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A review on phytochemical constituents and pharmacological potential of *Calotropis procera*

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Calotropis procera is locally known as *Aak* or *Madar* in Hindi, milk weed in English and belongs to the family Apocynaceae and subfamily Asclepiadoideae. Although a wasteland plant, it is of sacred use as its flowers are offered for worshipping Lord Shiva, a Hindu God. Tribes all over the world use the plant in treatment of various diseases like snake bite, body pain, asthma, epilepsy, cancer, sexual disorders, skin diseases and many more. This plant contains various phytoconstituents such as flavonoids, terpenoids, cardenolides, steroids oxypregnanes *etc.* Though literature searches reveal many reviews about ethnomedicinal uses, chemical composition and pharmacological activities, no recent papers are available that provide an overview of the therapeutic potential and toxicity of *Calotropis procera*. Hence, the insight of this review is to provide a systemic summary of phytochemistry, pharmacology, toxicology and therapeutic potential of *Calotropis procera* and to highlight the gaps in the knowledge so as to offer inspiration for future research.

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1. Introduction

Calotropis belongs to the Apocynaceae family, which is commonly known as milkweed or *Aak*. Plants of this genus are known as milkweeds due to the exudation of white and sticky latex from different plant parts. Genus *Calotropis* has two common species *viz. Calotropis procera* (Rakta arka) and *Calotropis gigantea* (Sweata arka), which are described as possessing vital pharmacological properties in Ayurvedic toxicology and therapeutics. Other species are *C. sussuela* and *C. acia*.

Calotropis procera (Aiton) W. T. Aiton is an erect, soft wooded, evergreen perennial shrub and commonly known as 'Sodom apple' or 'Madar shrub'. In Bengali, it is known as '*Akanda*' and in Hindi as '*Aak*'. It manifests its wide utilization in Indian, Arabic and Sudanese traditional medicinal systems for healing global range of diseases.

The Dangas tribe in Gujarat,[1] Singhum tribe in Bihar,[2] tribes of Ghatigaon forest in Gwalior,[3] tribes of Andhra Pradesh[4] have been using this plant in the treatment of various disorders such as ear pain, cough, fever, abdominal pain, dysentery and elephantiasis.

Calotropis procera is more toxic than *Calotropis gigantea* and assumed to be even more poisonous than cobra venom. It is interesting that the cobra and other poisonous snakes cannot

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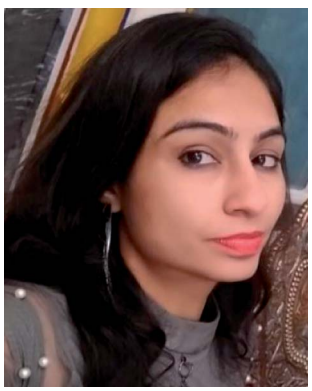

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even bear its smell; hence snake charmers of Bengal use this plant for controlling or taming cobras.[5]

Earlier reviews[6–16] have discussed on phytochemistry, ethnobotany and pharmacological potential of *Calotropis procera*. Review on *Calotropis* species[17–20] comparing *procera* and *gigantea* have deliberated their therapeutic importance. The present review summarizes the phytochemistry, pharmacology, commercial aspects, traditional medicinal uses, toxicology and recent studies on *Calotropis procera*. The future scope of *Calotropis procera* has also been affirmed with a view to establish its multiple biological activities and mode of action.

2. Unique properties of *Calotropis procera*

2.1 Toxicity

C. procera finds its widespread distribution over many regions of the globe. What makes its phytochemistry interesting is the exudation of milky and toxic latex from all the plant parts. The latex is referred to as vegetable mercury as it shows mercury like effects on human body.[21]

Every part of this plant is toxic, but stem (latex) and roots are more poisonous than leaves. The leaves of this plant have three toxic glycosides calotropin, calotoxin and uscharin, whereas its latex contains calotropin, calotoxin and calactin, which are caustic and considered poisonous in nature. Besides this, the concentration of calactin, which is a toxic glycoside, gets increased as defense mechanism on encounter of grasshopper or insect attack and this is the rationale behind the plant not being consumed by cattles or other grazing animals.[22] Other than this, osmotin, a laticifer protein purified from latex also provides protection to plant against phytopathogens.[23] Its milk is irritant, neurotoxic and has anticholinergic activity, which causes toxicity and fatal complications. Madar juice and latex has bitter taste and a burning pain which causes salivation, stomatitis, vomiting, diarrhoea, dilated pupils, titanic convulsion, collapse and death. The fatal period varies from half an hour to eight hours.[24] If latex enters into the eye, it causes kerato-conjunctivitis, corneal edema and dimness of vision without any pain.[25–27] Some cases showed permanent endothelial cell damage, which was evident after three weeks.[5,28] *C. procera* was found toxic at the dose of 100 mg kg^{-1} to chick embryo. Its toxicity caused hepatocellular degeneration in liver, brain congestion, dilation of central veins, sinusoids, underdeveloped lung and kidneys.[29] Hence, bearing in mind the toxic effects of certain extracts and glycosides, further studies should be focused to explain toxicity and safe use of *C. procera*.

2.2 Ability to survive under extreme climatic conditions

Another interesting aspect of this plant is its ability to tolerate adverse environmental conditions like scarcity of water, arid environment or any kind of harsh climate. To understand this, Akhkha[30] studied the effect of stress caused due to water scarcity and found that photosynthetic machinery remained uninfluenced, infact rate of photosynthesis gets raised at mild water

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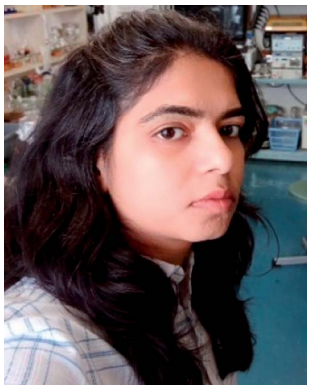

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Table 1 Ethnomedicinal applications of *C. procera*

Plant part	Disease	Preparation/administration	References
Root/root bark	Amoebic dysentery	Paste with/without opium taken orally	44–46
	Cholera	Powder orally taken or paste along with black pepper and ginger juice	44
	Dysentery	Powder orally taken	47
	Elephantiasis and hydrocele	Paste mixed with fermented rice water applied on the affected area	48–50
	Epilepsy	Grounded with goat milk and used as nasal drops	46
	Indigestion	Powder orally taken	47
	Jaundice	Taken with rice in grounded form	51
	Neuritis	Orally administered with cow butter	46
	Rheumatism	Powder taken with milk and sugar	48
	Snake bite	Powder orally taken. Paste applied on wounds and internally taken with ghee	47 and 52
	Spider and insect bite	Powdered and taken with vinegar	48
	Syphilis	Root bark powder taken orally	46
Latex	Boils	Applied externally	46
	Black scar on the face	Applied along with turmeric paste	44
	Ascites	Applied externally	47
	Liver and spleen disorder	Taken after dilution	47
	Leprosy	Applied on the affected area	47
	Migraine	Applied on the affected side vein of forehead	44
	Piles (haemorrhoids)	Applied externally	44
	Dog/jackal bite	Applied on wound	44 and 48
	Ring worm	Applied externally	46
	Scabies	Applied externally	46
	Snake bite	Applied on wounds or taken orally (20–30 drops for adults and 15–20 for infants)	46
		Five drops with 50 drops of distilled water injected hypodermally	46
	Syphilis, leprosy and odema	Applied externally with sesame oil	48 and 50
	Tooth ache	Applied on affected tooth	48 and 50
	Vertigo	Applied on affected parts	53
Leaf	Cold, cough, asthma and bronchitis	Warmed along with ghee and bandaged on the chest of infants	44
	Calculus, liver and spleen disorder	Powder taken orally	48
	Ear ache or ear troubles	Juice along with fermented boiled rice water used as ear drops	50
	Eczema and skin eruptions	Applied externally along with turmeric and sesame oil	48, 50 and 53
	Enlargement of abdominal viscera and spleen	Oral administration of powder	48 and 51
	Gonorrhoea	Decoction used for washing and taken orally	51
	Inflammatory swellings	Covered on affected part after warming	51
	Joint pain	Powder taken	47
	Malaria and intermittent fever	Oral administration of fresh juice	46, 49 and 51
	Body pain	Paste applied after warming	51
	Paralysis and sciatica	Massaged after preparing decoction with sesame oil	47
	Snake bite	Oral administration of fresh juice	50
	Ulcers, wounds, sores	Powder orally administered or external application	47, 49 and 51
Flowers	Health tonic	Oral administration of powder	47
	Cough	Burnt to produce ash, then taken with honey	44
	Rat bite	Oral administration of powder	47 and 49
	Dog/jackal bite (rabies)	Seven tepals chewed with fine rice on seventh day of biting, continued for seven days decreasing one tepal everyday	44
	Feet pain	Decoction used for fomentation	46
	Epilepsy	Oral administration of paste with black pepper	46
	Asthma and bronchitis	Fruit taken with jaggery	3
	Liver and spleen disorder	Administered along with milk	46
Fruit	Eye disorder	Decanted ash water applied on eye lids	44
	Anemia	Mixed with same quantity of red chilli, mineral salt and taken with milk.	46
Whole plant	Rheumatic pain and hyperacidity	Paste directly taken	44
Young twigs	Purgative	Juice taken	54

Table 2 Brief summary of the pharmacological properties

S. no.	Pharmacological activities	Parts/extracts/possible chemical constituents	References
1	Wound healing potential	Latex: aqueous extract	67
		Latex	68
		Bark: ethanolic extract	69
		Leaves: aqueous extract	70
		Bark: aqueous extract	71
2	Anticoccidial activity	Dried leaves powder	72
3	Toxicity activity	Leaves: aqueous extract	73 and 74
		Leaves and stem bark extracts	75
		Leaves and stem: ethanolic extract	29
		Leaves: ethanolic extract	79
4	Biopesticidal/insecticidal activity	Leaves: extract	80 and 81
		Leaves: methanolic extract, latex protein fraction, flavonoids (quercetin-3-*O*-rutinoside)	35
5	Antimycoplasmal activity	Leaves: acetone extract	82
6	Hepatoprotective activity	Root bark: methanolic extract	83
		Flowers: hydroethanolic extract	84
		Roots: chloroform extract	85
7	Antimicrobial/antibacterial activity	Leaves: methanolic extract, flavonoids (quercetin-3-*O*-rutinoside)	86
		Leaves and latex: ethanol, aqueous, and chloroform extract	87
		Leaves and stem: aqueous, ethanolic, methanolic extract	88 and 89
		Endophytic fungi of *C. procera*	90
		Seeds: chloroform extract	91
		Root: pet. ether, methanolic extract	92
		Flowers: ethanolic extract	93
		Latex	94
		Leaves: methanolic extract	95
		Leaves, flower, root bark: ethanolic extract	96
		Leaves and latex: aqueous, ethanolic extract	97 and 98
		Leaves: aqueous, methanolic extract	99
		Latex: aqueous extract	78
8	Central nervous system activity	Latex proteins	100
9	Antioxidant activity	Leaves, flower, fruit, latex	101
		Leaves: aqueous, methanolic extract, quercetin and its derivatives	76
		Leaves: aqueous and methanolic extract	102
		Leaves, flowers and fruits: methanolic extract	103
		Bark: ethanolic extract	69
10	Antinociceptive activity	Latex protein	104
11	Antihelmintic activity	Flowers: crude powder, aqueous and methanolic extract	105
		Latex: fresh, dried aqueous extract	106 and 107
12	Antiinflammatory activity	Dry latex	108 and 109
		Stem bark: chloroform and hydro-alcoholic extract	110
		Latex: hexane, dichloromethane, ethyl acetate, *n*-butanol and aqueous extract	77
		Latex: pet. ether, acetone, methanol extract	111
		Leaves: aqueous extract	112
		Flowers: ethanolic extract	93
13	Antidiarroheal activity	Bark: Arkamula Tvarka (Ayurvedic preparation)	45
		Latex	113
14	Antifungal activity	Aqueous bark extract	114
		Leaves: aqueous, methanol, acetone and ethanol extract	115
		Root bark	116
	Antimycotic activity against dermatophytes	Latex	117
	Antimycofloral activity (fungi in wheat)	Fresh latex	118
15	Larvicidal activity	Crude latex and ethanolic extract of leaf	119
		Leaves: ethanolic extract	120
		Leaves: aqueous extract	121
		Flower, young bud, mature leaves and stems: ethanolic extract	122
		Flowers: aqueous extract	123
16	Tobacco mosaic virus (TMV) inhibitor activity	Latex	124
17	Antifertility activity	Ethanolic extract of roots	125

