Phytopharmacologic aspects of *Canscora decussata* Roem and Schult.

Sethiya Neeraj K., Patel M. B., Mishra S. H.

Herbal Drug Technology Laboratory, Pharmacy Department, Faculty of Technology and Engineering, The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat, India

Submitted: 08-03-10 Revised: 13-05-10 Published: 10-04-2010

ABSTRACT

Nature is an inexhaustible source of secondary metabolites—different types of alkaloids, terpenoids, phenolics, and other classes of organic compounds. In the process of isolation, purification and determination of the structures of lead, with their biological effectiveness, every type of experimental tool and strategy, known too and developed over the years by various practitioners. The present review is an attempt to compile information on various aspects of *Canscora decussata*, "Shankhpushpi" of Indian traditional system of medicine. The phytoconstituents, such as phenolic compounds, xanthones, and triterpenoids were isolated from different parts of the plant. The plant possesses immunomodulatory, analgesic, anticonvulsant, antitubercular, antiinflammatory, spermicidal, central nervous system–depressive, and cardiostimulant properties. Clinical trials of marketed formulation showed very encouraging results.

Key words: Shankhpushpi, phenolic compounds, xanthones, triterpenoids

INTRODUCTION

India has an ancient heritage of traditional medicine. Materia Medica of India provides a lot of information on the folklore practices and traditional aspects of therapeutically important natural products. Alternative systems of medicine, namely, *Ayurveda*, *Siddha*, and *Chinese* Medicine have become more popular in recent years.[1] Natural products have been our single most successful source of medicine. Each plant is like a chemical factory capable of synthesizing a limited number of highly complex and unusual chemical substances derived from plants that are considered as important drugs currently in use, while several other drugs are simple synthetic modifications of the natural products.[2] Numerous drugs have entered the international pharmacopoeia through the study of ethnopharmacology of traditional medicine.[3] The research and development thrust in the pharmaceutical sector is focused on the development of new innovative/indigenous plant-based drugs through the investigation of leads from the traditional system of medicine.[4] Drugs acting on the central nervous system (CNS) were among the first to be discovered by the primitive human and are still the most widely used group of pharmacologic agents. The drugs that act on the CNS are invaluable therapeutically, because they can produce specific physiologic and psychologic effects. From the vast array of Materia Medica of the indigenous system, many plants have been reported to have activity against CNS disorders and thus act as very useful remedies for the alleviation of human suffering.[5]

Address for correspondence:
Mr. Neeraj K Sethiya,
Herbal Drug Technology Laboratory, G. H. Patel Pharmacy Building, Donor's Plaza, Fatehgunj, Vadodara,
Gujarat – 390002, India. E-mail: nscognosy2006@gmail.com

DOI: 10.4103/0973-7847.65326

CANSCORA DECUSSATA SCHULT (GENTIANACEAE)

In India, *Canscora decussata* Schult. is popularly known as "Shankhpushpi" and found throughout India, up to an altitude of 1300 m. It is also grown in Sri Lanka and Myanmar. It is much branched, annual plant propagated by seeds. The flowering season of this plant is from Oct–Dec. The plant is cultivated in the gardens as ornamental plant for its flowers. This is an erect annual herb with 4-winged stem and half a meter in length with decussate branches. It grows well in moist conditions. Leaves are sessile, 2.5-4 cm in length, lanceolate, decussate with 3 prominent vertical lines; flowers are axillary, solitary, and white or yellowish in color. The entire plant, as well as fresh juice, is used in the traditional medicine for the treatment of insanity, epilepsy, and nervous debility. This plant contains bitter substances and an oleoresin. It is also found to contain triterpines, alkaloids, and xanthones.[6] It is also a natural source of pentaoxygenated, hexaoxygenated, and dimeric xanthones.[7]

TRADITIONAL MEDICINAL USES

Shankhpushpi is a reputed drug of *Ayurveda* and reported as a brain tonic.[8] *C. decussata* was identified as shankhpushpi and finds use in the indigenous system of medicine for a variety of purposes.[9] It has been reviewed as a psychoactive plant of India with its botanical distribution.[10] Shankhpushpi, an important drug of indigenous system of medicine is reputed as a nervine tonic, alternative, and laxative.[11] It has also been found effective in anxiety and neurosis, due to its clinical antianxiety effects and improved mental function, highly esteemed by ancient Indian physicians as a wonderful nervine tonic and memory invigorator. It is used in cerebral abnormalities, epilepsy, insomnia, burning sensation, edema, urinary disorders, snake-bites, and diseases caused by evil spirits. It is the best tonic for brain and nerves and was also recommended for sexual and seminal debilities.[12]

Common vernacular name

Sanskrit: Sankhapuspi, Sankhini. Hindi: Sankhabati, Shankhaphuli, Shankhapuspi, Samkhaphuli. Bengali: Dankuni. Malayalam: Kancankora, Samkhapuspi. Telugu: Kancakura, Kannada: Sankinisoppy.

PHARMACOGNOSTIC PROFILE

See Table 1 for the various pharmacognostic features of *C. decussate* Schult.

