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Research and Medicinal Potential of the genus *Cestrum* (Solanaceae) – A Review

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ABSTRACT
The genus *Cestrum* belonging to Solanaceae family comprises about 300 species. *Cestrum*, which was mainly distributed in South America ranges from Southern Florida and Northern Mexico to Chile is now distributed all over the world as an ornamental plant. The genus is rich in saponins and most of the species exhibit toxicity supporting their use as potential insecticide, herbicide, molluscicide, antimicrobial agent and anticancer agent. A characteristic species of this genus, *Cestrum diurnum* is known for its calcinogenic potential, which can be used as a source of vitamin D in poultry. The present review explores the distribution, chemical composition, pharmacological activity and traditional uses of different species of genus *Cestrum*.
KEY WORDS: *Cestrum*, Solanaceae, *Cestrum diurnum*, calcinogenesis, vitamin D_3, saponins.

INTRODUCTION

Plants are considered to be promising source of medicine in the traditional health care system. The efficacy and safety of herbal medicine have turned the major pharmaceutical population towards medicinal plant's research. In view of the widespread interest on Solanaceous plants, this work reviews the scientific information of the genus *Cestrum*. The present work discusses the botanical, ethnopharmacological, phytochemical, pharmacological and toxicological information identified in the literature concerning genus *Cestrum*. Species of *Cestrum* range from trees and shrubs to vines with sympodial, polyaxial, and monochasial branching (1). Species of *Cestrum* are well known for their ornamental, chemical, and pharmacological potential (2-4). Literature survey has revealed the presence of saponins, lignans, flavonoids, phenolic compounds, volatile oils and trace amounts of alkaloids. Most of the species in the genus are toxic especially to livestock, some are invasive species, notably *C. parqui*. The species *Cestrum* diurnum in particular possesses calcinogenic potential i.e., Vitamin D_3 like activity which can be used as cheap source of Vitamin D_3.

***Classification** (5)*

Kingdom	*Plantae* – Plants
Subkingdom	*Tracheobionta* -Vascular plants
Superdivision	*Spermatophyta* - Seed plants
Division	*Magnoliophyta* - Flowering plants
Class	*Magnoliopsida* - Dicotyledons
Subclass	*Asteridae*
Order	*Solanales*
Family	*Solanaceae* – potato family
Genus	*Cestrum* L. - Jessamine

Traditional uses

Most of the species of *Cestrum* have found several applications in folk medicine (Table 2). *Cestrum parqui* is used in Chilean folk medicine as antifebrile and for the treatment of fever and inflammation (4). Chinese people use leaves of *C. nocturnum* for their pharmacological significance in burns and swellings. It is also used for treating epilepsy and as stupefying charm medicine in West Indian Islands. The volatile oil of the species is known to be mosquito repellent and hence *C. nocturnum* and *C. diurnum* are used to prevent malaria in several African nations (6). *C. laevigatum* is traditionally applied as sedative dressings to wounds and ulcers and used as antispasmodic and diuretic (7). Leaves of *C. auriculatum* are used in Peru and Canta externally to reduce wound inflammations and kill domestic fleas. It is also used for its antimicrobial, anti infective and anti inflammatory properties (8). Community of Pamporomas uses the leaves of *C. auriculatum* for treatment of skin infection and allergies. The leaves are usually rubbed with water and extract obtained is applied directly to skin. The aqueous extract of leaves is also taken orally in small quantity for fever and diarrhea. Other popular uses found in literature for *C. auriculatum* are for treating hemorrhoids and head ache. It also possesses antirheumatic and astringent properties (9). C. *parvifolium* is also reported to be used traditionally for fever, ulcers and skin disorders (10). The plants of the genus have further found use in perfumery, as ornamental plants, floral scent production etc.

PHYTOCHEMISTRY

The genus *Cestrum* is mainly enriched with volatile oils, saponins and lignans. Chemistry of a few species like *C. parqui, C. nocturnum, C. sendtenerianum* etc. has been elaborated (Table 1). Chemical investigation report of genus was first of all reported by Peckolt TH. in 1909.

Saponins

The occurrence of steroidal saponins in several species of *Cestrum* has been documented. Recently saponins have received scientific attention because of their structural diversity and significant biological activities. A number of species like *C. nocturnum, C. parqui, C. diurnum, C. sendtenerianum, C. kunthii, C. axillare, C. laevigatum* etc. are reported to contain saponins.

Some of the earlier works on *C. parqui* had reported presence of Parquinoside with a foam index of 1/4.0 and hemolytic index from 1/5.0 to 1/10.0 (11). Fresh green berries of *C. parqui* have shown the presence of gitogenin and digitogenin and dried leaves showed the presence of digallogenin (12-13). The presence of kaurene glycoside in the leaves has been identified to be responsible for its toxicity in grazing animals. Further research on the leaves have shown the presence of an unusual steroidal sapogenin (25*R*)-isonautigenin, which could be used as a taxonomic marker for the species (14). The presence of neotigogenin, along with two terpenoid saponins possessing molluscicidal potential and parquisosides A and B possessing anti-inflammatory property have also been identified in *C. parqui* (15-16).

Reports on *C. sendtenerianum* have shown the presence of polyhydroxylated spirostanol saponins of two types i.e., tetrahydroxylated and trihydroxylated (Fig. 1). The trihydroxylated spirostanol saponins have hydroxyl group at C-1ß, C-2α and C-3ß positions and bear a di- or trisaccharidal glycoside at C-3. The tetrahydroxylated derivatives are additionally hydroxylated at *12ß* position i.e., spirosta-5,25(27)-diene - 1ß,2α,3ß,12ß-tetrol 3-*O*- ß-D-galactopyranoside (17-18).

Phytochemical studies on another species of *Cestrum* i.e., *C. nocturnum* have shown the presence of spirostanol glycosides. Nocturnoside A, a yuccagenin pentasaccharide, and nocturnoside B, a diosgenin tetrasaccharide (Fig. 2) have been reported along with sapogenin like yuccagenin and tigogenin. Cesternoside A (2-sec-butyl-4,6-dihydroxyphenyl-ß-*D*-glucopyranoside) and its acetyl derivative cesternoside B, two novel glucosides have also reported from *C. nocturnum* (Fig. 3) (19-22). Several other steroidal saponins i.e., flavonoidal saponin, furostanol saponin, pseudofurostanol saponin, pregnane glycoside, cholestane glycoside, pregnane-carboxylic acid lactone glycoside etc. have also been described from the species (23).