Table 2 (*Contd.*)

S. no.	Pharmacological activities	Parts/extracts/possible chemical constituents	References
		Leaves: ethanolic extract	79
		Roots (calotropin)	59
	Abortifacient activity	Latex	126
	Antisperm activity	Root: chloroform extract	127
	Oestrogenic/antiovulatory activity	Roots: ethanolic and aqueous extract	128
18	Plasma clotting activity	Protein fraction isolated from fresh latex	129
19	Antiplasmodial activity	Different plant parts: ethyl acetate, ethanolic and acetone extract	130
		Leaves extract	131
20	Antipyretic activity	Dry latex: aqueous extract	132
		Flowers: ethanolic extract	93
21	Antiasthmatic activity	Flowers	133
22	Anticonvulsant activity	Root extracts	134
23	Cytotoxic activity	Root (2″-oxovoruscharin)	62
		Laticifer proteins (LP) recovered from latex	135
		Root: methanolic, aqueous, ethyl acetate, hexane extracts	136
		Plant: methanolic extract	137
		Stems: uzarigenin	138
		Root bark: calotroprocerol A	139
		Root: alcoholic, hydro-aqueous and aqueous	140
		Leaf: ethanolic extract	149
24	Analgesic activity	Flowers: Ethanolic extract	93
25.	Antihyperglycemic activity	Leaves: pet ether, methanol and aqueous extracts	141
26	Antiarthritis activity	Latex	142
		Protein sub fraction of latex	143
27	Antimolluscicidal activity	Latex: 95% aqueous ethanol (uscharin)	144
28	Antitermites activity	Latex	145
29	Antimigraine activity	Dried terminal leaves	146
30	Anti-ulcer activity	Root: chloroform extract	147
		Plant: 50% ethanolic extract	148
		Leaf: ethanolic extract	149
		Stem bark: chloroform and hydroalcoholic extract	110
31	Spasmolytic activity	Plant: aqueous extract	150
32	Allelopathic activity	Leaves: aqueous extract	151
33	Anti-keloidal activity	Latex	68
34	Anti-hyperbilirubinemic activity	Leaves: aqueous extract	70
35	Antiapoptotic activity	Latex	152

regime (50%) which can be considered as a compensatory mechanism. Further Ramadana *et al.*[31] studied the influence of light and irrigation on cumulation of β-sitosterol in *C. procera*. They hypothesized that β-sitosterol biosynthesis pathway supported the plant to bear drought and light intensity stress.

2.3 Commercial prospective

2.3.1 As biofuel. *C. procera* is rich in hydrocarbons and contains biologically degradable materials similar to that found in other agricultural crops. Traore[32] conducted fermentation experiments and found that it is a good substrate for biogas synthesis. Barbosa *et al.*[33] found that oil composition of its seeds varies from 19.7 to 24.0% which proves its future potential as biodiesel, specially in those areas where people rely mainly on wood as source of energy production.

2.3.2 As biopesticide. Laticifer proteins (LP) from *Calotropis procera* were assayed for insecticidal activity against different crop pests to assess the biological role of latex. Diets containing 4% latex led to decreased weight gain (ED_{50} = 3.07%) and affected survival (LD_{50} = 4.61%) of third instars of *Ceratitis capitata*.[34] The crude flavonoid fraction (Cf), the latex protein fraction (LP) and the leaf methanolic extract showed significant insecticidal activity.[35] These studies suggest that it can be developed as natural biopesticidal agent.

2.4 Industrial prospective

2.4.1 Cheese making agent. In West Africa, crude aqueous extract of *C. procera* is used as milk clotting enzyme in traditional method of cheese production.[36] It displayed an optimum activity at a temperature of 75 °C, which is essential for cheese production.[37] Calotropain enzyme found in the plant is more efficient than papain, ficin and bromelin, moreover it can lead to milk coagulation, digestion of meat, casein and gelatin.[38,39] These studies supported its traditional use as cheese making agent.

2.4.2 As surfactant. *C. procera* milk latex was used as a surfactant for facile synthesis of Eu^{3+} activated $La(OH)_3$ and

Table 3 Summary of cytotoxic studies of *C. procera*

C. procera: plant part/chemical constituent	Cancer cell lines/model	Method of analysis/assay	Mechanism of action/investigation	Observation	References
Uscharin and its derivatives 2″-Oxovoruscharin and its derivatives	Lung cancer (A549) Two glioblastoma (Hs683, U373) and two colon cancer (HCT-15 and LoVo)	MTT colorimetric assay, intraperitoneal (ip) injection-related toxicity	Na^+/K^+-ATPase inhibition activity	Cardenolides derived from 2″-oxovoruscharin exhibited significant *in vitro* antitumor activity and high *in vivo* tolerance	62
Laticifer proteins (LP) recovered from latex	HL60 (promoyelocytic leukemia), HCT-8 (colon), MDA-MB-435(breast), SF-295(brain)	3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2*H*-tetrazolium bromide MTT	LP is a target for DNA topoisomerase I triggering apoptosis in cancer cell lines	IC_{50} values for LP ranged from 0.42 to 1.36 μg mL^{-1} to SF-295, MDA-MB-435 respectively	135
Root: methanolic, aqueous, ethyl acetate, hexane extracts (1, 5, 10, 25 μg mL^{-1})	Human Hep 2	Tetrazolium bromide (MTT), colorimetry	Treatment initiated apoptotic mechanism by blocking the cell cycle at S-phase and thus preventing cells from entering proliferative (G2/M) phase	Ethyl acetate extract showed strongest cytotoxic effect	136
Plant: methanolic extract (0, 5, 10, 20 and 40 μg mL^{-1})	Human skin melanoma cells (SK-MEL-2)	Annexin-V FITC flow cytometry method, MTS assay	Methanolic extract induced apoptosis as shown by the accumulation of cells in the G2/M phase and the decrease of cell percentage in the G0/G1 phase	At 40 μg mL^{-1} late apoptotic cell percentage was increased up to 80%. *C. procera* exerted cytotoxic potential	137
5-Hydroxy-3,7-dimethoxyflavone-4-*O*-β-glucopyranoside; uzarigenin; β-anhydroepidigitoxigenin; 2β,19-epoxy-3β,14β-dihydroxy-19-methoxy-5α-card-20(22)-enolide; β-anhydroepidigitoxigenin-3β-*O*-glucopyranoside	HT 29, HepG2 (human cancer cell lines), NIH-3T3 (mouse fibroblast cell line)	CellTiter-Blue® cell viability assay	—	Uzarigenin showed moderate cytotoxicity	138
Calotroprocerol A; calotroproceryl acetate A; calotroprocerone A, B; pseudo-taraxasterol acetate; taraxasterol; calotropursenyl acetate B; stigmasterol; (*E*)-octadec-7-enoic acid	A549 non-small cell lung cancer (NSCLC), the U373 glioblastoma (GBM) and the PC-3 prostate cancer cell lines	3-(4,5-Dimethylthiazol-2-yl)- 2,5-diphenyltetrazolium bromide (MTT) assay	Growth inhibition action	Calotroprocerol A exhibited *in vitro* growth inhibitory activity in all the three cancer cell lines with effects comparable to those of cisplatin and carboplatin	139
Calotroposide H; calotroposide I; calotroposide J; calotroposide K; Calotroposide L; calotroposide M; calotroposide N	A549 non-small cell lung cancer (NSCLC), U373 glioblastoma (GBM), and PC-3 prostate cancer cell lines	MTT colorimetric assay	Calotroposide K and M exhibited subnanomolar growth inhibition activity with IC_{50} ranging from 0.5 to 0.7 μM against U373 glioblastoma (GBM) and PC-3 prostate cancer cell lines	*C. procera* exhibited cytotoxic potential	153
Calotroposide S	PC-3 prostate cancer, A549 non-small cell lung cancer (NSCLC), and U373 glioblastoma (GBM) cell lines	MTT colorimetric assay	Calotroposide S showed potent anti proliferative activity	*C. procera* exerted anti-proliferative activity	154
Latex: hexane, chloroform, ethyl acetate and aqueous extract. Calactin; 15β-hydroxy calactin;	A549 (lung) and hela (cervix) cancer cell lines using cisplatin as a positive control	MTT colorimetric assay	Growth inhibition action	Highest cytotoxic activity was displayed by chloroform extract. Amongst isolated compounds,	65

Table 3 (*Contd.*)

C. procera: plant part/chemical constituent	Cancer cell lines/model	Method of analysis/assay	Mechanism of action/investigation	Observation	References
afroside; uscharin; 15β-hydroxy uscharin; calotoxin; 12β-hydroxycoroglaucigenin; afrogenin; calactoprocin; procegenin A; procegenin B				calactin displayed highest cytotoxic activity	
Root: alcoholic, hydro-aqueous and aqueous extracts(10 μg mL^{-1}, 30 μg mL^{-1}, 100 μg mL^{-1})	Human oral (KB) and central nervous system (SNB-78) cancer cell lines	Sulforhodamine-B (SRB) assay	Alcoholic extract showed significant growth inhibition action	*C. procera* roots exhibited *in vitro* cytotoxicity against oral and CNS human cancer cell lines	140

La_2O_3 nanophosphors through green mediated hydrothermal route. The latex reflected good capping potency for controlling the morphology and phase of the nanophosphor.[40] Hence its latex can be a good source of natural surfactant.

2.4.3 As corrosion inhibitor. Extract of *C. procera* was studied for its corrosion inhibition action by weight loss, electrochemical, SEM and UV methods, significant corrosion inhibitive effect in sulphuric acid medium on mild steel was observed.[41] Hence, it can be used as green corrosion inhibitor.

2.4.4 As dehairing agent of leather. Latex peptidases of *C. procera* when assayed against skin representative substrates, revealed complete dehairing process, while no changes in leather structure were observed. Thus, it can be an appropriate environment friendly dehairing agent as compared to toxic sodium sulphite treatment for tanneries.[42]

3. Ethnomedicinal uses

An insight into Ayurveda, Unani and folk uses of different parts of *C. procera* and *C. gigantea* to cure various ailments was compiled by Misra *et al.*[43] Ethnomedicinal uses of plant parts of *C. procera* in curing various diseases have been summarized in Table 1.

