant is given in disorders of liver. The plant is used as analgesic and antipyretic, it is a remedy for malaria and fever. It is also applied in blood poisoning, anthrax and leprosy. It also works as anti-dysenteric and antidiabetic, it is used for the removal of abdominal obstruction [10]. The extract of the flower inhibits the ovarian function and stimulate the uterine function in albino rats. Fruits are used in the treatment of diabetes [9]. The fruits of the plant are antipyretic, abortifacient, demulcent, lessen inflammation and heat of the body; useful in chest complaints, throat troubles, liver complaints, diseases of eye and gripping. Juice of leaves is useful as dressing for ringworm, relieving irritation and relief of dropsical swelling. The pulp of the fruit around the seeds is a mild purgative [15]. It is also used in biliousness and in diabetes. Externally, it is useful for evacuation in flatulent colic, as dressing for gouty or rheumatic joints [14]. The pith is particularly useful if there is swelling in stomach, liver or intestine. The seeds are emetic, used in constipation and have cathartic properties [14]. The seeds are slightly sweet, laxative, carminative, cooling and they improve the appetite and possess antipyretic activity [10]. They are useful in jaundice, biliousness, skin disease and in swollen throat. A seed dried produce marked [10] hypoglycaemic activity. Seed powder is used in amoebiasis [10, 16]. The fruit pulp is used for constipation colic, chlorosis and urinary disorders [16]. The bark of the plant possesses tonic and anti-dysenteric properties, it is also used for skin complaints, the powder or decoction of the bark is administered in leprosy, jaundice, syphilis and heart diseases. The aqueous extract of the root bark exhibits anti-inflammatory activity. The root is used in cardiac disorders, biliousness, rheumatic condition, hemorrhages, wounds, ulcers and boils and various skin diseases [10, 15]. The stem bark of the plant is used against amenorrhea, chest pain and swellings.

Phytoconstituents

A majority of the ascribed biological effects of *C. fistula* extracts have been attributed to their primary and secondary metabolite composition. Primary metabolite analysis has essentially been focused on the seed, pollen, fruit, leaf and pod. The seeds are rich in glycerides with linoleic, oleic, stearic and palmitic acids as major fatty acids together with traces of caprylic and myristic acids. It has been reported that the stem bark of *C. fistula* is also a potential source of lupeol, ß-sitosterol and hexacosanol. In an earlier study it was reported that one of the major carbohydrates in the seeds was galactomannan consisting of different types of sugar moieties. A detailed biochemical analysis of the flower's pollen, suspected to play a significant allergenic role, showed a protein composition of 12% with appreciable amounts of free amino acids such as phenylalanine, methionine, glutamic acid and proline. Carbohydrate, lipid and free amino acid contents were of the order of 11.75, 12 and 1.42%, respectively [16].

The edible fruit tissue of the Indian laburnum fruit was reported to be a rich source of potassium, calcium, iron and manganese than fruits like apple, apricot, peach, pear and orange The protein (19.94%) and carbohydrate (26.30%) contents are indicative of the potential of the fruit to be an important source of nutrients and energy. A polar compounds including 5nonatetracontanone, 2- hentriacontanone, triacontane, hentriacontanol and sitosterol along with an oil (probably an isoprenoid compound) showing antibacterial activity have also been isolated in C. fistula pods [17]. *C. fistula* plant organs are known to be an important source of secondary metabolites, notably phenolic compounds. Fistucacidin, an optically inactive leucoanthocyanidin (3, 4, 7, 8, 4' pentahydroxyflavan) was first extracted from the heartwood. The presence of kaempferol and a proanthocyanidin whose structure has been established as a leucopelargonidin tetramer having a free glycol in the acetone extract of the flower has been documented. Proanthocyanidins containing flavan-3-ol (epiafzelechin and epicatechin) units with an abnormal 2S-configuration have also been observed in pods together with the common flavan-3-ols and proanthocyanidins like catechin, epicatechin, procyanidin B-2 and epiafzelechin [18].

Pharmacological Activity

Antioxidant Activity

Antioxidants are natural or manmade substances which may prevent or delay cell damage by scavenging free radicals and other oxidants. These free radicals lead to the formation of chain reactions that may damage cells as they tend to oxidize biomolecules like, cellular proteins, lipids genetic materials etc altering their structures and functions [19]. Antioxidants like thiols or ascorbic acid, phenols etc can terminate these chain reactions. Phenolic compounds are the secondary metabolites obtained from natural sources which have great antioxidant potential. They can easily breakdown the chain reaction by radical scavenging. It was shown by Irshad, Md, *et al*. (2012) that methanolic extract of pulp and seed showed the lowest EC50, 0.915 and 1.088 mg/ml for DPPH scavenging activity. They have also performed various other antioxidant measurements for this plant and found *C. fistula* to a very good radical scavenger. The antioxidant potential of this plant could be directly linked to its phenolic content [20].

