


CASSIA FISTULA: PHYTOCHEMICAL AND BIOLOGICAL REVIEW**Khaled Rashed*1, Chistiane Feitosa2, Felipe Pereira da Silva Santos3**¹Pharmacognosy Department, National Research Centre, 33 El-Bohouth St.-Dokki, Giza, Egypt- P.O.12622.²Federal University of Piaui, Laboratory of Natural Products, Chemistry Department, Ininga, 64049-550, Teresina-Pi, Brazil.³Chemistry Department, Federal university of piaui-Brazil

<p>*For Correspondence: Pharmacognosy Department, National Research Centre, 33 El- Bohouth St.-Dokki, Giza, Egypt- P.O.12622.</p>	<p>ABSTRACT Cassia fistula Linn is an ornamental, and flowering tree. It is a plant from Leguminosae family and it cultivated in all over the world because of its yellow flowers and its several medicinal uses. The pulp from the fruit is an effective laxative. The leaves are used for skin disorders. The root is used as a tonic and also help in reducing fever. Phytochemical evaluations showed tha it is a valuable medicinal plant. C. fistula is known to be a good source of phenolic compounds, it is rich source of tannins, flavonoids and glycosides. Pharmacological investigations proved antibacterial, antidiabetic, antifertility, anti-inflammatory antioxidant, hypatoprotective, antitumor, antifungal activities from the plant. This review aimed to give detailed information about the several phytochemicals isolated from different parts and various bioactivities from all the parts of C. fistula. KEY WORDS: <i>Cassia fistula</i>, Phytoconstituents, bioactivities</p>
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INTRODUCTION

Nature has huge plant wealth, which has several medicinal properties that can be used for all the mankind. The importance of some plants was mentioned but there are large number of them remain unidentified up till now. So, there is a need to explore their medicinal uses and also to conduct phytochemical and bioactivity studies to prove their therapeutic properties. To know any information about any medicinal plant, there is a necessary to go through all the available texts of Ayurveda and also the previous reviews from recent research. Phytochemical investigations and biological reviews on the plants will led to the valuable information which can help the scientists to know more advanced knowledge about these plant species. *Cassia* species are of medicinal interest in phytochemical and biological research due to their important medicinal values (1). *Cassia fistula* Linn is a tree from *Leguminosae* family. It is well known as the golden shower and it is cultivated in India, Srilanka Brazil, and South Africa (2). *C. fistula* tree has beautiful yellow flowers. The fruit is cylindrical pod and the seeds are black, sweet pulp separated by transverse partitions. The long pods are green, when unripe, turn black on ripening (3). Pulp is dark brown, sticky, sweet and mucilaginous, and odour characteristic (3). The plant is well known with several medicinal uses, and its role in health care. its main use is as a mild laxative (4) and it was used to treat rheumatism (5, 6). The plant parts were used as a therapeutic agent in the hypercholesterolaemia treatment partially because it contained a mucilage content (7). Phytochemistry of the plant reveals that it is rich with phenolic derivatives, where *C.*

fistula leaves showed that it contained mainly flavonoids, tannins, and anthraquinones, while the fruits contained anthraquinones, flavonoids, and waxes (8). It showed antipyretic and analgesic activities (9). Some reports showed its antibacterial effect against a number of bacteria strains (10), Antitumor (11), hepatoprotective (12), antifertility (13), and antioxidant activities (14). Moreover, its pharmacological properties, the plant extract is also used as a pest and disease control agents in India (15). Thus *C. fistula* is well known for its traditional uses and it has now found widespread in all over the world.

The Main Traditional Medicinal Uses

C. fistula tree is well known as the disease killer. All the parts of the plant proved many medicinal properties. The root of *C. fistula* is used as a tonic, astringent, febrifuge and strong purgative and also it is useful in heart diseases (16). The fruit pulp is considered as a purgative and an effective laxative, and also it is used for colic, chlorosis and urinary disorders (16). *C. Fistula* leaves can be used for rheumatism ulcers, also the leaves are used in relieving skin irritation and in easing swelling as well as pain, as well as the problem of common cold can be relieved by using the *C. Fistula* plant, Juice of leaves can be used in skin diseases (16). Fruits are used for snake bite, Flowers and pods are used as purgative and astringent. The fruits are used for treatment of asthma and pulp is used in disorders of liver (17). The seeds of the plant are laxative and antipyretic and improve the appetite (17). Moreover, *C. Fistula* can help in relieving the problem of fever and also *C. Fistula* plant can be used for intestinal disorders in Children suffering from the problem of flatulence where *C. Fistula* pulp can be applied externally around the navel area to ensure evacuation (16). The seeds are also useful in skin disease and in swollen throat. As well as the seeds produce a significant hypoglycaemic effect (18). The stem bark of the plant is useful against amenorrhoea, chest pain and swellings (18).