4. Major milestone of *Calotropis* phytochemistry

Phytochemistry of *Calotropis procera* has always attracted the attention of researchers because despite its toxicity, it employs wide applications in traditional medicinal system till date. Dating back to 1936, Hesse *et al.*[55] identified calotropin as the first compound from this plant. Further Hesse and his coworkers[56,57] isolated heart poisons or cardiac glycosides namely calotropin, calotoxin, calactin, uscharin, voruscharin and uscharidin.[58] Root powder of this plant is used in tribes to induce abortion in women and as an uterotonic since ancient period. Later it was found that it was due to the compound calotropin. Gupta *et al.*[59] administered calotropin to gerbils and rabbits and observed reduction in spermatids count by 65% and 94% respectively.

In 1955, Rajagopalan *et al.*[60] identified chemical constituents of seed *viz.* coroglaucigenin, corotoxigenin and frugoside (cardenolides). Later Bruschweiler *et al.*[61] identified three additional cardenolides *viz.* uzarigenin, syriogenin and procerosid. A novel cardenolide, 2″-oxovoruscharin was isolated from the root bark by Quaquebeke *et al.*[62] and modified into its semi-synthetic derivative, *i.e.*, UNBS1450. Akhtar and Malik[63] isolated a new cardenolide named proceragenin from the hexane-insoluble fraction of *C. procera*.

A fascinating feature of the plant is its potential to curb Alzheimer's disease (AD), the most predominant root cause of dementia, a neurodegenerative disease. Its dried latex showed attenuation of β-amyloid deposition in mouse brain and cerebral protective activities.[64] Hence, it is imperative to evaluate the mechanism of metabolites, so that it can lead to promising direction to search new scaffolds for AD treatment. In 2015,

Table 4 Summary of *in vivo* studies of wound healing potential of *C. procera*

Model	*C. procera* extract/dose/ duration	Negative control	Investigation	Result	References
Guinea pigs	20 mL of 1.0% sterile solution of the latex twice daily for 7 days	Excision wounds	Wounds exhibited marked dryness, no visual sign of inflammation	Significant prohealing property	67
Male albino-Wistar rats	Ethanolic extract of bark (50 mg per wound)	Incision and excision wounds	Extract demonstrated wound healing effect by accelerating wound closure and epithelialization	Excellent dermal wound healing potential	69
Wistar rats	Aqueous extract of *C. procera* (25 mg and 50 mg kg^{-1})	Incision and excision wounds	Significant ($P < 0.05$) increase in breaking strength and percentage wound contractions with decreased epithelization period was observed	Significant wound healing property	70

Mohamed *et al.* isolated three non-glycosidic cardenolides namely calactoprocin, procegenin A and procegenin B from the latex.[65]

A patent claimed that polar extract of *C. procera* showed anti-ulcerative colitis activity in dose-dependent manner in a subject mammal and was found to be more effective than the standard drug Prednisolone.[66]

5. Pharmacology

Over the last many years, researchers have carried out numerable pharmacological activities, which are summarized in Table 2.

The details enumerated in the Table 2 is indicative of the fact that the different plant parts demonstrate large number of

Table 5 Summary of *in vivo* anti-inflammatory potential of *C. procera*

Model	*C. procera* extract/dose/ duration	Negative control	Investigation	Result	References
Male albino rats and albino guinea pigs	50 mg, 200 mg 500 mg and 1 g kg^{-1} dry latex	Carrageenan-induced oedema test, cotton pellet granuloma and vascular permeability *etc.*	Dry latex suppressed fluid exudation, due to its influence on vascular permeability and also delayed the onset and intensity of UV induced erythema	Significant anti-inflammatory potential	108
Male albino rats	Dry latex	Carrageenin and formalin-induced pedal oedema test	At dose 5 mg per rat, showed 71% inhibition in the case of the carrageenin-induced oedema ($P < 0.005$) and 32% inhibition for the formalin-induced oedema ($P < 0.05$). At higher dose (50 mg per rat), 96% and 98%, for carrageenin- and formalin-induced oedema groups respectively	Potent anti-inflam-matory activity	109
Albino rats of either sex	Stem bark: chloroform and hydro-alcoholic extract	Carrageenan-induced paw oedema	Significant reduction in the inflammation at 100, 200 and 400 mg kg^{-1} displayed by chloroform extract	Significant anti-inflammatory potential	110
Male Wistar rats	Dry latex: petroleum ether, acetone, methanol and aqueous extracts (50 mg per rat)	Carrageenan induced paw oedema	Maximum anti-inflammatory effect (59% and 53% inhibition) by the aqueous and acetone extracts respectively compared to (63%) inhibition exhibited by phenylbutazone	Latex of *C. procera* exerted anti-inflammatory property	111
Male Wistar rats	Crude latex: hexane, dichloromethane, ethyl acetate, *n*-butanol and aqueous fractions (1.0, 5.0 or 10.0 mg kg^{-1} and 0.2 mL)	Carrageenan-induced peritonitis	Dichloromethane, ethyl acetate, and aqueous fractions inhibited carrageenan-induced neutrophil migration in rats at the ratios 67%, 56%, and 72%, respectively	Latex of *C. procera* possess anti-inflammatory property	77

Table 6 Summary of larvicidal potential of *C. procera*

Vector species	*C. procera* extract/dose/ duration	Observation	Result	References
Culex quinquefasciatus 3rd instar larvae	Crude latex and ethanolic extract of leaves	100% larval mortality at 300 ppm concentration of latex and at 1000 ppm concentration of ethanolic leaf extract. LC_{50} values of the latex and ethanolic leaves extract were 57.3 and 388.7 ppm respectively	Crude latex exerted stronger larvicidal potential than ethanolic extract	119
Musca domestica 3rd instar larvae	Ethanolic extract of leaves (500 mg L^{-1})	100% mortality at 500 ppm. LC_{50} value of the extract 282.5 ppm	Leaves exerted insecticidal potential	120
Anopheles arabiensis and *Culex quinquefasciatus* 2nd, 3rd, 4th instar larvae	Aqueous extract of leaves (1000, 500, 200 ppm)	LC_{50} value 273.53, 366.44, 454.99 ppm for 2nd, 3rd and 4th instar larvae	Leaves showed oviposition deterrent, larvicidal and adult emergence activity	121
Anopheles stephansi 3rd instar larvae	Ethanolic extracts of different parts *viz.* flower, young bud, mature leaves and stems (100 to 5000 ppm)	Mature leaves extract exhibited 100% mortality at 2000 ppm after 48 hours of incubation	Mature leaves showed high larvicidal activity against tested larvae	122
Culex species 4th instar	Aqueous extract of flowers (1%, 2.5% and 5%)/24 h	At 1% concentration, the mortality rate was 0%, 60% and 100% and at 2.5% concentration, mortality rate was 20%, 80% and 100% at the end of 1, 3 and 4 days of exposure, and at 5% concentration, 100% mortality was recorded at the end of third day	Flowers exhibited remarkable larvicidal properties against the pupae and late 4th instar larvae of *Culex* sp.	123

Table 7 Summary of *in vivo* and *in vitro* studies of anthelmintic potential of *C. procera*

Model	*C. procera* extract/dose	Compared with drug	Observation	Result	References
In vivo: sheep infected with mixed species of nematodes *in vitro*: *Haemonchus contortus*	Crude powder (CP), crude aqueous (CAE) and crude methanolic extracts (CME)	Levamisole	88.4%, 77.8% and 20.9% reduction in egg count percent for CAE, CP and CME respectively	Aqueous extract of *C. procera* has good anthelmintic potential	105
Earthworms	Aqueous extract of dry latex (5, 10, 50 and 100 mg mL^{-1}) and fresh latex (1.45, 7.25, 29, 72.5 and 145 mg mL^{-1})	Piperazine	At 5 to 10 mg mL^{-1} concentration paralysis at 90 min, at 100 mg mL^{-1} death within 60 min. Fresh latex also showed dose-dependent paralysis	Latex showed wormicidal activity, hence can be used as an anthelmintic agent	106

pharmacological activities. Moreover, maximum number of activities were conducted at extract level, therefore horizons for further research is still bright, wherein the active principle constituents responsible for the activities may be identified. Here some of the very vital biological activites are being discussed in detail.

5.1 Cytotoxic potential

Various phytoconstituents and plant extracts were examined for their *in vitro* anticancer potential on various cancer cell lines, and showed significant cytotoxic activities as summarized in Table 3.

Over past decade, cytotoxic activities of various extracts and chemical constituents of *C. procera* have been carried out. Majority of studies were conducted on various cancer cell line models *in vitro*, except the one conducted using UNBS1450. UNBS1450, a semi-synthesized cardenolide was compared to reference anticancer agents and classic cardenolides in prostate cancer cell line *in vitro* and *in vivo* following s.c. (subcutaneous) and orthotopic prostate cancer cell grafting into mice; it was

Table 8 Summary of *in vitro* studies of antioxidant potential of *C. procera*

C. procera part	Extract/dose/duration	Investigation	Result	References
Leaves, fruits, flowers and latex	Methanolic solution of dried extract	DPPH radical scavenging assay	Leaves exhibited maximum DPPH radical scavenging activity with $IC_{50} = 0.18$ mg mL^{-1}, whereas latex showed minimum activity with $IC_{50} = 0.42$ mg mL^{-1}	101
Leaves	Aqueous and methanolic extract (1, 5, 10, 50, 100 and 500 μg mL^{-1})	DPPH radical scavenging assay	IC_{50} of the methanol extract was 110.25 μg mL^{-1}, the aqueous extract showed mild antioxidant activity	102
Leaves	2–100 mg mL^{-1} for quercetin in methanol and 20–100 mg mL^{-1} for AME and quercetin derivatives with different methoxy substitution	DPPH radical scavenging assay	Varying degrees of antioxidant activity was exerted by quercetin derivatives, but quercetin was found to be most active	76
Leaves, flowers and fruits	Methanolic extracts of the samples of different concentrations (100–1000 ppm)	DPPH radical scavenging assay	IC_{50} values in leaves, fruits and flowers were 16.08, 16.06 and 10.31 μg mL^{-1} respectively, showing strong antioxidant activity of *C. procera*	103

Table 9 Summary of *in vitro* schizontocidal activity of *C. procera*

Model	*C. procera* extract/dose	Investigation	Result	References
Chloroquine sensitive strain, MRC 20 and a chloroquine resistant strain, MRC 76 of *Plasmodium falciparum*	Ethyl acetate, acetone, methanol fractions of flower, bud, root: (62–125 mg mL^{-1})	Percentage inhibition varied from 7.51 to 61.38% between the various fractions against MRC 20 and for MRC 76, percentage inhibition varied from 3.437 to 41.08% between the various fractions	At the lower dose range, the root extracts of *C. procera* found to be the most effective for both *P. falciparum* MRC 20 and MRC 76. Hence, *C. procera* exerted antiplasmodial potential	130

Table 10 Summary of *in vivo* hepatoprotective potential of *C. procera*

Model	*C. procera* extract/dose	Negative control	Investigation	Result	References
Albino rats of either sex	Methanol extract (MCP) of root and its sub fractions *viz.* hexane (HCP), ethyl acetate (ECP) and chloroform (CCP) (200 mg kg^{-1})	Carbon tetra chloride	MCP and its sub fractions HCP, ECP displayed hepatoprotective effect by reducing the elevated serum levels of, serum glutamic pyruvic transaminase, alkaline phosphatase and serum glutamic oxaloacetic transaminase, it increased high density lipoprotein. CCP does not show effective results	*C. procera* exerted hepatoprotective potential	83
Wistar rats of either sex	Hydro-ethanolic extract of *C. procera* flowers (200 mg kg^{-1} and 400 mg kg^{-1})	Paracetamol-induced hepatitis	Improvement in the hepatic architecture was observed	*C. procera* flowers have hepatoprotective effect	84

found to be more effective than tested reference compounds, such as mitoxantrone, taxol, oxaliplatin, irinotecan and temozolomide and less toxic than cardenolides.[155,156] Mechanism of UNBS1450 was studied and proven to be a potent sodium pump inhibitor as it inhibits NF-kB transactivation and triggers apoptosis by recruitment of pro-apoptotic Bak and Bax protein thereby leading to cell death.[157,158] Carrying out further *in vivo* studies will play a crucial role in ascertaining the safer use of UNBS1450. Therefore, further studies are necessary to obtain the clinically important lead molecules for the development of potent anticancer drugs.

