Available online on www.ijppr.com
International Journal of Pharmacognosy and Phytochemical Research 2016; 8(5); 777-787

ISSN: 0975-4873

Review Article

Chemical Constituents and Biological Activities of Cleome Genus: A Brief Review

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Available Online: 1st May, 2016

ABSTRACT

Family *Cleomaceae* is an important plant family, it includes seventeen genera and one hundred and fifty species in which *Cleome* genus is the most common one. This review summarizes the researches carried out on this genus concerning with it's chemical constituents and the biological activity. It was found that the plants of this genus contain many chemical classes like essential oils, terpenes, flavonoids, glucosinolates, anthocyanins and alkaloids. Also it exhibited different biological activities as antidiabetic, anticancer, anti-schistomiasis, antibacterial, antidiarrheal analgesic anti-inflammatory and antimalarial.

Key words: *Cleome*, *Cleomaceae*, chemical constituents and biological activity.

INTRODUCTION

Herbal drugs is the oldest form of treatments known to the world. Different cultures have used herbs throughout history. Chemical constituents of herbs have high therapeutic value. Most of the prescribed drugs contain plant extracts or active substances obtained from the plant extracts. *Cleome* is a genus of flowering plants in the family *Cleomaceae*. The genus includes about 170 species of herbaceous annual or perennial plants and shrubs. The genus has a sub-cosmopolitan distribution throughout the tropical and warm temperate regions of the world[1,2]. The antihyperglycemic activities of different extracts of most plants of this genus have been validated by several studies[3,5]. Phytochemical screening studies proved that, *Cleome* enrichment with a diverse array of beneficial secondary products including essential oils, terpenoids, flavonoids, phenolics, and alkaloids, supporting use of the genus for culinary and therapeutic purposes[6,8]**.** This study summaries the chemical constituents, uses, and pharmacological activities of *Cleome* genus.

Chemical constituents

Essential oils and fatty acids

It was found that, many plants of this genus are rich in their essential oil content either in the herb or in the seeds. 65 compounds forming about 99.3% of the total composition were identified in oil of *C. droserifolia*, while thirty compounds were detected and corresponding to 95.9% of the total in the oil of *C. trinervia*. All the data about the other species are found in table 1

Terpenes and sterols

Terpenes are formed from the union of isopreneunits (2-methyl 1,3-butadiene,C_5H_8) and they are replications of that unit. The isoprene units combined together in a"head to tail" manner to form linear chains or rings, which may be mono, sesqui, di, siter, tri, or tetra terpenenes …etc, while the sterols structure contain perhydrocyclopentano phenantherene nucleus. The isolates terpenes and sterols from *Cleome*genus are summarized in table 2

Flavonoids

The flavonoids were found in a number of plants of *Cleome* genus either in aglycone or glycosidic form as in table 3

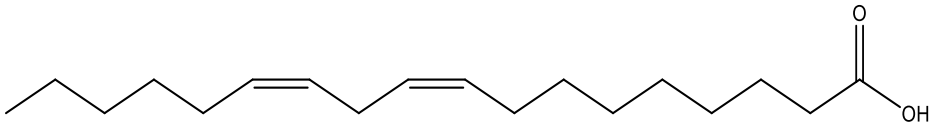
Glucosinolates and isothiocyanates

The Glucosinolates(Gls.)are a class of naturalcompoundswhich includesulfur and nitrogen and are derived from glucose and an amino acid. They are water-solubleanions and can be leached into the water during cooking. Every Gls. contains a central carbonatom, which is bound to the thioglucose group, a nitrogen atom attached to a sulfate group and a side group. Different Gls. have different side groups whichupon hydrolysis gave different products and the variation in the biological activities of these compounds due to it'svariation in their side chains.

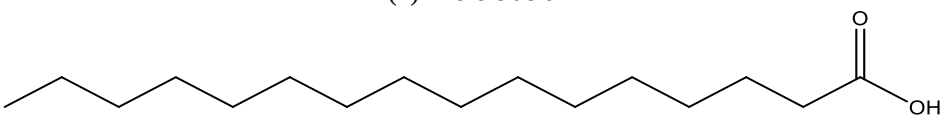
Alkaloids

investigation of the alkaloidal constituents from the ethyl acetate extract of *C.viscosa* seeds during large scale extraction at a level of 100 kg/batch, resulted in the isolation and identification of dipyridodiazepinone which known asnevirapine (**70**), with a yield of 0.004%[20].

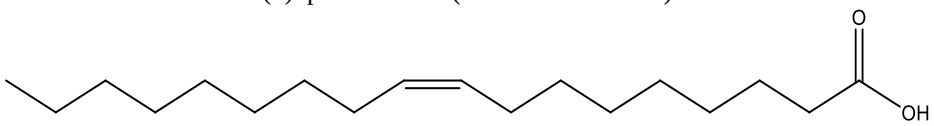
**Author for Correspondence*



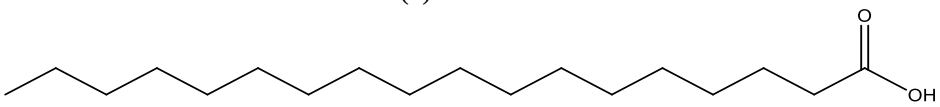
(1) linoleic acid



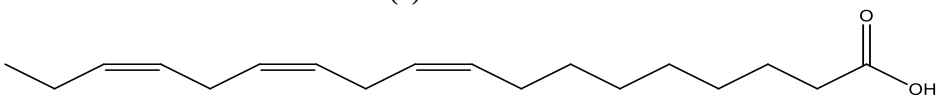
(2) palmitic acid (hexadecanoic acid)