Hepatoprotective Activity

Hepatotoxicity is a condition when liver is damaged, which can lead to malfunctioning to liver, or to function irregularly. One of its most important tasks is to filter out toxic substances from the body, including alcohol, carbon tetra chloride (CCl_4), different medications like paracetamol, chemotherapyand antibiotics etc. Dawada *et al*. (2012) [21] observed that ethanolic extract of Cassia fistula's root can be protective against CCl_4 induced hepatotoxicity [21]. This study was conducted by injecting CCl_4 and Olive oil, in ratio 1:1; 2ml/kg, to adult Wistar albino rat's colony. The rats were divided into 6 groups for 7 days: I-control, II- CCl_4treated, III- standard silymarine treated, IV-ethanol extract (100 mg), V- ethanol extract (200mg).The levels of the marker enzymes (SGOT, SGPT, ALP, S. bilirubin) of liver functions were initially elevated, and then start decreasing. There was an increase in the body weight in rats. The Serum total protein and the Serum albumin also reached normal level. *C. fistula* (200g/kg and 100g/kg) was showed comparable results with a standard drug Silymarin. In another study even ethanolic extract of leaves of Cassia were

found to have hepatoprotective activity against Diethyl nitrosamine [22].

Wound Healing

One experimental study suggests that *Cassia fistula* can be used in healing, as well. In a study conducted on albino rat model found out that ethanolic extract of leaves of C. fistula could kill microbes like Staphylococcus aureus ATCC 29213 and Pseudomonas aeruginosa ATCC 27853. The ethanolic extract was applied in the form of a formulation and it was observed that formulated ointment could treat rats in terms of better wound closure, improved tissue regeneration at the wounded site [23].

Anti-Diabetic Effect

John Wilking Einstein *et al*. (2013) did comparative evaluation of anti-diabetic effects of methanol extracts of different parts of *Cassia fistula* [24]. The extract was tested in normoglycemic as well as, streptozotocin nictotinamide induced type 2 diabetic rats. Different extracts of *Cassia fistula* were administered (for 21 days) to the diabetic rats at 250 mg/kg and 500 mg/kg doses. Biochemical parameters like insulin, blood glucose, glycosylated hemoglobin, serum marker enzymes and lipid profile were determined. The methanol extract of leaves and the bark showed to be more effective in causing hypoglycemia in normoglycemic rats. After oral administration of the bark and leaf methanolic extracts, the diabetic rats that showed that increased levels of glycosylated haemoglobin, plasma insulin, were reverted to near normal levels. Glucose uptake studies in isolated rat hemi diaphragm showed enhanced peripheral utilization of glucose. Dose of 500 mgkg−1 of methanol extract of the leaves and bark showed significant anti-lipid emic and anti-hyperglycemic activity, as well. The extracts also showed improvement in parameters like insulin profile and glycosylated haemoglobin as well as, in the regeneration of pancreatic βcell sand so might be of value in treatment of diabetes. Daisy *et al*. (2010) also conducted an experiment showing insulin mimetic impact of Catechin (from *Cassia fistula*) on the oxidation of glucose and molecular mechanisms of its uptake on Streptozotocin-induced diabetic Wistar rats [25].

Antipyretic Activity

The *Cassia fistula* pod was found to be devoid of antipyretic activity in experimental models. The pods extracts showed a marked antipyretic effect by causing a reduction in yeast induced fever. The extract caused a better hypothermal activity against yeast-induced pyrexia in rats. Subcutaneous injection of yeast induces pyrexia by increasing synthesis of prostaglandin and is used to screen [26].

Antibacterial and Antifungal

The microbial activity of hydro alcohol extracts of leaves of *Cassia fistula* Linn. Was evaluated for potential antimicrobial activity against medically important bacterial and fungal strains. The antibacterial and antifungal activities of extracts (5, 25, 50, 100, 250 µg/ml) of *Cassia fistula* were tested against two Gram-positive— Staphylococcus aureus, Streptococcus pyogenes; two Gram-negative— Escherichia coli, Pseudomonas aerie nose human pathogenic bacteria; and three fungal strains—Aspergillus Niger, Aspergillus clavatus, Candida albicans. The results revealed that in the extracts for bacterial activity, S. pyogenes and S. aureus were more sensitive as compared with E. coli and P. aeruginosa, and for fungal activity, C. albicans shows good result as compare with A. Niger and A. clavatus. The results show that the extracts of *Cassia fistula* were found to be more effective against all the microbes. The present study claimed uses of leaves in the traditional system of medicine to treat various infectious disease caused by the microbes [27].

