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Ethnomedicinal, phytochemical and pharmacological properties of *Cassia fistula*: A medicinal plant

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Cassia fistula L., locally known as amaltas, is a deciduous flowering ornamental tree of the family Fabaceae. It is commonly called a "golden shower" for its bright yellow flowers. *C. fistula* is a time-tested remedy and is a well-accepted drug in Ayurvedic and Unani Pharmacopoeia, as well as in the traditional medicinal system in India. This review provides a comprehensive overview of the botany and ethnomedicinal uses of this plant. The various plant parts are used medicinally by local people throughout their geographical distribution as remedies for various diseases. In this review, the available information on the phytochemistry and biological studies of different parts of *C. fistula* is assessed and systematically organised. All the literature on *C. fistula* was critically reviewed with an emphasis on the qualitative and quantitative chemical analysis of the extract. Chemically, *C. fistula* is enriched with phenolic compounds, *viz*., flavonoids, anthraquinones, and chromones. The bioactivity is attributed to the plant's secondary metabolites. Many commercial formulations have been standardised by researchers with respect to the plant part used in medicine for their enhanced activity.

Keywords: Amaltas, Biological studies, Botanical description, *Cassia fistula* L., Chemical composition

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Introduction

Medicinal plants are the primary source of secondary metabolites that are directly or indirectly involved in maintaining health. Some of these secondary metabolites, such as terpenoids, alkaloids, phenols, and flavonoids, are associated with antimicrobial, antioxidant, and analgesic activities, making these plants a key source of new pharmaceutical drugs and healthcare products[1,2]. Bioactive compounds, being naturally occurring, have fewer side effects as compared to the synthesised compounds. Moreover, the demand for natural remedies is constantly increasing, thereby motivating researchers to search for diverse medicinal plants with possible potent activities[3,4].

Cassia fistula L. is a semi-wild Indian Laburnum also referred to as pudding pipe, Bahava (Marathi), Amaltas (Hindi, Urdu), Garmala/Girmala (Gujarati), Konrai (Tamil), Kola Ponna (Telugu) and Kakke gida (Kannada)[1,5]. *C. fistula* is also called 'golden shower' due to its attractive bunches of bright yellow coloured flowers blooming in April to June[6,7]. After flowering, the pods develop quickly and attain full length by October, which ripen between December and March. In May, the ripened pods begin to fall.

C. fistula originated in South-East Asia and is now widely distributed throughout tropical countries. It grows natively in India, Pakistan, and Sri Lanka[1,8], and is also found in Egypt, Australia, Ghana, Mexico, and Zimbabwe[9]. The species is dispersed widely in Thailand, China, Malaysia, East Africa, South Africa, Brazil, and Mauritius[7,10]. It occurs from sea level up to an altitude of approximately 1300 m.

It is commonly found in dry areas on mountain slopes and plains. The optimum temperature and rainfall requirements of amaltas range from 18 to 29°C and 480 to 720 mm annually, respectively. The plant can grow on a wide range of soil types; however, soils with a pH of 5.5–8.7 (slightly acidic to slightly alkaline) are considered most suitable. Its growth is notably enhanced in red volcanic and calcareous soils. It can withstand drought and frost and exhibit some salt tolerance. However, it does not possess the ability to fix atmospheric nitrogen[11].

Materials and Methods

A comprehensive survey of scientific databases, including PubMed, Scopus, Research Gate, Science Direct, and Google Scholar, was conducted to collect

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all relevant literature available on the traditional/ethnomedicinal uses, phytochemical composition, and biological studies related to *C. fistula* published till 2025. Additionally, high-impact-factor journals such as Springer, Elsevier, Taylor & Francis, and Wiley, as well as local journals/books, were also accessed. Keywords such as "chemical composition", "biological activities", "pharmacological activities", "antibacterial", "antioxidant", "antimicrobial", "anti-inflammatory", "anticancer", etc., along with *Cassia fistula*, were used to identify relevant literature for review writing. The collected data were thoroughly scrutinised to exclude irrelevant literature. More than 150 research articles were selected for compiling this review.

Botanical description

C. fistula is a mid-sized tree of about 10-20 m height[12,6]. The roots of *C. fistula* are shallow, with a taproot system and multiple branches. Its main trunk is about 5-6 m tall and 1-2 m in diameter, with branches that spread to form a crown-like appearance. The bark is pale/greenish grey to reddish brown. It is laminated and fragmented (flat/curved), with the outer surface smooth or rough, often with wart-like spots, whereas the inner surface is rough. The colour and texture of the bark vary as the plant matures. It has a peculiar sweet taste and fragrance[12]. Leaves are shiny green, about 30-40 cm in length, alternate, pinnately compound, pubescent, with a main rachis, stipules minute, linear-oblong and obtuse[13], with 4-8 pairs of large, ovate leaflets, 2-5 cm broad, and 7.5-15 cm long[9,12]. Flowers are bright yellow, fragrant, 30-50 cm long, 3-4 cm broad, slightly zygomorphic, sessile, and have drooping racemes. Corolla has five subequal, shortly clawed, obovate, and veined petals. Calyx is oblong, obtuse, glabrous, pubescent, caduceus, and divided at the base. Stamens are 10 in number, bearing basifixed anthers, with the lowest 3 being the longest, with oblong anthers dehiscing longitudinally and very long curved filaments, the 4 lateral with versatile anthers opening by pores at the base and short straight filaments, and the remaining 3 much smaller, erect with indehiscent anthers. Stigma is terminal, trunk-shaped with an incurved style. The ovary is sessile with many ovules[12,13]. The fruit of *C. fistula* is a dark brownish black, long (50-100 cm), pendulous, cylindrical, hard, intact, and septate pod with a diameter of 1-3 cm, bearing 25-100 seeds[14]. The pulp is dark brown, sweet, mucilaginous, and has a characteristic rather unpleasant odour[12,15] Seeds are reddish brown, flat, lustrous, broadly ovate, lenticular, and are separated by transverse partitions. They are about 5 mm thick and 8 mm long[13-16].

Taxonomic description

C. fistula belongs to the kingdom Plantae and the subkingdom Tracheobionta. Phylum and subphylum are Spermatophyta and Angiospermae. The plant belongs to the class Magnoliopsida-Dicotyledonae, subclass Rosidae, order Fabales, family Fabaceae, genus *Cassia*, and species *fistula.*

Traditional and medicinal uses

C. fistula is mentioned as Argvadha, which means "disease killer" in Ayurvedic literature[1]. The plant parts of *C. fistula* show effectiveness against a variety of skin and liver diseases, as well as in treating rheumatism, nasal infection, hypercholesterolemia, and diarrhoea[17]. It is also used to cure syphilis, leprosy, burning sensations, jaundice, boils, bronchitis, dyspepsia, colic, ringworm, constipation, cardiac problems, diabetes, dry cough, fever, malaria, inflammations, gout, fatty liver, and stomach disorders[10] (Fig. 1).

The roots of the plant have a very strong purgative property and act as an antidote for fever, cardiovascular disorders, biliousness, syphilis, haemorrhages, skin diseases, wounds, joint pain, ulcers, migraine, blood dysentery, tonic, astringent,

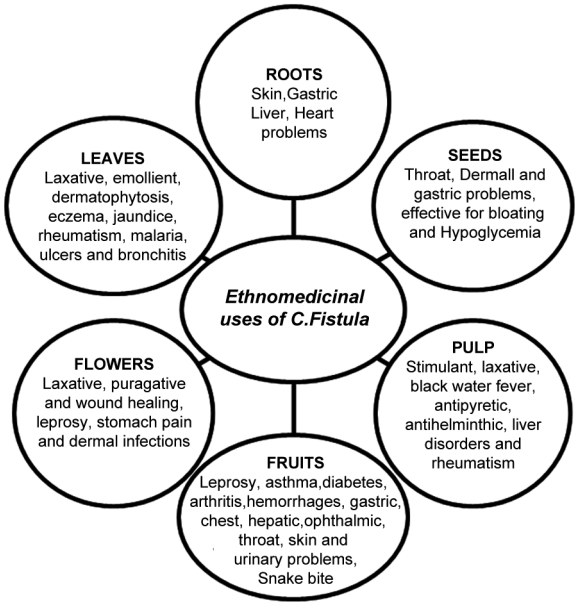

Fig. 1 — Traditional medicinal applications of different parts of *C. fistula*.

and febrifuge[1,18-20]. Leaves of *C. fistula* have mild laxative and external emollient properties. Their juice has been used for relieving irritation, dropsy, dressing for ringworm, dermatophytosis, eczema, inflammation, jaundice, rheumatism, malaria, ulcers, bronchitis, fever, and dry cough[1,4,10,19]. Flowers of *C. fistula* are beneficial in treating leprosy, dermal, and stomach infections. It has laxative, purgative, and wound healing potential[19,20]. Its fruit is used to treat leprosy, fever, chest problems, asthma, diabetes, arthritis, haemorrhages, stomach problems, hepatic and ophthalmic problems, throat troubles, urinary infections, snake bite, colic, and skin diseases[1,19,20]. The pulp is utilised as a stimulant, laxative, antimalarial, antipyretic, and antihelminthic. It is considered a safe laxative for both pregnant women and children, and it is also used to treat rheumatism and liver disorders such as biliousness[18,19]. The seeds have a mild, sweet taste and a cooling effect with antipyretic, carminative, laxative, emetic, cathartic, and marked hypoglycemic activity (when dried). They can treat constipation, stomach pain, dermal diseases, and a swollen throat. The seed powder is used as an antiamoebic agent[18-20].