Phytochemical review on *Cassia fistula*

This recent review composed of almost the previous phytochemical investigations which are isolated from different parts of *C. fistula* plant.

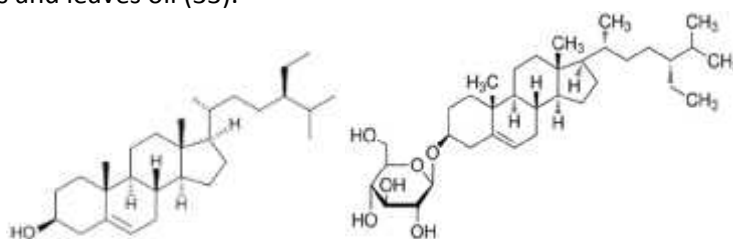
Primary metabolites composition

The seeds of *C. fistula* are very rich with linoleic, oleic, stearic and palmitic acids as major fatty acids and also the seeds are rich with carbohydrates and the major sugars present were galactose and mannose. The flowers of *C. fistula* have 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 with amounts of 11.75, 12 and 1.42%, respectively (19). The fruit of *C. fistula* was reported that it is a rich source of minerals such as potassium, calcium, iron and manganese than fruits like apple, and orange. Also, it has a good protein content (19.94%) and carbohydrate content (26.30%) and this is a prove that the fruit can be as a potential and an important source of nutrients and energy (19).

Secondary metabolites composition

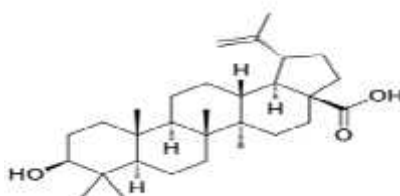
C. fistula is a rich source of chemical constituents and some previous reports showed the isolation and identification of these compounds from *C. fistula* parts: The pulp of fruit contained anthraquinone glycosides, sennosides A and B, rhein and its glucoside, barbaloin, formic acid, butyric acid and their ethyl esters, and oxalic acid, also it is reported that pectin and tannins, sugars, oxalate of calcium are present (20, 21). The flowers contained ceryl alcohol, kaempferol, rhein and a bianthraquinone glycoside (fistulin), (20). The leaves has free rhein, its glycosides, and anthraquinone glycosides, sennosides A and B (20). Leaves and flowers contained anthraquinones, tannin, oxyanthraquinone, rhein and volatile oils (3, 22). Root bark contained tannins, phlobaphenes and oxyanthraquinone substances, rhein glucoside, rhein, fistulic acid, and sennoside A and B (23). Some reports indicated that the flowers of *C. fistula* contained β -sitosterol and its β -D glucoside (23). The roots of *C. fistula* was reported that it contained 7-methylphyscion, betulinic acid and β -sitosterol (23). Previous studies on *C. fistula* plant revealed the presence of chrysophanol, rhein, physcion, and kaempferol (23). Rhamnetin 3-*O*-gentiobioside was isolated from the roots of *C. fistula* (24). The hexane fraction from the fruits of *C. fistula* contained β -sitosterol (25). A diterpene, 3 beta -hydroxy-17-norpimar-8(9)-en-15-one was isolated from the pods of *C. fistula* (26). Meena and Kalidhar(27) reported 3-formyl-1-hydroxy-8-methoxy-anthraquinone was isolated from the pods of *C. fistula* (27). Some previous reports indicated that twenty-seven compounds were isolated and identified from the aerial of *C. fistula*. The chemical structures of these compounds were determined by different spectroscopic analyses (28). The compounds, 5-