PHYTOCHEMICAL PROFILE

Chaudhuri and Ghosal reported, in 1971, that the roots of *C. decussata* Schult. have been shown to contain 16 xanthones (I–XVI), 6 of which (II, VII, IX, XII, XIII, XVI) have not been previously reported.[15] They established their identity with the use of various chemical, spectral methods, and in most cases, comparison with authentic synthetic samples, such as mangiferin (1,5-dihydroxy-3-methoxy (X), 1-hydroxy-3,5-dimethoxy (VII), 1,3,5-trihydroxy-6-methoxy (II), 1,3,8-trihydroxy-7-methoxy (III), 1,8-dihydroxy-3,7-dimethoxy (XI), 1-hydroxy-3,7,8-trimethoxy (VIII), 1,3,8-trihydroxy-6,7-dimethoxy (XIII), 1,8-dihydroxy-3,6,7-trimethoxy (XII), 1-hydroxy-3,6,7,8-tetramethoxy (IX), 1,3,5,6-tetrahydroxy (XIV), 1,3,7-tetrahydroxy (XV), and 1,3,6,7,8-pentahydroxy (XVI) xanthones [Figure 1]. During course of investigation they have been isolated and partially characterized, three more minor xanthones namely IV, V and VI. They also discussed biogenetic and chemotaxonomic significance of the co-occurrence of mangiferin and the other aforementioned xanthones in a single plant species, C. *decussata*. They preceded it by taking alcoholic mother liquor, which after the separation of mangiferin, gave a syrupy mass from which the nitrogenous constituents were removed by aqueous acetic acid treatment in the usual way. The chloroform-soluble fractions of the aqueous acidic suspension, consisting of a mixture of xanthones, were separated into 3 broad fractions (Fractions A–C) by solvent extractions. They isolated individual entities (II–XVI) from the above fractions by preparative chromatography.

Classification (Taxonomic)

Kingdom	Plantae	Plants
Subkingdom	Tracheobionta	Vascular plants
Super division	Spermatophyta	Seed plants
Division	Magnoliophyta	Flowering plants
Class	Magnoliopsida	Dicotyledons
Subclass	Asteridae	
Order	Gentianales	
Family	Gentianaceae	
Genus	*Canscora*	
Species	*decussata*	

Vernacular Names

Ghosal *et al,* reported that petroleum (60–80°) extract (Soxhlet) of the ground roots (2.4 kg), after removal of weak bases and minor phenolic constituents, afforded several triterpene constituents, which were separated by solvent extraction and preparative chromatography.[16] Those were identified as β-amyrin (melting point [m.p.], mixed m.p., co-thin layer chromatography [tlc], $[\alpha]_D$, infrared [IR], m.p., and mixed m.p. of the acetate), friedelin (m.p., mixed m.p., co-tlc, $[\alpha]_D$, M^+, *m/e*), and epifriedelanol (m.p., co-tlc, $[\alpha]_D$, IR, *m/e*). In addition, 2 apparently new triterpene acids were also isolated from the sparingly soluble fraction [Figure 2]. Mass spectrometry (MS) study indicated the presence of 4 xanthones in the ratio shown in parenthesis: (I) a tetrahydroxydimethoxyxanthone, M^+ 320 {26}; (II) a trihydroxytrimethoxyxanthone, M^+ 334 {42}; (III) a pentamethoxyxanthone, M^+ 346{12}; and (IV) a hexamethoxyxanthone, M^+ 376 {20}.

Ghosal *et al,* isolated the 3 naturally occurring xanthones, namely, l-hydroxy-3,5,6-trimethoxyxanthone, 1,6-dihydroxy-3,5-dimethoxyxanthone, and 1,3,6-trihydroxy-5-methoxyxanthone from the roots.[17] The identity of these xanthones was established by chemical reactions and spectral (ultraviolet [UV], IR, nuclear magnetic resonance [NMR], and MS) evidence. They also discussed phylogenetic significance of the co-occurrence of these and other polyoxygenated xanthones in the plant. The solid obtained from the petroleum ether fraction showed several spots on TLC plates, but repeated column chromatography failed to separate any individual xanthone. The mixture of xanthones remained unchanged upon treatment with dimethyl sulfate and potassium carbonate, indicating that they are permethylated. The solid obtained from the benzene fraction showed several spots on TLC plates. Finally, these were isolated by dissolving in chloroform and chromatographed over silica gel.

Ghosal *et al,* isolated 5 triterpenes (gluanone, canscoradione, friedelin, fridelan-3-β-ol, and β-amyrin), 3 sterols (sitosterol, stigmasterol, and campesterol), and liberal amount of a mixture of *n*-alkanes (C_{27}–C_{31}) and *n*-alkanols (C_{26}–C_{32}) from the aerial parts of *C. decussata* Schult.[18] The identity of isolated compounds has been established by chemical transformations,

Table 1: Different pharmacognostic features of *Canscora decussata* Schult.[13,14]

S. No.	Characters	Evaluated plant characters
1.	Habit	Erect, branching, annual herb
Stems structures		
1.	Length	Main stem 20–60 cm bearing opposite decussate branches
2.	Surface	Glabrous
3.	Internodes	Usually 3.5–4.5 cm, up to 6.2 cm
4.	Taste	Bitter
5.	Outline in transverse section	Annular with 4 wings
6.	Cuticle	Ridged
7.	Trichomes covering	Absent
8.	Glandular trichomes	Absent
9.	Chlorenchyma	Absent
10.	Collenchyma	Absent
11.	Endodermis	Distinct; secondary radial walls in old stems
12.	Pericyclic fibers	Absent
13.	Phloem fibers	Absent
14.	Pith	Intact, cells pitted when mature
Leaf structure		
1.	Phyllotaxy	Opposite decussate
2.	Shape	Oblong, lanceolate
3.	Size	25–38 mm × 8–15 mm
4.	Apex	Acute
5.	Surface	Glabrous
Midrib		
1.	Outline in transverse section	Concavo-convex; dorsal bulge irregularly lobed
2.	Collenchyma	Absent on either side
3.	Calcium oxalate	Absent
Lamina		
1.	Lamina	Dorsiventral, palisade in 1 layer
2.	Cuticle	Ridged
3.	Trichomes	Absent
4.	Stomata	Anisocytic; upper epidermis has a few stomata
Quantitative analysis		
1.	Stomatal number (lower surface)	52–72–108
2.	Stomatal index (lower surface)	16.9–21.0–24.6
3.	Vein-islet number	1–2.5–3.25
Extractive values (% w/w)		
1.	Water soluble	10.00
2.	Alcohol soluble	13.92
Fluorescence characteristics		
1.	Powder as such	Green
2.	Powder treated with 1 N NaOH in methanol	Bluish green
3.	Powder treated with 1 N NaOH in methanol, dried and mounted in nitrocellulose	Blue
4.	Powder treated with 1 N NaOH (aqueous)	Yellowish green

spectral evidence, and by direct comparison with authentic reference materials. Gluanone and canscoradione have not been encountered before in nature. From the petroleum ether extract of the stems, leaves, and flowers of the plant, the neutral fraction was separated from the weakly acidic methoxy xanthones in the usual way. The neutral fraction afforded 4 different types of compounds, that is, *n*-alkanes, *n*-alkanols, triterpenes, and sterols, by repeated column and preparative chromatography.

