

Phytochemical and pharmacological profile of *Cassia tora* Linn. — An Overview

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Cassia tora Linn. is one of the well-known anthraquinone containing plant and has been used in Chinese and Ayurvedic medicine. In the present review, an attempt has been made to explore a literature survey on its traditional uses, phytochemical studies and pharmacological properties. The whole plant as well as specific parts such as roots, leaves and seeds have been widely used and claimed against different diseases by rural and traditional practitioners of Satpura region of Madhya Pradesh. This plant has great contribution in modern system of herbal medicine for new drug development.

Keywords: Anthraquinone, Ayurvedic medicine, *Cassia tora*, Foetid Cassia, Pharmacological properties, Satpura region, Traditional medicine.

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Introduction

The nature has provided the storehouse of remedies to cure all ailments of mankind. The traditional herbal medicines are still practiced in large part of our country mostly in tribal and rural areas. In many developing countries large section of population relies on traditional practitioners, who are dependent on herbal folk medicines for their primary health care and has deep faith in it. Since the usages of these herbal medicines are increased, the issues regarding their safety, quality and efficacy in industrialized and developing countries are cropped up¹. Growing interest has also prompted researcher to screen scientifically various claims regarding properties and uses of medicinal plant materials. Presently both common consumers and health care professional seek updated, authoritative information towards safety and efficacy of any recommended medicinal plant as drug prior to its use^{2,3}.

Cassia tora Linn. (Family — Caesalpinaceae) is generally distributed throughout India, Sri Lanka, West China and tropics. It is known as *Charota* (Hindi); Foetid Cassia (English) and *Jui Ming Zi* (Chinese). In India it occurs as wasteland rainy season weed, grows in dry soil throughout tropical parts and

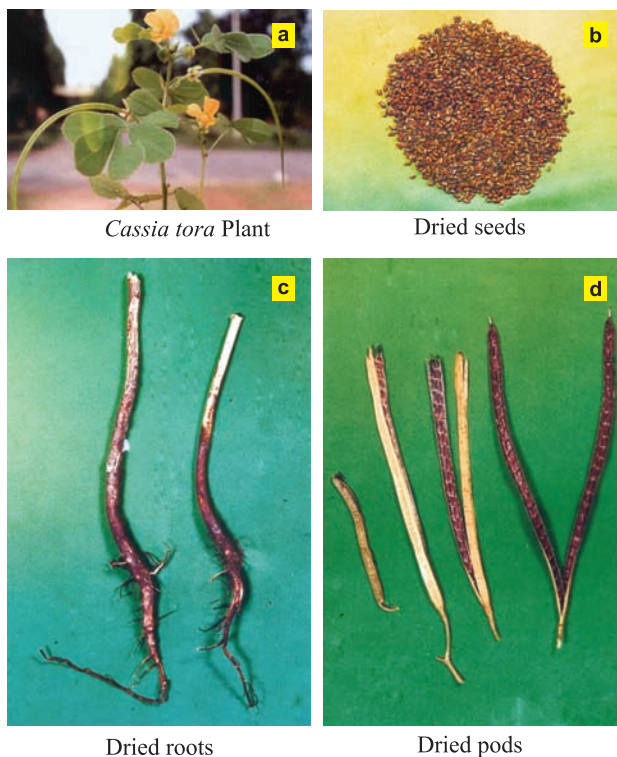
high hills of elevations up to 1,800 m as well as in plains⁴. The plant is an annual herbaceous foetid herb, almost an under-shrub, up to 30-90 cm high, with pinnate leaves. Leaflets are in 3 pairs, opposite, obovate, oblong with oblique base and up to 10 cm long. Flowers are in pair in axils of leaves with five petals and pale yellow in colour. In Indian conditions, flowering time is favourable after the monsoon rain. Pods are somewhat flattened or four angled, 10 to 15 cm long and sickle shaped, hence the common name sickle-pod. The seeds are 30-50 in a pod, rhombohedral and gathered in autumn and dried in sun⁵⁻⁷.

The present attempt is to review and compile updated information on various aspects of *C. tora* plant used in Indian system of medicine for variety of purposes. It highlights the several epidemiological, pharmacological and experimental studies on it, which demonstrated the correlation between the active constituents and uses in different fields.