(2-hydroxyphenoxymethyl)furfural, (2'S)-7-hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl) chromone, benzyl 2-hydroxy-3,6-dimethoxybenzoate and benzyl 2β-O-D-gluco-pyranosyl-3,6-dimethoxybenzoate, and two oxyanthraquinones compounds named, chrysophanol and chrysophanein were identified from *C. fistula* seeds and the structures of all the compounds were determined by different spectroscopic analyses (29). An active flavone glycoside named, 5, 3', 4'-trihydroxy-6-methoxy-7-O-α-L-rhamnopyranosyl-(1→ 2)-O-β-D-galactopyranoside was isolated and identified from the acetone fraction of the defatted seeds of *C. fistula* (30). Three lectins were isolated and purified from *C. fistula* seeds. The sugar composition of these lectins was found to be galactose, glucose and mannose moieties (31). An isoflavonoid named biochanin A was isolated and identified from dichloromethane extract of *C. fistula* fruits and this compound showed a significant antileishmanial activity (32). The chemical compositions of essential oil from the flowers and leaves of *C. fistula* were determined by GC and GC/MS analyses. Forty-four compounds were identified which represent 92.6% and 90.7% of the flowers and leaves oil (33).

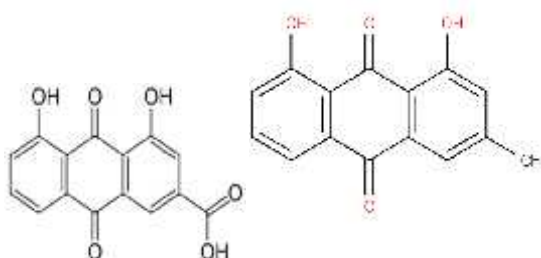


-Sitosterol

-Sitosterol- 3-O- -glucoside

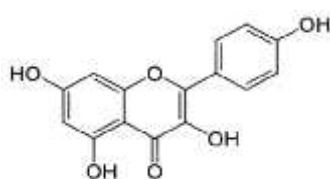


Betulinic acid

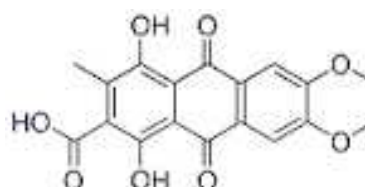


Rhein

Chrysophanol



Kaempferol



Fistulic acid



Biochanin A

Rhamnetin 3-*O*-gentiobioside

Figure 1. Chemical structures of the main phytoconstituents isolated from *C. fistula*

Biological review on *Cassia fistula*

Antioxidant activity

The importance of *C. fistula* is due to it has very high content of antioxidants. There is A modern study for evaluating the antioxidant and protective activities of *C. fistula* Linn. on hydrogen peroxide-induced oxidative damage in erythrocytes and the results proved ethanol extract from *C. fistula* contained a significant antioxidant activity while the aqueous extract from *C. fistula* showed a good antioxidant and protective activities with the percentage of 75% (34). The parts of *C. fistula* (bark, stem, leaf, and root) extracts were subjected to antioxidant assay and the results indicated that the bark extracts has a significant high antioxidant effect (35). Ethyl acetate extract of the bark proved a higher antioxidant activity than methanol and n-hexane extracts (36). Antioxidant effect of ethanol 90% extract of the leaves, stem bark, pulp and flowers of *C. fistula* was determined. The results proved stem bark extract showed a high antioxidant effect (37). Previous reports showed that n-hexane, ethyl acetate, and aqueous fractions of *C. fistula* pods were measured for its antioxidant effect. The results proved a significant antioxidant potential of ethyl acetate fraction (38). The aqueous extract of *C. fistula* flowers showed a decreased activity of antioxidant enzymes including superoxide dismutase, catalase, glutathione peroxidase (39) and these enzymes were return back to their normal level. The extracts of fruit pulp of *C. fistula* were studied for their antioxidant activity. The results indicated that the extracts have a significant antioxidant potential and this is through inhibiting DPPH and hydroxyl radical and reducing power (40).