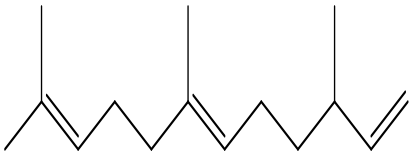
(3) oleic acid



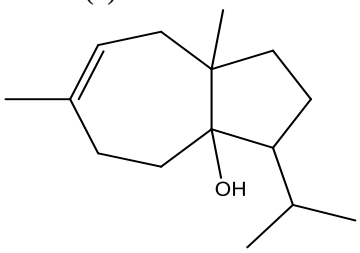
(4) Stearic acid



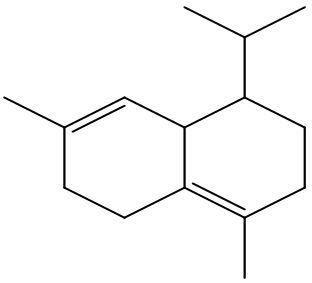
(5) Linolenic acid



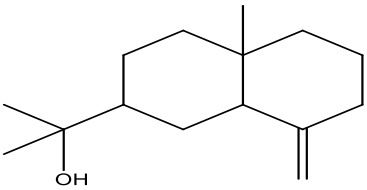
(6) 3,7,11-trimethyldodeca-1,6,10-triene



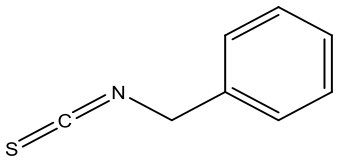
(7) Carotol



(8) δ-cadinene



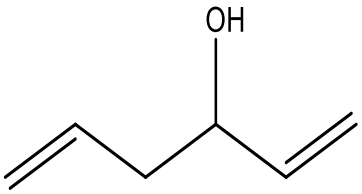
(9) β-eudesmol



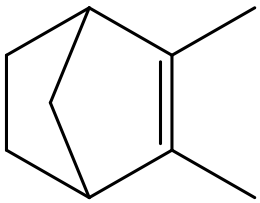
(10) benzyl isothiocyanate

(11) Arachidic acid

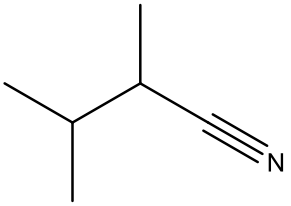
(12) Eicosenoic acid



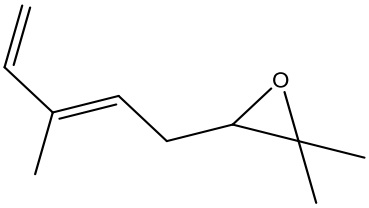
(13) 1,5-hexandien-3-ol



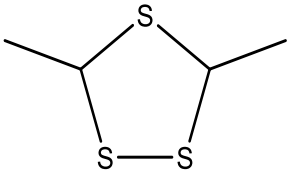
(14) santene



(15) 3-methyl-2-methylbutanitrile

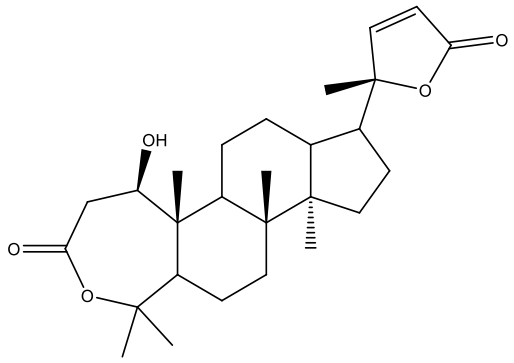


(16) Z-myroxide

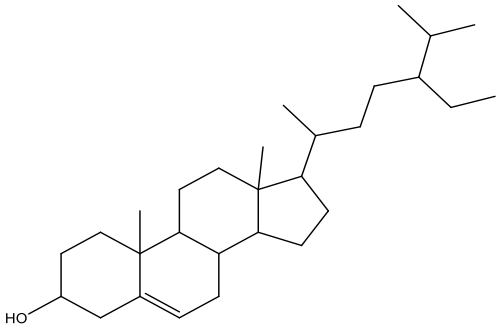


(17) 3,5-dimethyl-1,2,4-trithiolane

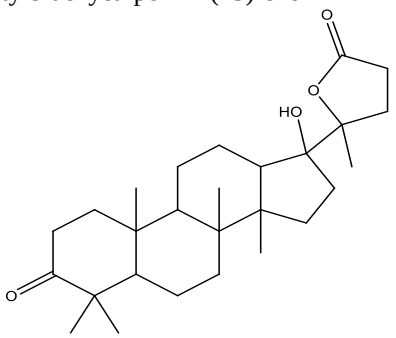
Figure 1: Chemical structure of some compounds in essential oil and fatty acids of *Cleome* genus



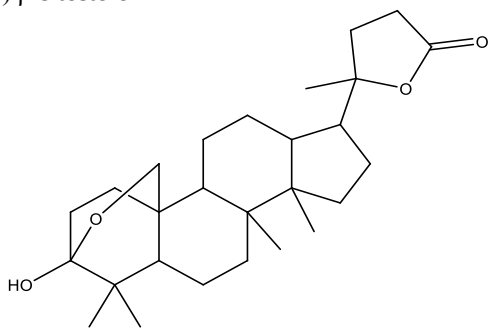
(**18**) 1-deacetylbrachycarpon-22(23)-ene