5.2 Wound healing potential

C. procera has folk medicinal reputation as a wound healing agent. *In vivo* studies proved its wound healing potential as summarized in Table 4.

These data strongly support its ethnomedicinal use in wound healing potential and skin problems. *In vivo* screening showed considerable results in dose-dependent manner when compared to positive controls. A future perspective of studying the side effects and toxicity of the extracts at the dose level can also be unravelled.

5.3 Anti-inflammatory potential

Anti-inflammatory potential of extracts from *C. procera* have been summarized in Table 5.

On the basis of studies mentioned in Table 5, it can be concluded that the anti-inflammatory effect of dry latex needs to be further characterized as well as the nature of active principle leads responsible for anti-inflammatory activity remains to be identified.

5.4 Larvicidal/insecticidal potential

Aqueous and ethanolic extracts of leaves and other parts of *C. procera* showed significant larvicidal activities against various vector species as summarized in Table 6.

Above studies indicated that aqueous and ethanolic extracts of leaves of *C. procera* possessed phenomenal oviposition deterrent and larvicidal effect, thus it can be developed as environment friendly alternative for the synthetic insecticides for mosquito control.

5.5 Anthelmintic potential

C. procera is used as an anthelmintic by ruminant farmers as proved by activities summarized in Table 7.

5.6 Antioxidant potential

Leaves of *C. procera* displayed highest antiradical activity as evident from activities summarized in Table 8.

Above activities proved that quercetin, aqueous and methanolic extracts of leaves of *C. procera* possessed remarkable antiradical activity. Evaluation of the *in vivo* antioxidant potential would be indispensable, so that it can be used as natural antioxidant ingredients in food and drug industries.

5.7 Antiplasmodial potential

Traditional practitioners use *C. procera* as antimalarial agent. Activity summarized in Table 9.

Over past decades, reduction in efficiency of chloroquine has been observed, thus resistivity to antimalarial drugs can be a threat to control malaria. The hunt for analogues with reduced toxicity and improved antimalarial activity still prevails. The possibilities of finding active compounds and correlating with specific dose effective antimalarial activity, from those parts of the plant, which are used separately or together could be further pursued.

5.8 Hepatoprotective activity

In vivo experimental study proves that *C. procera* has hepatoprotective potential as summarized in Table 10.

5.9 Miscellaneous activities

Antiapoptotic activity of latex of *C. procera* was carried out by Sayed *et al.* (2016) on catfishes exposed to (100 $\mu g\ L^{-1}$) 4-nonylphenol as chemical pollutant. Significant ($P < 0.05$) decrease in apoptotic cells, enzymes (superoxidase dismutase, acetylcholinesterase cortisol *etc.*) and ions validified antiapoptotic activity of the crude latex against the toxicity of 4-nonylphenol.[152] Hence, crude latex exerted antiapoptotic activities against the toxicity of 4-nonylphenol.

Anti-hyperbilirubinemic activity of leaves was evaluated using phenylhydrazine and paracetamol induced Wistar rats. Significant ($P < 0.05$) decrease in concentrations of serum total bilirubin in hyperbilirubinemic rats proved bilirubin lowering activity of aqueous extracts of *C. procera*.[70]

Recent studies indicated that *C. procera* has significantly broader range of beneficial effects as it contains bioactive phytochemicals with therapeutic potential. By far only cytotoxic studies on cancer cell lines have been well established in clinical trials, whereas other activities have been evidenced by basic studies. Most of the studies are limited to *in vitro* studies which lack exploration of molecular mechanism of action. Therefore, mechanism based *in vitro* and *in vivo* studies should be carried out, which can lead to understanding of underlying mechanism related to traditional uses.

6. Phytochemistry

C. procera contains cardenolides, flavonoids, sterols, oxypregnanes triterpenoids, glycosides and other constituents as elaborated in Table 11.[7] Flavonoid and its glycosides (Fig. 1) are the major compounds isolated from the leaves of *C. procera*. Steroids (Fig. 2) and cardenolides (Fig. 3) are the major secondary metabolites found in the latex. Cardenolides have also been reported from other plant genera of the family Apocynaceae or Asclepiadaceae like *Strophanthus*, *Cerbera*, *Apocynum*, *Nerium*, and *Thevetia*.[159] Traditionally they are employed in curing of congestive heart failure.[160] Cardenolides are C23 steroids with steroid nucleus having a glycoside moiety at C-3 and a lactone moiety at C-17.[6] Cardiac glycosides can be novel antineoplastic agents as cancer cells are more prone to these compounds.[159] Terpenoids (ursane, olenane type and pentacyclic triterpenes *etc.*) (Fig. 4) have been

Table 11 Compounds isolated from *Calotropis procera*

S. No.	Compound name (molecular formula)	Extract/fraction	Eluent	Plant part & references
Flavonoids				
1	5-Hydroxy-3,7-dimethoxyflavone-4′-*O*-β-glucopyranoside ($C_{23}H_{24}O_{11}$)	Ethanolic extract	Benzene-chloroform	Stem[138]
2	Isorhamnetin 3-*O*-β-D-rutinoside ($C_{28}H_{32}O_{16}$)	85% methanolic extract	10–40% methanol	Leaves[76,164]
3	Isorhamnetin 3-*O*-β-D-robinoside ($C_{28}H_{32}O_{16}$)	85% methanolic extract	10–40% methanol	Leaves[76,164]
4	Isoquercitrin ($C_{21}H_{20}O_{12}$)	85% methanolic extract	70% methanol	Leaves[76]
5	Quercetagetin-6-methyl ether 3-*O*-β-D-$^4C_1$-galacturonopyranoside ($C_{22}H_{20}O_{14}$)	85% methanolic extract	40–60% methanol	Leaves[76]
6	Quercetin ($C_{15}H_{10}O_7$)	85% methanolic extract	80% methanol	Leaves[76]
7	Isorhamnetin ($C_{16}H_{12}O_7$)	85% methanolic extract	80% methanol	Leaves[76]
8	Azaleatin ($C_{16}H_{12}O_7$)	85% methanolic extract	80% methanol	Leaves[76]
9	3,3′-Dimethoxy quercetin ($C_{17}H_{14}O_7$)	85% methanolic extract	50–60% ethyl acetate	Leaves[76]
10	3,6,3′,4′-Tetramethoxy quercetin ($C_{18}H_{16}O_7$)	85% methanolic extract	50–60% ethyl acetate	Leaves[76]
11	3,6,7,3′,4′-Pentamethoxy quercetin ($C_{19}H_{18}O_7$)	85% methanolic extract	60–100% ethyl acetate	Leaves[76]
12	Kaempferol-3-*O*-rutinoside ($C_{27}H_{30}O_{15}$)	Methanolic extract	Ethyl acetate : water : formic acid : glacial acetic acid (100 : 26 : 11 : 11, v/v)	Leaves[86]
13	Quercetin-3-*O*-rutinoside ($C_{27}H_{30}O_{16}$)	Methanolic extract	Ethyl acetate : water : formic acid : glacial acetic acid (100 : 26 : 11 : 11, v/v)	Leaves[86]
14	Luteolin ($C_{15}H_{10}O_6$)	Ethanol–water extract (60 : 40)/butanol fraction	*n*-Hexane–acetone (70 : 30)	Stem bark[165]
15	Epicatechin ($C_{15}H_{14}O_6$)	Ethanol–water extract (60 : 40)/butanol fraction	*n*-Hexane–acetone (60 : 40)	Stem bark[165]
16	Kaempferol 3-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside ($C_{27}H_{30}O_{15}$)	Ethanolic extract	Water–methanol (1 : 1)	Fruits[149]
Steroids				
17	Stigmasterol ($C_{29}H_{48}O$)	Methanolic extract/ hexane fraction	Hexane–ethyl acetate	Flowers,[166] root bark,[139] latex[167]
18	β-Sitosterol ($C_{29}H_{50}O$)	Ethanolic extract/ chloroform fraction	Hexane–ethyl acetate	Flowers,[166] latex,[167] aerial part[168]
19	Daucosterol or β-sitosterol glucoside ($C_{35}H_{60}O_6$)	Ethanolic extract/ chloroform fraction	10% aq. methanol and hexane	Latex, aerial part,[168] roots[169]
20	Benzoyllineolone ($C_{28}H_{36}O_6$)	Ether extract/chloroform fraction	Benzene–chloroform	Root bark[170]
21	Benzoylisolineolone ($C_{28}H_{36}O_6$)	Ether extract/chloroform fraction	Benzene–chloroform	Root bark[170]
22	Lineolone ($C_{21}H_{32}O_5$)	Ether extract	—	Root bark[170]
23	Isolineolone ($C_{21}H_{32}O_5$)	Ether extract	—	Root bark[170]
24	Cyclosadol ($C_{31}H_{52}O$)	Methanolic extract	—	Flowers[166]
25	β-Sitost-4-en-3-one ($C_{29}H_{48}O$)	Methanolic extract	*n*-Hexane–ethyl acetate (95 : 5)	Flowers[166]
Steroids : cardenolides				
26	Calactin ($C_{29}H_{40}O_9$)	Ethanolic extract/ chloroform fraction	10% aq. methanol and hexane	Roots,[62] latex,[65] aerial part[168]
27	15β-Hydroxycalactin ($C_{29}H_{40}O_{10}$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
28	Calactoprocin or 14β,15β-dihydroxy-19-oxo-2α,3β-[(2*S*,3*S*:4*R*,6*R*)-tetrahydro-3-hydroxy-4-methoxy-6-methyl-2*H*-pyran-2,3-diyl] bis(oxy)-5α-card-20(22)-enolide (3′β-methoxy-15β-hydroxy calactin) ($C_{30}H_{42}O_{10}$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
29	Afroside ($C_{29}H_{42}O_9$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
30	Calotoxin ($C_{29}H_{40}O_{10}$)	Ethanolic extract/ chloroform fraction	—	Aerial part,[168] latex[65]
31	Calotropin ($C_{29}H_{40}O_9$)	Ethanolic extract/ chloroform fraction	—	Root bark,[62] latex and aerial part[168]
32	12β-Hydroxycoroglaucigenin ($C_{23}H_{34}O_6$)	Ethanolic extract/ chloroform fraction	—	Latex[65]

Table 11 (*Contd.*)