In 1960, the first report on the presence of saponin in *C. diurnum* was published and later a tigogenin trisaccharide, Tigonin and a tigogenin pentasaccharide, diurnoside 1 (Fig. 4) were identified (24-25). *C. laevigatum* and *C. elegans* have been elaborated for the presence of gitogenin, digitogenin and tigogenin, gitogenin respectively (26- 27).

Alkaloids

Traces of alkaloids were detected in a few species. The alkaloid parquine from *C. parqui* leaves was identified by Mercier in 1914 (28). It has been shown to cause motor incordination. Alkaloids have also been detected from *C. nocturnum* and *C. diurnum*. Chattraj Mousmi *et al*. isolated and characterized 1-carbamoyl pyrrolidin-2-one from *C. nocturnum* on the basis of chemistry and spectroscopy (29). Halim *et al*., in 1971, reported the presence of cotinine and myosmine (Fig. 5) in *C. nocturnum* for the first time from a non-nicotiana genus, along with nicotine and nor nicotine which are also reported in *C. diurnum* (30). Steroidal alkaloids like solanodine and solasodine although found to be present in *C. purpureum*, were absent in both *C. diurnum* and *C. auriculatum* (31-32).

Volatile Oils

Many of the species of the genus are grown for ornamental purposes and for floral scent production in perfumery. This property is attributed to the presence of volatile oils in *Cestrum*. Essential oils in *C. nocturnum* were examined by Gupta G N *et al*. in 1954 (33). Later on in 1972, Collins R. and others identified *trans*-2-hexenal, *cis*-3-hexenyl acetate, *cis*-3-hexenol and *trans*-2-hexenal as common constituent of volatile oils of *C. nocturnum* and *C. diurnum*. The oil of *C. nocturnum* has shown the presence of benzyl alcohol, ß-phenylethyl alcohol, eugenol and methyl anthranillate (34). Chao li *et al*. identified the presence of linalool and phenyl acetaldehyde as main contributor to characterstic flower fragrance of *C. nocturnum* (35). Further *cis*-jasmone, methyl jasmonate, 1,8-cineole, borneol, linalyl acetate, citronellyl propionate were also identified from the same species (36). Zhixing *et al*. analysed the volatile oil content of *C. nocturnum* in night time and found it to contain 1-heneicosyl formate, docasone, 2-monolinolein, dibutyl phthalate, 10-heneicosane, 1,3-dimethylbenzene, 1,2,3-trimethylbenzene, 4-ethyl 1,2-dimethylbenzene, tetracosane, 2,4-bis(1,1-dimethyl) phenol and 1-ethyl 2-methyl benzene (37).

The constituents of essential oils of *C. diurnum* mainly included palmitic acid, stearic acid and oleic acid possessing antimicrobial activity against pathogenic strains of gram positive *Staphylococcus aureus* and gram negative *Pseudomonas auereginosa* (38).

Terpenes

Different *nor*-isoprenoids and sesqiterpenes have also been identified from the genus. The hydroalcoholic extract of *C. parqui* leaves when fractionated with dichloromethane yielded C_{13} *nor*-isoprenoids, most of which were already established from different species like (6*R*,9*R*) 9-hydroxy-4-megastigmen-3-one isolated from Greek tobacco, (3*S*,7*E*,9*R*)-3,9-dihydroxy-5,7-megastigmadiene previously isolated as glucoside from *Bunias orientalis* leaves, (3*R*,6*R*,7*E*)-3-hydroxy-4,7-megastigmadien-9-one, a C_{13} *nor*-terpene isolated from *Vilburnum dilatatum* etc. Along with these a new *bisnor* sesquiterpene i.e., (2*R*, 6*R*, 9*R*)-2, 9-dihydroxy-4-megastigmen-3-one (fig. 6) was also isolated and characterized. The ethyl acetate fraction of hydralcoholic extract yielded (3*S*,5*R*,6*R*,7*E*,9*R*)-3,5,6,9, tetra hydroxyl-7-megastgmene, a C_{13} *nor*-isoprenoid; 26-*O*-(3'-isopentanoyl-ß-D-glucopyranosyl-5α-furost-20(22)ene-3ß, 26diol, a pseudosapogenin glycoside; 5α-spirostane-3ß,12ß,15α-triol, a spirostanol terpene and 1,2,2α,3,6,7,8,8α-Octahydro-7-hydroxy-2α,7,8-trimethylacenaphthylen-4(4H)-one, an unusual tricyclic sesquiterpene. (39-40). Ito *et al* in 1997 isolated a *nor* isoprenoid i.e., (6*E*,9*S*)-9-hydroxy, 4,6-megasigmadien-3-one and its geometric isomer for the first time from a natural source although they were earlier

obtained synthetically (41). Some of the terpene are shown to be phytotoxic and their activity was found to be similar to that of the herbicide pendemethalin. Recently Khaled Mohd. *et al*. have disclosed the presence of a white amorphous powder of megastigmane derivative named citroside B (Fig. 6) from the leaves of *C. diurnum* (42)

Triterpene i.e., ursolic acid is reported to be present in *C. diurnum*, *C. parqui* and *C. kunthi* leaves. Oleanolic acid, an isomer of ursolic acid (Fig. 7) has also been isolated and identified in *C. kunthi* leaves (13, 43-44).

Lignans

The presence of lignans in the genus cestrum is only recently explored from two species i.e., from *C. parqui* and *C. diurnum*.

Khaled Mohd. *et al*. have reported the presence of a novel *nor*lignan glycoside, cestrumoside (Fig. 6) along with epoxylignan glycoside berchemol-4-O-ß-glucopyranoside, lignan and neolignan glycosides liriodendrin, dehydrodiconiferyl alcohol-4-O-ß-glucopyranoside, (+)-lyoniresinol 3a-O-ß-glucopyranoside and (−)-lyoniresinol 3a-O-ß-glucopyranoside from the leaves of *C. diurnum* (42).