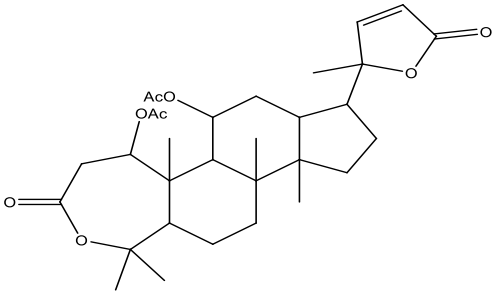
(**19**) β-sitosterol



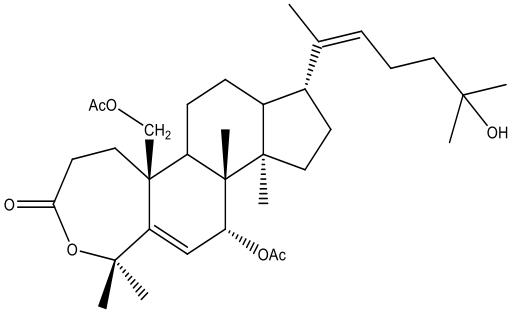
(**20**) 17-α- hydroxycabraleactone



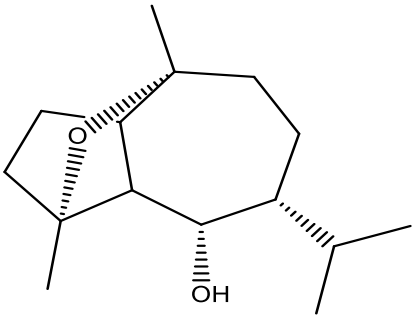
(**21**) amblyone



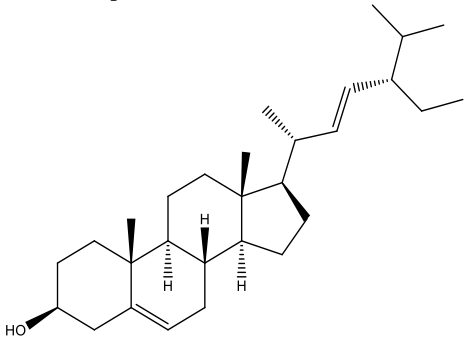
(**22**) 11-α-acetylbrachy-carpone-22(23)-ene



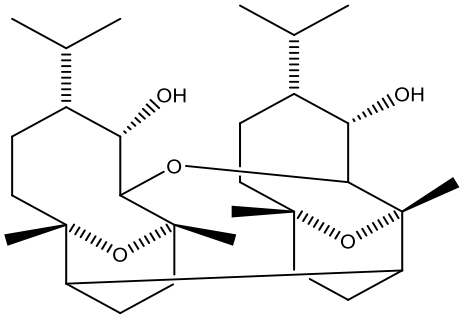
(**23**) drosericarpone



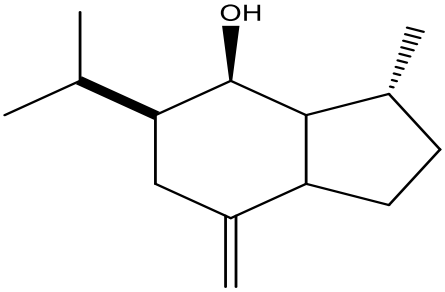
(**24**) Buchariol



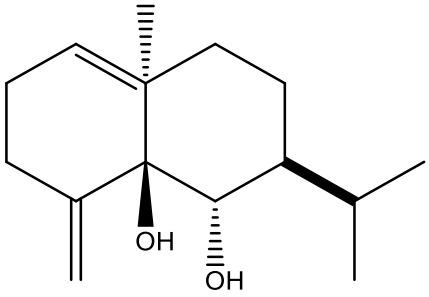
(**25**) stigmasterol



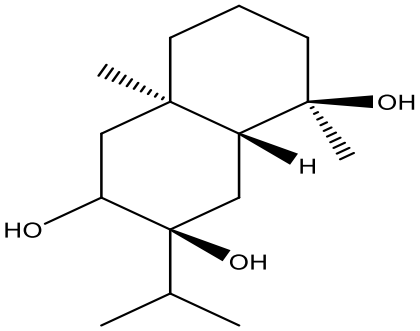
(**26**) 6-di(7-hydroxy, 1, 5-epoxy germacrane)



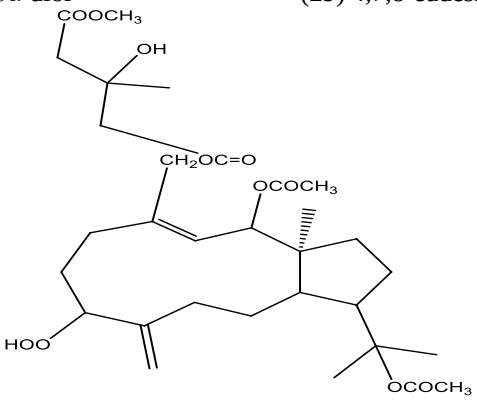
(**27**) 4(15)-guaiane-6-ol



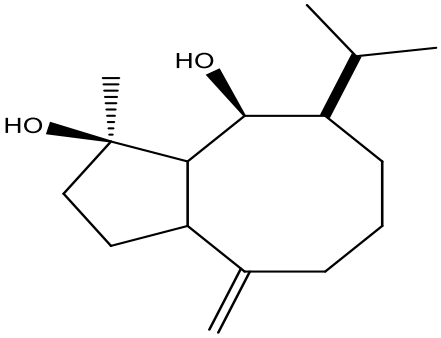
(**28**) 7-germacra-1, 4(15)-diene-5β, 6α-diol



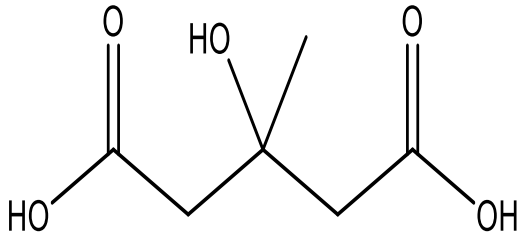
(**29**) 4,7,8-eudesma-triol



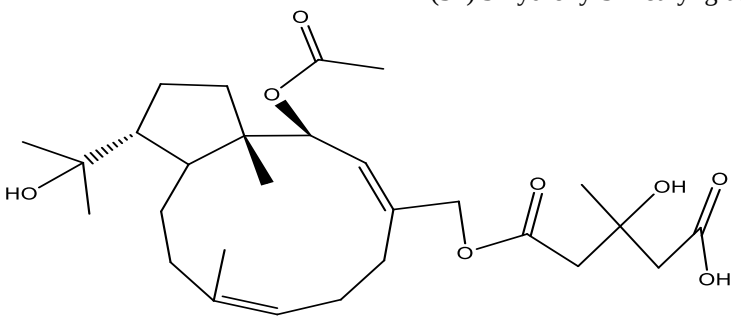
(**31**) 2,18-O-diacetyl-16-O-(3-hydroxy-3-methylglutaryl)- 7-hydroperoxydolabella-3,8(17)diene-2,16,18 triol