Ghosal and Chaudhuri isolated and identified the previously unreported 1,3,6,7-tetrahydroxyxanthone (I), 1,3,5,6-tetrahydroxyxanthone-C_2-glucoside (II), and 1,5,6-trihydroxy-3- methoxyxanthone (III) from the alcoholic extract of the plant.[19] The structures of these xanthones have been established by chemical transformations, synthesis (in case of III), and spectral (UV, IR, proton magnetic resonance [PMR], MS) evidence. Compounds II and III have not been encountered before in nature, whereas compound I was reported for the first time in this genus. The significance of mass spectral fragmentation in the structural elucidation of oxygenated xanthones is discussed. From the more polar fraction of the alcoholic extract of flowers, 3 previously unreported xanthones (I–III) were isolated. One was identified as 1,3,6,7-tetrahydroxyxanthone (I) by direct comparison with material prepared from mangiferin. Xanthone II, $C_{19}H_{18}O_{11}$ (M^+, 422, 6%) was obtained as a minor constituent along with xanthone III. Xanthone II showed UV absorption λ_{max} 240 sh (log ε 4.32), 250 (4.44), 280 (3.88), and 335 (3.90), characteristic of

CHEMICAL STRUCTURES

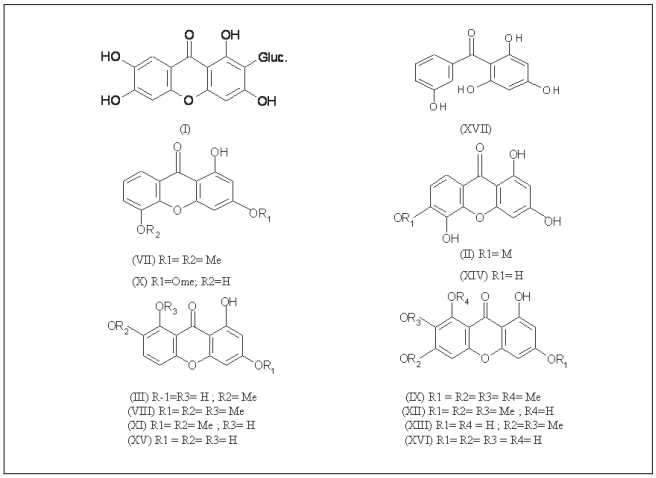

Figure 1: Structures of different xanthones of the plant

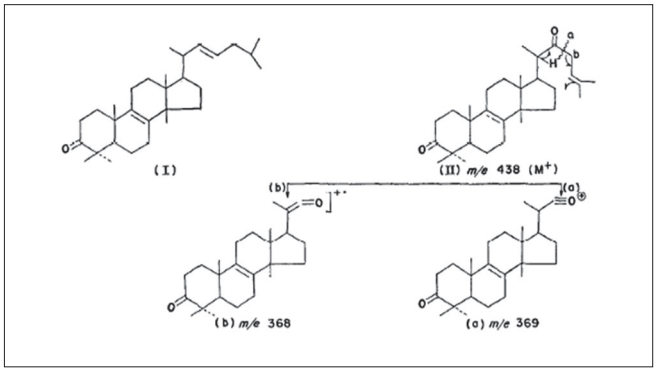

Figure 2: Structures of different lanostrene triterpenoids of plant

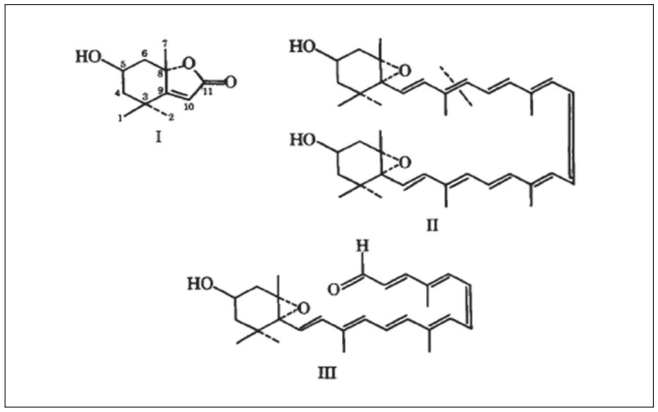

Figure 3: Structures of different loliolides of plant

1,3,5,6-tetraoxygennted xanthones. Xanthone III, $C_{14}H_{10}O_6$ (M+, 274, 100%), is a monomethoxytrihydroxyxanthone in which one of the hydroxyl groups is strongly chelated because it forms a dimethyl ether with $CH_2{\cdot}N_2$ and a diacetate but a trimethyl ether with $(CH_3)_2{\cdot}SO_4$. It has a UV spectrum λ_{max} 248 ($\log_{\epsilon}$ 4.61), 280 (3.94), and 335 (3.98), characteristic of 1,3,5,6-tetraoxygenated xanthones.