Phytochemical constituents

C. fistula L. fruit is rich in macro and micro nutrients and can be a good source of minerals owing to the presence of higher potassium, calcium, iron, and manganese content. The amount of potassium and calcium is sufficient for daily human requirements, while the iron and manganese content are more than that present in highly consumable fruits[21]. Kadam *et al.*[22] carried out a proximate analysis and reported that the percentage composition of moisture, ash, total protein, crude fibre, crude fat, and total carbohydrates in the leaves was 5.25, 12.0, 12.39, 19.63, 9.38, and 41.33, respectively. In the fruits, the corresponding values were 3.20, 4.93, 16.62, 7.48, 3.06, and 64.6, respectively. The calorific value and fat-to-protein ratio were 299.39 and 0.76:1.0 in the leaves, whereas in the fruits, these values were 352.82 and 0.18:1.0, respectively.

C. fistula is also a good source of both primary and secondary metabolites. It is mainly composed of phenols, flavonoids, alkaloids, steroids, glycosides, and anthraquinones[24,25]. The chemical composition of flowers, leaves, seeds, pulp, stem, and bark of *C. fistula* is discussed below and summarised in Table 1.

Flowers

The metabolite analysis of *C. fistula* flowers indicated the occurrence of 12% protein, 11.75% carbohydrates, 1.42% free amino acids (proline, phenylalanine, methionine, and glutamic acid), and 12% lipids[23,24,26]. The secondary metabolites proanthocyanidin and kaempferol were identified in the acetone extract of the *C. fistula* flowers[24,27]. Isolation of rhein, kaempferol, ceryl alcohol, fistulin, a bianthraquinone glycoside, and a leucopelargonidin tetramer with a free glycol unit was carried out from the *C. fistula* flower's ethanol extract[28,29]. The alkaloids, phenolics, and traces of triterpenes were also reported in the flowers[24,30,31]. A compound, 4-hydroxy benzoic acid hydrate, was isolated and confirmed using X-ray crystallography from the EtOAc extract of the flowers[32]. Rhein was also isolated from the EtOAc extract of *C. fistula* flowers[5,33,34]. The GC-MS analysis of the ethanolic extract reported twelve compounds from the *C. fistula* flowers namely-quinoline,5-nitro-1-oxide,1,4-methanoazulene-9-methanol,decahydro-4,8,8-trimethyl-[1s-(1a`,3aa`,4a`,8aa`,9R'')-], tetradecanoic acid, pentadecanoic acid, 13-methyl-, methyl ester, ethanone,1-[4-methoxy-3-[methylphenoxy]phenyl-, phytol, octodec-9-enoic acid, *Z*, E-2-Methyl-3,13-octadecadien-1-ol, coumarine, 3-[2,4-dinitrophenyl]-, isopropyl stearate, 1a`-n-butyl-1a`[2-methoxycarbonyl-ethyl]1,2,3,4,6,7,12,12ba`-octahydroindolo[2,3-a]quinolizine and Eicos-9-ene-1,20-diacetate[35].

Leaves

Ethanolic extract analysed by Gas Chromatography-Mass Spectrometry revealed the presence of 19 compounds, including phytol, oleic, myristic acids, etc.[36]. The spectroscopic analysis (FTIR and NMR) of the methanol extract of leaves showed various functional group peaks corresponding to bioactive compounds such as hopane (triterpene), rhein and catechin (phenolics) and amentoflavone (flavonoid)[1]. The presence of (-)-epiafzelechin 3-O-β-D-glucopyranoside, 2 triflavonoids, 7-biflavonoids, procyanidin B-2, (-)-epicatechin, and (-)-epiafzelechin was reported in the acetone extract of the *C. fistula* leaves[24,37]. The anthraquinones physcion, chrysophanol, and rhein were also reported in the ethanol extract of leaves[24,38]. The leaves contained free rhein along with its glycosides, sennosides A and B[29]. The presence of two compounds, namely (2′S)-7-hydroxy-5-hydroxymethyl-2-(2′-hydroxypropyl) chromone and Benzyl-2β-O-D-glucopyranosyl-3,6-dimethoxybenzoate, was also identified in the

Table 1 — Chemical composition of aerial parts of *C. fistula*

Plant part	Solvent used	Chemical constituents	References
Flowers	Acetone	Kaempferol and a proanthocyanidin	24,27,
	Ethanol	Bianthraquinone glycoside, fistulin, kaempferol and rhein	24,28
	-	Phenolics, alkaloids and traces of triterpenes	24,30,31
	-	Kaempferol, ceryl alcohol, rhein, bianthraquinone glycoside, fistulin, and leucopelargonidin tetramer with a free glycol unit	29
	Ethyl acetate	4-hydroxy benzoic acid hydrate (crystals)	32
	Ethyl acetate	Rhein	5,33,34
	Ethanol	Quinoline,5-nitro-1-oxide,1,4-Methanoazulene-9 methanol,decahydro-4,8,8-trimethyl-[1s-(1a`,3aa`,4a`,8aa`,9R'')-], Tetradecanoic acid, Pentadecanoic acid, 13-methyl-, methyl ester, Ethanone,1-[4-methoxy-3-[methylphenoxy]phenyl-, Phytol, Z, E-2-Methyl-3,13-octadecadien-1-ol, Octodec-9-enoic acid, Coumarine,3-[2,4-dinitrophenyl]-, Isopropyl stearate, 1a`-n-butyl-1a`[2-methoxycarbonyl-ethyl]1,2,3,4,6,7,12,12ba`-octahydroindolo[2,3-a]quinolizineand Eicos-9-ene-1,20-diacetate	35
Leaves	Acetone	(-)-epiafzelechin 3-O-B-Dglucopyranoside, two triflavonoids, seven biflavonoids, procyanidin B-2, (-)-epiafzelechin and (-)-epicatechin	24,37
	Ethanol	Chrysophanol, rhein and physcion (anthraquinones)	24,38
	--	Free rhin along with its glycosides, sennosides A and B	29
	Methanol	(2′S)-7-hydroxy-5-hydroxymethyl-2-(2′-hydroxypropyl) chromone (II) and Benzyl-2β-O-D-glucopyranosyl-3,6-dimethoxybenzoate (III)	39,40
	Ethanol	Amentoflavone (Biflavonoid)	41
	Methanol	hopane (triterpene), rhein and catechin (phenolics) and Amentoflavone (flavonoid)	24
Seeds		5-(2-hydroxy phenoxy methyl) furfural, benzyl 2-O-D-glucopyranosyl-3,6-dimethoxybenzoate, benzyl 2-hydroxy-3,6- dimethoxybenzoate, (22 S) -7-hydroxy -5-hydroxymethyl -2-(22-hydroxypropyl) chromone, (22 S) -7-hydroxy-2-(22-hydroxypropyl)-5- methylchromone, 5-hydroxymethylfurfural, chrysophanol and chrysophanein (oxyanthraquinones)	45
Pods	-	Sennosides A and B, aloin, barbaloin, rhein and its glucoside, oxalic acids, formic acid and butyric acid	29
	-	1,8-dihydroxy-3-anthraquinone carboxylic acid	24,48
	-	Free rhin complexed with sennidin-like compounds.	24,49
	-	Fistulic acid (an anthraquinone acid)	50
	Methanol	3-formyl-1- hydroxy-8-methoxy anthraquinone	51
	-	3β-hydroxy-17-norpimar-8(9)-en-15-one (diterpene)	24,52
Fruit	Hexane	5-nonatetracontanone, 16-hentriacontanol, 2- hentriacontanone, triacontane, - sitosterol and an oil (an isoprenoid compound)	24,53
Fruit	Acetone	Epiafzelechin, catechin, epicatechinprocyanidin B-2 (Proanthocyanidins containing flavan-3-ol)	24,54
Pulp	-	Rhein	55,48
Pulp and seeds	n-hexane (oil)	stigmasterol, lathosterol, β-sitosterol, fucosterol, campesterol, and ergosta-4,22-dien-3-one (sterols), 5-(4,8-dimethylnonyl)-5-methyldihydro-2 (3H)- furanone, tetramethyl-hexadeca-1,6,10,14-tetraen-3-ol, 2,5-furandione, 3-dodecenyl and 3-(6-hydroxy-3,7-dimethyl-octa-2,7-dienyl)-4-methoxy-phenol	56
Bark	-	(+)-catechin, kaempherol, epicatechin, leucocyanidin, fistacacidin, leucopelargonidin trimer, hexacosanol, rhein glycoside, β-sitosterol and lupeol	29
Stem	-	Fistucacidin	58
Stem bark	-	(5,7,4'-trihydroxy-6,8,3'-trimethoxyflavone-3-*O*-α-L-rhamnosyl (1→2)-*O*-β-D-glucopyranoside, 5,7,3',4'-tetrahydroxy-6,8-dimethoxyflavone-3-*O*-α-arabinopyranoside) (Flavonol glycosides) and (1,8-dihydroxy-3,7- dimethoxyxanthone-4-O- α-L-rhamnosyl (1→2)-O-D-β glucopyranoside) (a xanthone glycoside)	57,71

(*Contd.*)

Table 1 — Chemical composition of aerial parts of *C. fistula* (*Contd.*)

Plant part	Solvent used	Chemical constituents	References
Bark and stem	-	Fistulaflavonoids B and C, licoisoflavone, (3S)-3', 7-dihydroxy-2',4',5',8-tetramethoxyisoflavan, (3S)-7-hydroxy-2',3',4',5',8-pentamethoxyisoflavan, morusyunnansins F, (2S)-2',4' -dihydroxy-7-methoxy-8-prenylflavan (flavonoids)	60-64
Stem	-	5-methoxy-2,2-dimethyl-7-(2-oxopropyl)-2,3-dihydrochromen-4-one,5- methoxy-2,2-dimethyl-8-(2-oxopropyl)-2,3-dihydrochromen-4-one, 1-(3,4-dihydro-5-meth- oxy-2,2-dimethyl-2H-chromen-7-yl) propan-2-one, pestaloficiol G, greveichromenol,7-hydroxy-2-methyl-5-(2-oxopropyl)-4H-chromen-4-one and perforatic acid	65-69
Roots	-	rhamnetin 3-O-gentibioside	24,70

methanolic extract of *C. fistula* leaves[39,40]. A biflavonoid, amentoflavone, was reported recently in the ethanolic extract of *C. fistula* leaves[41].