Hydroalcoholic extract of green *Cestrum* (*Cestrum parqui*) has shown the presence of sesquilignans, oxyneolignans and *nor*lignans. The *nor*lignan, trihydroxy-3,5-dimethoxy lig-7-eno-9`,7-lactone is most active of all in inhibiting shoot length of tomato by about 50%. The two sesquilignans are isomers i.e., (±)-herpetotriol, already reported from *Herpetospermum caudigerum*. Some diepoxylignans like (+)-pinoresinol, (+)-mediaresinol and (+)-syringresinol; epoxylignans like (+)-lariciresinol, and (+)-justiciresinol; the furanoid lignan like 5'-methoxy lariciresinol and (-)-berchemol and neolignans like (-)-simulanol, (±)dehydro coniferyl alcohol are also reported from *C. parqui*. All compounds are reported to be stimulant on shoot elongation of *C. album* and *P. oleraca*. The diepoxylignans are most active in *A. retroflexus* and *P. oleraca* germination while epoxylignans are toxic to it (45-46).

Phenolic compounds

The occurrence of chlorogenic acid, an ester of quinic acid and phenolic compound is reported in leaves of *C. aurantiacum*, *C. elegans* and *C. poeipigii*. Cinnamic acid and caffeic acid are hypothesized to be secondary precursors for the biosynthesis of chlorogenic acid. A new phenolic ester, cestreic acid (fig.8), which is caffeic acid ester of glucaric acid, has been identified from *C. euanthes* (47).

Investigations on the aerial parts of *C. lanatum* exhibited the presence of polyphenolic compounds. Turnock *et al*. has revealed the existence of N-*trans*-feroyl tyramine (fig.8) was also reported for the first time from the genus *Cestrum* (48).

Aqueous fraction of fresh leaves of *C. parqui* was found to contain low molecular weight phenols *viz*., 4-hydroxy benzaldehyde, 3,5-dimethoxy benzaldehyde, 4-hydroxy benzoic acid, vanillic acid, syringic acid, methyl 4-hydroxy benzoate, methyl vanillate, methyl syringate, triosol, 3'5'-dimethoxy-4'-hydroxy(2-hydroxy)acetophenone, methyl ferulate, caffeic acid, methyl caffeoate and N-(*p*-carboxy methyl phenyl)-*p*-hydroxy benzamide.

All phenolic compounds have shown slow inhibitory values on testing for possible phytotoxicity (49).

Flavones and flavonoids

Two flavones are described to be present in aqueous portion of *C. parqui* leaves and are characterized to be 4'-hydroxy-4-methoxy chalcone and quercetin (49).

Some flavonol gycosides have also been found in methanolic fraction of *C. nocturnum* leaves (fig.9) (50). An anthocyanine containing cyanine is found to be present in fruits of *C. hediondium* (51).

Vitamin D_3

Cestrum diurnum or day jasmine is particular species of genus in possessing a calcinogenic glycoside called 1, 25- dihydroxy cholecalciferol or 1α, 25 dihydroxy vitaminD3 (Fig. 10), that leads to vitamin D toxicity in livestock. Vitamin D_3 like activity in *C. diurnum* was initially reported by Krook *et al*. in 1975 (52). The presence of 1, 25-dihydroxy vitamin D_3 glycoside was then confirmed by development of radio-receptor assay for 1, 25-dihydroxy vitamin D_3 by which the plant factor showed identical results to pure 1, 25-dihydroxy vitamin D_3. However effects were slightly slow indicating that some *in-vivo* metabolism is needed. It was later assumed that the factor is present as a glycoside in position *O*-25 of the molecule and hydrolysis liberates an active fragment (53-54).

The activity was later on quantified, but different studies came up with different results ranging from 30,000 IU/Kg of cholecalciferol equivalent to about 100,000 IU/Kg. The large difference is accounted to be because of variation in exposure to sunlight of plants grown in different places (55-57).

PHARMACOLOGY

The genus cestrum is endowed with a number of medicinally important activities (Table2) such as antiinflammatory, antipyretic, antimicrobial, antioxidant, cytotoxic, antimalarial, molluscicidal etc. Some species are also used as herbicide because of their phytotoxicity.

The medicinal potential of the genus *Cestrum* was first realized by Peckolt *et al*. in 1909.

Some of the early works regarding pharmacological effects of saponins of cestrum species have reported that saponins of both *C. diurnum* and *C. nocturnum* possess cardiotonic property on isolated heart of guinea pigs and frogs. *C. diurnum* produces systolic contracture of frog heart. It causes an initial stimulation of amplitude of heart followed by a decrease till the heart stopped with the auricles still beating (58). The saponins differed from ouabin in that they did not show emetic property. The saponins of the two species differed from each other in that the saponin of *C. diurnum* causes no spasm of smooth muscle (59).

Antimicrobial activity

Because of the appearance of bacterial resistance to antimicrobial agents more efforts are being made to find alternate antimicrobial compounds. As some plants of the genus are used traditionally as anti-infective agent, pharmacological works to reinforce the same fact have been done.

The alcoholic extract of leaves of *C. auriculatum* (Hiever santa) is reported to be potentially active against *Staphylococcus capititis*, *Streptococccus pneumoniae*,

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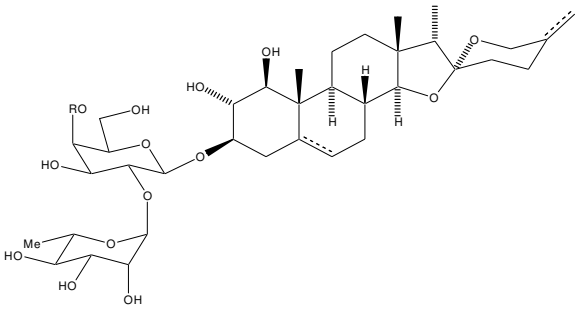
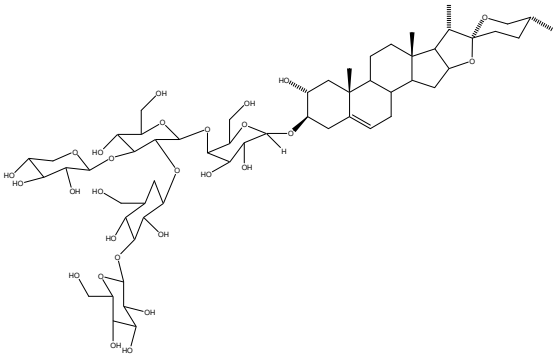
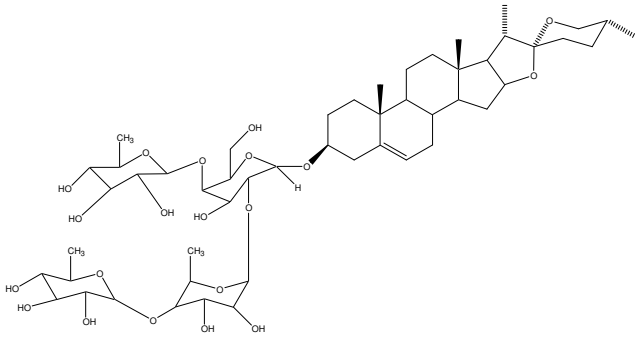