Anti-Inflammatory Activity

The anti-inflammatory activities of the aqueous (CFA) and methanolic extracts (CFM) of the *Cassia fistula* bark were assayed in Wistar albino rats. The extracts were found to possess significant anti-inflammatory effect in both acute and chronic models [28].

Antitussive Activity

The methanol extract of leaves of *C. fistula* was investigated for its effect on a cough model induced by sulfur dioxide gas in mice and the extract exhibited significant, dose-dependent anitussive activity compared with the control. The antitussive activity was comparable with that of codeine phosphate, a prototypes antitussive agent. *C. fistula* extract (400 and 600 mg/kg, p .o.) inhibited coughing by 44.44 and 51.85%, respectively, with respect to the control group confirming its anitussive potential [29].

CNS Activities

The methanol extract of seeds of *C. fistula* was tested for different pharmacological actions in mice and the extract significantly potentiated the sedative actions of sodium pentobarbitone, diazepam, meprobamate and chlorpromazine. It also potentiated analgesia induced by morphine and pethidine in a dose-dependent manner. The extract also influenced behaviour in mice [30]. These studies have shown that the methanol extract of seeds of *C. fistula* possesses significant CNS activities.

Leukotriene Inhibition Activity

Studies have shown that the methanol extract of fruits of *C. fistula* inhibited the 5- lipoxygenase catalysed formation of leukotriene B4 in bovine polymorphonuclear leukocytes (IC value of 38 micro 50 g/ml). Lipid peroxidation in bovine brain phospholipid liposomes induced with 2,2'-azo-bis-(2amidinopropane) dihydrochloride (AAPH) was inhibited (IC of 40 micro g/ml). A linear correlation 50 was obtained between the effects of the extract in the two assays suggesting a redox-based mechanism for the inhibition of the 5-lipoxygenase enzyme [31].

Clastogenic Effect

Anthraquinone glycosides of *Cassia fistula* were investigated for their ability to induce a clastogenic effect on the bone marrow cells of Swiss albino mice. The endpoints screened were chromosomal aberrations and frequency of aberrant cells. Oral exposure to doses of these anthraquinones and their equivalent amount in leaf and pod extracts did not induce significant numbers of chromosomal aberrations or aberrant cells. The results of the study indicate that anthraquinone sennoside B and rhein are weakly genotoxic. Pure sennoside B and rhein were weakly clastogenic. Crude extracts of C. fistula (leaves and pods) each containing sennoside B and rhein were also weak clastogens. The CA/cell and % DC were lower than

those induced by an equivalent amount of pure sennoside B. Therefore, these phytolaxatives do not behave as potent clastogens and pods or leaves of *C. fistula* can be used as an alternative source of sennosides [32].

Laxative Activity

The in-vitro effect of *Cassia fistula* infusion on isolated guinea-pig ileum was studied where the acute and sub-chronic toxicity of the infusion of C. fistula and Cassia acutifolia sp. Del. Pod-(Senokot tablet) as the reference drug were also determined. C. fistula infusion, when compared with senokot tablet, showed that the infusion of Cassia fistula pods possessed very low levels of toxicity, having the LD of 6600 mg/kg 50 and also without any pathological effects on the organs examined microscopically. Thus, C. fistula pod infusion could be safely utilized as laxative drug and as a substitute for the official Senna [33].

Larvicidal and Ovicidal Activity

The ovicidal effect of leaf extracts of *C. fistula* (at 0.5, 1.0 and 2.0%, topically applied) was evaluated on the viability and hatching of eggs (0, 1 and 3 days old) of D. koenigii. The results of the study have shown that application of leaf extracts of the plant inhibited hatching of the eggs and increasing concentration of the extract resulted in increased non-viability of 3-day old eggs [34]. In another study, the methanolic leaf extract of *Cassia fistula* was tested for larvicidal and ovicidal activity against Culex quinquefasciatus and Anopheles stephensi. The extract was found to be more lethal to the larvae of A. stephensi than C. quinquefasciatus with LC values of 17.97 and 20.57 50 mg/l, respectively. Mean percent hatchability of the ovicidal activity was observed 120 h after treatment. The percent hatchability was found to be inversely proportional to the concentration of extract and directly proportional to the eggs. The egg raft of C. quinquefasciatus was found to be more hatchable than A. stephensi. The results of the study show that the leaf extract of *C. fistula* is a promising larvicidal and ovicidal agent against C. quinquefasciatus and A. stephensi [35].