Seeds

The seeds of *C. fistula* are an abundant source of glycerides, fatty acids (linoleic, oleic, stearic, palmitic, caprylic (traces), myristic (traces) acids, cephalin, and lecithin phospholipids[42]. About 31% crude proteins (mainly globulin and albumin) and 11.8% carbohydrates (major-galactomannan) were also found in the seeds[24,43,44]. The presence of compounds (2′ S)-7-hydroxy-5-hydroxymethyl-2-(2′-hydroxypropyl) chromone, (2′S)-7-hydroxy-2-(2′-hydroxypropyl)-5-methylchromone, 5-(2-hydroxyphenoxymethyl) furfural, benzyl 2-hydroxy-3,6-dimethoxybenzoate, benzyl 2-O-D-glucopyranosyl-3,6-dimethoxybenzoate, oxyanthraquinones chrysophanol and chrysophanein, and 5-hydroxymethylfurfural was documented in the seeds[45].

Fruit and pods

The fruit was considered an abundant source of calcium, potassium, manganese, iron, protein (19.94%), and carbohydrate (26.30%)[46,47]. The pod contained protein, carbohydrates, tannin, maltose, pectin, glucose, sucrose, and a small amount of volatile oil along with secondary metabolites sennosides A and B, rhein, its glucoside, barbaloin, and oxalic acids, butyric acid, and formic acid[29]. In the pods, the compound 1,8-dihydroxy-3-anthraquinone carboxylic acid and free rhein complexed with sennidin-like compounds was also identified[24,48,49]. The anthraquinones such as fistulic acid and 3-formyl-1-hydroxy-8-methoxy anthraquinone were isolated from the methanol extract of pods[50,51]. A diterpene, 3β-hydroxy-17-norpimar-8(9)-en-15-one, was isolated from the pods of *C. fistula*[24,52]. Non-polar compounds such as 2,2-hentriacontanone, 5-nonatetracontanone, 16-hentriacontanol, triacontane, and β-sitosterol, along with oil, were reported in the pods[24,53]. Proanthocyanidins, flavan-3-ols like epiafzelechin, epicatechin, catechin, and procyanidin B-2 were also documented in pods[24,54].

Pulp

In the fruit pulp, 15.3% aspartic acid, 13% glutamic acid, and 7.8% lysine were reported[46]. Rhein was also identified in the pulp of *C. fistula*[48,55]. The total anthraquinone and anthraquinone glycosides content in pod pulp extracts was found to be greater than 0.10 and 0.03% w/w, respectively[55].

Oil

Oil extracted with n-hexane from *C. fistula* pulp and seeds contained 35 and 41 compounds, respectively, with 20 compounds shared by both. Steroids and terpenoids were the main compounds in pulp and seed oils, along with typical sterols like β-sitosterol, stigmasterol, lathosterol, fucosterol, ergosta-4,22-dien-3-one, and campesterol. Other compounds present in the seed oil were 5-(4,8-dimethylnonyl)-5-methyldihydro-2 (3H)- furanone, tetramethyl-hexadeca-1,6,10,14-tetraen-3-ol, 3-(6-hydroxy-3,7-dimethyl-octa-2,7-dienyl)-4-methoxy-phenol and 2,5-furandione, 3-dodecenyl[56].

Bark and stem

Bark extract reported to contain flavonols and xanthone glycosides[57]. The bark contained (+)-catechin, kaempherol, epicatechin, leucocyanidin, fistacacidin, leucopelargonidin trimer, hexacosanol, rhein glycoside, β-sitosterol, and lupeol[29], along with fistucacidin[58]. Two flavonol glycosides, 5,7,3', 4'-tetrahydroxy-6,8-dimethoxyflavone-3-O-α-arabinopyranoside and 5,7,4'-trihydroxy-6,8,3'-trimethoxyflavone-3-O-α-Lrhamnosyl (1→2)-O-β-D-glucopyranoside, and a xanthone glycoside (1,8-dihydroxy-3,7-dimethoxyxanthone-4-O-α-L-rhamnosyl (1→2)-*O*-D-β glucopyranoside) were identified in the

stem bark[59]. The flavonoids, i.e., fistula flavonoids B and C[60], licoisoflavone[61], (3S)-7-hydroxy-2',3',4',5',8-pentamethoxyisoflavan, (3S)-3',7-dihydroxy-2',4',5',8-tetramethoxyisoflavan[62], (2S)-2',4'-dihydroxy-7-methoxy-8-prenylflavan[63] and morusy unnansins F[64] were extracted from the bark and stems of plant. Li *et al.*[65] isolated chromones *i.e.* 5-methoxy-2,2-dimethyl-7-(2-oxopropyl)-2,3-dihydrochromen-4-one (VII), 5- methoxy-2,2-dimethyl-8-(2-oxopropyl)-2,3-dihydrochromen-4-one (VIII) and 1-(3,4-dihydro-5-meth- oxy-2,2-dimethyl-2H-chromen-7-yl)propan-2-one (IX), pestaloficiol G[66], greveichromenol[67], 7-hydroxy-2-methyl-5-(2-oxopropyl)-4H-chromen-4-one[68], and perforatic acid[69] (X- XII) from the stems of *C. fistula*.

Roots

The presence of rhamnetin 3-*O*-gentibioside in *C. fistula* roots was reported[24,70]. To date, the compounds belonging to the terpenoids, flavonoids, anthraquinones, and chromones classes of secondary metabolites have been isolated from different parts of *C. fistula*. The structures of the compounds isolated from different parts are shown in Fig. 2.

Pharmacological activities

The traditional ethnomedicinal potential of various parts of *C. fistula* has been well documented since the time of Ayurveda. Numerous biological studies have been conducted so far that have justified these traditional claims to a large extent[71,72]. In this section, we have comparatively assessed different biological and pharmacological studies, such as antioxidant, antifungal, antibacterial, antiplasmodial, hepato protective, antifeedant, and anticancer, conducted using extracts of different plant parts (Fig. 2). Table 2 summarises the biological studies of *C. fistula* extracts published since 2000.

Antioxidant activity

Medicinal plants are the main source of natural antioxidants. These natural antioxidants prevent the regeneration of harmful free radicals and thus prevent many diseases from occurring. These are also utilised in food items to increase their shelf life[73]. Siddhuraju *et al.*[74] prepared methanol (flowers, stem bark, and pulp) and ethanol extracts (leaves) (90%) of *C. fistula* and found that the antioxidant activity of stem bark was higher as compared to leaves, flowers, and pulp in correlation with the total polyphenolic content. The existence of some prooxidants, such as reducing sugars and chrysophanol, might have lowered the antioxidant potential of the flower and pulp extracts, whereas the high phenolic content in the stem attributed to its higher antioxidant potential with reference to its reducing power, DPPH radical scavenging ability, and inhibition of peroxidation, O_2^-. In rat liver and kidney homogenates, the aqueous and methanolic bark extracts inhibited lipid peroxidation initiated by CCl_4 and $FeSO_4$. In DPPH, Nitric oxide, and Hydroxyl radical-induced *in vitro* assays, both extracts exhibited significant antioxidant activity[75]. In alloxan-induced diabetic rats, the aqueous extract of the flowers restored the activities of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione)[76]. Bhatnagar *et al.*[14] also mentioned that the high antioxidant potential, as depicted by a concentration-dependent increase in FRAP value of *C. fistula*, is due to its high phenolic (22 mg/kg) and flavonoid (4 mg/kg) content. The high antioxidant action of the fruit methanolic extract was demonstrated by the Fenton reaction model, with IC_{50} at 1200 µg[77]. Acharya *et al.*[78] observed significant antioxidant and antiradical potential of hydro alcoholic extracts of dried seed powder using DPPH (2,2-diphenyl-1-picryl hydrazyl) assay, taking ascorbic acid as a standard. Similarly, the antiradical potential of hydroalcoholic extract of flowers and fruit pulp was attributed to a high amount of total phenols[17,79]. The DPPH, FRAP, Fe^{3+} reducing power, and hydrogen peroxide scavenging assays revealed that *C. fistula* pulp and seeds methanol extracts had higher activity than hexane extracts[56]. The radical scavenging activity exhibited by methanol extracts increased with an increase in dose, with IC_{50} value of 79.42 ppm using ascorbic acid as a standard[80]. The radical scavenging activity of the ethanolic extract of bark (IC_{50} value = 10.613 ppm) was lower than standard ascorbic acid (IC_{50} value = 4.716 ppm)[81]. The EC_{50} values of *C. fistula* leaves methanolic extract (70%) evaluated by CUPRAC (Cupric ion reducing antioxidant capacity assay) and DPPH assay were 170±0.55 µg/mL and 52.6±0.86 ppm, respectively[82]. Among the various fractions of leaves, the ethyl acetate fraction showed maximum antioxidant potential as determined by FRAP, ABTS, and NO radical scavenging assay[83].