Traditional uses

Different parts of *C. tora* (Plate 1a-d) are known to possess various ailments by rural and tribal people of Satpura region of Madhya Pradesh along with its uses in Ayurvedic and Chinese system of medicine. Due to its moist quality, sweet flavour and cold property of herb, it acts on liver and large intestine channels, clear the heat and liver fire, improve vision and ease the

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Plate 1 — *Cassia tora* : Plant, Seeds, Pods, Roots

bowels by clearing the heat and nourishing the large intestine. Therefore, this herb is used for treating conjunctival congestion caused by liver fire, blurring vision due to yin and constipation caused by intestinal dryness⁸. The leaves and seeds are also useful in treatment of leprosy, ringworm, flatulence, bronchitis, cough, dyspepsia and cardiac disorders and it is the most popular ingredient in Ayurvedic formulation, *Chakramadha tailam*. Generally traditional Chinese healers use this herb to treat blindness, xerophthalmia and conjunctivitis. The seeds are reputed in Chinese medicine as vision improving, antiasthenic, asperient, diuretic and an effective agent in lowering cholesterol and reducing blood pressure^{9,10}.

Externally it is applied as a germicide and anti-parasitical. About 60 ml of leaf decoction prepared by adding one part water is given to children to cure fever during teething. The herb also eases skin itch and eruptions when it is given mixed with lime juice. Warmed leaves reduce gout, sciatica and joint pain. Dried seeds contain 20 to 24% protein and are given as a protein rich feed to livestock and birds. They also yield tannins, yellow, blue and red coloured dyes and 7.5% gums which is good suspending and binding agent and having gelling properties. Roasted seeds are substituted for coffee like

Tephrosia seeds and also used in preparation of sweet dishes. Due to its fungicidal activity, it is also used as a natural pesticide in organic farms. Seed powder is most popular in pet food industry and also useful in mining and other industrial application when mixed with guar gum¹¹⁻¹³.

Phytochemical studies

Chrysophanol is the marker constituent of *C. tora*¹⁴. The roots showed the presence of 1, 3, 5-trihydroxy-6-7-dimethoxy-2-methyl anthraquinone and β -sitosterol. Seeds contain naphtho- α -pyrone-toralactone, chrysophanol, physcion, emodin, rubrofusarin, chrysophonic acid-9-anthrone. The leaves are rich in emodin, tricontan-1-ol, stigmaterol, β -sitosterol- β -D-glucoside, freindlen, palmitic, stearic, succinic and d-tartaric acids, uridine, quercitrin and iso-quercitrin¹⁵⁻¹⁸. The flowers are reported to contain kaempferol and leucopelargonidin¹⁹.

The seed oil contains different percentage of mixed fatty acids composition as palmitic, 6.70; stearic, 7.56; lignoceric, 10.05; oleic, 39.55; and linoleic, 36.14 (Ref. 20).

C. tora mainly consist of anthraquinone glycosides and flavonoids (Fig. 1). Three naphopyrone glucosides, cassiaside, rubrofusarin-6-O- β -D-gentiobioside and toralactone-9-O- β -D-gentiobioside isolated from the BuOH-soluble extract of the seeds were used *in vitro* bioassay evaluation based on inhibition of activity on advanced glycation end products (AGEs) formaton²¹. In another study by Jang *et al*, nine anthraquinones, aurantio-obtusin (1), chryso-obtusin (2), obtusin (3), chryso-obtusin-2-O- β -D-glucoside (4), physcion (5), emodin (6), chrysophanol (7), obtusifolin (8) and obtusifolin-2-O- β -D-glucoside (9) isolated from an EtOAc-soluble extract of the seeds of *C. tora* were subjected to *in vitro* bioassays to evaluate their inhibitory activity against advanced glycation end products formation and rat lens aldose reductase (RLAR). Among the isolates, compounds 6 and 8 exhibited a significant inhibitory activity on AGEs formation with observed IC₅₀ values of 118 and 28.9 μ m, respectively, in an AGEs-bovine serum albumin (BSA) assay by specific fluorescence. Furthermore, compounds 6 and 8 inhibited AGEs-BSA formation more effectively than aminoguanidine, an AGEs inhibitor, by indirect AGEs-ELISA and N(epsilon)-carboxymethyllysine (CML)-BSA formation whereas compounds 1, 4, and 6 showed a significant inhibitory activity on RLAR with IC₅₀

values of 13.6, 8.8 and 15.9 μm , respectively²². Seeds yield sitosterol from petroleum ether extract, chrysophanol, physicon, emodin, rubrofusarin from CHCl_3 extract and glycoside II and I from ethanolic extract. Glycoside II was identified as nitrofurarin-6-