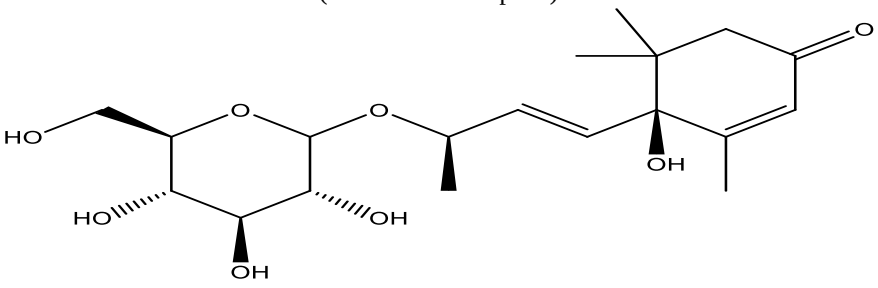
(**30**) teucladiol



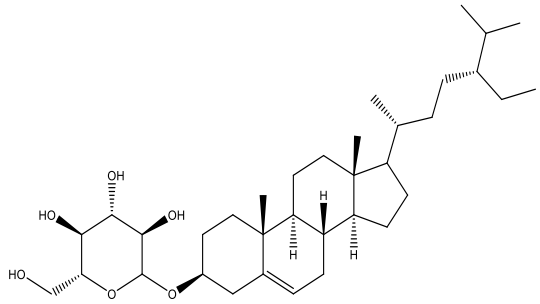
(**32**) 3-hydroxy-3-methyl glutaric acid



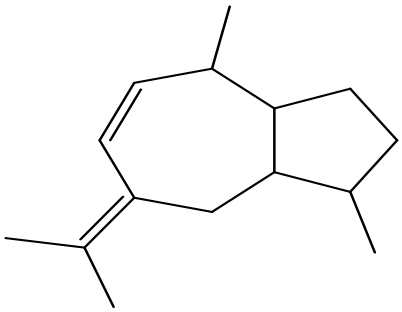
(**33**)(1R,2R,3E,7E,11R,12S)-2-O-acetyl-16-O-(3-hydroxy-3-methylglutaryl)-dolabella-3,7-dien-2,16,18-triol (dolabellanediterpene)



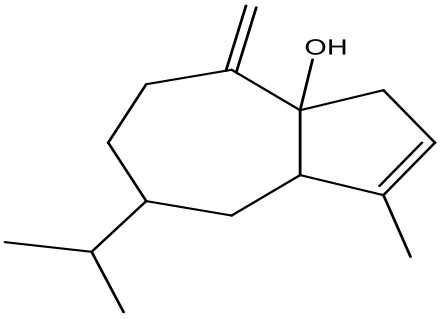
(**34**) (6S,9R)-roseoside (megastigmanenorterpene)



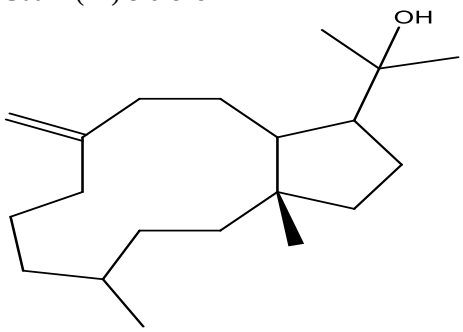
(**35**) daucosterol



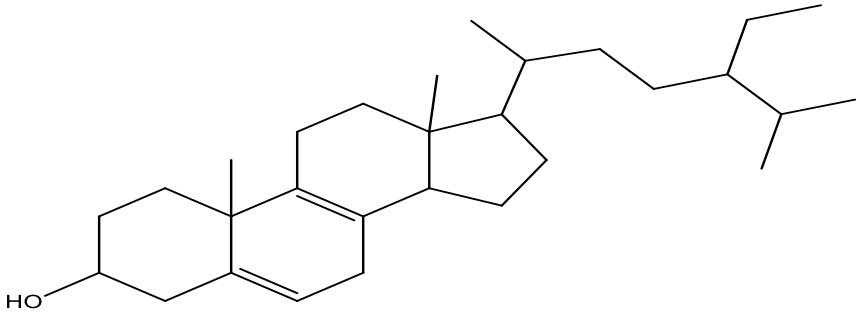
(**36**) Guai-7(11) 8-diene



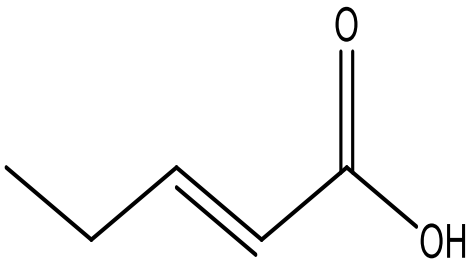
(**37**) 1-Hydroxy-guai-3,10 (14)-diene



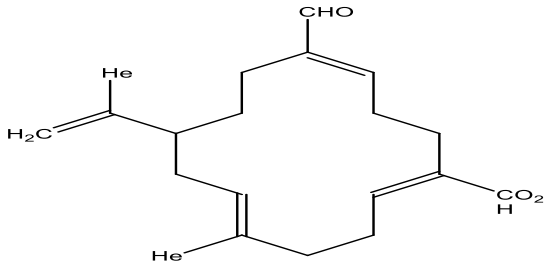
(**38**) 18-Hydroxy-dollabela-8 (17)-ene



(**39**) 24 E-Stigmasta-5,8-dien-3β-Ol



(**40**) paradoxenoic acid



(**41**) cleomaldeic acid

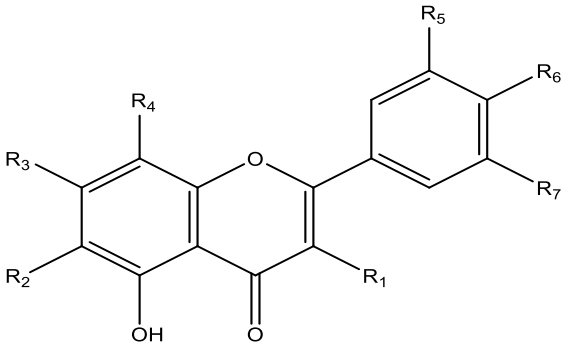
Figure 2: Chemical structure of terpenes and sterols isolated from *Cleome* genus

Two alkaloids were isolated from the chloroform fraction of the methanolic extract of *C.paradoxa*. They identified asparadoxonine (**71**) and paradoxenoline (**72**)[7].