Hypolipidemic Activity

The effect of 50% ethanolic extract of *Cassia fistula* legume was investigated on serum lipid metabolism in cholesterol fed rats where oral feeding of cholesterol (500 mg/kg b.wt./day) dissolved in coconut oil (0.5 ml/rat/day) for 90 days caused a significant ($P<0.001$) elevation in total and LDL-cholesterol, triglycerides and phospholipid in serum of rats. Administration of C. *fistula* legume extract at the doses 100, 250 and 500 mg/kg b.wt./day along with cholesterol significantly prevented the rise in the serum total and LDL cholesterol, triglycerides and phospholipid in a dose dependent manner. The ratio of HDL-cholesterol/total cholesterol ratio was elevated in serum of *C. fistula* extract treated groups as compared to cholesterol alone fed control rats [28].

Anti-fertility Activity

Research studies have demonstrated that petroleum ether extract of seeds of *Cassia fistula*, as screened for anti-fertility activity in proven fertile female albino rats at the doses 100, 200 and 500 mg/kg b.wt./day, produced significant anti-fertility activity. The results of the study have revealed that oral administration of the extract to mated female rats on days 1-5 of pregnancy resulted in a decline in the fertility index, numbers of uterine implants and live fetuses in a dose dependent manner as was confirmed by laparotomy on day 15 of pregnancy. The extract (100 mg/kg b.wt.) exhibited weak estrogenic activity when given alone and tested in immature bilaterally ovariectomized female albino rats, but exhibited slight anti-estrogenic activity when administered along with estradiol valerate (0.1 mg/kg b.wt.). In this experimental animal study, blood sugar and haematological parameters were within normal range. Thus, the results of the present study indicate that the petroleum ether extract of *Cassia fistula* seeds possesses pregnancy terminating effect by virtue of anti-implantation activity [36].

Anti-Leishmaniatic Activity

The effectiveness of *Cassia fistula* in the treatment of leishmaniasis, the efficacy of concentrated boiled extract and hydroalcoholic extract of *C. fistula* on leishmaniasis was compared with intralesional injection of Glucantime [meglumine antimonate] in this study. 63.6% of patients treated with the concentrated boiled extract, 52.7% of patients treated with the hydroalcoholic extract, and 45.5% of patients treated with Glucantime. In total, 22 patients (40%) given the concentrated boiled extract of *C. fistula*, 20 patients (36.4%) given the hydroalcoholic extract of C. fistula, and 36 patients (65.5%) of the Glucantime group showed complete cure. The efficacy in the third group was significantly higher than the first ($P<0.02$) and second groups ($P<0.005$), but there was no difference between the efficacy of concentrated boiled extract and hydroalcoholic extract of C. fistula. These results show that this plant could be used topically along with Glucantime for decreasing the time and dose of treatment with Glucantime. The potential of *Cassia fistula* boiled extract in the treatment of cutaneous leishmaniasis, to evaluate the efficacy of intralesional meglumine antimonate-*C. Fistula* fruit gel combination for the treatment of cutaneous leishmaniasis. A total of 140 patients with cutaneous, one group received intralesional meglumine antimonate injection and C. fistula fruit gel, and the second group (control) was treated with intralesional meglumine antimonite plus placebo gel. Improvement was defined as complete cure, partial cure and treatment failure. At week 12, forty-seven (67.1%) patients in the experimental group achieved complete cure, compared to 29 (41.4%) patients in the control group ($P<0.001$). Results indicate that the *C. fistula* fruit gel increases the efficacy of intralesional meglumine antimonate for the treatment of cutaneous leishmaniasis. Combination therapy with intralesional meglumine antimonate and *C. fistula* fruit gel should be considered for the treatment of acute cutaneous leishmaniasis [37].

Anti-Ulcer Activity

The ethanol leaf extract (ELE) of *Cassia fistula* Linn. (Caesalpinaceae) was evaluated for anti-ulcer activity against pylorus ligation - Induced gastric ulcer [38].

Anti-Itching Activity

Eczema is a chronic skin disease with no permanent cure in modern medicine. Raising serum IgE level is the commonest immunological marker for eczema. This study suggests of significant efficacy of Aragvadha on the patients of eczema [39].

Conclusions

Cassia fistula L. is widely used in traditional medicinal system of Bangladesh and India and has been reported to possess laxative, anti-ulcer, antioxidant, hepatoprotective, anti-inflammatory, antitussive, antifungal and also used to check wounds healing and antibacterial properties. It is known as a rich source of tannins, flavanoids and anthraquinone glycosides. The plant is rich in carbohydrates, Linoleic, Oleic, and Stearic. Leaf of *Cassia fistula* mainly contains Oxalic Acids, Tannins, Oxyanthraquinones, and Anthraquinones Derivatives. Phytochemical and Pharmacological reviews on this plant will give valuable information which will assist the scientists in getting more advanced knowledge about a plant species.

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