β -gentiobioside²³. Seeds were found to have gums and mucilage, which have the ability to sustain the release of freshly soluble drugs like propranolol HCl from tablet²⁴. Nitric oxide plays an important role in protecting the *C. tora* plant against Al-induced

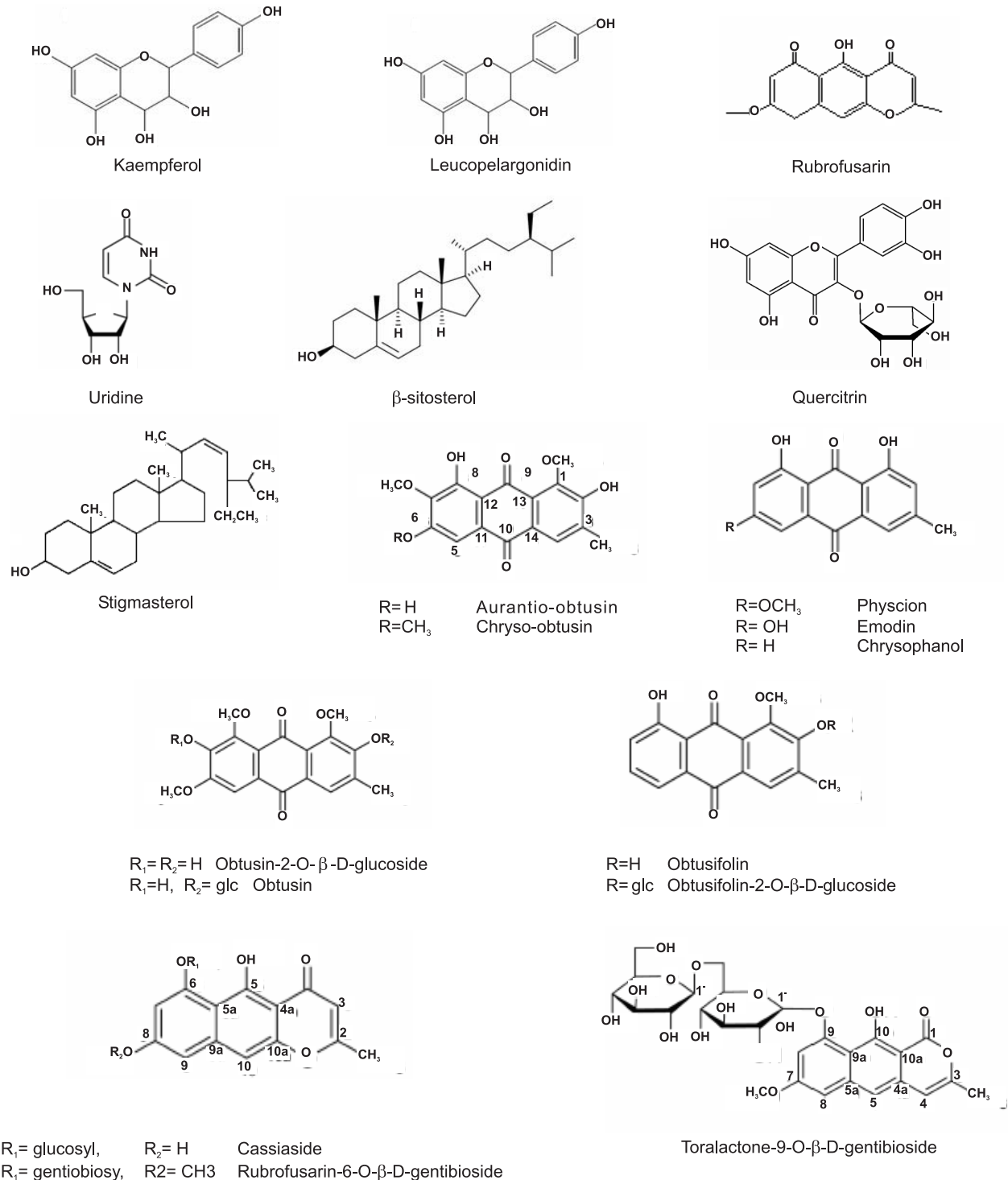


Fig. 1 — Structures of phytochemicals of *Cassia tora* Linn.