In another study, the antioxidant effects of petroleum ether, n-hexane, ethanol, and methanol extracts of pods, flowers, leaves, and barks using different extraction techniques were evaluated.

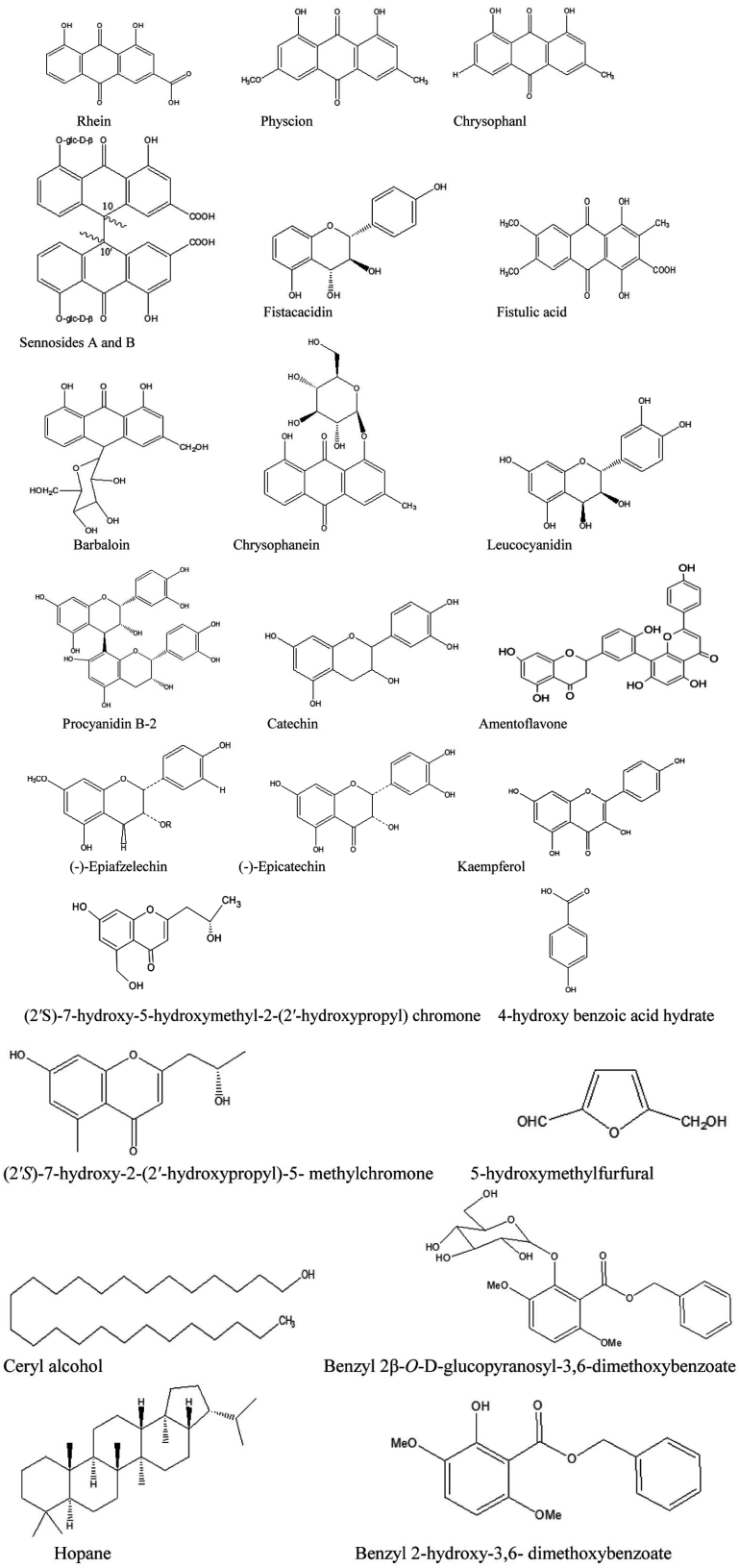

Fig. 2 — Chemical structure of compounds identified in *Cassia fistula*.

Table 2 — Biological activities of *C. fistula* plant extracts

Activity	Target cell/ organism	Plant part	Solvent	Model used	Result	Reference
	in vivo/Mice	Pod pulp	Ethanol	Ferric reducing antioxidant power (FRAP) assay	Active	14
	in vitro	Seeds, fruit pulp	Hexane and methanol	DPPH, FRAP, Fe^{3+} reducing power, and hydrogen peroxide scavenging assay	Pulp (methanol) > seed (methanol) pulp > (hexane) seed (hexane)	56
Antioxidant activity	*in vitro*	flowers, Stem bark, fruit pulp Leaves	Methanol (90%) Ethanol (90%)	Inhibition of peroxidation, Reducing power, and DPPH radical scavenging ability	Active Stem bark > leaves > flowers > pulp	74
	in vivo/Rat	Bark	Aqueous, methanol	DPPH, Nitric oxide and Hydroxyl radical induced *in vitro* assay	Both extracts active	75
	Alloxan-induced Female Wistar strain diabetic rats	Flowers	Aqueous		Active	76
	in vitro	Fruit	Methanol (50%)	Fenton reaction	IC_{50}=1200 µg/mL	77
	in vitro	Leaves	Methanol	DPPH free radical scavenging assay	IC_{50} = 79.42µg/mL	80
	in vitro	Bark	Ethanol	DPPH free radical scavenging assay	IC_{50} = 10.613 µg/mL, ascorbic acid (IC_{50} = 4.716 µg/mL	81
	in vitro	Leaves	70% Methanol	CUPRAC (Cupric ion reducing antioxidant capacity assay) and DPPH assay	EC_{50}=170 ± 0.55 µg/mL and 52.6 ± 0.86 µg/mL	82
	in vitro	Pods, flowers, leaves and barks	Ethanol, methanol, n-hexane and petroleum ether	DPPH free radical scavenging assay	70% methanolic leaf extracts showed 89% and 84.7% DPPH scavenging activity	84
	in vitro	Bark, leaf, stem and roots	Methanol	DPPH free radical scavenging assay	Methanolic bark extracts (IC_{50} value of 0.04 g/mL)	85
	in vitro	Seeds, fruit pulp, flowers	Hydro alcohol	DPPH free radical scavenging assay, total phenol content by Folinciocalteu reagent and reducing power methods using the OYAIZU method	All extracts active	17,79,101
	in vitro	All parts	Aqueous, Methanol, and petroleum ether	DPPH and FRAP assay	Methanol > aqueous > pet ether	86
	in vitro	Leaves	Aqueous	DPPH free radical scavenging assay	AgNPs showed IC_{50} value of 92.2 ± 1.2 µg/mL	88
Analgesic and Anti-inflammatory activity	Wistar albino rats	Bark	Aqueous, Methanol	Carrageenan paw oedema model, cotton pellet granuloma model	standard> methanol = aqueous (at 240 min); model, standard > aqueous > methanol.	75

(*Contd.*)

Table 2 — Biological activities of *C. fistula* plant extracts (*Contd.*)

Activity	Target cell/ organism	Plant part	Solvent	Model used	Result	Reference
	Wistar albino rats	Leaves	Methanol	Carrageenin, histamine and dextran induced paw oedema	Percent inhibition = 34.6%	90
	Wistar albino rats	Stem bark	Aqueous, ethanol	Carrageenan-induced paw oedema	Percentage inhibition = 26.98% (aqueous extract), 44.44% (ethanolic extract) and 82.53% (aspirin).	91
	Male Wistar albino rats	Fruit	Aqueous	Carrageenan-induced paw oedema	Percentage inhibition = 41.15%	92
	Swiss albino mice	Leaves, bark	Ethanol	The hot plate, formalin-induced paw licking, and acetic acid-induced writhing methods	Active	93
	Wistar albino rats	Pulp of *C. fistula* and fruits of *Solanum xanthocarpum*	Water	Carragenan-induced paw oedema model	ED50 = 408.52 mg/kg	95
	Human WBC's	Leaves	Deionised water		EC_{50} =558.03 µg/mL	96
	Human red blood cells (HRBC)	Leaves	Ethanol	Human red blood cells (HRBC) membrane stabilisation method	Percentage inhibition ~ 60- 70%	97
Anti-plasmodial activity	*P. falciparum*		DCM		IC_{50} = 38 g/mL	98
	P. falciparum	Leaves, bark, fruits	n-hexane		Active	99
Antibacterial activity	*E. coli, B. cereus*	Leaves	Methanol	Well diffusion method	Active	1
	S. aureus, *E. coli*	Leaves		Disc diffusion method	Active	9
	S. aureus, *Streptococci faecalis*, *E. coli* and *Salmonella typhi*	Bark	Methanol, acetone and aqueous	Agar cup diffusion method	Methanolic most active	18
	Gram-positive and Gram-negative bacteria	Flowers	Hexane, $CHCl_3$, ethyl acetate, methanol and water	Disc diffusion method, MIC	MIC = 0.078 and 2.5 mg/mL	32
	B. subtilis and *S. aureus*	Leaves	Acetone	Disc diffusion method	Active	39
	B. subtilis, S. *epidermidis*, *S. aureus*, *P. aeruginosa*, *Shigella flexineri* and *E. coli*	Fruit	Methanol	Disc diffusion method, MIC	Zone of inhibition = 9-12mm (Gram-positive); 9mm (Gram negative)	77
	Klebsiella aerogenes, *E. coli*, *Plasmodium desmolyticum* and *S. aureus*	Leaves	Water	Well diffusion method	Active	87
	B. subtilis, *S. aureus,* *E. coli* and *P. aeruginosa*	Leaves	Water	Agar-cup method	Strains were inhibited >95% (gram positive) and>80% (gram negative).	88