S. No.	Compound name (molecular formula)	Extract/fraction	Eluent	Plant part & references
33	Procegenin A or 3α,12β,14β-trihydroxy-19-hydroxymethyl-5α-card-20(22)-enolide or 3-*epi*,12β-hydroxycoroglaucigenin ($C_{23}H_{34}O_6$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
34	Procegenin B or 3α,12β,14β-trihydroxy-19-oxo-5α-card-20 (22)-enolide or 12β-hydroxy carpogenin ($C_{23}H_{32}O_6$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
35	Afrogenin ($C_{23}H_{34}O_6$)	Ethanolic extract/ chloroform fraction	—	Latex[65]
36	Desglucouzarin ($C_{29}H_{44}O_9$)	Ethanolic extract/ chloroform : ethyl acetate fraction	Chloroform–methanol (9 : 1)	Stem[171]
37	Frugoside ($C_{29}H_{44}O_9$)	Ethanolic extract/ chloroform : ethyl acetate fraction	Chloroform–methanol (9 : 1)	Seeds,[60] stem,[171] root bark[172]
38	Uzarigenin ($C_{23}H_{34}O_4$)	Ethanolic extract/ chloroform : ethyl acetate fraction	Chloroform–methanol (9.5 : 0.5)	Latex[61] Stem[168,171,173]
39	Uzarigenone ($C_{23}H_{32}O_4$)	Ethanolic extract/ benzene	Chloroform–methanol (9.5 : 0.5)	Stem[171]
40	β-Anhydroepidigitoxigenin-3β-*O*-glucopyranoside ($C_{29}H_{42}O_8$)	Ethanolic extract/ benzene : chloroform	Chloroform–methanol (9 : 1)	Stem[138]
41	β-Anhydroepidigitoxigenin or 3β-hydroxy-5α-carda-14(15),20(22)-dienolide ($C_{23}H_{32}O_3$)	Ethanolic extract → benzene : chloroform	Chloroform–methanol (9 : 2)	Stem[138]
42	Calotropagenin ($C_{23}H_{32}O_6$)	Chloroform extract	Hexane–diethyl ether (9 : 11)	Aerial part[174]
43	Ischarin ($C_{31}H_{41}NO_8S$)	Ethanolic extract	Chloroform	Aerial part[168]
44	Ischaridin ($C_{29}H_{42}O_8$)	Ethanolic extract/10% aq. methanol and hexane fraction	Chloroform–methanol (98 : 2)	Aerial part[168]
45	2″-Oxovoruscharin ($C_{31}H_{41}NO_9S$)	Methanolic extract	Dichloromethane–methanol (98 : 2)	Root bark[62]
46	Proceraside A ($C_{31}H_{44}O_{10}$)	Methanolic extract/ethyl acetate fraction	Chloroform–methanol	Root bark[172]
47	Syriogenin ($C_{23}H_{34}O_5$)	Methanolic extract	Water–methanol	Latex[61]
48	Proceroside ($C_{29}H_{40}O_{10}$)	Methanolic extract	Water–methanol	Latex[61]
49	Uscharidin ($C_{29}H_{38}O_9$)	Ethanolic extract	—	Aerial part[56]
50	Voruscharin ($C_{31}H_{43}NO_8S$)	Methanolic extract	Acetone–methanol (8 : 2)	Roots[62]
51	Coroglaucigenin ($C_{23}H_{34}O_5$)	Chloroform extract	—	Seeds[60]
52	Corotoxigenin ($C_{23}H_{32}O_5$)	Ether extract	—	Seeds[60]
53	3-[β-(4-*O*-β-D-Glucopyranosyl-β-D-6-desoxyallopyranosyl)oxy] uzarigenin ($C_{35}H_{54}O_{13}$)	70% ethanolic extract/ benzene : chloroform	Chloroform–methanol (9 : 1.5)	Stem[173]
54	Uzarin or 3-[β-(2-*O*-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy] uzarigenin ($C_{35}H_{54}O_{14}$)	70% ethanolic extract/ benzene : chloroform	Chloroform–methanol (9 : 2)	Stem[173]
55	15β-Hydroxyuscharin ($C_{31}H_{41}NO_9S$)	Ethanolic extract	Chloroform	Latex[65]
56	Uscharin ($C_{31}H_{41}NO_8S$)	Methanolic extract	Chloroform–methanol (70 : 30)	Aerial part,[168] latex[65,168]
57	Proceragenin or 7β,14β-dihydroxy-5α-card-20(22)-enolide ($C_{23}H_{34}O_4$)	Methanolic extract/ chloroform fraction	Hexane–chloroform (1 : 9)	Aerial part[63]
58	2β,19-Epoxy-3β,14β-dihydroxy-19-methoxy-5-α-card-20(22)-enolide ($C_{24}H_{34}O_6$)	Ethanolic extract/ benzene : chloroform fraction	Chloroform–methanol (9 : 2)	Stem[138]
59	Procesterol or (24*S*)-24-ethyl-stigmast-4-en-6α-ol-3-one ($C_{29}H_{48}O_2$)	Ethanolic extract/ chloroform fraction	Hexane–chloroform (3 : 2)	Fresh and undried flowers[176]
Terpenes/terpenoids				
60	α-Amyrin ($C_{30}H_{50}O$)	Methanolic extract/ hexane : ethyl acetate gradients	Dichloromethane–methanol (1 : 1)	Flowers[176]
61	β-Amyrin ($C_{30}H_{50}O$)	Methanolic extract/ hexane : ethyl acetate gradients	Dichloromethane–methanol (1 : 1)	Flowers[176]
62	α-Amyrin acetate ($C_{32}H_{52}O_2$)	Methanolic extract	Pet. ether–chloroform (1 : 9)	Roots[169]
63		Methanolic extract	Pet. ether–chloroform (1 : 1)	Roots[177]

Table 11 (*Contd.*)

S. No.	Compound name (molecular formula)	Extract/fraction	Eluent	Plant part & references
	Procerursenyl acetate or urs-18α-*H*-12,20(30)-diene-3β-yl acetate ($C_{32}H_{50}O_2$)			
64	Calotropenyl acetate or urs-19(29)-3β-yl acetate ($C_{32}H_{52}O_2$)	Chloroform extract	Benzene–hexane (60 : 40)	Flower,[175] latex and aerial part[168]
65	Calotropoleanyl ester or olean-13(18)-en-3β-yl acetate ($C_{32}H_{52}O_2$)	Ethanolic extract	Pet. ether	Root bark[178]
66	Calotroprocerol A or ursa-5,12,20(30)-trien-18αH-3β-ol ($C_{30}H_{46}O$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
67	Calotroproceryl acetate A or ursa-5,12,20(30)-trien-18α*H*-3β-yl acetate ($C_{32}H_{48}O_2$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
68	Calotroprocerone A or ursa-5,12,20(30)-trien-18α*H*-3-one ($C_{30}H_{44}O$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
69	Calotroproceryl acetate B or ursa-5,12,20-trien-18α*H*-3β-yl acetate ($C_{32}H_{48}O_2$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
70	Calotropursenyl acetate B or urs-12,19(29)-diene-3β-yl acetate ($C_{32}H_{50}O_2$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139,180]
71	Pseudo-taraxasterol acetate ($C_{32}H_{52}O_2$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
72	Taraxasterol ($C_{30}H_{50}O$)	Methanolic extract	*n*-Hexane–ethyl acetate	Root bark[139]
73	Proceroleanenol A or olean-13(18)-en- 9α-ol ($C_{30}H_{50}O$)	Ethanolic extract	Benzene–chloroform	Root bark[178]
74	Proceroleanenol B or olean-5,13(18)-dien-3α-ol ($C_{30}H_{48}O$)	Ethanolic extract	Benzene–chloroform (1 : 1)	Root bark[178]
75	Cycloart-23-ene-3β,25-diol ($C_{30}H_{50}O_2$)	Ethyl acetate extract	Hexane–ethyl acetate (2 : 1)	Flowers[166]
76	Lupeol ($C_{30}H_{50}O$)	Ethanolic extract	—	Latex[179]
77	3-*epi*-Moretenol ($C_{30}H_{50}O$)	Ethanolic extract	—	Latex[179]
78	Multiflorenol ($C_{30}H_{50}O$)	Pet. ether fraction	Chloroform–ethyl acetate (3 : 2)	Flowers,[166] latex[167]
79	Urs-19(29)-en-3-β-ol ($C_{30}H_{50}O$)	Acetone fraction	Pet. ether–acetone (8 : 2)	Latex[167]
80	Calotropenyl acetate or urs-19(29)-en-3-yl acetate ($C_{32}H_{52}O_2$)	Pet. ether fraction	Chloroform–ethyl acetate (3 : 5)	Latex[167]
81	3β,27-Dihydroxy-urs-18-en-13,28-olide ($C_{30}H_{46}O_4$)	Ethyl acetate fraction	Benzene–ethyl acetate (8 : 2)	Latex[167]
82	Calotropfriedelenyl acetate or friedelin-1-ene-3 β-yl acetate ($C_{32}H_{52}O_2$)	Ethanolic extract	—	Root bark[180]
83	Calotropterpenyl ester or 6,10,14-trimethylpentadec-6-enyl-2′,4′,8′,12′,16′-pentamethyl nonadecane ester ($C_{42}H_{82}O_2$)	Ethanolic extract	—	Root bark[180]
84	Phytyl iso-octyl ether or 3,7,11,15-tetramethyl hexadecanyl-6′-methyl hept-5′-enyl ether ($C_{28}H_{56}O$)	Methanolic extract	Pet. ether–chloroform (1 : 3)	Roots[181]
85	Dihydrophytoyl tetraglucoside or 3,7,11,15 tetramethylhexadecanoyl-β-D-glucopyranosyl-(2 → 1)-β-D-glucopyranosyl-(2 → 1)-β-D-glucopyranosyl (2 → 1)-β-D-glucofuranoside ($C_{44}H_{80}O_{22}$)	Methanolic extract	Chloroform–methanol (3 : 2)	Roots[181]
86	Procerasesterterpenoyl triglucoside or 2,6,10,14,18-pentamethylnonadecanoyl-β-D-glucopyranosyl-(2 → 1)-β-D-glucopyranosyl-(2 → 1)-β-D-glucopyranoside ($C_{42}H_{78}O_{17}$)	Methanolic extract	Chloroform–methanol (3 : 1)	Roots[181]
87	Oleanolic acid ($C_{30}H_{48}O_3$)	Chloroform extract/ butanol fraction	Benzene–ethyl acetate (10 : 1–1 : 10)	Stem bark[165]
88	Lupeol-3-*O*-acetate ($C_{32}H_{52}O_2$)	Ethanolic extract	Chloroform–methanol (9.3 : 0.7)	Leaves[149]
89	Proceraursenolide or 18-α*H*-urs-12-en-3,25-olide ($C_{30}H_{46}O_2$)	Ethanolic extract	Pet. ether–chloroform (1 : 3)	Roots[183]
	Oxypregnane oligoglycosides			
90	Calotroposide H or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-cymaropyranosyl ($C_{63}H_{96}O_{21}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
91	Calotroposide I or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl ($C_{63}H_{96}O_{21}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
92	Calotroposide J or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-(6-*O*-acetyl)-β-D- glucopyranoside ($C_{71}H_{108}O_{27}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
93	Calotroposide K or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]

Table 11 (*Contd.*)