oxidative stress. It acts as a key signaling molecule, which has been involved in mediation of various biotic and abiotic stress-induced physiological responses in plants. Pre-treatment of the plant with sodium nitroprusside (SNP), as an NO donor, exhibited significantly greater root elongation when compared with the plants without SNP treatment²⁵. The capillary electrophoresis used for simultaneous determination of emodin, chrysophanol and their 8- β -D-glucosides of *C. tora*, which were achieved by cyclodextrin, modified capillary zone electrophoresis²⁶. The protein, anthraquinone glycosides (in seeds) and total sennoside contents (in pods), crop yield, quality attribute and growth of plant are significantly enhanced by calcium application on crop²⁷.

Pharmacological activities

Hypolipidemic

An ethanolic extract of seeds was evaluated by Patil *et al*²⁸ for its hypolipidemic activity on triton induced hyperlipidemic profile. Ethanolic extract and its ether soluble and water-soluble fraction decreased serum and triglyceride level of total LDL-cholesterol but increased the serum HDL-cholesterol level by different percentages.

In another study by Cho *et al*²⁹, soluble fibres were isolated from the seeds showed the hypolipidemic effect due to their phenomenal rheological behaviour and lipid metabolism. It showed significant reduction in serum concentration of total cholesterol and triglyceride levels but increased level of the serum high-density lipoprotein cholesterol level. The soluble fibres enhance fecal lipid excretion and showed the hypolipidemic effect due to marked reduction in serum and hepatic lipid concentrations in rats.

Antitumour

Emodin (1, 3, 8-trihydroxy methylanthraquinone) is a naturally occurring anthraquinone present in the roots and barks of *C. tora* as an active ingredient. At present, its role in combination chemotherapy with standard drugs to reduce toxicity and to enhance efficacy is pursued vigorously. Its additional inhibitory effects on angiogenic and metastasis regulatory processes make emodin a sensible candidate as a specific blocker of tumour associated events. Additionally, because of its quinone structure, emodin may interfere with electron transport process and in altering cellular redox status, which may

account for its cytotoxic properties in different systems. This biological property of emodin molecule is offering a broad therapeutic window, which in future may become a member of anticancer³⁰.

Antigenotoxic

An aqueous seed extract has a dose dependent inhibitory effect on benzo[a]pyrene (B[a]P)-induced DNA damage in human hepatoma cell line HepG2 due to its anthraquinones derivatives like chrysophanol, emodin and rhein present in it. Antigenotoxicity of the drug might be decreased due to a reduction in their anthraquinones content. Aqueous extract alone, at low concentrations of (0.1-2 mg/ml) showed neither cytotoxic nor genotoxic effect toward HepG2 cells^{31,32}.

Anti-inflammatory

The methanolic extract of leaves exhibited significant anti-inflammatory activity against carageenin, histamine, serotonin and dextran induced rat hind paw oedema as a dose dependent manner³³.

Antihepatotoxic

Protective effect of leaf extract against CCl₄ induced hepatotoxicity has been reported. The extract showed the ability to stabilize biliary dysfunction in rat liver during chronic hepatic injury with CCl₄^{34,35}.

In another study new antihepatotoxic naphthopyrone glycosides, 9-[β -D-glucopyranosyl-(1 \rightarrow 6)-O- β -glucopyranosyl]oxy]-10-hydroxy-7-methoxy-3-methyl-1H-naphtho [2,3-c] pyran-1-one and 6-[$(\alpha$ -apio-furanosyl-(1 \rightarrow 6)-O- β -D-glucopyranosyl)oxy]-rubrofusarin, together with cassiaside and rubro fusarin-6- β -gentiobioside were isolated from the seeds showed the significant hepatoprotective effects against galactosamine damage, which were higher than that of silybin from *Silybum marianum* Gaertn³⁶.