(*Contd.*)

Table 2 — Biological activities of *C. fistula* plant extracts (*Contd.*)

Activity	Target cell/ organism	Plant part	Solvent	Model used	Result	Reference
	Bacillus cereus, *S. aureus*, *S. pyogenes*, *Streptococcus mutans*, *Clostridium perfringens*, *Salmonella* spp., *E. coli* and *K. pneumoniae*	Leaves of *C. fistula* and *Ocimum basilicum*	Deionised water	MIC	EC_{50}= 746.39±8.4 µg/mL	96
	S. aureus, *E. coli* and *K. pneumoniae*	Leaves	Ethanol	Agar well diffusion method	Inhibitory zone for *S. aureus*19 ± 0.43 mm, *E. coli* (22 ± 0.33 mm) and *K. pneumoniae* (22 ± 0.63 mm).	97
	S. aureus, *Streptococcus pyogenes*, *E. coli, P. aeruginosa*	Fruit pulp, leaves	Hydro alcohol and chloroform	Agar disc diffusion method	Active	100,101
	Bacillus cereus, *S. aureus*, *S. epidermidis*, *Salmonella typhi*, *K. pneumoniae*, *E. coli*, *P. aeruginosa and Proteus mirabilis*	Flowers	Methanol, ethanol	Disc diffusion method, MIC, MBC	Active	103
	S. aureus, E. coli, and *P. aeruginosa*	Flowers	Methanol, ethanol, chloroform, petroleum ether and aqueous (hot and cold)	Agar disc diffusion method	methanol> petroleum ether>hot aqueous	104
	Salmonella typhosa and *Shigella dysenteriae*	Bark	Ethanol	MIC	MIC = 0.3125% w/v	108
	S. mutans, *S. mitis*, *S. sanguinis*, *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Actinomyces naeslundii*	Flowers	Ethanol	MIC	Active	106
	E. coli, *K. pneumoniae*	Fruit	Ethanol	MIC	100% and 91% activity after 1 hour and 5 hours, respectively	107
Antifungal activity	*Trichophyton mentagrophytes*, *Epidermophyton floccosum*	Flowers	Hexane, chloroform, methanol, ethyl acetate, and water	MIC	Active	32
	C. albicans, C. glabrata and *C. tropicalis*	Pulp and seeds	Oil extracted	Zone of inhibition, MIC	MIC = 250-300 µg/mL (pulp oil), 350-500 µg/mL(seed oils)	56

(*Contd.*)

Table 2 — Biological activities of *C. fistula* plant extracts (*Contd.*)

Activity	Target cell/ organism	Plant part	Solvent	Model used	Result	Reference
	A. niger, *A. clavatus* and *C. albicans*	Fruit pulp	Hydro alcohol, chloroform	Agar disc diffusion method	Zone of inhibition = 12-21 µg/mL	100
	C. albicans, *C. glabrata, C. tropicalis*	Fruit pulp, seed	Hexane	MIC	Seed extract: MIC= were 350, 300 and 300µg/mL Pulp extract: MIC=150, 250 and 100 µg/mL	110
	C. albicans, *C. krusei*, *C. parapsilosis, C. tropicalis, A. fumigatus*, *A. flavus* and *A. niger*	Bark, fruit and leaves	Chloroform, petroleum ether, ethanol, methanol and aqueous	Agar cup method, MIC, MFC	*Candida* sp.: methanol > ethanol > aqueous Petroleum ether and ethanol showed zone of inhibition against all three.	112
	C. albicans, *C. krusei*, *C. glabrata*, *C. kefyr*, *C. tropicalis*, and *C. parapsilosis*	Leaves, bark and seeds	Petroleum ether, chloroform, ethanol and aqueous	Agar well diffusion method, MIC	Active	113
	A. niger and *Penicillium digitatum*	Leaves and fruits	Aqueous	Inhibition zone method	Active	115
Antivirus activity	Tobacco mosaic virus	Bark, stems	Aqueous methanol (70%)	Half-leaf method	Inhibition rate = 28.5% - 31.3%	61
	Tobacco mosaic virus	Stems	Acetone	Half-leaf method	Inhibition rate = 15.6-22.1%	65
	Bovine rhinotracheitis virus	Fruits and leaves	Aqueous			122
	COVID-19 virus	Fruit pulp	Aqueous			123
Hepato-protective activity	Female mice	Bark	Ethanol		IC_{50} = 10.613 µg/mL	81
	White albino rats (Wistar strain)	Leaves	Methanol (90%)	Paracetamol-induced hepatotoxicity	Active	126
	Male Wistar rats	Leaves	Ethanol		Active	130
Antifeedant and larvicidal activity	*Culex quinquefasciatus* and *Anopheles stephensi*	Leaves	Methanol		LC_{50}=20.57 mg/l, LC_{50} = 17.97 mg/l	131
	Aedes aegypti	Leaves	Methanol, benzene, acetone		LC_{50} = 10.69 mg/l LC_{50} = 18.27 mg/l LC_{50} = 23.95 mg/l	132
Anticancer activity	Human cervical cancer (SiHa) and breast cancer (MCF-7) cell lines	Fruit pulp and seeds	Ethyl acetate, n-butanol	Clonogenic cell survival assay	IC_{50}= 415.5-535.3 µg/mL (SiHa cells), IC_{50}= 422.2-564.5 µg/mL (MCF-7)	135
	Breast cancer (MCF-7) cell	Flower	Aqueous, AgNPs	3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide (MTT) assay	IC_{50}= 7.19mg/mL	136
Antidiabetic activity	Male albino Wistar rats	Stem/ Bark	methanol	Streptomycin-induced diabetics	20 ppm/bw	140,145

(*Contd.*)

Table 2 — Biological activities of *C. fistula* plant extracts (*Contd.*)

Activity	Target cell/ organism	Plant part	Solvent	Model used	Result	Reference
	in vitro	Flowers	Petroleum ether, chloroform, acetone, ethanol, aqueous		Ethanol extract most potent	143
	Rats	Stem		Alloxan-induced diabetics		144
Antiulcer	Rats	Leaf	Ethanol	Pylorus ligation induced gastric ulcer		157
	Rats	Leaf, bark, flower, fruit pulp		ethanol induced gastric ulcer		158

Macerated methanolic leaf extracts (70%) showed 89% and 84.7% DPPH scavenging activity, when ascorbic acid and quercetin were separately used as standards, respectively, whereas the macerated methanolic (70%) extract of pods, barks, and flowers showed per cent inhibition of 66, 81, and 83.4 with ascorbic acid as standard. However, extracts prepared by the Soxhlet method resulted in lower free radical scavenging activities[84]. The antioxidant potential of leaves, stems, bark, and roots at three classes based on the age of the plant, as class A (2-3 years), B (5-10 years), and C (10-15 years), was determined. The methanolic bark extracts showed optimum activity with an average IC_{50} value of 0.04 g/mL[85]. The methanol extract (IC_{50}=69 and 714.86) displayed the highest inhibition to free radical, followed by aqueous (IC_{50}=60 and 448.14) and petroleum ether (IC_{50}=25 and 387.51) by DPPH and FRAP assay[86].

The multifunctional zinc oxide (ZnO) nanoparticles prepared using *C. fistula* extract as fuel *via* green formation route displayed significant antioxidant activity by scavenging DPPH free radicals[87]. The biogenic-synthesised silver nanoparticles (AgNPs) obtained by treatment of Ag ions with a water extract of *C. fistula* leaves showed IC_{50} value of 92.2±1.2 µg/mL by DPPH scavenging assay[88]. In light of the results from the above studies, *C. fistula* can be considered a potentially novel source of free radical-scavenging compounds. On the basis of these studies, it may be inferred that *C. fistula* is rich in flavonoids and phenolics and thus may be used as a natural and safe antioxidant[89].

Anti-inflammatory and analgesic activity

The comparative anti-inflammatory potency of the methanolic extract of *C. fistula* leaves and the standard drug was studied in contrast to phenylbutazone by applying histamine, carrageenan, and dextran-induced paw oedema in Wistar albino rats. The maximum percentage inhibition at 800 mg/kg after 4 h of the injection of the inflammatory agent was 34.6%, whereas in the case of phenylbutazone (reference standard), the inhibition was 35.6% after the injection of carrageenin[90]. In case of the aqueous (CFA) and methanolic (CFM) *C. fistula* bark extracts (250 and 500 mg/ kg) assayed in Wistar albino rats, the carrageenan paw oedema model exhibited significant reduction in paw oedema volume with the percentage inhibition (at 240 min) of 57.89% (CFA, 250 mg/Kg), 63.15% (CFA, 500 mg/Kg), 57.89% (CFM, 250 mg/Kg), 63.15% (CFM, 500 mg/Kg) and 71.05% (Diclofenac, reference standard). In the cotton pellet granuloma model, CFA and CFM at the concentration of 500 mg/kg caused a significant reduction in the cotton pellet-induced granuloma dry weight in rats with percentage inhibition of 42.69 and 22.31, respectively, as compared to Diclofenac (reference standard) with per cent inhibition of 50.42. Hence, both the extracts had anti-inflammatory potential[75]. The aqueous and ethanolic stem bark extracts displayed significant activity at a 400 mg/Kg dosage in Wistar albino rats with carrageenan-induced paw oedema. The percentage inhibition at the 5th hour was 26.98% (aqueous extract), 44.44% (ethanolic extract), and 82.53% (aspirin, reference)[91]. Similarly, the dried fruits aqueous extract demonstrated maximum activity at a 400 mg/kg dose, with a maximum percentage inhibition of 41.15%, when compared to diclofenac sodium, which demonstrated a maximum percentage inhibition of 47%[92].