S. No.	Compound name (molecular formula)	Extract/fraction	Eluent	Plant part & references
	oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D- glucopyranoside ($C_{69}H_{106}O_{26}$)			
94	Calotroposide L or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranoside ($C_{68}H_{104}O_{28}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
95	Calotroposide M or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranoside-(1 → 4)-(6-*O*-acetyl)-β-D-glucopyranoside ($C_{78}H_{120}O_{30}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
96	Calotroposide N or 12-*O*-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-glucopyranoside-(1 → 4)-β-D-gluopyranoside ($C_{75}H_{116}O_{31}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[153]
97	Calotroposide S or 12-benzoylisolineolon-3-*O*-β-D-cymaropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-cymaropyranosyl-(1 → 4)-β-D-oleandropyranosyl-(1 → 4)-β-D-oleandro-pyranosyl-(1 → 4)-β-D-oleandropyranoside ($C_{84}H_{132}O_{30}$)	Methanolic extract/*n*-butanol fraction	Chloroform–methanol (85 : 15)	Root bark[154]
Aliphatic and phenolic glycoside				
98	Methyl resorcinyl triglycoside or *O*-methyl resorcinyl-β-D-glucuronopyranosyl (2 → 1)-β-D-glucopyranosyl-(2 → 1)-β-D-glucopyranoside ($C_{25}H_{36}O_{18}$) (phenolic glycoside)	Methanolic extract	Chloroform–methanol (3 : 2)	Roots[169]
99	Butanediol diglucuronoside or (*n*-butan-1,4-diol-1,4-β-D-diglucuronopyranoside) ($C_{16}H_{26}O_{14}$) (aliphatic glycoside)	Methanolic extract	Chloroform–methanol (4 : 1)	Roots[169]
100	(*E*)-3-(4-Methoxyphenyl-2-*O*-β-D-$^4C_1$-glucopyranoside)-methyl propenoate ($C_{17}H_{22}O_9$)	85% methanolic extract	40–60% aqueous methanol	Leaves[76]
101	Methyl 4-*O*-β-D-glucopyranosyl ferulate ($C_{17}H_{22}O_9$)	Ethanolic extract	Water–methanol (1 : 1)	Flowers[149]
Lignan glycoside				
102	7′-Methoxy-3′-*O*-demethyl-tanegool-9-*O*-β-D-glucopyranoside ($C_{26}H_{34}O_{12}$)	Ethanolic extract	Water–methanol (6 : 4)	Flowers[149]
103	Pinoresinol-4-*O*-glucoside ($C_{26}H_{32}O_{11}$)	Ethanolic extract	Water–methanol (1 : 1)	Flowers[149]
104	Syringaresinol-4-*O*-glucoside ($C_{28}H_{36}O_{13}$)	Ethanolic extract	Water–methanol (1 : 1)	Fruits[149]
Terpene glycoside				
105	Labdan-18-ol-β-D-galactofuranoside ($C_{26}H_{48}O_6$)	Methanolic extract	Chloroform–methanol (9 : 1)	Roots[182]
106	Proceralabdanoside/labdan-3β-ol-11,15-olide-18,20-dioic acid-3β-D-galactofuranoside ($C_{26}H_{40}O_{12}$)	Methanolic extract	Chloroform–methanol (9 : 1)	Roots[182]
Caffeic acid derivatives				
107	Methyl caffeate ($C_{10}H_{10}O_4$)	85% methanolic extract	30–50% aqueous methanol	Leaves[76]
108	Caffeic acid ($C_9H_8O_4$)	85% methanolic extract	30–50% aqueous methanol	Leaves[76]
109	Rosmarinic acid ($C_{18}H_{16}O_8$)	Ethanolic extract	Chloroform–methanol (8.5 : 1.5)	Flowers[149]
110	Methyl rosmarinate ($C_{19}H_{18}O_8$)	Ethanolic extract	Chloroform–methanol (8.5 : 1.5)	Flowers[149]
Others				
111	2-Propenyl-2*Z*-hydroxyethyl carbonate	—	—	Leaves[186]
112	Glyceryl mono-oleolyl-2-phosphate ($C_{21}H_{41}O_7P$)	Methanolic extract	Pet. ether–chloroform (1 : 3)	Roots[177]
113	Methyl behenate ($C_{23}H_{46}O_2$)	Methanolic extract	Chloroform–methanol (99 : 1)	Roots[177]
114	*N*-Dotriacont-6-ene ($C_{32}H_{64}$)	Methanolic extract	Pet. ether–chloroform (3 : 1)	Roots[177]
115	Methyl myrisate ($C_{15}H_{30}O_2$)	Methanolic extract	Chloroform	Roots[177]
116	Glyceryl-1,2-dicapriate-3-phosphate ($C_{23}H_{45}O_8P$)	Methanolic extract	Chloroform–methanol (97 : 3)	Roots[177]
117	(*E*)-Octadec-7-enoic acid ($C_{18}H_{34}O_2$)	Methanolic extract/*n*-hexane fraction	*n*-Hexane–ethyl acetate	Root bark[139]
118	Proceranol or *n*-triacontan-10β-ol ($C_{30}H_{62}O$)	Methanolic extract	Chloroform–methanol (99 : 1)	Roots[177]
119	Methyl ferulate	Methanolic extract	Chloroform–methanol (8.5 : 1.5)	Flowers[149]
120	1,2-Dihexadecanoyl-3-phosphatyl glycerol ($C_{35}H_{69}O_8P$)	Methanolic extract	Chloroform–methanol (99 : 1)	Roots[181]
121		Methanolic extract	Pet. ether–chloroform (1 : 3)	Roots[183]

Table 11 (*Contd.*)

S. No.	Compound name (molecular formula)	Extract/fraction	Eluent	Plant part & references
	n-Tetradecanyl palmitoleate/*n*-tetradecanyl *n*-hexadec-9-enoate ($C_{30}H_{58}O_2$)			
122	Tricapryl glyceride ($C_{33}H_{62}O_6$)	Methanolic extract	Pet. ether	Roots[183]
123	Oleodipalmityl glyceride ($C_{53}H_{100}O_6$)	Methanolic extract	Pet. ether–chloroform (9 : 1)	Roots[183]
124	Tribehenyl glyceride ($C_{69}H_{134}O_6$)	Methanolic extract	Pet. ether–chloroform (1 : 1)	Roots[183]
125	Capryl glucoside/*n*-decanoyl-β-D-glucopyranoside ($C_{16}H_{31}O_7$)	Methanolic extract	Chloroform–methanol (49 : 1)	Roots[182]
126	Palmityl glucoside/*n*-hexacosanoyl- β-D-glucopyranoside ($C_{22}H_{43}O_6$)	Methanolic extract	Chloroform–methanol (19 : 1)	Roots[182]
127	Stearyl glucoside/*n*-octadecanoyl-β-D-glucopyranoside ($C_{24}H_{47}O_7$)	Methanolic extract	Chloroform–methanol (93 : 7)	Roots[182]
128	*n*-Heptanoate/heptylate ($C_8H_{16}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
129	*n*-Octanoate/caprylate ($C_9H_{18}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
130	*n*-Nonanoate ($C_{10}H_{20}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
131	*n*-Tridecanoate/tridecylat ($C_{14}H_{28}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
132	*n*-Pentadecanoate/pantadecylate ($C_{16}H_{32}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
133	*n*-Hexadecanoate/palmitate ($C_{16}H_{34}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
134	*n*-Heptadecanoate/margorate ($C_{18}H_{36}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
135	Methyl nonanotetracnoate ($C_{10}H_{12}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
136	*n*-Decenoic acid ($C_{10}H_{18}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
137	9-Decenoate ($C_{11}H_{20}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
138	Undecadienoate ($C_{12}H_{20}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
139	9-Dodecenoate ($C_{13}H_{24}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
140	Tridecatrienoate ($C_{14}H_{22}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
141	2,4,5-Tetradecatrienoate ($C_{15}H_{24}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
142	Hiragonate ($C_{17}H_{28}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
143	Heptadecadienoate ($C_{18}H_{22}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
144	Heptadecenoate ($C_{18}H_{38}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
145	9-Eicosenoate/gadoleate ($C_{21}H_{40}O_2$)	Ethanolic extract	Hexane–chloroform	Aerial part[162]
146	Gallic acid ($C_7H_6O_5$)	Ethanolic extract	HPLC analysis	Aerial part[184]
147	Ferulic acid ($C_{10}H_{10}O_4$)	Ethanolic extract	HPLC analysis	Aerial part[184]
148	*p*-Coumaric acid ($C_9H_8O_3$)	Ethanolic extract	HPLC analysis	Aerial part[184]
149	Vanillic acid ($C_8H_8O_4$)	Ethanolic extract	HPLC analysis	Aerial part[184]
150	Rutin ($C_{27}H_{30}O_{16}$)	Ethanolic extract	HPLC analysis	Aerial part[184]
151	4-Hydroxy-4-methylpentan-2-one ($C_6H_{12}O_2$)	Acetone extract	GC-MS analysis	Latex[161]
152	2,3,4-Trimethylhexane (C_9H_{20})	Acetone extract	GC-MS analysis	Latex[161]
153	Decane ($C_{10}H_{22}$)	Acetone extract	GC-MS analysis	Latex[161]
154	*n*-Pentadecane ($C_{15}H_{32}$)	Acetone extract	GC-MS analysis	Latex[161]
155	2,6-Dimethyl tetra-1,5-decaene ($C_{16}H_{28}$)	Acetone extract	GC-MS analysis	Latex[161]
156	*n*-Eicosane ($C_{20}H_{42}$)	Acetone extract	GC-MS analysis	Latex[161]
157	3,7,11-Trimethyl-2,6,10,12-pentadecatrien-1-ol ($C_{18}H_{30}O$)	Acetone extract	GC-MS analysis	Latex[161]
158	2,6,10,15,19,23-Hexamethyl-2,6,10,14,18,22-tetracosahexaene ($C_{30}H_{50}$)	Acetone extract	GC-MS analysis	Latex[161]
159	1,3,5-Tri-isopropylbenzene ($C_{15}H_{24}$)	Acetone extract	GC-MS analysis	Latex[161]
160	6,10,14-Trimethyl-pentadecanone-2 ($C_{18}H_{36}O$)	Hexane extract	GC-MS analysis	Leaves[185]
161	9-Octadecenoic acid (*Z*)-($C_{18}H_{34}O$)	Hexane extract	GC-MS analysis	Leaves[185]
162	(6*Z*,9*Z*)-Pentadecadien-1-ol ($C_{15}H_{28}O$)	Hexane extract	GC-MS analysis	Leaves[185]
163	Farnesol isomer ($C_{15}H_{26}O$)	Hexane extract	GC-MS analysis	Leaves[185]
164	Tetratetracontane ($C_{44}H_{90}$)	Hexane extract	GC-MS analysis	Leaves[185]
165	Ergost-5-en-3-ol ($C_{28}H_{48}O$)	Hexane extract	GC-MS analysis	Leaves[185]

isolated from flowers, root bark and latex. Oxypregnane glycosides (Fig. 5) have recently been reported from root bark of this plant.[153,154] They have steroidal skeleton containing a 2-deoxy sugar moiety. These oxypregnanes have benzoyl moiety at C-12 and a straight 5–7 units sugar chain connected to C-3 of the aglycone.[6] Some glycosides (Fig. 6), lignan glycosides (Fig. 7), terpene glycosides (Fig. 8) and caffeic acid derivatives (Fig. 9) have also been isolated from this plant.