Ghosal *et al,* reported that the aerial parts of the plant have been shown to contain l-methoxy-3,5-dihydroxyxanthone and its 3-O-rutinosyl derivative.[20] The identity of these compounds was established by chemical transformation and spectral (UV, IR, PMR, MS) evidence of the compounds and their derivatives. It was the first demonstration of the occurrence of these 2 compounds in nature. *Xanthone I:* This compound, $C_{14}H_{10}O_5$ (M^+ 258), was a monomethoxydihydroxyxanthone (m.p. 354–355°C) in which the 2 hydroxyl groups were not chelated (PMR spectrum). It formed dimethyl ether with ethereal diazomethane and a diacetate. The UV spectrum was characteristic of 1,3,5-trioxygenated xanthones. The compound was soluble in dilute Na_2CO_3 solution and showed a strong bathochromic shift of the K-band on addition of NaOAc, typical of 3-hydroxyxanthones. *Xanthone II*: This compound, $C_{26}H_{30}O_{14}{\cdot}H_2O$, was a monohydroxymonomethoxy-xanthone-O-disaccharide (m.p. 252–255°C) as evidenced from its PMR spectrum and formation of octamethyl ether and a heptaacetate. It showed UV absorption characteristic of 1,3,5-trioxygenated xanthones. On acid hydrolysis, it furnished l-methoxy-3,5-dihydroxyxanthone, glucose, and rhamnose.

Ghosal *et al*, isolated (-)-loliolide, and reported that it is a native compound from *C. decussata* Schult.[21] Its identity was established by physical and spectral (UV, IR, PMR, carbon magnetic resonance (CMR), and MS) properties of the compound and its acetate derivative. The significance of the co-occurrence of loliolide with a number of carotenoids in *C. decussata* and the facile transformation of violaxanthin into loliolide and violoxin are discussed in the light of the biogenesis of the degraded carotenoid. (-)-Loliolide (I) [Figure 3] was isolated previously[22] in low yields (10^{-6} to 10^{-4}%) from 3 plant species, namely, *Lolium perenne* (Gramineae), *Digitalis purpurea*, and *Digitalis lanata* (Scrophulariaceae). However, the process of isolation and the plant parts used did not eliminate the possibility of its formation from the carotenoids present in these plants in appreciable quantities. Thus, the question of whether loliolide is an artifact or a native compound in these plants remained unsettled. It has now been obtained in an appreciable yield (7×10^{-3}%) from aerial parts and in a lower yield (1×10^{-4}%) from the roots. The isolation of loliolide from the roots, therefore, suggests that it is a native compound in *C. decussata* and is not formed by the autoxidation of any of the oxycarotenoids during the extraction of these compounds. A portion of loliolide probably is formed as a metabolite of one of the oxycarotenoids (or equivalent) *in vivo* and moves to the roots from the flowers and fruits of the plant during the growth of the plant.

Ghosal *et al,* isolated and reported the structures of new 1,3,5-tri- and 1,3,5,6,7-pentaoxygenated xanthones of *C. decussata.*[23]

Ghosal and Biswas isolated and characterized one new pentaoxygenated free xanthone and a new pentaoxygenated xanthone-O-glucoside from the flowering top of a fresh batch of *C. decussata.*[24] Compound 1, $C_{16}H_{14}O_7$ (M^+-318), showed UV

and IR spectra characteristic of a 1,3,5,6,7-pentaoxygenated xanthone. The MS spectrum showed, aside from the molecular ion peak, significant fragment ion peaks arising from the loss of CH_3, OH, H, O, and CHO from the M^+, indicating it to be a dihydroxy-trimethoxyxanthone with a 1-OMesubstituent. The changes in the UV maxima in the presence of the usual shift reagents indicated the presence of a 3- and/or 6-OH, and the absence of 1-OH and ortho-dihydroxy function.

The compound formed a diacetate which, in its ^1H NMR spectrum in $CDCl_3$, showed the H-8 signal at δ 7.48 ppm, suggesting only one OAc function in the B-ring and locating it at C-6 position. Selective methylation with dimethyl sulfate and $NaHCO_3$, afforded 1,3,5,6,7-pentamethoxyxanthone. This result suggested that the 2 OH groups in C-1 are acidic in nature and therefore located at the C-3 and C-6 positions. Finally, selective de-methylation of 1,3,5,6,7-pentamethoxyxanthone afforded 1,5,7-trimethoxy-3,6-dihydroxyxanthone, which was identical with the natural product. Compound 2, $C_{21}H_{22}O_{12}\cdot H_2O$, showed a close similarity to 7-glucosyloxy-1,6-dihydroxy-3,5-dimethoxyxanthone in its UV spectrum and in chemical reactions. The changes in the UV spectrum in the presence of the usual shift reagents suggested the presence of a C-l and C-3 or C-6 hydroxyl groups. As expected for an O-glycoside, the mass spectrum showed only the ion of the aglucone (*m/e* 304); hydrolysis with emulsin gave glucose and aglucone. The latter was found to be identical with 1,5,6-trihydroxy-3,7-dimethoxyxanthone (xanthone 4) in all respects.

Sethiya *et al,* developed spectrofluorimetric method for the simultaneous estimation of scopoletin and mangiferin,[25] and also investigated using comparative tlc on various available commercial sources of the plant and its formulation.[26]

PHARMACOLOGIC PROFILE

The following literature has been reported for various pharmacologic activities:-

Acute toxicity

Bhattacharya *et al,* reported the LD_{50} of mangiferin; the major and most polar xanthone of *C. decussata* in albino rats (based on a total of 16 animals) was 365 mg/kg (303–416 mg/kg at 95% fiducial limits). The total xanthones in a dose range of 500–1000 mg/kg caused no deaths in albino rats for a period extending 5 days after a single intraperitoneal injection.