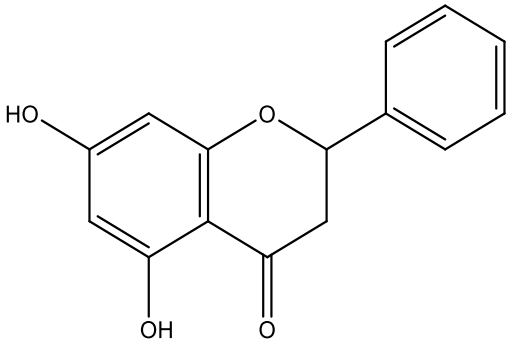
Anthocyanins

It was found another group of compounds are closely related to the flavonoids which known as anthocyanins, that may appear red, purple, or blue depending on the pH. They are present in all tissues of higher plants, and are derived from anthocyanidins by adding sugars. Jordheimet al in 2009[21] studied the anthocyaninsin the flowers of *C.hasslerianaand* identified the following compounds cyanidin 3-(2″-(6‴-caffeoyl-β-glucosyl)-6″-(*p*-coumaroyl)-β-glucoside)-5-β-glucoside (**74**), cyanidin 3-(2″-(6‴-sinapoyl-β-glucosyl)-6″-(*p*-coumaroyl)-β-glucoside)-5-β-glucoside (**75**), cyanidin 3-(2″-(6‴-feruoyl-β-glucosyl)-6″-(*E-p*-coumaroyl)-β-glucoside)-5-β-glucoside (**76**), pelargonidin 3-(2″-(6‴-sinapoyl-β-glucosyl)-6″-(*p*-coumaroyl)-β-glucoside)-5-β-glucoside (**80**)pelargonidin 3-(2″-(6‴-*p*-coumaroyl-β-glu-cosyl)-6″-(*p*-coumaroyl)-β-glucoside)-5-β-glucoside (**82**), together withone monoacylated and four diacylatedcyanidin 3-sophoroside-5-glucosides (**73**,**77**,**78**,**79**,**81**).

Other compounds



(**62**)



(**63**) pinocembrin

No.	R1	R2	R3	R4	R5	R6	R7
42	OH	H	O-Rhamn	H	H	OH	H
43	O-(Rhamn-1-6-Gluc)	H	OH	H	H	OH	H
44	O-Rhamn	H	O-Rhamn	H	H	OH	H
45	O-Gluc	H	O-Rhamn	H	H	OH	H
46	O-Rhamn	H	O-Gluc	H	H	OH	H
47	OH	H	O-Rhamn	H	H	OH	OH
48	O-(Rhamn-1-6-Gluc)	H	OH	H	H	OH	OH
49	OH	H	O-(Rhamn-1-6-Gluc)	H	H	OH	OH
50	O-Rhamn	H	O-Rhamn	H	H	OH	OH
51	O-Gluc	H	O-Rhamn	H	H	OH	OH
52	O-(Rhamn-1-6-Gluc)	H	OH	H	H	OH	OCH_3
53	O-Rhamn	H	O-Rhamn	H	H	OH	OCH_3
54	H	O-Gluc	OH	O-Gluc	H	OH	H
55	OCH_3	OCH_3	OCH_3	OCH_3	H	OH	H
56	OCH_3	OCH_3	OCH_3	H	OH	OCH_3	OCH_3
57	OCH_3	OCH_3	OCH_3	H	OCH_3	OCH_3	OCH_3
58	H	H	OH	H	H	OH	OH
59	OH	H	O-(Rhamn-1-2-Gluc)	H	H	OH	OCH_3
60	O-Gluc	H	OH	H	H	OH	OCH_3
61	O-Acety-Rhamn	H	O-Rhamn	H	H	OH	OCH_3
62	O-Rhamn	H	O-Rhamn	H	H	OCH_3	H

Figure 3: Chemical structure of Flavonoids of *Cleome* genus

Mnzava N.A. in 1990[12] investigated the amino acids in the defattedmealseeds of *Cleome*and he proved the existence Trolox, (+) catechin, p-coumaric acid and gallic acid) using DPPH and giving the highest activity. So, this plant may beconsider as an important source of chemopreventive and chemotherapeutic natural products[22]. Cleomiscosin b (**90**); cleomiscosin c (**91**) and cleomiscosin d (**92**) were isolated from *C. viscosa* extract of glutamic acid (**83**), arginine (**84**) and aspartic acid (**85**) in a relatively high values while Lysine (**86**), tyrosine (**87**) and histidine (**88**) were the lowest**.** It was found that, the phenolic extract of *C.arabica*is the most active as a radical scavenger,the extract was purified by semi-preparative HPLCwhich led to the isolation and identification of a steroid derivative known as, 17-(4-hydroxy-1,5-dimethylhexyl)-2,3,7-(acetyloxy) gona-1,3,5(10)-trien-15-ol) (**89**). The isolated compound was compared to six other standard antioxidants (ascorbic acid, α-tocopherol, and these compounds were used for production of a hepatoprotective natural coumarinolignoid drug named as Cliv-92[23,24].