A magnificent analgesic potential was reported by the ethanolic extract of leaves and bark at concentrations of 200 and 400 ppm in mice using

formalin-induced paw licking, hot plate, and acetic acid-induced writhing method[93]. *C. fistula* ethanol extracts were found to be as effective as diclofenac and indomethacin (the standard drugs) in relieving inflammation in both the carrageenan-induced hind paw oedema and cotton-pellet granuloma in rats. The activity increased with an increase in the concentration of extract[94].

The water extract of *C. fistula* dried pulp, along with dried fruits of *Solanum xanthocarpum* Schrad and Wendl, was studied on carragenan-induced paw oedema model in Wistar albino rats individually and in combination. The highest anti-inflammatory activity was shown at a 500 ppm concentration. The 1:1 combination of extracts exhibited 75% inhibition, as compared to diclofenac sodium (positive control), which showed 81% inhibition. Hence, *S. xanthocarpum* and *C. fistula* extracts interacted synergistically[95]. Similarly, the aqueous extracts of *C. fistula* and *Ocimum basilicum* leaves showed 85.9% and 76% depletion of human WBCs, respectively[96].

Recently, the anti-inflammatory potential of biosynthesised AgNPs using *C. fistula* leaves was assessed and compared with Diclofenac sodium (standard drug). The percentage inhibition for AgNPs was found to be ~60-70%, whereas for Diclofenac sodium, it remained between 70 and 80% hence, the authors reported that the fungal broth-capped AgNPs showed better anti-inflammatory property[97]. These studies ascertained that *C. fistula* alone or in combination can provide relief from inflammation and can act as a potential source of anti-inflammatory drugs.

Anti-inflammatory models, *viz.* Carrageenan-induced hind paw oedema, croton oil-induced ear oedema, cotton pellet-induced granuloma, and acetic acid-induced vascular permeability were used to evaluate rhein's anti-inflammatory activity in Wistar rats and mice. The activity of rhein (10, 20, 40 mg/kg) against carrageenan-induced paw oedema in rats and croton oil-induced ear oedema in mice was negatively correlated with concentration. Continuous administration of rhein to rats *via* implanted cotton pellets results in a significant reduction in granuloma formation (20 mg/kg: 17.24%; 40 mg/kg: 36.12%) compared with the control group. Rhein's administration also resulted in increased activities of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH-px), whereas the levels of nitrite, interleukin-6 (IL-6), interleukin-1b (IL-1b), tumour necrosis factor-a (TNF-a), malondialdehyde (MDA), and vascular endothelial growth factor were decreased. Western blotting test revealed that rhein lessened inducible nitric oxide synthase (iNOS) and carrageenan-induced cyclooxygenase (COX)-2 and increased heme oxygenase (HO)-1, nuclear factor erythroid 2–2-related factor 2 (Nrf2), peroxisome proliferator-activated receptor gamma (PPAR)-c and heat shock protein (HSP)-72 expression after 6 h in the paw oedema model. The anti-inflammatory action of rhein might be correlated with reduced concentrations of iNOS, MDA, and COX-2 and stimulating HO-1, Nrf2, and PPAR-γ expression via increased activities of SOD, CAT, and GSH-px through nitrite, T IL-6, NF-α, and IL-1β suppression[5].

Antiplasmodial activity

The DCM plant extract of *C. fistula* tested positive for *Plasmodium falciparum* with an IC_{50} value of 80 µg /mL[98]. The antiplasmodial activity of the n-hexane extract of leaves, fruit, and bark was also tested against *P. falciparum* (the chloroquine-sensitive strain). The maximum activity was noticed in the leaf extract. Hence, it was evident for the development of *C. fistula* as an antimalarial remedy[99].

Antibacterial activity

Medicinal plants have been regularly researched to develop new pharmaceutical drugs to treat communicable diseases. Different solvents (chloroform [$CHCl_3$], ethyl acetate [EtOAc], methanol [MeOH], and water [H_2O]) extracts of *C. fistula* caused significant inhibition to the growth of Gram-positive (*Staphylococcus aureus*, *S. epidermidis*, *Bacillus subtilis*, *Enterococcus faecalis*) and one Gram-negative (*Pseudomonas aeruginosa*) bacteria, with MIC (minimum inhibitory concentrations) values varied between 78 and 2500 µg/mL[32]. The MIC of methanolic (50%) fruit extract of *C. fistula* at various concentrations (i.e., 25-100%) against Gram-positive bacteria (*B. subtilis*, *S. epidermidis* and *S. aureus*) was 25% whereas in Gram-negative bacteria (*P. aeruginosa*, *Shigella flexneri* and *Escherichia coli*), inhibition was observed only in the case of pure extract[77]. Isolated (2′S)-7-hydroxy-5-hydroxymethyl-2-(2′-hydroxypropyl) chromone and Benzyl-2′-O-D-glucopyranosyl-3,6-dimethoxybenzoate showed promising antibacterial activity against *B. subtilis* and *S. aureus*[39]. Using the agar disc diffusion method, the

antimicrobial activity of hydro alcohol and $CHCl_3$ extracts of *C. fistula* fruit pulp was determined against *S. aureus*, *Streptococcus pyogenes*, *E. coli* and *P. aeruginosa*. The extracts displayed mild to strong inhibition against these strains[100,101]. Fistulin, a plant protease inhibitor extracted from *C. fistula* leaves, was found to be effective against *S. aureus*, *E. coli*, *B. subtilis* and *Klebsiella pneumoniae*, and its efficacy was comparable to the standard drug, streptomycin sulphate[102]. Another study reported that flower (MeOH and EtOH) extracts showed effectiveness against *Bacillus cereus*, *S. aureus*, *S. epidermidis, E. coli* and *K. pneumoniae*[103]. The aqueous extracts of *C. fistula* and *Ocimum basilicium* leaves, along with their mixture, were found to be potentially active against Gram-positive as well as Gram-negative bacteria[96]. The antimicrobial activity of Hydro alcohol and $CHCl_3$ extracts of *C. fistula* fruit pulp showed moderate to strong activity against *S. aureus*, *Streptococcus pyogenes*, *E. coli* and *P. aeruginosa*[100].

Among EtOH, $CHCl_3$, MeOH, Petroleum ether, and aqueous (hot and cold) extracts of flowers, the methanol extract exhibited maximum inhibition, whereas the hot aqueous extract exhibited the least inhibition against *S. aureus, E. coli* and *P. aeruginosa*[104,105]. In another study, among methanol, acetone, and aqueous extracts of bark, the methanolic extract was found to be most effective towards Gram-positive bacteria *S. aureus* and *Streptococci faecalis,* and minimal effect was observed against Gram-negative bacteria, *E. coli* and *Salmonella typhii*[18]. The fractions of methanolic leaves displayed inhibitory activity against *E. coli* and *B. cereus*[1]. The ethanol extract of flowers showed moderate activity against *S. mutans, S. mitis, S. sanguinis, Aggregatibacter actinomyce temcomitans, Porphyromonas gingivalis, Fusobac terium nucleatum,* and *Actinomyces naeslundii*[106]. Exceptional bactericidal activity was shown by the ZnO NPs synthesised by the green synthesis of *C. fistula* leaves extract on *K. aerogenes*, *S. aureus, E. coli* and *Plasmodium desmolyticum*[87]. Biogenic-synthesised silver nanoparticles (AgNPs) from *C. fistula* aqueous leaves extract caused more than 90% inhibition to the growth of bacterial strains, *viz. B. subtilis* and *S. aureus,* whereas recorded growth inhibition in the case of Gram-negative bacteria (*E. coli* and *P. aeruginosa*) was only 80% indicating that the latter are resistant to plant extract[88]. Rashid *et al.*[107] synthesised silver nanoparticles (AgNPs) using *C. fistula* fruit extract and reported 100% and 91% bactericidal activity against *K. pneumoniae* and *E. coli* after 1 hour and 5 hours, respectively.

Silver nanoparticles (AgNPs) fabricated from endophytic fungus extracted from *C. fistula* leaves displayed a considerable antibacterial effect against *S. aureus* (inhibitory zone of 19±0.43 mm), *K. pneumoniae* (22±0.63 mm), and *E. coli* (22±0.33 mm)[97]. Zinc nanoparticles prepared using *C. fistula* mediated ZnO NPs showed higher antimicrobial potential than the standard against *S. aureus* and *E. coli*[9]. Further, the enhancement of antibacterial activity was observed *via* the fabrication of metal nanoparticles using plant extract. Chaerunisaa *et al.*[108] evaluated the *in vitro* antibacterial activity of *C. fistula* bark extracts (Ethanol and hexane) and fractions (ethylacetate and water) against *Salmonella typhosa* and *Shigella dysenteriae*. The reported MIC values for the ethanol and ethyl acetate fractions were 0.3125 and 0.625% b/v, respectively. *In vivo* studies were conducted using *S. typhosa*-infected mouse models. *C. fistula* extract can be used safely below the 1000 ppm concentration. At higher concentrations, toxicological effects were observed. From all these studies carried out so far, it can be concluded that *C. fistula* and its isolated components displayed more inhibition to Gram-positive bacteria and alcoholic solvents are preferred for the preparation of extracts as compared to other solvents[109].