	R	A/B	
1	*H*	-	$\Delta^{5, 25(27)}$
2	*H*	-	Δ^{5}
3	*H*	*trans (H-5α)*	$\Delta^{5, 25(27)}$
4	*H*	*trans (H-5α)*	-
5	*β-D-Glcp*	-	$\Delta^{5, 25(27)}$



Nocturnoside A



Nocturnoside B

Fig. 1: Structures of steroidal saponins from Cestrum sendtenerianum

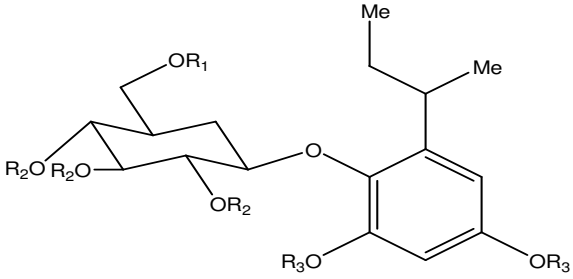


Fig. 2: Sturctures of steroidal saponins from Cestrum nocturnum

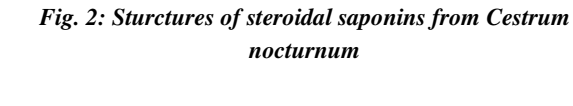


Fig. 3: Structure of Cesternoside A and B

A R1 = R2 = R3 = H
B R1 = Ac, R2 = R3 = H

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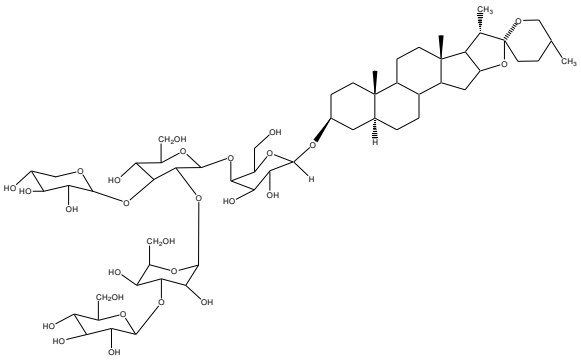
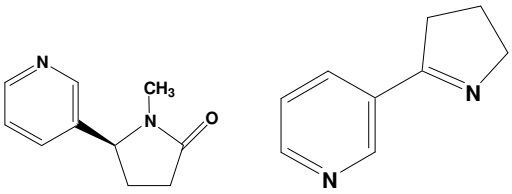
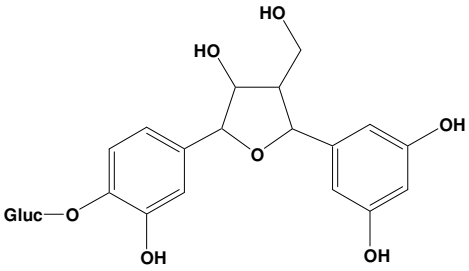


Fig. 4: Structure of Diurnoside 1

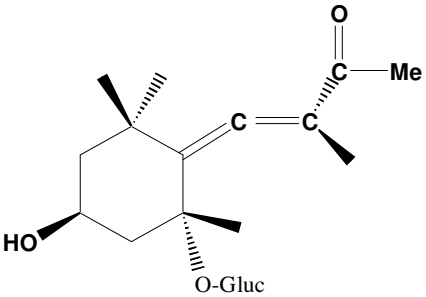


Cotinine *Myosmine*

Fig. 5: Structures of noted Alkaloids from Cestrum

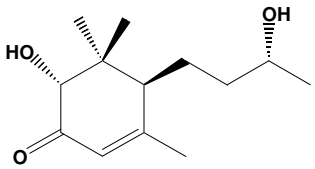


Cestrumoside



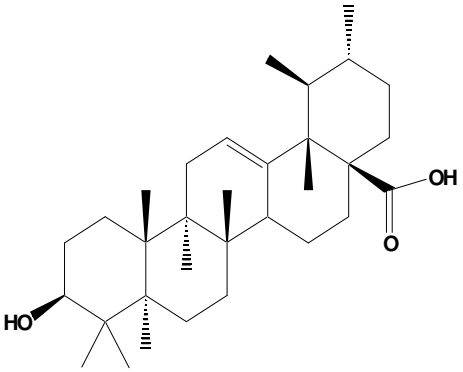
O-Gluc

Citroside B

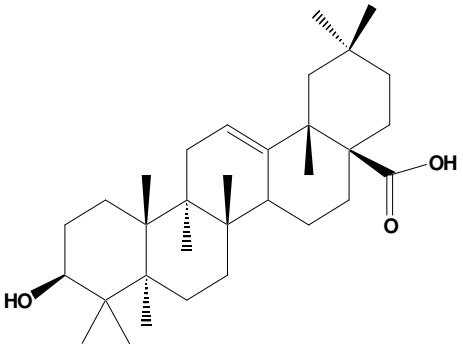


(2R, 6R, 9R) 2, 9-dihydroxy-4-magastigmen-3-one

Fig. 6: Structures of novel Lignans from Cestrum



Ursolic Acid



Oleanolic acid

Fig. 7: Structures of Triterpenes from Cestrum diurnum

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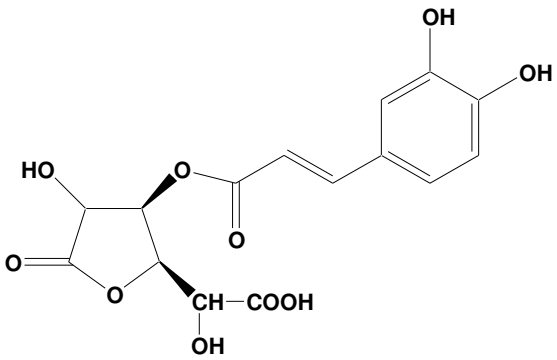
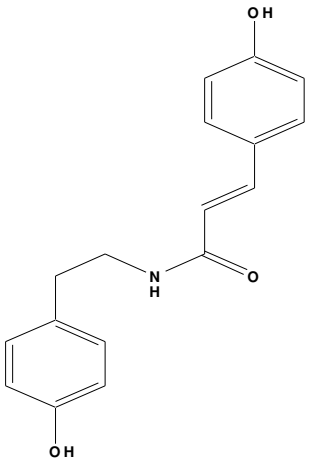
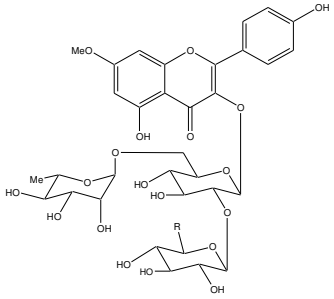