Biological activity

Table 1: Isolated essential oils and fatty acids from *Cleome* genus

S No.	Plant species	Compounds	Ref.
1	*C. chelidonii*	linoleic (**1**) and palmitic acid (**2**)	9
2	*C. dolichostyla*	linoleic acid (**1**) oleic (**3**) 30·6%; palmitic (**2**) 10·1%; stearic (**4**) 4·49% and linolenic (**5**) 1·17%.	10
3	*C. droserifolia*	3,7,11-trimethyldodeca-1,6,10-triene (11.8%) (**6**), carotol (10.1%) (**7**), δ-cadinene (8.9%) (**8**), β-eudesmol (7.0%) (**9**) and benzyl isothiocyanate (5.9%) (**10**).	11
4	*C. gynandra*,	linoleic (**1**), palmitic acid (11·2%) (**2**), Oleic (**3**) stearic (6·55%) (**4**), Arachidic (**11**) and eicosenoic acids (**12**)	9,12
5	*C. simplicifolia*,	linoleic (**1**) and palmitic acid (**2**)	9
6	*C. speciosa*.	linoleic (**1**) and palmitic acid (**2**)	9
7	*C. trinervia*	1,5-hexandien-3-ol (28.3%) (**13**), santene (20.0%) (**14**), 3-methyl-2-methylbutanitrile (14.9%) (**15**), Z-myroxide (9.3%) (**16**) and 3,5-dimethyl-1,2,4-trithiolane (7.0%) (**17**).	11
8	*C. viscosa*	palmitic acid (**2**)	9

Table 2: isolated terpenes and sterols from *Cleome* genus

S No.	Plant species	compounds	Ref.
1	*C.arabica*	1-deacetylbrachycarpon-22(23)-ene)(18), β-sitosterol(19), 17-α hydroxylcabraleactone (20), amblyone (21), 11-α-acetylbrachy-carpone-22(23)-ene (22)	13
2	*C. droserifolia*	Drosericarpone(23), buchariol(24), stigmasterolglucoside(25), 6-di(7-hydroxy, 1, 5-epoxy germacrane) (26), 4(15)-guaiane-6-ol (27), 7-germacra-1, 4(15)-diene-5β, 6α-diol (28) and 4,7,8-eudesma-triol (29), teucladiol (30), 2,18-O-diacetyl-16-O-(3-hydroxy-3-methyl-glutaryl)-7-hydroperoxydolabella-3,8(17)diene-2,16,18 triol(31), 3-hydroxy-3-methyl glutaric acid (32), (1R,2R,3E,7E,11R,12S)-2-O-acetyl-16-O-(3-hydroxy-3-methyl-glutaryl)-dolabella-3,7-dien-2,16,-18-triol (33), (6S,9R)-roseoside (34), daucosterol (35) Guai-7(11) 8-diene (36); 1-Hydroxy-guai-3,10 (14)-diene (37); 18-Hydroxy-dollabela-8 (17)-ene (38); (24 E) Stigmasta-5,8-dien-3β-Ol (39)	1,6, 14, 15, 16
3	*C.paradoxa*.	paradoxenoic acid (40)	7
4	*C. viscosa*	cleomaldeic acid (41)	17

Table 3: isolated flavonoids from *Cleome* genus

S No.	Plant species	Compounds	Ref.
1	Cleome sp.	K-7-*O*-rhamnoside (**42**), K-3-*O*-rutinoside (**43**), K- 3,7-*O*-dirhamnoside (**44**), K-3-*O*-glucoside-7-*O*-rhamnoside (**45**), K- 3-*O*-rhamnoside-7-*O*-glucoside (**46**), Q-7-*O*-rhamnoside (**47**), Q-3-*O*-rutinoside (**48**), Q-7-*O*-rutinoside (**49**), Q- 3,7-*O*-dirhamnoside (**50**), Q- 3-*O*-glucoside-7-*O*-rhamnoside (**51**), isorhamnetin 3-*O*-rutinoside (**52**), isorhamnetin 3,7-*O*-dirhamnoside (**53**), and vicenin-2 (**54**).	4
2	*C. arabica*	Calycopterin (**55**)	13
3	*C. droserifolia*	5,3′-dihydroxy-3,6,7,4′,5′-pentamethoxyflavone(**56**), 5-hydroxy-3,6,7,3′ ,4′,5′ hexamethoxyflavone(**57**), luteolin(**58**), 3′-methoxy-3,5,4′-tri-hydroxy flavone-7-neohesperidoside (**59**)**,** Q-3-*O*-glucoside-7-*O*-rhamnoside(**51**), isorhamnetin-3-*O*-glucoside(**60**),Q-3′-methoxy-3-*O*-(4″-acetylrhamnoside)-7-*O*-α-rhamnoside(**61**), K-4′-methoxy-3,7-*O*-dirhamnoside (**62**) and pinocembrin (**63**)	6,14, 15,16

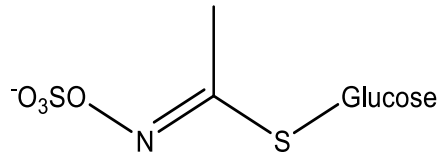
K= keampferol, Q= quercetin

Table 4: Isolated Glucosinolates and isothiocyanates from *Cleome* genus

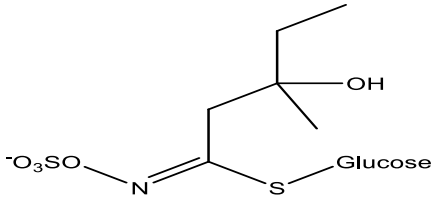
S No.	Plant species	Compounds	Ref.
1	*C. chelidonii*	glucocapparin(**64**), glucocleomin (**65**) (2-hydroxy-2-methylbutyl-Gls.), Methyl isocyanate (**66**) and 5-ethyl-5-methyl-oxazolidine-2-thione (**67**).	12,18, 19
2	*C. droserifolia*	benzyl isothiocyanate (**68**)	11
3	*C. trinervia*	3-Methyl-2-methylenebutanitrile (**69**).	11
4	*C. viscosa*	glucocapparin (**64**), glucocleomin (**65**) (2-hydroxy-2-methylbutyl-Gls.), (Methyl isocyanate (**66**) and 5-ethyl-5-methyl-oxazolidine-2-thione (**67**).	12,18, 19