Antifungal activity

Medicinal plants/trees are considered as a primary candidate to develop antifungal drugs due to their novel mode of action and minimum side effects[110,111]. The fungitoxic effect of *C. fistula* can be confirmed *via* various studies conducted time to time. The fruit pulp and seed extracts of *C. fistula* were found to possess good anticandidal activity. The minimum inhibitory concentration (MIC) for seed extract was 350, 300, and 300 ppm, and those for pulp extract were 150, 250, and 100 ppm, respectively, against *Candida albicans*, *C. glabrata*, and *C. tropicalis*[112]. Antifungal activity of *C. fistula* oil was measured by disrupting ergosterol biosynthesis against *Candida* species. The MIC value of the pulp oil (MIC 250-300 µg/mL) and seed oils (MIC 350-500 µg/mL) can be directly correlated with the decrease in ergosterol content in the cell wall. The pulp and seed extracts reduced the ergosterol content

up to 68 and 47%, as compared to 90% reduction in the case of standard fungicide[113].

Among the chloroform, ethanol, petroleum ether, methanol, and aqueous extracts, the highest antifungal effect was shown by the methanol extract, followed by EtOH and water extracts against *C. albicans* (zone of inhibition-12.6 mm), *C. parapsilosis* (14.0 mm), *C. krusei* (13.3 mm), and *C. tropicalis* (14.3 mm). Petroleum ether and ethanol extracts inhibited all three *Aspergillus* species, with the highest zone of inhibition for *A. fumigatus* (12.0 mm), followed by *A. flavus* and *A. niger*[114]. Sony *et al.*[115] observed the anticandidal activity of petroleum ether, $CHCl_3$, ethanol, and aqueous extracts of bark, seeds, and leaves of *C. fistula* against Microbial Type Culture Collection (MTCC) *Candida* strains and 21 fluconazole-resistant clinical isolates. Antifungal activity analysed by agar diffusion and broth dilution techniques revealed that the ethanol seed extract had the highest inhibitory activity against *C. krusei* and *C. parapsilosis,* whereas the least inhibitory activity against *C. kefyr.*

Hada and Sharma[116] reported that pure $CHCl_3$ extracts of *C. fistula* fruit at a concentration of 1.25 mg/mL cause a significant increase in the mycelium width and a decrease in conidia size up to 77.89 and 97.61% of *A. solani*. Antifungal activity of methanolic extracts of *C. fistula* was also observed against *M. phaseolina* with 68.07 per cent inhibition. The activity was attributed to the presence of high amounts of phenolics, flavonoids, alkaloids and tannins[117]. The antifungal activity might be attributed to compounds, *i.e.*, butanoic acid, 2-methyl-, Penthiophane (2H-Thiopyran, tetrahydro), and isopropyl acetate (Acetic acid, 1-methyl ethyl ester), identified by GC-MS analysis of the most active fraction.

Hydro alcohol and chloroform extracts of *C. fistula* fruit pulp showed promising antifungal activity against *A. niger*, *A. clavatus* and *C. albicans*[100]. The application of aqueous extracts of fruits and leaves resulted in inhibition of the radial growth of *A. niger* and *Penicillium digitatum*[118]. The bioactive compounds (4-hydroxy benzoic acid) isolated from ethyl acetate crude extract validated its antifungal activity against *Trichophyton mentagrophytes* and *Epidermophyton floccosum*, with a minimum inhibitory concentration (MIC) of 0.5 mg/mL[32]. The growth of fungi such as *Trichophyton simii* (MIC 125 µg/mL), *Trichophyton rubrum* (MIC 62.5 µg/mL), *Trichophyton mentagrophytes* (MIC 31.25 µg/mL) and *Epidermophyton floccosum* (MIC 31.25 µg/mL) was inhibited by Rhein[119].

Antiviral activity

Recent studies have proved the antiviral activity of extracts of *C. fistula via* preventing the multiplication of viruses in host cells[120,121]. Antiviral activity of aqueous fruit and leaves extract of *C. fistula* against infectious bovine rhinotracheitis (IBR) virus in cattle varied with concentration[122]. The flavonoids isolated from *C. fistula* exhibited anti-tobacco mosaic virus (anti-TMV) activity. Compared with standard Ningnanmycin (24.7%), the anti-TMV activity of isolated flavonoids (fistula flavonoid B and C) showed higher inhibition rates (28.5 and 31.3%) than other isolated compounds, with inhibition rates varying between 18.5-22%[60]. Li *et al.*[65] evaluated anti-TMV activity and reported that one of the compounds showed high anti-TMV activity, with an inhibition rate of 30.8% while the inhibition rates of other compounds ranged from 15.6–22.1% at a concentration of 20 mM. The antiviral and immunemodulatory properties of *C. fistula* pod extract were primarily attributed to the anthraquinone component present in it[123]. Recently, Ravi *et al.*[124] suggested using fruit pulp extract as a supplement along with other medicinal measures to cure COVID-19. The fruit pulp of *C. fistula* contained the maximum amount of procyanidin B2 molecule that can act as an inhibitor of protease enzyme in patients having COVID-19 infection.

Hepatoprotective activity

Improper functioning of the liver led to the accumulation of toxic chemicals in the body. Many medicinal plants have shown hepatoprotective properties and help in the detoxification of the cells[125]. The hepatoprotective activity of methanol leaf extract against paracetamol-induced hepatotoxicity in rats was observed. Oral administration of extract @ 400 ppm body weight caused a significant reduction in serum levels of bilirubin, along with enzymes serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and alkaline phosphatase (ALP) in rats[126]. In a study carried out by Pradeep and co-workers[127,128], it was observed that prior administration of *C. fistula* leaves ethanolic extracts at a dose of 500 ppm body weight to the rats having CCl_4 and diethylnitrosamine induced hepatotoxicity after 7 and 30 days,

respectively, reversed the lipid peroxidase activity entirely, and normalised the functioning of glutathione and catalase reductase enzymes in the tissue. *C. fistula* aqueous extracts at a concentration of 250 and 500 ppm showed hepatoprotective activity and significantly reduced total bilirubin, ALP, SGOT, SGPT, aspartate transaminase (AST), alanine transaminase (ALT), and increased total protein (serum and liver) in CCl_4-induced liver damage in rats. *C. fistula* extracts can diminish the toxic effect of CCl4 in the liver[129]. An equivalent high dose of ethanolic leaves extract (500 mg/kg) of *C. fistula* displayed hepatoprotection against isonicotinic acid hydrazide/Rifampicin induced hepatitis in rats[130]. The ethanol extract of bark showed hepatoprotective activity with SGPT levels of 60.83 and 56.95 IU/L and SGOT levels of 134.30 and 110.17 IU/L at doses ranging from 150 to 300 ppm in female mice. Thus, it was indicated that the ethanolic bark extract belonged to the non-toxic category[81]. The findings support the use of *C. fistula* bark and leaves as a hepatoprotector.

Antifeedant and larvicidal activity

The leaves extract demonstrated promising insecticidal activity. The higher ovicidal and larvicidal effect of methanolic leaf extract was observed against *Culex quinquefasciatus* and *Anopheles stephensi* with LC_{50} values of 17.97 and 20.57 mg/L, respectively. The hatchability of the *C. quinquefasciatus* egg raft was found to be much higher than *A. stephensi*[131]. The leaves extract (benzene, methanol, and acetone) of *C. fistula* exhibited significant mortality of Aedes aegypti with LC50 values of 18.27, 10.69, and 23.95 mg/L, respectively. The hatchable tendency varied inversely with the concentration of extract[132]. Rhein showed promising antifeedant and larvicidal activities against lepidopteran pests *Helicoverpa armigera* and *Spodoptera litura*. The reported LC_{50} values were 606.50 and 1192.55 µg/mL against *H. armigera* and *S. litura*, respectively. The deformities were also observed in surviving larvae, which hindered development to the pupal and adult stages[33].

Anticancer activity

Modernisation and changed lifestyles led to the emergence of various health-related problems. Cancer is the second most prevailing health issue after heart disease in both developed and developing countries. There is a continuous increase in cancer patients worldwide. Medicinal plants have been regularly investigated for the development of anticancer drugs[133]. Gupta *et al.*[134] reported a reduction in tumour size and an increased lifespan of the mice having a tumour *via* administration of *C. fistula* seeds' methanolic extract. They also observed improvements in red blood cell and bone marrow cell counts in infected mice.

Seeds and pulp extracts of *C. fistula* fruit in two solvents (ethyl acetate and n-butanol) were tested for anticancer activity against human cervical cancer (SiHa) and breast cancer (MCF-7) cell lines. The fruit pulp and seed extracts inhibited the growth of MCF-7 and SiHa cells and induced cell death by modulating the expression of apoptosis regulatory genes and caspase enzymes. The pulp and seed extracts' anticancer activity might be attributed to the presence of active anticancer compounds[135]. The AgNPs prepared from aqueous extract of flowers had an IC_{50} value of 7190 µg/mL[136]. All the above studies suggested the potential of *C. fistula* for development as an anticancer agent.