Antifungal

The dealcoholized leaves extract has shown the significant antifungal activity to inhibit the growth of *Candida albicans*, *Aspergillus niger*, *Sachharomyces cerevisiae* and *Trichophyton mentagrophytes* when tested by turbidity and spore germination methods in a concentration dependent fashion. The effects produced by the extract were compared with a standard antifungal agent Griseofulvin³⁷.

Anthraquinones (emodin, physcion and rhein) isolated from *C. tora* seed show an antifungal property against phytopathogenic fungi i.e. *Botrytis cinerea*, *Erysiphe graminis*, *Phytophthora infestans*,

Puccinia recondita, *Pyricularia grisea* and *Rhizoctonia solani*, using a whole plant method *in vivo* and were compared with synthetic fungicides and three commercially available anthraquinones. The chloroform fraction of *C. tora* showed a strong fungicidal activity against *B. cinerea*, *E. graminis*, *P. infestans* and *R. solani*. Furthermore, aloe-emodin showed strong and moderate fungicidal activities against *B. cinerea* and *R. solani*, respectively, but did not inhibit the growth of *E. graminis*, *P. infestans*, *P. recondita* and *Py. grisea*. Little or no activity was observed for anthraquinone and anthraquinone-2-carboxylic acid when tested. Chlorothalonil and dichlofluanid as synthetic fungicides were active against *P. infestans* and *B. cinerea* at 0.05 g/l, respectively³⁸.

Antimutagenic

The antimutagenic activity of anthraquinone aglycones and naphthopyrone glycosides from a methanolic extract of seeds against aflatoxin B₁ (AFB₁) was demonstrated with the *Salmonella typhimurium* assay. The MeOH extract was then sequentially partitioned with CH₂Cl₂, n-BuOH and H₂O. The CH₂Cl₂ and n-BuOH fractions possessed antimutagenic activity but the H₂O fraction was inactive. Neither the MeOH extract nor its fractions were capable of inhibiting the direct-acting mutagen N-methyl-N'-nitro-N-nitrosoguanidine suggesting that these fractions may prevent the metabolic activation of AFB₁ or scavenge the electrophilic intermediate capable of inducing mutations. Column chromatography using silica gel yielded pure chrysophanol, chryso-obtusin and aurantio-obtusin from the CH₂Cl₂ fraction and cassiaside and rubrofusarin gentiobioside from the n-BuOH fraction. Each of these compounds showed significant antimutagenic activity³⁹.

Antioxidant

Phenolic active components, alaternin and nor-rubrofusarin glucose isolated from extract of *C. tora* showed a potent ONOO-scavenging activity. Spectrophotometric analysis demonstrated that alaternin and nor-rubrofusarin glucose led to a decrease in the ONOO-mediated nitration of tyrosine through electron donation. In bovine serum albumin, alaternin, but not nor-rubrofusarin glucose, showed significant inhibition of ONOO-mediated nitration in a dose-dependent manner. Alaternin can be developed as an effective ONOO-scavenger for the prevention of ONOO-associated diseases⁴⁰.

In another study radical scavenging principles on 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical were isolated from the seeds. Assignments of the 1H- and 13C-NMR data showed the active components to be an anthraquinone, alaternin and two naphthopyrone glycosides, norrubrofusarin-6-β-D-glucoside (cassiaside) and rubrofusarin-6-D-gentiobioside. Alaternin showed more potent radical scavenging effect than the others⁴¹.

The effects of water extracts from *C. tora* (WECT) treated with different degrees of roasting (unroasted and roasted at 150, 200 and 250°C) on the oxidative damage to deoxyribose, DNA and DNA base *in vitro* were investigated. It was found that WECT alone induced a slight strand breaking of DNA. In the presence of Fe³⁺/H₂O₂, WECT accelerated the strand breaking of DNA at a concentration of 2 µg/ml; however, it decreased with increasing concentrations (>5 µg/ml) of WECT, which also accelerated the oxidation of deoxyribose induced by Fe³⁺-EDTA/H₂O₂ at a concentration of 0.2 mg/ml but inhibited the oxidation of deoxyribose induced by Fe³⁺-EDTA/H₂O₂/ascorbic acid. Furthermore, WECT accelerated the oxidation of 2'-deoxyguanosine (2'-dG) to form 8-OH-2'-dG induced by Fe³⁺-EDTA/H₂O₂. The pro-oxidant action of WECT on the oxidation of 2'-dG was in the order of unroasted > roasted at 150°C > roasted at 200°C > roasted at 250°C. The decrease in the pro-oxidant activity of the roasted sample might be due to the reduction in its anthraquinone glycoside content or the formation of antioxidant and Maillard reaction after roasting. Thus, WECT exhibited either a pro-oxidant or an antioxidant property in the model system that was dependent on the activities of the reducing metal ions, scavenging hydroxyl radical and chelating ferrous ion⁴².