Antidiabetic

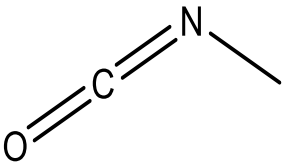
C. droserifolia is widely used traditionally in Egypt and Jordan to counteract hyperglycemia. There are many research efforts confirmed it's utility as a hypoglycemic



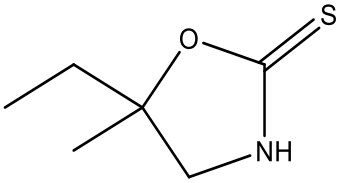
(**64**) glucocapparin



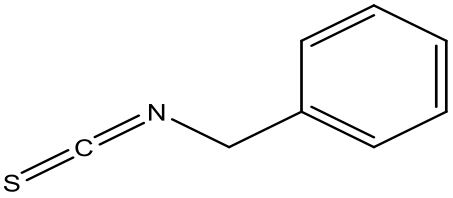
(**65**) glucocleomin



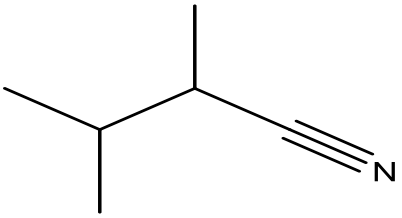
(**66**) Methyl isocyanate



(**67**) 5-ethyl-5-methyl-oxazolidine-2-thione

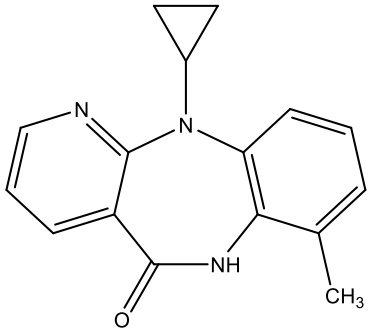


(**68**) benzyl isothiocyanate

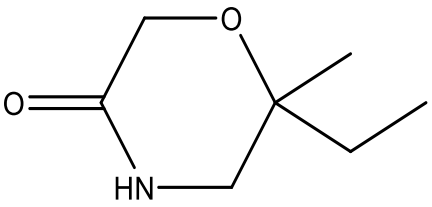


(**69**) 3-Methyl-2-methylenebutanitrile

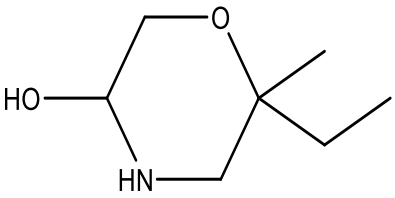
Figure 4: Chemical structure of Glucosinolates and isothiocyanates isolated from *Cleome* genus



(**70**) nevirapine



(**71**) paradoxonine



(**72**) paradoxenoline

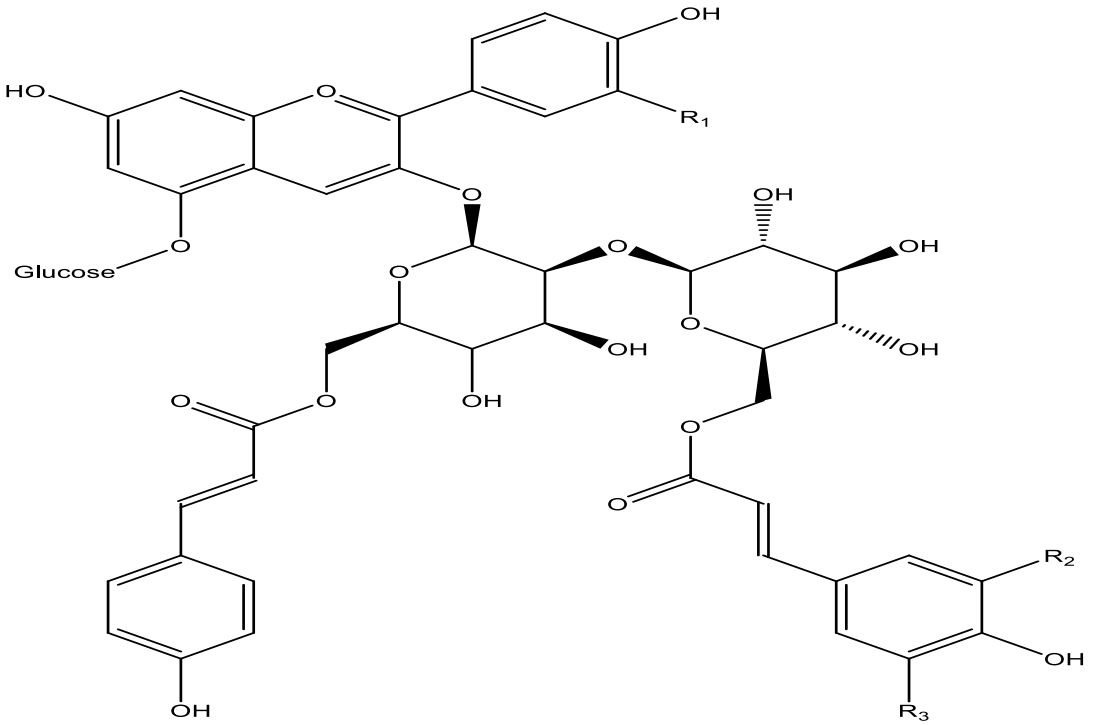
Figure 5: Chemical structure of Alkaloidal compounds of *Cleome* genus

herb[25]. The aqueous and ethanolic extracts of this plant was examined for their antidiabetic activity in cultured C2C12 skeletal muscle cells and 3T3-L1 adipocytes. It was proved that,the activity is attributed to significant insulin-like effects in peripheral tissues of quercetin-3′-methoxy-3-*O*-4″-acetyl-rhamnoside-7-*O*-α-rhamnoside andkaempferol-4′-methoxy-3,7-dirhamnoside [16].Also the same activity as well as the effect on lipid peroxidation of three different doses (50, 100, and 200 mg/kg) of methanolic extract of the plantaerial parts in comparison with glibenclamide in alloxan-induced diabetic rats were studied by El Naggar*et al*., 2005[26]. whoexplain these activities due to the presence of three flavonoids (isorhamnetin, kaempferol, andquercetin) together with three phenolic acids (4-coumaric acid, ferulic acid andsinapinic acid). Nicola *et al*.[27] and El-Shenawy in 2006[28] reported about significant suppression in the rise in peripheral blood glucose concentrations caused by *C. droserifolia* extract, both in the basal (fasting) state and after glucose intake. Suppression of fasting glucose indicated a lowering effect of the extract on hepatic glucose output (HGO). The antihyperglycemic and antihyperlipidemic effects of the methanolic extracts of the aerial parts of *C. ramosissima*, were evaluated in STZ induced diabetic rats at a dose of 500 mg/kg bw. It was found that *C. ramosissima* have both antihyperglycemic and hypolipidemic effects with high insulin-secreting activity[29].