Cestreic Acid

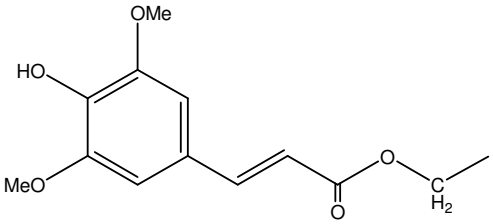


N-trans-feroyl tyramine

Fig. 8: Structures of unusual phenolic compounds from Cestrum

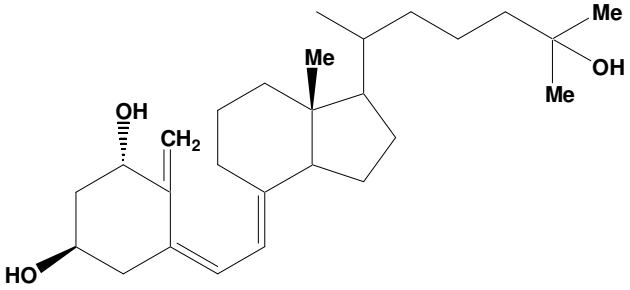


I: R =



II:R = H

Fig. 9: Structures of Flavonol glycosides from Cestrum nocturnum.



1α, 25-dihydroxycholecalciferol

Fig. 10: Structure of Vitamin D_3

Table 1: Phytochemical constituents of various Cestrum species

Species	Chemical Constituents
C. diurnum	***Saponins**:* Diurnoside, tigonin, tigogenin. ***Volatile oils**: trans*-2-Hexenal, *cis*-3-hexenyl acetate, *cis*-3-hexenol, *trans*-2-hexenol, palmitic acid, stearic acid, oleic acid. ***Terpenes:*** Ursolic acid. ***Lignans:*** Berchemol-4'-O-β-glucopyranoside, liriodendrin, dehydrodiconiferyl alcohol-4-O-β-glucopyranoside, (+) and (–)-lyoniresinol 3a-O-β-glucopyranoside, citroside B, cestrumoside. ***Alkaloids**:* Nicotine, *nor* nicotine. ***Others**:* Vit-D_3 and its glycoside.
C. nocturnum	**i** Yuccagenin, tigogenin, nocturnoside A & B, cesternoside A & B, (25*R*)-2α,17α-dihydroxyspirost-5-en-3*β*-yl *O*-*β*-D-glucopyranosyl-(1→2)-*O*-[*β*-D-xylopyranosyl-(1→3)]-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-galactopyranoside. (25*R*)-2α,15*β*-dihydroxyspirost-5-en-3*β*-yl *O*-*β*-D-glucopyranosyl-(1→3)-*O*-β-D-glucopyranosyl-(1→2)-*O*-[α-D-xylopyranosyl-(1→3)]-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-galactopyranoside. (25*R*)-2α,17α-dihydroxyspirost-5-en-3*β*-yl *O*-*β*-D-glucopyranosyl-(1→3)-*O*-*β*-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1→3)]-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-galactopyranoside. (25*R*)-2α-hydroxyspirost-5-en-3*β*-yl *O*-α-L-rhamnopyranosyl-(1→2)-*O*-[*O*-α-L-rhamnopyranosyl-(1→4)-α-*L*-rhamnopyranosyl-(1→4)]-*β*-D-glucopyranoside. (24*S*, 25*S*)-24[(β-D-glucopyranosyl) oxy]-2α-hydroxyspirost-5-en-3β-yl *O*- β-D glucopyronosyl-(1→3)-*O*- β-D-glucopyranosyl-(1→2)- *O*-[β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- *β*-D-galactopyranoside. (25*R*)-26-[(β-D glucopyronosyl)oxy]- 2α-hydroxy-22α-methoxy furost-5-en-3 *β*-yl *O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- *β*-D-galactopyranoside. (25*R*)-26-[(β-D glucopyronosyl)oxy]- 2α-hydroxy furosta-5,20(22)-dien-3 *β*-yl- *O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)- *O*-[β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- *β*-D-galactopyranoside. ***Cholestane glycosides**:* (25*R*)- 3 *β*-[(*O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)- *O*- [β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- β-D-glactopyranosyl)-oxy]-26-[(β-D glucopyronosyl)-oxy]-2α-hydroxycholesta-5,17-diene-16,22-dione. (25*R*)- 3 *β*-[(*O*- β-D-glucopyranosyl-(1→2)- *O*- [β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- *O*- β-D-glactopyranosyl)oxy]- 26-[(β-D glucopyronosyl)-oxy]-2α-hydroxycholesta-5,17-diene-16,22-dione. ***Pregnane glycosides**:* 3β-[(*O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)- *O*-[β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- β-D-glactopyranosyl)-oxy]-16 β-[[(4*R*)-5-(β-D glucopyronosyloxy)-4-methyl-1-oxopentyl] oxy]-2 α-hydroxypregn-5-en-20-one. 3β-[(*O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)- *O*- [β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- β-D-glactopyranosyl)-oxy]- 2 α-hydroxypregna-5,16-dien-20-one. 3β-[(*O*- β-D-glucopyranosyl-(1→3)- *O*- β-D-glucopyranosyl-(1→2)- *O*- [β-D-xylopyranosyl-(1→3)]- *O*- β-D-glucopyranosyl-(1→4)- β-D-glactopyranosyl)-oxy]- 2α,16β-dihydroxypregn-5-ene-20-carboxylic acid γ-lactone. ***Flavonol glycosides**:* 4′,5-Dihydroxy-7-methoxyflavonol 3-*O*-[6-*O*-(*E*)-3,5-dimethoxy-4-