Effect on central nervous system

Bhattacharya *et al* reported that signs of CNS stimulation were observed with mangiferin in the gross behavioral studies. In the doses of 50 and 100 mg/kg, mangiferin induced tremors, pilo erection, compulsive gnawing, and increased motor activity in all of the test animals. The behavioral changes reached a peak by 30 min of drug administration, were sustained up to 60 min, and then gradually declined by 120 min; all these were blocked by chlorpromazine pretreatment. The total xanthones from the petroleum extract did not elicit any hyperactivity, but the animals showed excessive signs of CNS depression (decreased motor activity, sedation, and diminished response to external stimuli).

Sethiya et al investigated that the ethanolic extract at dose of 400 mg/kg p.o. significantly reduced the neuromuscular coordination indicative of the muscle relaxant activity at a high dose. They used Diazepam (1 mg/kg i.p.) as a standard in all the animal models. They also isolated, characterized and evaluated its effects, a biomarker viz., mangiferin, in the animal models along with the ethanolic extract.[48]

Effect on pentobarbitol sleeping time

Bhattacharya *et al* investigated that both mangiferin and the total xanthones (50 mg/kg) significantly potentiated ($P < 0.05$) pentobarbitol sleeping time. Rats pretreated with mangiferin and the total xanthones slept for 56.2 ± 7.8 and 58.7 ± 6.7 min (± SEM), respectively, as compared with 36.2 ± 5.3 min (± SEM) sleeping time in the control group.

Effect on subnarcotic dose of ethanol

Bhattacharya *et al,* investigated that, only mangiferin (50 mg/kg) significantly ($P < 0.001$) potentiated the effect of a subnarcotic dose of ethanol. In this dose, 60% of the treated mice showed a loss of the righting reflex as against none in the untreated control group. The total xanthones had no demonstrable effect in this dose.[27]

Effect on reserpine-induced ptosis and depression

Bhattacharya *et al* reported that mangiferin exhibited a dose-related inhibition of reserpine-induced ptosis, sedation, and depression of locomotor activity in the doses studied. The ED_{50} against reserpine-induced ptosis was 42.4 mg/kg (31.5–49.8 mg/kg at 95% fiducial limits). The total xanthones did not show any significant activity against these parameters.

Effect on amphetamine group toxicity

Bhattacharya *et al* reported that mangiferin also produced a dose-related potentiation of amphetamine group toxicity. The ED60 was determined as 76.2 mg/kg (56.5–94.0 mg/kg at 95% fiducia1 limits). The total xanthones did not exhibit any significant effect in this parameter. The behavioral effects of mangiferin together with its ability to potentiate pentobarbital, ethanol, antiamphetamine-induced pharmacologic effects indicate the potential antidepressant nature of the compound.[13]

Effect on heart

Bhattacharya *et al* reported that both mangiferin and the total xanthones produced a transient positive inotropic effect on perfused frog heart in doses of 1–2 mg. Because the effect was not blocked by propranolol, it was a direct cardiostimulant action. A similar transient positive inotropic effect was observed in hypodynamic frog heart.

Analgesic effect

Bhattacharya *et al* investigated mangiferin or the total xanthones did not elicit any analgesic activity of its own in doses up to 40 mg/kg. However, in this dose, mangiferin significantly ($p < 0.001$) potentiated the analgesia produced by subanalgesic doses of morphine. In the vehicle-pretreated control group, the latent period of tail flick induced by a subanalgesic dose of morphine was 11.14 ± 0.25 sec. (± SEM), whereas in the mangiferin-pretreated (40 mg/kg) group, the same dose of morphine (2 mg/kg) induced a latent period of 17.170 ± 0.31 s (± SEM). The total xanthones did not produce any significant effect in this parameter.

Diuretic effect

Bhattacharya *et al* reported that the compounds had no significant diuretic effect up to dose levels of 100 mg/kg.[27] The present investigations failed to substantiate the diuretic effect reported with mangiferin.[28]

Effect on blood pressure, respiration, and intestine

Bhattacharya *et al* reported that there were no significant effects on the dog's carotid blood pressure, respiration, and intestinal movements were observed with mangiferin or the total xanthones up to a dose of 20 mg/kg.

Effect on biliary flow

Bhattacharya *et al* investigated that mangiferin produced a moderate increase in bile flow in doses of 20 mg/kg. From preinjection control levels, the bile flow started increasing after 30 min of the drug administration (180% increase); by 60 min, it reached a peak effect (290% increase). This choleretic effect started waning by 90 min (220 %) and had almost passed off (56%) by 240 min). There was an increase in the bile secretion at 30, 60, and 90 min of drug administration. Over the preinjection basal level, *P* value was statistically significant ($P < 0.001$). The total xanthones from the petroleum extract had no effect on bile flow up to a dose of 50 mg/kg.[27]

Anticonvulsant activity

Dixit, tried *C. decussata* in its both forms, that is, crude fine powder and alcoholic extraction against maximal electroshock test (MES), metrazol seizure test (MST), and for hypnosis potentiation tests, experimentally. He observed encouraging results against the above tests. The drugs were also tested for toxicity studies before the clinical trial. They administered the drug compound in two groups; Group A with acute type of convulsions showed no effect, whereas Group B with chronic type of convulsions showed better effect.[29]

Dikshit *et al*, reported that crude dried powder and its alcoholic extract with reference to phenytoin sodium (serves as a positive control) were found to provide 100% protection against supramaximal electroshock. This can be defined as a convulsion induced with a current of 150 mA for 0.2 s by an electroconvulsometer.[5] They also reported their ED_{50} value, which was found to be 62 mg/100 g, 7.6 mg/100 g, and 1.4 mg/100 g for crude powder, alcoholic extract, and phenytoin sodium, respectively.[30]

Bhattacharya *et al* reported mangiferin; major and most polar xanthones of *C. decussata*, and total xanthones did not elicit any anticonvulsant activity against maximal electroshock and pentylenetetrazol-induced convulsion in doses up to 100 mg/kg.[27]