A number of hydrocarbons, saturated and unsaturated fatty acids were also identified from *C. procera* extract by GC-MS.[161,162] Similarly fatty acid ester, phthalate derivatives, and pentacyclic triterpenes were identified from chloroform extract of roots of *Calotropis procera*.[163]

Apart from the compounds mentioned in Table 11, terpenoids named α-calotropeol and β-calotropeol have been isolated from ethanolic extract of latex.[179] A cardenolide named 19-

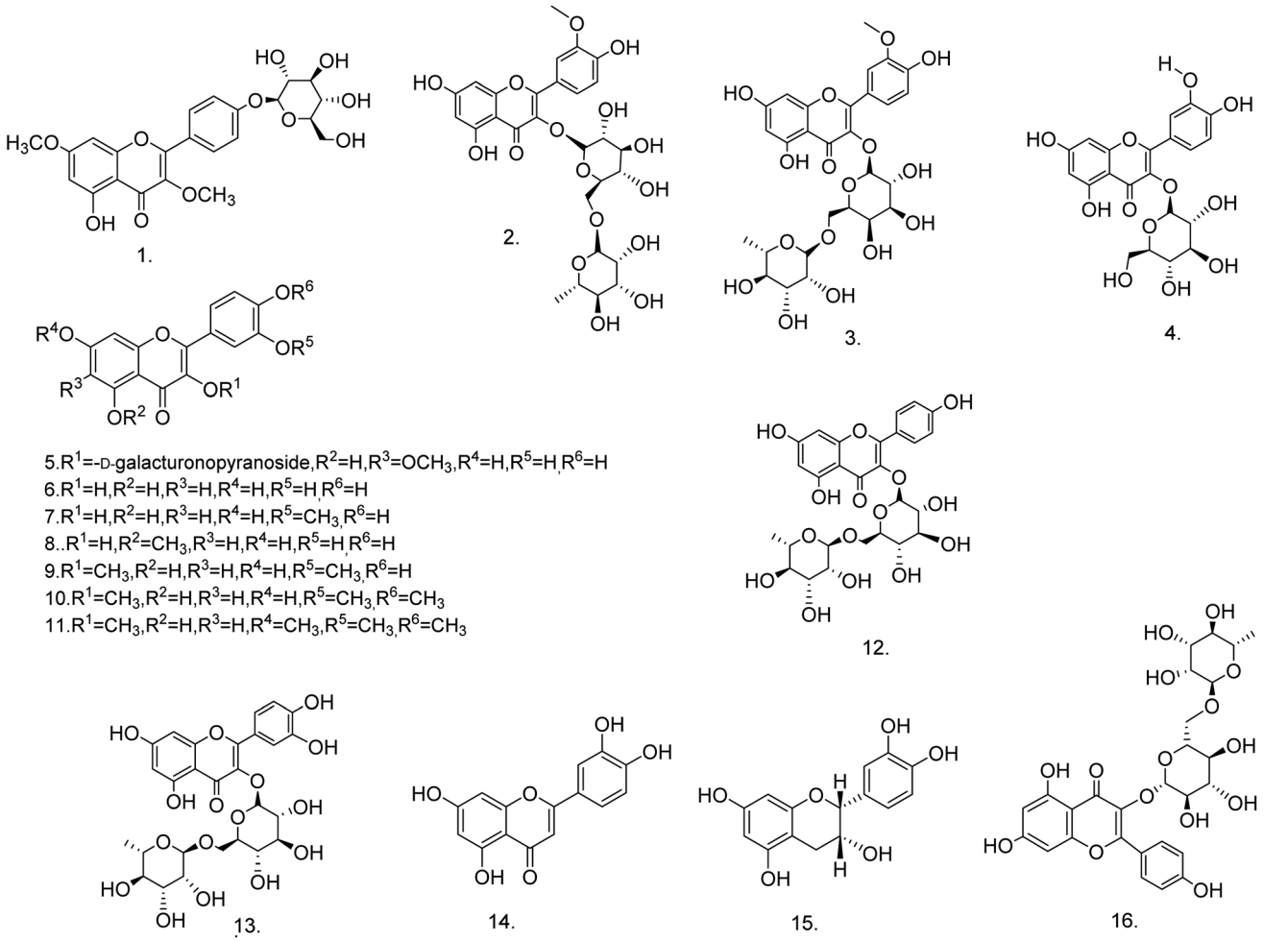

Fig. 1 Chemical structures of flavonoids.

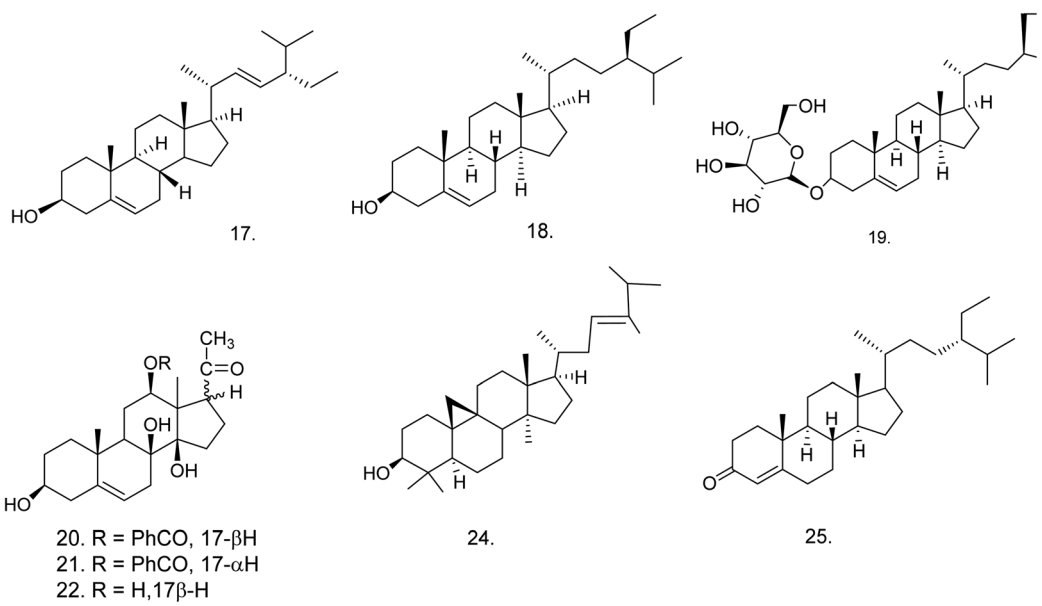

Fig. 2 Chemical structures of steroids.

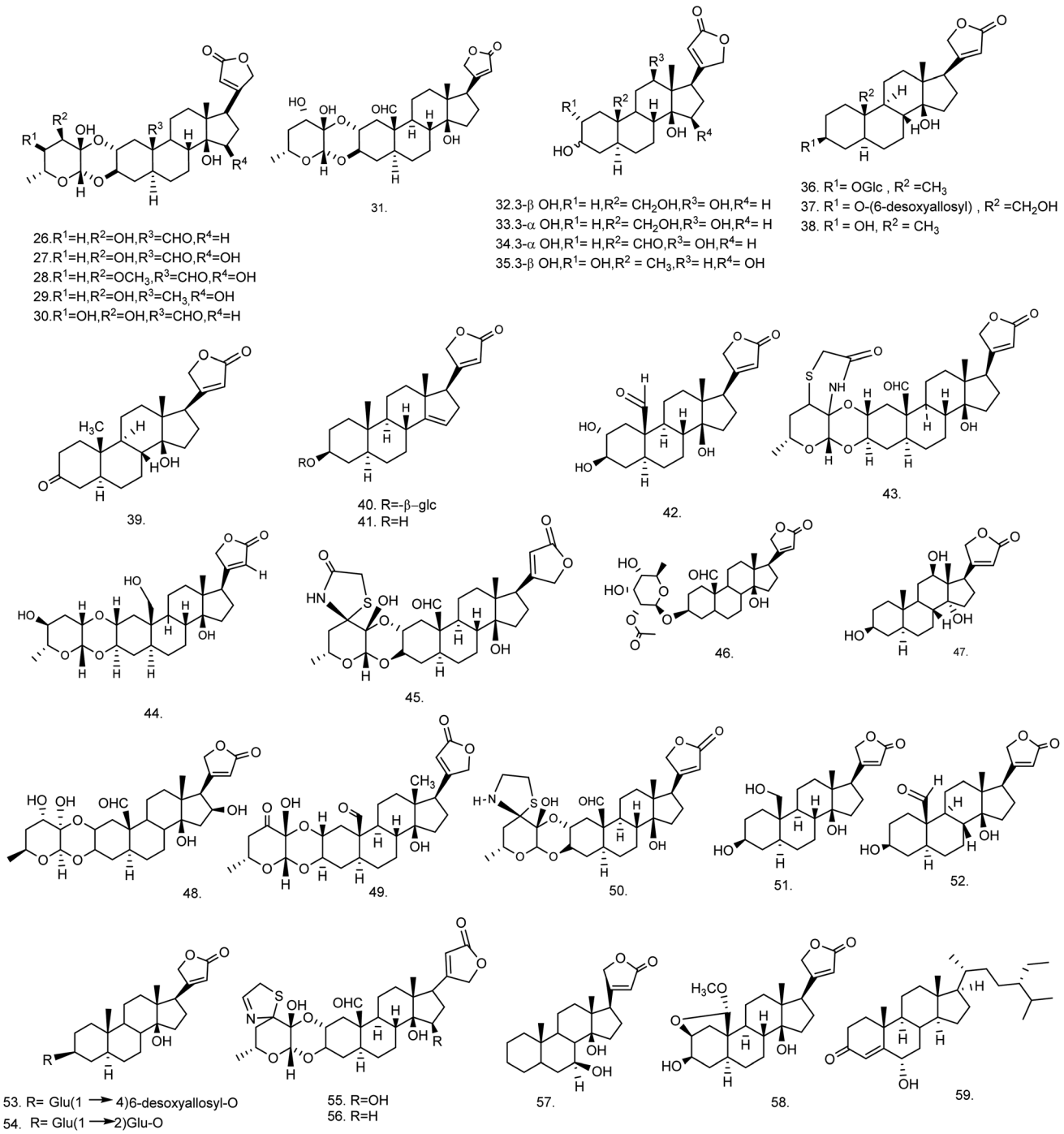

Fig. 3 Chemical structures of cardenolides.

dihydrocalotropagenin and flavonoid named 3′-*O*-methyl-quercetin-3-*O*-rutinoside have also been reported from ethanolic extract of aerial parts.[168]

7. Conclusion, discussion and future perspectives

In the present review, the research progress in phytochemistry and pharmacology of *C. procera* have been summarized. There have been acquirements in the research; still some gaps came across our studies which are as follows:

(1) Folks and tribes have been using *C. procera* since ancient times; still investigations can be carried out on inception time of traditional uses of *C. procera*.

(2) Secondary metabolites of plant vary according to several factors like region, environment, quality of soil, age of plant *etc.* Moreover, latex and root bark seem to be exhaustively investigated for phytoconstituents, not much research on flowers, pods and seeds for phyoconstituentsis have been conducted.