	hydroxycinnamoyl-*β*-D-glucopyranosyl]-(1→2)-*O*-[α-L-rhamnopyranosyl-(1→6)]-*β*-D-glucopyranoside, 4′,5-dihydroxy-7-methoxyflavonol 3-*O*-*β*-D-xylopyranosyl-(1→2)-*O*-[α-L-rhamnopyranosyl-(1→6)]-*β*-D-glucopyranoside. ***Volatile oils****: trans*-2-Hexenal, *cis*-3-hexenyl acetate, *cis*-3-hexenol, *trans*-2-hexenol, linalool, eugenol, β-phenylethyl alcohol, *cis*- jasmone, methyl jasmonate, 1, 8-cineole, borneol, linalyl acetate, citronellyl propionate, methyl anthranillate, 1-heneicosyl formate, docosane, 2-mono linolein, dibutyl phthalate, 10-heneicosane, tetracosane. ***Alkaloids****:* Nicotine, nor nicotine, cotinine, myosmine.
C. parqui	***Saponins:*** Gitogenin, digitogenin, digallogenin, (25R)-isonautigenin, neotigogenin, parquinoside, parquisoside A & B**.** ***C_{13} norisoprenoids:*** (6*R*,9*R*) 9-hydroxy-4-megastigmen-3-one, (3*R*,6*R*,7*E*)-3-hydroxy-4,7-megastigmadien-9-one, (6*R*,7*E*,9*R*) - 9 - hydroxy - 4,7 - megastigmadien-3-one, (3*R*,6*R*,7*E*,9*R*)-3,9-dihydroxy-4,7-megastigmadiene, (3*S*,7*E*,9*R*)-3,9-dihydroxy-5,7-megastigmadiene, (3*S*,5*R*,6*S*,7*E*)-5,6-epoxy-3-hydroxy-7-megastigmen-9-one., (3*S*,5*R*,6*R*,7*E*,9*R*)-3,5,6,9-tetrahydroxy-7-megastigmene, (2*R*,6*R*,9*R*)-2,9-Dihydroxy-4-megastigmen-3-one, (3*S*,5*R*,6*S*,7*E*,9*R)*-5,6-epoxy-3,9-dihydroxy-7-megastigmene, (7*E*,9ξ)-9-Hydroxy-5,7-megastigmadien-4-one, (6*E*,9*S*)-9-Hydroxy-4,6-megastigmadien-3-one, (6*Z*,9*S*)-9-Hydroxy-4,6-megastigmadien-3-one. ***Sesquiterpene:*** 1,2,2α,3,6,7,8,8α-Octahydro-7-hydroxy-2α,7,8-trimethylacenaphthylen-4(4H)-one. ***Spirosatnol terpene:*** 5 α -Spirostane-3 β ,12 β ,15 α –triol. ***Triterpene****:* Ursolic acid. ***Lignans****:* (+)-Pinoresinol, (+)-mediaresinol, (+)-syringresinol, (+)-lariciresinol, (+)-justiciresinol, 5'-methoxy lariciresinol, (-)-berchemol, (-)-simulanol, dehydro coniferyl alcohol, threo and erythro-4′,4″,7″,9″-tetrahydroxy-3,3′,3″,5′-tetramethoxy-4,8″oxy-7,9′:7′,9-diepoxylignan, herpetotriol. ***Flavones:*** 4′-Hydroxy-4-methoxy chalcon, quercetin. **Phenolics**: 4-Hydroxy benzaldehyde, 3,5 dimethoxy benzaldehyde, 4-hydroxy benzoic acid, vanillic acid, syringic acid, methyl-4-hydroxy benzoate, methyl vanillate, methyl syringate, triosol, 3′-5′ dimethoxy -4′-hydroxy(2-hydroxy)acetophenone methyl ferulate, caffeic acid, methyl caffeoate, N-(p-carboxymethylphenyl)-p-hydroxybenzamide
C. purpureum	***Alkaloids****:* Solandine, solasodine.
C. aurantiacum	***Phenolics****:* Chlorogenic acid.
C. sendtenerianum	***Saponins****:* 1β, 2α-Dihydroxyspirosta-5, 25(27)-dien-3β-yl *O*-α-D-rhamnopyranosyl-(1→2)-β-L-galactopyranoside. (25R)-1β,2α-dihydroxyspirost-5-en-3β-yl *O*-α-L-rhamnopyranosyl-(1→2)-β-D-galactopyranoside. 1β,2α-dihydroxy-5α-spirost-25(27)-en-3β-yl *O*-α-L-rhamnopyranosyl-(1→2)-β-D-galactopyranoside. (25R)-1β,2α-dihydroxy-5α-spirostan-3β-yl *O*-α-L-rhamnopyranosyl-(1→2)-β-D-galactopyranoside. 1β,2α-dihydroxyspirosta-5,25(27)-dien-3β-yl *O*-α-L-rhamnopyranosyl-(1→2)-*O*-[β-D-glucopyranosyl-(1→4)]-β-D-galactopyranoside. spirosta-5,25(27)-diene-1β,2α,3β,12β-tetrol, spirosta-5,25(27)-diene-1β,2α,3β,12β-tetrol 3-*O*-β-D-galactopyranoside.
C. laevigatum	***Saponins:*** Gitogenin, digitogenin.

C. elegans	***Saponins:*** Gitogenin, tigogenin.
	Phenolics: Chlorogenic acid.
C. kunthii	***Triterpenes****:* Ursolic acid.
C. poepigii	***Phenolics****:* Chlorogenic acid.
C. euanthes	***Phenolics****:* Cestreic acid.
C. lanatum	***Phenolics:*** N-trans feroyl tyramine.

Table 2: Ethnopharmacological and Pharmacological uses of Cestrum species

Species	Ethnopharmacological use	Pharmacological use
Cestrum diurnum	Antimalarial.	Cardioactive, antibacterial, antimalarial, insect attractant, antifungal, calcinogenic
Cestrum nocturnum	Antiinflammatory, antibacterial, antiepileptic, antimalarial.	Cardioactive, insect attractant, anticancer, antifungal.
Cestrum parqui	Antiinflammatory, antipyretic.	Antiinflammatory, antipyretic, insecticidal, molluscicidal, antipyretic, herbicide, spermicidal
Cestrum auriculatum	Antiinflammatory, antipyretic insecticidal, antiallergic, astringent.	Antiinflammatory, antibacterial, antifungal.
Cestrum sendtenerianum	-	Anticancer
Cestrum laevigatum	Antiinflammatory, antispasmodic, diuretic, antiulcer.	-
Cestrum purpureum	-	Antiinflammatory, insecticidal.
Cestrum parvifolium	Antipyretic, antiulcer.	Anticancer

Streptococcus agalactiae and *Bracteroides fragilis* (60). The ethanolic extract of leaves also showed potent antifungal activity against *C. albicans*, *Tricophyton mentagrothytes*, *Microsporum gypseum* and *Sporothrix schenckii* (9).