Antitubercular activity

Ghosal and Chaudhuri reported that the chloroform-soluble fraction of ethanolic extract gave a mixture of about dozens of polyoxygenated xanthones. These polyoxygenated and some unidentified minor xanthones were used for the assessment of the anti-*Mycobacterium tuberculosis* H37RV, using Youmanin medium by tube dilution methods on these xanthones. They found that the total xanthones (II–IV) were more active than mangiferin and minimum inhibitory concentration (10μg/mL) of total xanthones was comparable to that of streptomycin.[31]

Ghosal *et al*, reported a potent anti *M. tuberculosis* component of *C. decussata*. Findings of these studies suggested that, there is moderate to significant anti-*M.tuberculosis* activity by the various plant isolates. They also reported that the xanthones nucleus should contain oxygen functions at 1,3 and 5,6, or 8- position. Among the 7 types of oxygenated xanthones, 1,3,5,6,7- and 1,3,6,7,8-pentaoxygenated xanthones were the most potent. Furthermore, in these 2 types of oxygenated xanthones, those containing hydroxyl groups at 1,3 and 6, or 8 position were more active than those at other positions.[32]

Immunomodulatory activity

Madan and Ghosh (2002) reported that *C. decussata* can be used for promoting the adhesion of peripheral neutrophils to human umbilical vein endothelial cells. CdAqE promotes the adhesion of neutrophils by inducing the expression of cell adhesion molecules ICAM-1 and E-selectin on endothelial cells. There real time-polymerase chain reaction results demonstrate that CdAqE increases the steady state transcript levels of these adhesion molecules suggesting that it may be activating at an early stage of signaling event.[33] Although several medicinal properties, such as antibacterial and anticonvulsant activities, have been attributed to *C. decussata* in the traditional medicine in India, not much experimental evidence is present.[34] There results showed the activation of cell adhesion molecules by the aqueous preparation of *C. decussata.*

Antiinflammatory activity

Shankarnarayan *et al* reported that significant antiinflammatory activity was observed in rats by carrageenan hind paw edema, cotton pellet granuloma, and granuloma pouch techniques.[35]

Madan *et al*[36] observed that the migration of the leukocytes to the site of inflammation is regulated in part by the expression of cell adhesion molecules, such as intercellular adhesion molecule-1 (ICAM-1) and E-selectin.[37] These cell adhesion molecules

are induced on endothelial cells by various proinflammatory cytokines, such as interleukin-1, tumor necrosis factor-1, and also by bacterial lipopolysaccharide (LPS).[38] It is well established that in various inflammatory diseases, the expression of these proteins is upregulated on endothelial cells.[39] Inhibition of these molecules using specific monoclonal antibodies (mAbs) has been found to be beneficial for controlling various inflammatory diseases.[40,41] In the present study, we investigated the effect of the extract prepared from the plant *C. decussata* on the expression of ICAM-1 and E-selectin on endothelial cells and on inflammatory response in rat model of carrageenan-induced paw edema. Our results show that an extract of *C. decussata* inhibits the expression of ICAM-1 and E-selectin on endothelial cells and is also effective *in vivo* as it reduces the edema formation in rats in carrageenan-induced paw edema assay. There results for the first time demonstrate that CdEE can be used for controlling cell trafficking by inhibiting the expression of ICAM-1 and E-selectin. CdEE effectively inhibits LPS-induced expression of ICAM-1 and E-selectin in a dose-dependent manner and it is also effective *in vivo* as it decreases the carrageenan-induced rat paw edema.

Hepatoprotective activity

Shankarnarayan *et al* reported that magostin-3,6-di-O-glucoside and mangiferin, a C-glucoside from *C. decussata* roots provides a definite protection against experimentally induced carbon tetrachloride liver injury in albino rats.[42] De *et al* reported *C. decussata* to possess hepatoprotective activity.[43]

Monoamine oxidase-inhibiting activity

Bhattacharya *et al* reported that mangiferin gave positive response in all the experimental parameters, such as potentiation of hexobarbitone necrosis in mice, reversal of reserpine-induced sedation and ptosis in mice, potentiation of amphetamine toxicity in aggregated rats, potentiation of dihydroxyphenylalanine (DOPA) effect in mice, potentiation of 5-hydroxytryptophan effects in albino mice, and potentiation of subanalgesic dose of morphine in albino rats. However, the dose required to produce monoamine oxidase inhibition was very large. It may also explain the use of the plants in traditional Indian system of medicine for melancholia and nervous debility.[44]

Spermicidal activity

Madan reported *Canscora decussata* to possess spermicidal activity.[45] Tyagi *et al* reported that the aqueous extract of this herb in a dose of 25 mg/100 g body weight arrested spermatogenesis in albino rats.[46]

Postmenopausal effect of its formulation

The Himalaya Drug Company, Bangalore (India), has formulated a safe and effective herbomineral preparation Menotab to relieve the distressing symptoms of postmenopausal syndrome. Menotab comprises *Withania somnifera*, *Elletaria cardamomum*, *Bombax malbaricum*, *Centella asiatica*, *Embelia ribes*, *C. decussata*, *Asparagus racemosus*, Oyster shell extract, *Glycyrrhiza glabra*, *Adhatoda vasica*, *Tinospora cordifolia*, and *Boerhaavia diffusa*. The herbs in the formulation restored a feeling of well-being in postmenopausal women. They relieve irritability, promote confidence, and keep them energetic. Menotab has a mild antidepressant activity and prevents hot flushes, insomnia, and fatigue. It has a high content of natural calcium, which helps to control postmenopausal osteoporosis. This study has shown that Menotab is an ideal medication for relief of postmenopausal symptoms as a short-term therapy. It is also safe, effective, with