The anticancer effect of Rhein was also evaluated in the human colon adenocarcinoma cell line COLO 320 DM and the normal cell line VERO. Rhein showed cytotoxicity against COLO 320DM cells at varying concentrations and times, whereas it had no effect on VERO cells. Rhein demonstrated 40-80% cytotoxicity at 200 g/mL over a 6-72 h incubation period. The lowest IC_{50} value was obtained at a 15 µg/mL concentration of Rhein after 48 h of incubation. Apoptosis in COLO 320DM cells was observed after 24 h in the treated cells. Apoptosis increased from 1.94 to 4.36 per cent with increasing rhein concentration. These findings suggested that rhein could be used to treat cancer[34]. The anticancer property of rhein may be attributed to its ability to suppress the proliferation of cancer cells by inhibiting the enzymes of the mitogen-activated protein (MAP) kinase pathway[137]. Rein has an inherent property to protect DNA from damage and thus prevent uncontrolled cell growth in cancer[138].

Wound healing potential

Wound healing is a necessary physiological process; failure may result in serious infections. Demand for the plant-derived drugs increased manyfold as resistance to synthetic antibiotics has developed in many cases. Topical application of *C. fistula (*alcoholic) extract formulation on the infected wound resulted in a decrease in wound size, improvement in tissue regeneration in the albino rat model. The results were positively correlated

with the biochemical analysis and enzymes functioning at the infected site[139].

Antidiabetic potential

A reduction in blood glucose levels was observed following administration of *C. fistula* stem (methanol) extract in Streptozotocin-induced diabetic rats. Further, a noticeable increase in tissue glycogen, and (14)C-glucose oxidation without any change in plasma insulin and C-peptide when Catechin (isolated from the methanolic extract) was orally administered at the dose of 20 ppm body weight. Enzyme activity was also normalised in male albino Wistar rats treated with catechin[140,141]. Daisy and Saipriya[142] also observed that the antidiabetic effect of gold nanoparticles prepared from aqueous extract was higher than that of the pure aqueous extract of *C. fistula* stem bark in curing streptozotocin-induced diabetic rats. A noticeable increase in body weight, total protein levels, and high-density lipoprotein was also achieved in treated rats.

Different solvents (petroleum ether, $CHCl_3$, acetone, EtOH, H_20, and crude aqueous) extracts and ethanol fractions of *C. fistula* Linn. flowers were evaluated at 200 and 400 mg/kg concentration and found to have hypoglycemic potential in controlling glucose levels in the diabetic rats. The activity of the water-soluble fraction of ethanol was found to be equivalent to the standard, glibenclamide[143]. A similar observation was reported in a study by Agnihotri *et al.*[144] on alloxan-induced diabetic rats. They observed that the stem barks of *Tamarindus indica* and *C. fistula* exhibited strong antihyperglycemic activity. In another study, a significant reduction in the blood sugar and serum insulin level was observed in the Streptozotocin-induced type 2 diabetic male albino rats *via* administration of hexane extract of *C. fistula* bark at the concentration of 0.45g/kg in 1.0 mL of 0.3 % Carboxymethyl cellulose solution[146].

The hypoglycemic potential of catechin was also confirmed by Pitchai and coworkers[146], who observed improvement in glucose tolerance in Streptozotocin-induced diabetic male albino Wistar rats administered with catechin at the same dose as mentioned in the previous study. The results were authenticated through in silico studies indicating that catechin has the potential to activate the insulin receptor and the Peroxisome proliferator-activated receptor gamma, and can be used to treat hypoglycemic patients. All these studies supported the potential of *C. fistula* and its isolated compounds as antidiabetic drugs[147].

Oral administration of *C. fistula* pod extract (100, 250, and 500 mg/kg body weight per day) to streptozotocin-induced Type-I diabetes rats notably improved sperm vitality, fertility rate, and progeny number. The treatment also enhanced epididymal antioxidant levels and reversed histopathological abnormalities in comparison to the untreated diabetic group[148].

Antipyretic potential

C. fistula ethanol extract was examined for its antipyretic activity against Typhoid vaccine-induced pyrexia in rats. At a concentration of 500 mg/kg body weight, vaccine-induced elevated body temperature was reduced after 1 hour, while it decreased in 30 minutes after administration of a higher dose[93]. Singh *et al.* [149] further confirmed the greater antipyretic effect of the methanolic extract of *C. fistula* in treated rats. They attributed this potential to the synergetic effect of phytochemical constituents present in *C. fistula* extracts.

Laxative potential

C. fistula showed a good laxative property and can be used to treat constipation. *In vitro* infusion of aqueous extract in the ileum of the guinea-pig resulted in low toxicity (LD_{50} value 6600 mg/kg) and thus is safe to be used as a substitute for Senna, a standard drug for treatment of constipation[150]. Nikhat[151] carried out a study to compare the toxic effects of *C. fistula* extracts and the Senokot tablet (a standard drug used to treat constipation) using *in vitro* infusion in the small intestines of selected guinea pigs. *C. fistula* pods extract displayed very low toxic effects and no visible pathological effects in the tested pigs.

Hypolipidemic activity

Abid *et al.*[152] observed that *C. fistula* fruit ethanol extract administered orally at concentrations ranging between 100 to 500 ppm body weight per day caused a significant increment in the level of liver serum lipid, malondialdehyde (MDA), and enzyme activities in HFD (High Fat diet) induced hyperlipidemic mice. Jangir and Jain[147] also observed a significant boost in insulin secretion and improved antioxidative status of the pancreas in streptozotocin-induced diabetic rats when administered orally with ethanolic extracts of *C. fistula* pods at a dose of 100-500 mg/kg body weight per day. The results were comparable to the standard drug, glibenclamide. Hence, *C. fistula* fruit extract can be used for curing cardiac problems.

Antiparasitic potential

Sartorelli *et al.*[153] reported the antiparasitic action of biochanin A (isoflavone isolated from the fruits of *C. fistula*) with EC_{50} values of 18.96 and 18.32 µg/mL against promastigotes of *Leishmania chagasi* and *Trypanosoma cruzi*, respectively. The extract was found to be two-fold more effective than benznidazole. The positive results were obtained in clinical trials conducted on patients (age group 6-60 years) to compare the effect of concentrated extract of *C. fistula*, hydroalcoholic extract of *C. fistula,* to the intralesional injection of meglumine antimoniate (MA) for treating leishmaniasis lesions. More than 40% of patients were relieved from their diseases. *C. fistula* extracts can be successfully used as a substitute for MA for curing leishmaniasis and decreasing the load of MA doses[154]. Recently, Tabrez *et al*. [155] conducted molecular docking studies to demonstrate the antileishmanial activity of *C. fistula* leaves. In antileishmanial assay (*in vitro*), leaves methanol extract of leaves inhibited the growth and multiplication of *L. donovani* promastigote (IC_{50}= 43.31± 4.202 µg/mL) along with inhibition of the growth of intra-macrophagic amastigotes (IC_{50} value= 80.76±3.626 µg/mL). In a similar study, alcoholic and aqueous extracts at higher doses of *C. fistula* completely inhibited the growth of Fasciola gigantica parasites, which were found to be more effective than albendazole (50 mg/mL), a standard drug, 8 h after application. However, extracts were ineffective at lower dosages[156]. *C. fistula* extract proved to be cytotoxic at very high doses on human macrophages. Thus, *C. fistula* extract can be used for curing parasitic infections.

Antiulcer activity

Ethanolic leaf extract of *C. fistula* Linn. significantly reduced gastric volume, pH, and acidity in rats with pylorus ligation-induced gastric ulcer in a dose-dependent manner. The antiulcer activity was comparable to standard drug (ranitidine). The protective action of the extract might be attributed to its antioxidant potential, thereby strengthening the mucosal defence mechanism[157]. Gastric ulcers were induced in male Wistar rats using ethanol, and the effect of different extracts was assessed on the basis of ulceration in the stomach, ulcer index, and percentage protection. Among different extracts of *C. fistula*, ethanolic bark extract (100 mg/kg/day) showed the highest protection (52.0%), followed by leaf, flower, and fruit pulp[158].

Antifertility

Oral administration of the aqueous seed extract of *C. fistula* to mated female rats during days 1–5 of pregnancy at doses of 100 and 200 mg/kg body weight resulted in 57.14 and 71.43% inhibition of pregnancy, respectively. Complete (100%) pregnancy inhibition was observed at a dose of 500 mg/kg body weight[159]. The antifertility effect of *C. fistula* in male rats was reversible, with organ weights, hormonal levels, tissue biochemistry, and fertility restored to normal 120 days after treatment withdrawal[160].

Conclusion

This review comprehensively and critically compiled the scientific information available on the phytochemistry and pharmacological properties of this important ornamental medicinal tree. This detailed information will be helpful in the proper evaluation of the plant for utilisation in agriculture and medicinal sectors. *C. fistula* extracts are enriched in phenolic compounds, *viz.* flavonoids, anthraquinones, and chromones that are responsible for the variety of biological activities exhibited by the plant extracts. Methanol is the ideal solvent for preparing extracts from different plant parts. The powdered extracts are an integral part of many commercially available drugs. Clinical studies confirmed the extracts' non-toxic effects in humans. Despite the high potential, limited work has been reported on the isolation of bioactive compounds. Rhein (a natural anthraquinone) is the only bioactive compound isolated from various parts of the plant and shows promising biological potential. Research work needs to be focused on the standardisation of extraction methods and isolation of other more potent compounds from *C. fistula*. Furthermore, molecular target elucidation and pharmacokinetic profiling need to be conducted. Integrating omics-based strategies, including metabolomics and proteomics, with molecular docking and AI-driven drug discovery can facilitate the identification of novel lead compounds. Additionally, advances in nanotechnology provide promising strategies to enhance solubility, bioavailability, and targeted drug delivery; however, comprehensive nanotoxicological evaluations remain crucial.

Conflict of interest

The authors declare that there is no conflict of interest.

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