Similarly, volatile oils of *C. diurnum* have been described to possess antimicrobial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Essential oil of *C. diurnum* having a strong anti bacterial agent may be considered as a potential source in search of newer drugs (38).

Antiinflammatory activity

C. parqui and *C. auriculatum* are used traditionally as antidiarrhoeal because of their antimicrobial and anti-inflammatory effect. Aerial parts of *C. parqui* are capable of inhibiting carageenin induced paw-oedema and ADP (adenosine diphosphate) and PAF (platelet activating factor) induced platelet aggregation (61). The effect has been attributed to parquinoside A and B. Infusions of *C. parqui* has been found to be potent antiinflammatory agent, the methanolic extract of which is also active but to a lesser extent (4).

Ursolic acid, a pentacyclic triterpenoid, present in *C. diurnum* possess anti-inflammatory property. It acts by inhibiting T-Helper-1 (T-h1) i.e., IL-1, IFN-α and TNF-γ (pro-inflammatory cytokines) and by increasing T-helper-2 (T-h2) cytokines (anti-inflammatory agent) and thus act as immunomodulator explaining its use in arthritis (62).

Anticancer activity

Cestrum is rich in saponin content which possess a number of important biological properties. A spirostanol triglycoside of *C. sendtenerianum* has shown weak cytotoxic activity on human promyelolytic leukaemia cell (HL-60) with IC_{50} value of 7.7µg/ml (17). Brine shrimp lethality test performed to determine cytotoxicity has shown a LD_{50} of 6.907µg/ml for n-butanol extract of *C. diurnum* while LD_{50} of 128.711µg/ml for nocturnoside (a steroidal saponin of *C. nocturnum*) and 420µg/ml for whole plant extract of *C. parvifolium*. Possible cytotoxicity of *C. parvifolium* was tested by inhibition of cell division test (ICDT) using sea urchin and by potato disk bioassay (inhibition of crown gall tumours induced by *A. tumefacians*). While, no activity was observed in ICDT, a 24% inhibition was seen in potato disk bioassay (10).

Reports on the cytotoxicity studies of steroidal saponin and flavonoid glycoside of *C. nocturnum* by Yoshihiro M. *et al*. has ascertained that the flavonoid glycosides are not active (LD_{50}>400) while saponins showed activity predominantly against human oral squamous cell carcinoma (HSCZ cell) but was weakly active against normal human gingival fibroblast (HGF). Powder of *C. nocturnum* has anticancer activity against liver, stomach, intestinal, oesophageal, breast, lungs, and cervical cancer and even in melanoma and leaukemia (50, 63).

Insecticidal activity

There is a growing interest in natural product as insecticide either as a model to design new class of insecticide or as an object of genetic modification of crop species. The endocrinological system of insects is believed to be highly susceptible to disruption. Among the main protein targets for development of insecticides is insect steroid hormone especially molting hormone, ecdysone and ecdysteroid receptor. *C. nocturnum* (seeds), *C. parquii* (seeds, leaves, roots, stem) and *C. purpureum* (seeds) were tested for possible ecdysteroid agonist/ antagonist effect. While seeds of *C. parquii* showed cytotoxic effect in both agonist and antagonist bioassay, leaves of *C. purpureum* showed weak agonist activity but *C. nocturnum* was inactive (64).

C. parquii extracts have shown to possess anti-feedant effect on various damaging Lepidoptera (viz. *Pieris brassicae* L., *Spodoptera littoralis*, *Bois dural* and *Schisteocerca gregaria*); the effect being proportional to extract concentration in the diet. *C. parquii* is known to delay larval growth of *Spodoptera littoralis* (an insect pest of tomato) (65-67). Further the aqueous extract i.e., the polar components of *C. parquii* have shown to possess high toxicity to neonate larva when ingested through diet, inhibiting population at a concentration above 0.6%. Aqueous extract diminishes the reproductive potential of adults implying significant effect on offspring (68).

C. diurnum is also reported to be efficacious against larval anopheline mosquito suggesting a possible role in combating spread of malaria (69).

The pathology of effect can be hypothesized to indicate interaction of saponins with membrane cholesterol, as the insecticide potency decreases on addition of cholesterol to the diet. Thus they cause membrane destabilization and cell death (70).

Molluscicidal activity

A monodesmodic saponin viz. neotigogenin of *C. parqui* is reported to possess molluscicidal activity against *Biomphalaria alexandria* snails and *Theba pisana* snails. The activity is conferred only when the substance is used in crystal form suggesting that it acts by irritating mucus membrane because of its detergent nature. This leads to dehydration, excessive water loss and death (15, 71).

Phytotoxic (herbicidal) activity

Secondary metabolites isolated from higher plants could be useful as natural herbicides. Several studies have shown *C. parqui* to be active against *Lactuca sativa*, *Lycopersicon esculentum*, *Allium cepa*, *Amaranthus retoflexus*, *Chenopidum album* and *Portulaca oleraca*. The activity is attributed to the presence of low molecular weight phenols, flavones, lignans and other C_{13} *nor*-isoprenoids. Lignans are most active in influencing seed germination and radical elongation. This effect might be due to the variation in amino acids involved in photorespiration of lettuce plants. The results indicate that phytotoxic activity is greater than most of the commercially used herbicides suggesting their potential as natural herbicide (40, 45, 46, 49, 72).

Other pharmacological applications

Leaf extract of *C. parquii* produced dose and time dependent inhibitory effect on sperm motility and viability with the maximal effect at 250µg/ml. The study reveals a potential spermicidal effect of the extract *in-vitro* suggesting its possible use as an antifertility agent (73).

C. nocturnum shows sensitivity towards SO_2, indicating its usefulness for monitoring SO_2 pollution. Fumigation by SO_2 caused increase in –SH content of the plants (74-75).

Several species possess antioxidant activity. Certain species are used in nasal formulations for treating Alzheimer's disease with the active component containing eugenol, its salts or its isomers for improving memory and adjusting permeability of blood brain barrier (76-77).