Table 2: Different Indian marketed formulations of Canscora decussata Schult

Brand Name	Use	Manufacturing Company
Restore	The Revitalizer and Detoxifier feed for Horse	Global Herbs Products
Narvinol Syrup/ capsule	Narvinol exhibits prompt and sure action on Central nervous system and cardiovascular system. Narvinol produces moderate hypotension due to its depressive effect. Narvinol produces tranquilizing and sedative effect without addiction. Narvinol brings about a functional coordination between the body and mind, as Narvinol has anxiolytic and antitensive effects	Asoka Cordial and Asoka Compound
MenoCare	MenoCare® is a clinically researched herbal formula that helps support normal hormonal levels and their utilization in menopausal women. MenoCare® restores normal metabolism and contributes to overall fitness, comfort, and sense of well-being	Himalaya Herbal Healthcare
Safi	It relieves constipation, prevents and cures boils, pimples, skin eruption, and epistaxis.	Hamdard
Purex	Purex has special herbal formula that restores the optimum function of these organs of purification therefore cleansing the body of all the unwanted toxic elements. Purex corrects the digestive system and brings relief from constipation. As the function of excretion improves and the blood is purified, the skin improves remarkably in every way	Top Treatments; The Sign Of Health and Beauty
Brainta	This medicine is highly useful in strengthening and rejuvenating the mind. Improves concentration, comprehension, memory retention, and recall Perfect for students of all ages and those individuals who had to consume their mental energy in day-to-day workloads	Sharangdhar Pharmaceuticals Pvt. Ltd.

no adverse side effects. With reference to compliance, it also has the added advantage of not having side effects of withdrawal bleeding. Hence, it is an ideal alternative to other forms of hormone replacement therapy for short-term medication For short term medication[47]. Various polyherbal formulation of the plant were summarized in Table 2.

CONCLUSION

C. decussata is one of the traditional medicines practiced, as a controversial source of shankhpushpi for various brain-related disorders in Indian system of medicine. However, this plant proved its potential in CNS stimulation, hypertension, convulsion, tuberculosis, immunomodulation, inflammation, hepatoprotection, spermatogenesis, and postmenopausal osteoporosis. It is reported to contain several types of xanthones, triterpenoids, loliolide, sterols, and flavonoids. The most widely occurring xanthone, mangiferin, in this plant also proved its potential for CNS stimulation. The various pharmacologic studies reported in the present review confirm the therapeutic value of *C. decussata*.

Various types of xanthones and triterpenoids had been isolated from this plant, but there is lack of data that could correlate these chemical entities with specific biological efficacy. This plant was traditionally claimed to possess its potential for brain-related disorders and also widely used in marketed formulations for the same. But there is insufficient data that could conclude any underlying mechanism related to this. There is still lack of clinical data for its efficacy. With regard to globalization, in the changing scenario of medicinal plants, a thorough investigation and reinvestigation of the past is needed to get a lead on the basis of evidence.

REFERENCES

1. Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. N Engl J Med 1993;328:246-52.
2. Anonymous. Quality control methods for medicinal plant materials. World health organization, Geneva. Indian Edition Publ. Delhi: AITBS Publishers and Distributors; 2002. p 8-24.
3. Waxler-Morrison NE. Plural medicine in India and Sri-Lanka: do Ayurvedic and western medical practices offer?. Soc Sci Med 1988;27:531-44.
4. Patwardhan B, Ashok DB, Vaidya, Chorghade M. Ayurveda and Natural Products Drugs Discovery. Current Science 2004;86:789-99.
5. Suba V, Murugesan T, Rao RB, Pal M, Mandal SC, Saha BP. Neuropharmacological profile of Barleria lupulina Lindl. Extract in animal models. J Ethnopharmacology 2002;81:251-5.
6. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 19th ed., Nirali Prakashan, Pune; 2002. p. 524-5.
7. Peres V, Nagem TJ. Naturally occurring pentaoxygenated, hexaoxygenated and dimeric xanthones: a literature survey. Química Nova 1997;20:388-97.
8. Upadhya AS, Kumbhojkar MS. Studies on Ayurvedic Drug Shankhpushpi from Western Maharashtra Medicobotanical reported aspects. Bull Medicoethan Res 1993;14:64-9.
9. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi, India: CSIR; 1956. p. 49.
10. Jain SK, Ranjan V, Sikarwar RLS, Saklani A. Botanical distribution of Psychoactive Plants of India. Ethnobotany 1994;6:65-75.
11. Shah Y, Tangalos EG, Petersen RC. Mild cognitive impairment. When is it a precursor to Alzheimer's disease?. Geriatrics 2000;55:65-8.
12. Chunekar KC, Bhavaprakasa Nighantu (Commentary). Varanasi: Chowkhamba Vidyabhawan; 1969. p. 454-5.
13. Sinha P, Kumar A, Wahi SP. A comparative pharmacognostic study on Shankhpushpi - *Canscora decussata* Schult., Convolvulus pleuricaulis Chios and Evolvulus alsinoids Linn. Bull Med Ethanobo Res 1986;10:62-73.
14. Sethiya NK, Nahata A, Dixit VK, Mishra SH. Shankhpushpi: Cognition boosting ayurvedic medicine – An update. J Chin Integr Med 2009;7:1001-22.
15. Chaudhuri RK, Ghosal A. Xanthones of *Canscora decussata*. Phytochemistry 1971;10:2425-32.
16. Ghosal S, Chaudhuri RK, Nath A. Chemical constituents of the roots of *Canscora decussata*. Part II. J Ind Chem Soc 1971;48:589-92.
17. Ghosal S, Chaudhuri RK, Nath A. Chemical constituents of Gentianaceae IV New Xanthone of *Canscora decussata*. J Pharm Sci 1973;62:137-9.
18. Ghosal S, Chaudhuri RK, Nath A. Lanostane triterpenes of *Canscora decussata*. Phytochemistry 1973;12:1763-6.
19. Ghosal S, Chaudhuri RK. New tetraoxygenated xanthones of *Canscora decussata*. Phytochemistry 1973;12:2035-8.
20. Ghosal S, Ballava R, Chauhan PS, Biswas K, Chaudhuri RK. New 1, 3, 5-trioxygenated xanthones in *Canscora decussata*. Phytochemistry 1976;15:1041-3.
21. Ghosal S, Singh AK, Chaudhuri RK. Chemical constituents of Gentianaceae XX: Natural occurrence of (-) loliolide in *Canscora decussata*. J Pharm Sci 1976;65:1549-51.
22. Hodges R, Porte AL. The structure of loliolide: A terpene from Lolium perenne. Tetrahedron 1964;20:1463-7.
23. Ghosal S, Biswas K, Chaudhuri RK. Chemical constituents of Gentianaceae part 22, structure of new 1, 3, 5-tri and 1, 3, 5, 6, 7-penta oxygenated xanthones *Canscora decussata* Schult. J Pharm Sci 1977;14:1597-605.
24. Ghosal S, Biswas K. Two new two new 13 5 6 7-pentaoxygenated xanthones from *Canscora decussata*. Phytochemistry 1979;18:1029-31.
25. 25. Sethiya NK, Nahata A, Dixit VK. Simultaneous Spectrofluorimetric determination of scopoletin and mangiferin in a methanolic extract of *Canscora decussata*. Asian J Trad Med 2008; 3:224-9.
26. Sethiya NK, Nahata A, Dixit VK. Comparative thin layer chromatographic investigations on commercial sources of Shankhpushpi in India. Pharmacognosy Journal. 2009;1:224-6.
27. Bhattacharya SK, Ghosal S, Chaudhuri RK, Sanyal AK. C. decussata (Gentianaceae) Xanthones 3 Pharmacological Studies. J Pharm. Sci 1972;61:1838-49.
28. Finegan RA, Stephani RA, Ganguli G, Bhattacharya SK. Occurrence of mangiferin in Hiptage madablota Gaertn. J Pharm Sci 1968;57:1039.
29. Dixit SP. Effect of certain indigenous drugs in convulsion in children. Jrnl Res Ind Med 1971;6:2.
30. Dikshit SK, Tewari PV, Dixit SP. Anticonvulsant activity of C. decussata Roem and Schult. Ind J Physiol Pharmacol