Anti-inflammatory activity

An important study showed that *C. fistula* bark extracts have anti-inflammatory potentials in both acute and chronic models (36). The dried fruits of *Solanum xanthocarpum* and dried pulp of *C. fistula* water extracts were measured for their anti-inflammatory effect. The results showed that in different dose combinations of both the extracts with comparsion with positive control, diclofenac sodium and the inhibition of the inflammation was 81% (41). The anti-inflammatory potential of *C. fistula* was tested with comparsion with phenylbutazone, using carrageenin, histamine, and dextran induced paw edema in rats and *C. fistula* proved a significant anti-inflammatory effect against all phlogistic agents (42). Another study was done to evaluate the anti-inflammatory activity from *C. fistula* leaves ethanolic extract with different doses. The results proved that the ethanol extract significantly inhibited both carrageenan-induced hind paw edema and cotton-pellet granuloma in a dose-dependent manner (43).

Anti-tumor activity

Previous study was done to measure the effect of the methanolic extract of *C. fistula* seeds on the growth of Ehrlich ascites carcinoma and on the life span of tumor bearing mice. The results showed that the extract increase life span, and also it showed a decrease in the tumor volume and viable tumor cell count (11). An study was carried out to evaluate anticancer activity of rhein compound isolated from *C. fistula* flowers. The study showed that rhein proved a significant anticancer effect in a dose dependent mannar (44). The different extracts of *C. fistula* fruits were measured for their anticancer effect against some cell lines such as human

cervical cancer and breast cancer. The results proved that the extracts of fruits have a significant anticancer activity (45). Moreover, rhein compound isolated from *C. fistula* plant showed a significant inhibition of growth of human cervical cancer, breast adenocarcinoma and hepatocellular carcinoma in a dose-dependent manner (46).

Anti-diabetic activity

Previous reports showed that n-hexane extract of *C. fistula* bark at different doses 0.15, 0.30 and 0.45 g/kg body weight for 30 days gave a significant decrease the elevated glucose levels in diabetic rats (47). Another study showed that *C. fistula* bark and leaves methanolic extracts at a dose of 500 mg/kg indicated a significant anti-hyperglycemic and anti-lipidemic activity (48) and other reports revealed antidiabetic effect of the extract and fraction from *C. fistula* plant which the extract showed a significant decrease for the serum glucose level (49). A preparation of the aqueous extract from *C. fistula* and gold nanoparticles was carried out to evaluate the hypoglycemic activity. The results proved *C. fistula* extract gold nanoparticles are promising antidiabetic agents (50). *Tamarindus indica* and *C. fistula* stem barks extracts proved significant decrease in blood glucose level in diabetic rats treated (51). A recent study proved that catechin isolated from *C. fistula* at a dose of 20 mg/kg b.wt for a period of 60 days produced a better glucose tolerance pattern (52).

Anti-bacterial activity

C. fistula is a good plant which showed an important role in the management of infectious diseases due to its inhibitory effect on various types of the pathogens. The hydroalcohol extracts from the leaves of *C. fistula* were tested for their effects on gram-positive, gram-negative, fungal strains. The results indicated that the extracts gave a significant inhibition for the bacterial and fungal growth for all the tested organisms (53). The extracts of *C. fistula* were tested against gram-positive, gram-negative human pathogenic bacteria and fungi. The results indicated that the crude extracts have a moderate to strong activity against most of the bacteria tested (54). Previous report showed that the methanolic and ethanolic extracts of *C. fistula* were tested against gram-positive and gram-negative species. The results proved that the two extracts gave a significant inhibition for gram-positive bacteria and gram-negative bacteria (55). The different extracts from the flowers of *C. fistula* were tested for their antibacterial activity against some bacterial strains. The results indicated that all the extracts proved a significant antibacterial effect against all the bacterial strains (56). The methanol extract of *C. fistula* seeds exhibited a significant effect on all the tested microorganisms and the minimum inhibitory concentration values were in the range of 1.563–50.00 mg/ml (57). Some reports indicated that a flavone glycoside isolated from the seeds of *C. fistula* showed a good antibacterial activity against some gram-negative bacteria and gram-positive bacteria and also it showed antifungal effect (30). Another report revealed that isoflavone biochanin showed a moderate activity against promastigotes of *Leishmania* (L.) chagasi and also showed anti-trypanosoma-cruzi activity with the comparison with benznidazole (32).