***CESTRUM DIURNUM*: A CALCINOGENIC PLANT**

The day jasmine (*C. diurnum*) possesses Vitamin D_3 like activity. Some other plants of family Solanaceae *viz. Solanum malacoxylon*, *Nierembergia veitchii*, *Solanum torvum*, *Solanum esuriale*, *Solanum verbascifolium* etc. also come under the category of calcinogenic plants.

The biological activity of *Cestrum diurnum* was studied in connection with occurrence of calcinosis in grazing animals in Florida and it is reported to overcome inhibitory effects of high strontium diet fed to chicks. Since the high strontium diet blocks conversion of 25-hydroxy cholecalciferol to 1α, 25-dihydroxy cholecalciferol it was postulated to contain Vitamin D_3 like activity (78). *C. diurnum* causes osteoporesis and hypercalcitonism in cattle due to the action of Vitamin D_3. Even in horses, elevated calcium levels, calcinosis of elastic tissues and other abnormalities of mineral metabolism are found attributed to *C. diurnum* (79, 52). Even in lambs and pigs, addition of 3% *C. diurnum* leaf meal is reported to cause hypercalcemia, hypophosphatemia, retarded cell differentiation of cartilages and atrophy of parathyroid glands. The activity was found to be similar to ingestion of Viatmin D_3, but pigs were able to tolerate higher amount of Viatmin D_3 than *C. diurnum* leaf powder as in the latter case the feed back control of 1α-hydroxylase is also bypassed (80-81).

Though the calcinogenic plants are amongst the most noxious plants to animals they can also be beneficial. It is hypothesized that young, rapidly growing, broiler chicken are not able to produce 1α,25-dihydroxy Vitamin D_3 from dietary cholecalciferol rapidly and efficiently enough to meet their need for maximum Ca absorption and bone development. This inability makes the broiler chicken more susceptible to tibial dyschondroplasia due to insufficient Ca absorption resulting in under optimum body weight. The rate of egg production and egg shell strength decreases as the hen ages leading to about 12% egg losses due to poor egg shell quality. This is attributed to progressive deterioration in the ability of the hen's liver to hydroxylate Vitamin D_3 to 25-hydroxy Vitamin D_3. The economy of Ca utilization is under the control of Vitamin D_3, particularly its active metabolite 1, 25-dihydroxy cholecalciferol. The 1, 25 dihydroxy Vitamin D_3 available in the market is prohibitively expensive for supplementing the broiler feed. Incorporation of *C. diurnum* as a source of 1, 25-dihydroxy Vitamin D_3 could improve the Ca absorption in broilers and supplementation of *C. diurnum* leaves enhanced the serum Calcium, body weight, tibia weight, density and strength resulting in the disappearance of tibial

dyschondroplasia without producing lesions of toxicity in any soft tissue. It has been shown that egg specific gravity, shell weight, percentage of shell, and egg breaking strength are significantly increased with the supplementation of C. diurnum leaf powder. It restores calcium binding protein synthesis and increases calcium absorption in cholecalciferol deficient chicks suggesting that the incorporation of *C. diurnum* leaf powder in poultry feed could be beneficial to the poultry for benefiting the farmer effectively (56, 82-84).

Vitamin D deficiency can occur in Indian population particularly in overcrowded, illventilated and polluted environment. Hence Vitamin D activity of plant can be explored as a cheap source. *Cestrum diurnum* can be used for preparation of enriched calcitriol containing extracts. Calcitriol is used for the treatment of rickets, osteoporosis, psoriasis and renal Osteodystrophy in patients on dialysis. The plant material can be formulated into pharmaceutical and veterinary compositions of the calcitriol extract in oral and external dosage forms for treatment of osteoporosis, psoriasis and renal osteodystrophy in humans and oral formulations of the extract in dry powder form for admixture with poultry feed to increase meat weight and to improve FCR (food conversion rate) in broilers/poultry (85).

TOXICITY

Several species of the *Cestrum* are reported to be containing toxic constituents that can lead to poisoning. While *C. diurnum* may lead to calcinosis, *C. parquii* because of its toxic constituents is used as herbicide and insecticide. Parquin, carboxyparquin and other kaurene gycosides of *C. parquii* are poisonous to cattle (86). The crude aqueous extract of the species are toxic at 24 hrs. The LD_{50} is 0.81 gm/kg for mice producing severe periacinar coagulative necrosis of hepatocytes as well as acute necrosis of proximal renal tubular epithelium. Elevated levels of plasma aspartate transaminase and prolonged prothrombin time are demonstrated in experimental cases. The poisoning is mainly due to primary hepatotoxicity (87, 88).

C. axillare, a rich souce of saponins, is toxic to livestock and is used as pesticide. It inhibits oxidative phosphorylation in rat liver mitochondria (89).

C. laevigatum is responsible for wide spread poisoning of grazing animals. At doses of 5 to 10 gm/kg/day it produces signs of ataxia, muscle tremors, hypersensitivity and intermittent chewing. Hepatosis is characterized by midzonal coagulative necrosis whereas haemorrhage and congestion are also produced at higher doses. In sheep it produces elevation of serum aspartate transaminases, lactate dehydrogenase and γ-glutamyl transferase indicating liver involvement. Liver lesions in animals include disappearance of hepatocytes and collapse of reticulin stroma in centrilobular areas (90-91).

CONCLUSION

The botanical, ethnopharmacological, phytochemical, pharmacological and toxicological information on the genus *Cestrum* is reviewed and congregated. Survey of literature reveals the presence of saponins (steroidal) mostly in glycosylated forms, lignans and terpenes (norlignan, C_{13} *nor*-isoprenoid, epoxylignan and sesquilignan), alkaloids, phenols and volatile oils.

(25*R*)-isonautigenin is an unusual steroidal sapogenin used as taxonomic marker in *C. parqui*. The high concentration of saponins is responsible for cardiac activity and even insecticidal activities. The volatile oils account for the use of many species in perfumery as well as for ornamental purposes. These volatile oils are antimicrobial and insect attractant governing their pharmacological use. The triterpene, ursolic acid, is a potential antiinflammatory agent, further being immunomodulatory it can be used in arthritic conditions.

Most of the species in the genus are toxic implying their potential use as insecticide, molluscicide and herbicide. The selective toxicity shown by certain species has accounted for their use as antimicrobial and anti cancer agents.

The species *C. diurnum* is typical in the genus possessing calcinogenic potential. The herb is capable of inducing calcinosis in livestock. This can alternatively be used as a cheap source of Vitamin D for poultry feed and animals. It may even be substituted as dietary source of Vitamin D_3 for deficient people in underdeveloped nations.

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