1972;16:81-3.

31. Ghosal S, Chaudhuri RK. Chemical constituents of Gentianaceae XVI: Antitubercular activity of xanthones of *Canscora decussata* Schult. J Pharm Sci 1975;64:888-9.
32. Ghosal S, Biswas K, Chaudhuri RK. Chemical constituents of Gentianaceae XXIV: Anti-mycobacterium tuberculosis activity of naturally occurring xanthones and synthetic analogs. J Pharm Sci 1978;67:721-2.
33. Madan B, Ghosh B. *Canscora decussata* promotes adhesion of neutrophils to human umbilical vein endothelial cells. J Ethnopharmacology 2002;79:229-35.
34. Ramachandran K. Wealth of India (Raw materials). Publications and Information Directorate, Delhi: Council of Scientific and Industrial Research; 1992. p. 205.
35. Shankarnarayan D, Gopalkrishnan C, Kameswaran L. Pharmacology of mangiferin. Ind J Pharm Sci 1979;41:78-9.
36. Madan B, Mandal BC, Kumar S, Ghosh B. *Canscora decussata* (Roxb.) Schult. (Gentianaceae) inhibits LPS-induced expression of ICAM-1 and E-selectin on endothelial cells and carageenan-induced paw-edema in rats. Jrnl Ethnopharma 2003;89:211–6.
37. Springer TA. Traffic signals for lymphocyte recirculation and leukocyte emigration: the multi-step paradigm. Cell 1994;76:301–14.
38. Mantovani A, Bussolino F, Introna M. Cytokine regulation of endothelial cell function: from molecular level to bedside. Immunology Today 1997;18:231–40.
39. Calderon E, Lockey RF. A possible role for adhesion molecules in asthma. J Allergy Clin Immunol 1992;90:852–65.
40. Gorski A. The role of cell adhesion molecules in immunopathology. Immunology Today 1994;15:251–5.
41. Weiser MR, Gibbs SAL, Hechtman HB. Strategies to inhibit cellular adhesion molecules. In: Paul LC, Issekutz TB, editors. Adhesion Molecules in Health and Disease. New York: Marcel Dekker; 1997. p. 55.
42. Shankarnarayan D, Gopalkrishnan C, Kameswaran L. Effect of mangostin, 3,6-di-O-glucoside and mangiferin in CCl4, liver injury in rats. Mediscope 1979;22:65-8.
43. De S, Ravishankar B, Bhaskar GC. Plants with Hepatoprotective Activity – A Review. Indian Drug 1998;80:355-63.
44. Bhattacharya SK, Ghosal S, Sanyal AK. Monoamine oxidase-inhibiting activity of mangiferin isolated from *Canscora decussata*. Naturwissenschaften 1972;59:651.
45. Madan BR. Spermicidal Activity of *Canscora decussata*—An Indian Indigenous Drug Arch Int Pharmacodyn Ther 1960;20:88-94.
46. Tyagi SD, Singh N, Joneja S, Agarwal SC. Crude Powder of Canscora-decussata Roem and Schult. as Spermicidal Agent in Albino Rats. Acta Botanica Indica 1990;18:139-40.
47. Devi UK, Swarup A. Evaluation of Clinical Efficacy of Menotab in Alleviating Symptoms of Menopausal Syndrome: Phase III Open Clinical Trial. Antiseptic 2001;98:87-9.
48. Sethiya NK, Nahata A, Dixit VK. Anxiolytic Activity of Canscora decussata in Albino Rats. J. Compl. Integ. Med. 2010; 7(1): 19.

Source of Support: Nil, **Conflict of Interest:** None declared