Hepatoprotective effect

The aqueous extract of *C. fistula* bark proved a mild hepatocytic damage compared to the CCl₄ treated group (58). Another study revealed that the ethanolic extract of *C. fistula* leaves at the dose of (500 mg/kg body weight/day for 7 days) causes the lipid peroxidation (59). A study evaluated hepatoprotective activity of extract n-heptane of *C. fistula* leaves. The results indicated the extract of *C. fistula* at a dose of 400 mg/kg has a good hepatoprotective effect (12). The hepatoprotective effect of the n-heptane extract from the leaves of *C. fistula* at a dose of 400 mg/kg body wt. showed a potent protective effect (60). The aqueous extract from the leaves and bark of *C. fistula* was tested for hepatoprotective effect. The results showed that the extract revealed significantly reduced CCl₄-induced elevation in plasma enzyme and bilirubin concentration in rats (61). The methanolic extract of *C. fistula* at a dose of 200 mg/kg and 400 mg/kg causes the altered level of biochemical markers to the normal levels at the dose-dependent manner (62), and another study also reported the hepatoprotective activity of *C. fistula* (63).

Anti-pyretic effect

C. fistula plant and its constituents exhibited a significant role as anti-pyretic and some previous reports indicated the anti-pyretic effect of *C. fistula* based on the animal model. Anti-pyretic effect of the ethanolic extract of *C. fistula* was done. The results indicated that the extract at a dose of 250 and 500 mg/kg b.wt reduced TAB vaccine-induced pyrexia after 60 min, while at a dose of 750 mg/kg b.wt reduced the vaccine

induced elevated body temperature post 30 min of its administration (43). The methanolic extract from the pods of *C. fistula* proved a good antipyretic effect which was significantly higher than control rats (64).

Anti-infertility effect

A study based on animal model indicated that the oral administration of the seeds aqueous extract of *C. fistula* from day 1–5 of pregnancy at the different doses of 100 and 200 mg/kg body weight caused prevention of pregnancy, by the percentages of 57.14% and 71.43% respectively, and moreover, a total pregnancy inhibition was exhibited at the dose of 500 mg/kg bw of the extract (13).

Immunomodulatory effect

C. fistula gave a significant stimulation of the cell-mediated immunity and no effects on the humoral immunity (65).

Larvicidal and ovicidal activity

Larvicidal and ovicidal effects of the methanolic leaves extract of *C. fistula* against *Culex quinquefasciatus* and *Anopheles stephensi* was tested. The results indicated that the leaves extract is a potent larvicidal and ovicidal agent (66). The different solvents of the flower of *C. fistula* proved a potent larvicidal effect against *Culex tritaeniorhynchus*, *Aedes albopictus* and *Anopheles subpictus* and from these results, it can be concluded that the flowers extract from *C. fistula* is a good and potent agent for the control of *C. tritaeniorhynchus*, *A. albopictus* and *A. subpictus* mosquito larvae (67). The activity of methanol extract of leaves was evaluated against *Anopheles* mosquito and the results proved that the leaves extracts showed a significant mosquitocidal activity against *A. stephensi* (68).

Wound healing effect

A study was performed to examine the wound healing activity from the methanol extract of *C. fistula* in the form of an ointment in two types of wound models such as excision and inclusion wound model rats. The results indicated that ointment of two different concentrations gave a significant response in both models of wounds tested (69).

Toxicity and safe dose

Many studies were carried out to determine a safety of the plants and the results confirmed a safe dose of various plants based on animal model testing. The extracts from *T. indica* and *C. fistula* showed no signs of toxicity up to a dose level of 2000 mg/kg (51). The acute toxicity of the extracts of *C. fistula* was evaluated and the results indicated that no sign of toxicity up to a dose level of 2000 mg/kg (36).

CONCLUSION

This literature about *C. fistula* proved that it is very important plant with various bioactivities. The plant had different chemical constituents which proved many medicinal properties of the plant. It reported that phytochemical investigations and the isolated compounds of *Cassia fistula* can be investigated further to be a basic molecule in the search of novel herbal medicines. The safety and efficacy of *C. fistula* make it to be an important candidate in the treatment and prevention of many diseases. Modern studies which based on *in vivo* and *in vitro* studies confirmed that *C. fistula* plays an important role in diseases inhibition via modulation of various physiological and biochemical process. Detailed study based on molecular pathways should be done to confirm the exact mechanism of action of *C. fistula* in the diseases management.

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