Antibacterial

Torachryson, toralactone, aloe-emodin, rhein and emodin isolated from the seeds showed noticeable antibacterial effects on four strains of methicillin resistant *Staphylococcus aureus* with a minimum inhibitory concentration of 2-64 mg/ml. On the other hand, some phenolic glycosides were also isolated from seeds that did not show strong antibacterial effects on *Escherichia coli* and *P. aeruginosa*^{43,46}.

Anthelmintic

Alcohol and aqueous seed extracts showed the anthelmintic activity against *Pheretima posthuma* and *Ascaridia galli* due to the flavonoids present in it.

Three concentrations (25, 50, 100 mg/ml) of each extract were studied, which involved the determination of time of paralysis and time of death of the worm. Both the extracts exhibited significant anthelmintic activity at highest concentration of 100mg/ml using Piprazine citrate as a standard in same concentration as that of extract and distilled water as control⁴⁷.

Antinociceptive

The methanolic extract of leaves showed the antinociceptive and smooth muscle contracting activities and spasmogenic effects on guinea pig ileum, rabbit jejunum and mice intestinal transit in a concentration-dependent manner which is reversibly blocked by Atropine. Mepyramine also reduced the contractile amplitude due to the extract. The extract increased intestinal transit in mice dose dependently. *C. tora* extract significantly reduced the number of acetic acid induced abdominal constrictions in mice and the effect was comparable to that of Aspirin. The extract also significantly reduced the nociceptive response of mice to increased force (g), which is dose-dependent. Thus the use of *C. tora* traditionally as a purgative and in the treatment of other ailments is justifiable⁴⁸.

Hypotensive

The seeds of *C. tora* elicit hypotensive effects in anesthetized rats. Experimental results indicate that the hypotensive effect of the extract possibly involves a vagal reflex, which reciprocally alters the vasomotor tone of the centrally emanating sympathetic nervous system^{49,50}.

A study by Koo *et al* on pentobarbital-anesthetized rats revealed that the medial portion of the medullary reticular formation is directly involved in the hypotensive effect of extracts. The role of the medullary reticular formation in the *C. tora* induced hypotension was suggested to be one, which modulates the basic cardiovascular reflexes, favouring a decrease in vasomotor tone⁵¹.

Conclusion

C. tora is one of the most important sources of medicinally important phytochemicals and widely used in Ayurvedic as well as Chinese system of medicine. Most of the scientific works have been conducted on the seeds although activities of leaf extract are also reported. The major pharmacological work are on the anthraquinone glycosides and their

derivatives. Molecular mechanism of emodin action shows transition from laxative ingredient to an anti-tumour agent and mutagenic/genotoxic effects mainly in bacterial system. Emodin, first assigned to be a specific inhibitor of the protein tyrosine kinase *p65lck*, has now a number of cellular targets interacting with it. Its inhibitory effect on mammalian cell cycle modulation in specific oncogene over expressed cells formed the basis of using this compound as an anticancer agent. Some anthraquinones, phenolic glycosides including new naphthopyrone glucosides as cassiaside rubrofusarin-6-O- β -D-gentiobioside and toralactone-9-O- β -D-gentiobioside were isolated from seeds have been found to show various biological or pharmacological actions including radical scavenging effects, inhibitory effects on enzyme, antimicrobial effects. Some phenolic glycosides have also been used as traditional medicines for eye diseases and intestinal disorders in Asian countries. Experiments on the effect of *C. tora* extracts and some of pure compounds contained therein have shown that the traditional use of this plant is given considerable justification. There is no doubt that this plant is a reservoir of potentially useful chemical compounds which serve as drugs, are provided newer leads and clues for modern drug design by synthesis. Due to its many medicinal properties, there is enormous scope for future research on *C. tora* and further clinical and pharmacological investigation should be conducted to investigate unexploited potential of this plant.

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