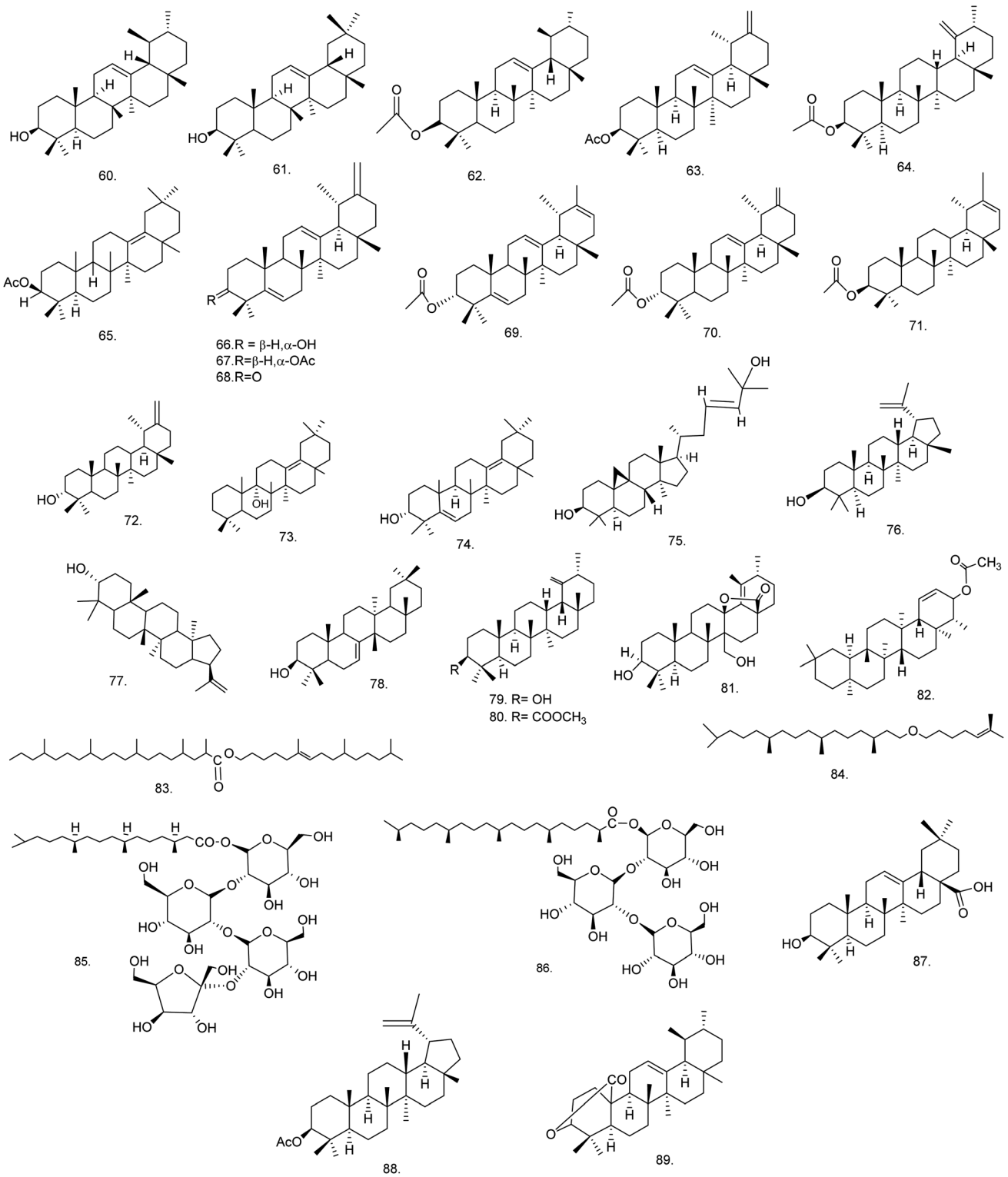

Fig. 4 Chemical structures of terpenoids.

Further exploring these parts can lead to discovery of new phytoconsituents of interest.

(3) The plant can be employed commercially as scientific studies have proved its use as cheese making agent, dehairing of leather, natural surfactant, biopesticide and corrosion inhibitor.

(4) Numerous activities on validation of its cytotoxic and anti-inflammatory potential have been conducted. A few have been carried out on its antimigraine, antiplasmodial and anti-convulsant effects. Carrying out further scientific studies in these fields can provide medical science with effective and promising new drugs.

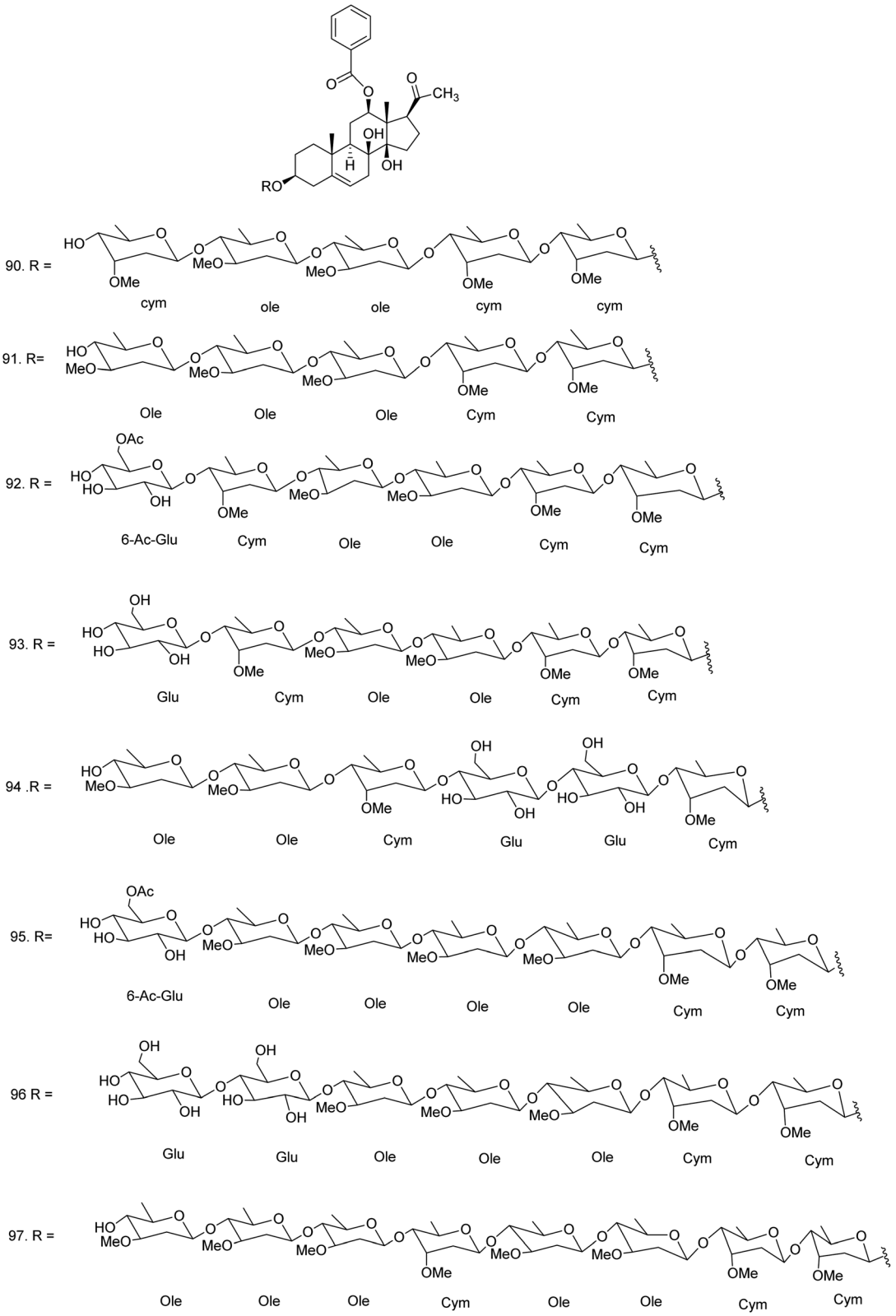

Fig. 5 Chemical structures of oxypregnanes.

(5) Most of the cytotoxic activities conducted are *in vitro* except the one conducted on UNBS1450; a semi-synthesized cardenolide. Further studies should be carried out to examine its *in vivo* potential.

(6) Right route and right dose can convert a dreadful toxicant into an outstanding drug whereas even a drug in lack of proper dosage and route can become a fatal poison. Folk practitioners have been employing *C. procera* as antifertility and uterotonic

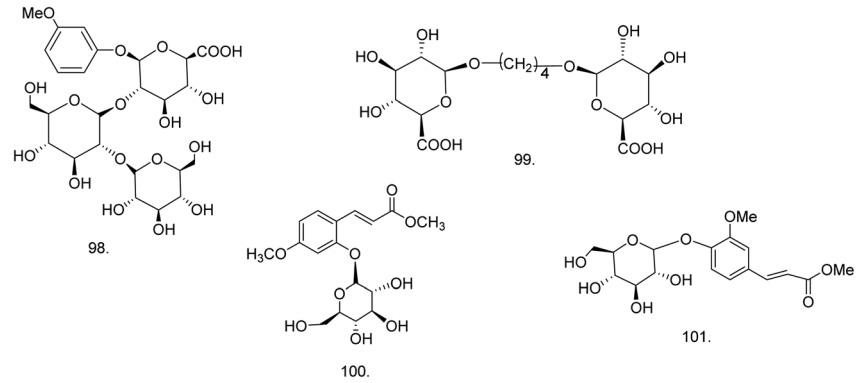

Fig. 6 Chemical structures of glycosides.

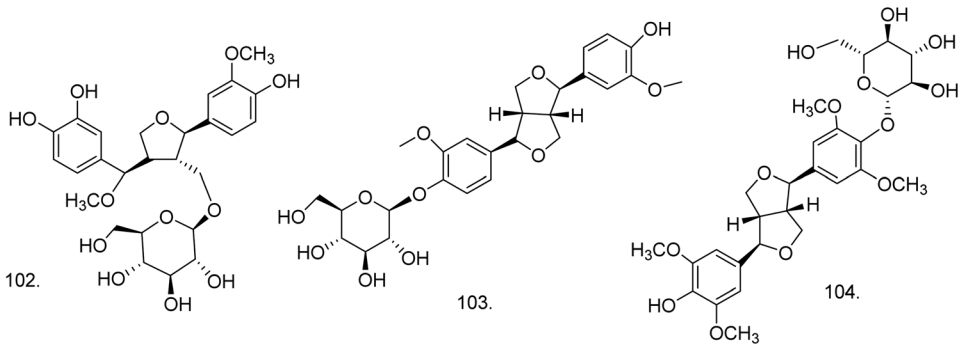

Fig. 7 Chemical structures of lignan glycosides.

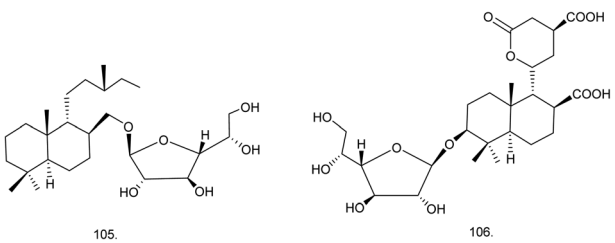

Fig. 8 Chemical structures of terpene glycosides.

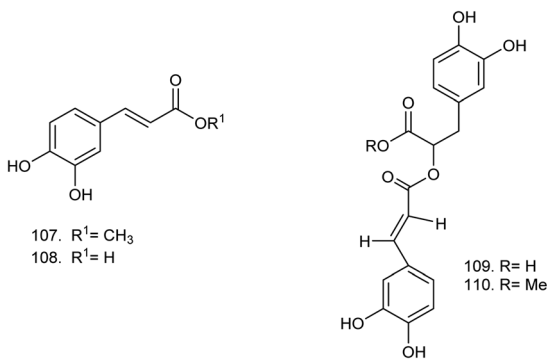

Fig. 9 Chemical structures of caffeic acid derivatives.

agent. Further studies using positive controls, study of toxicity and side effects can lead to discovery of effective and natural contraceptive drugs.

(7) Active principles behind many of the activities are unknown, except the one known for cytotoxic, antibacterial, antifertility, antimolluscicidal and insecticidal activity. More research can be carried out to know the active principles so that potent drugs can be made.

(8) Replicable and environment benign sources of energy are the need of hour, *Calotropis procera* being rich source of various hydrocarbons, thus can prove to be a promising biofuel agent.

Overall, the pharmacology, toxicology, traditional uses, use of secondary metabolites, clinical trials and quality control has been reviewed in this paper. However, there seems to be a good correspondence between pharmacological activities and traditional uses. Further research in this field is essential to determine the active principles and the underlying mechanisms.

Author contributions

Barkha Darra Wadhwani: literature collection, evaluation and draft manuscript preparation. Deepak Mali and Pooja Vyas: literature collection: pharmacological activity and analyses of chemicals constituents of *C. procera*. Rashmy Nair: reviewing and editing. Poonam Khandelwal: concept development; idea generation; manuscript preparation; reviewing and editing.

Conflicts of interest

The authors confirm that this article content has no conflict of interest.

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