Anticancer

The cytotoxicity of the aqueous and ethanolic extracts, respectively, of the aerial parts of *C. droserifolia* against two human cancer cell lines, breast (MCF7) and colon (HCT116) adenocarcinoma. The Aq.Ex.displayed high cytotoxic activity, thus it's four subfractions, namely n-hexane, chloroform, ethyl acetate, and n-butanol fractions were also tested. The results proved that, significant cytotoxic activities against the two tested cell lines comparable to those of the anticancer drug doxorubicin. The compound 18-hydroxydollabela- 8(17)-ene was the most active as it had the lowest IC_{50} value[30].

Antischistomiasis



No.	R1	R2	R3
73	OH	-	-
74	OH	OH	H
75	OH	OCH_3	OCH_3
76	OH	OCH_3	H
77	OH	H	H
78	H	-	-
79	H	OH	H
80	H	OCH_3	OCH_3
81	H	OCH_3	H
82	H	H	H

Figure 6: Chemical structure of Anthocyanins of *Cleome* genus

El-Shenawy, 2006[28] studied the antischistomiasis activity of alcoholic leaves extract of *C. droserifolia* (ALECD) on experimentally infected mice with *Schistosomamansoni*. He took two groups of mice which showed a potent infection of *S. mansoni*, one of them was daily treated with ALECD (0.31 g/kg b.wt, i.p.) for 21 days. The results after a weak showed a reduction in worm burden (32.46%) and affected the viability of both mature and immature eggs as substantiated by increasing in the percentage of dead eggs.

Antibacterial

The antibacterial activity of ethanolic extracts of both leaves and flowers of *C. viscosa* was investigated against *E. coli*, *P. vulgaris* and *Ps.Aeruginosa*.The results showed a broad spectrum of antimicrobial activity of both extracts, in addition to the leaves extract exhibited moderate activity against pathogenic fungi[31]. Muhaidat et al in 2015[11] studied the antibacterial activity of essential oilsof both*C. droserifolia* and *C. trinervia*against different pathogens usingthe agar-well diffusion and the micro-dilution methods. The study showed that, both of the two oils exhibited marked growth inhibitory effects. Most tested bacterial species were inhibited, despite the varying degrees of inhibition observed (MIC values of 150–550 μg ml^{-1}). The antibacterial activity was evaluated *in vitro* against bacteria by Further explorations for use as natural therapeutics (antibacterial agents) are suggested. It was found that, the glucosinolates and their hydrolysis products which were isolated from *Cleome*have a significant antimicrobial activity[32].

Analgesic and Anti-inflammatory

The ethanolic extract of *C. rutidosperma* aerial parts at doses of 200 and 400 mg/kg, p.o, showed a high analgesic activity in acetic acid-induced writhing and tail immersion tests, anti-inflammatory effect against carrageenan induced inflammation, induced polyarthritis and antipyretic activity against yeast-induced pyrexia[33]. The ethanolic extract of *C. gynandra* was administered orally at a dose of 150 mg/kg b. wt. for 30 days to the induced arthritic rats (which was assessed by paw volume measurement) and it's capacity to stabilize lysosomal

enzyme activities in the plasma and liver of control and experimental rats. Pathophysiological enzymes such as AST, ALT, ALP, cathepsin-D, β-glucuronidase, *N*-acetyl-β-glucosaminidase, LDH activity and the levels of glycoproteins were also estimated in plasma and liver. The increased levels of both lysosomal enzymes and protein-bound carbohydrates in arthritic rats were highly reduced to near normal values. Furthermore, the elevated plasma level of TNF-α found in arthritic rats wasfound to be decreased to near normal levels[34]. The analgesic and antipyretic activities of *C.viscosa* methanolic extract(given orally) were examined in mice using the acetic acid-induced writhing and the tail flick, tail clip, tail immersion methodsand yeast-provoked elevated temperature rats. The extract gave promising activity in all the testes and caused a high reduction in body temperature in a dose-dependent manner in relative to paracetamol (150 mg/kg. bwt)[35].

Antidiarrheal activityC. viscosa methanolic extract was investigated for it's anti-diarrheal potential against some of the experimental models of diarrhea in rats. It exhibited significant inhibitory activity against castor-oil-induced diarrhea and PGE_{2-} induced enteropooling in rats and also a significant reduction in gastrointestinal motility in the charcoal meal test in rats. The results obtained establish the efficacy and substantiate the folklore claim as an anti-diarrheal agent[36].

Anti- malarial activity

Elufioye and Onoja in 2016[37] evaluated the methanolic extract of *C. viscosa*as anti-malarial in treatment and prophylactic in chloroquine sensitive infected mice. The results showed that, the extract has a high activity in both ways in a dose dependent behavior.

CONCLUSION

In conclusion, considering all available evidence present review suggested that, *Cleome* genus comprises different chemical constituents (essential oils, terpenes, flavonoids, glucosinolates and alkaloids) and has many pharmacological functions including anti-diabetic, anticancer, antibacterial, antiinflammatory, analgesic, antidiarrheal and antimalarial[38]. So, the plants of Cleome genus may be useful to the health professionalsand scientist's scholars to develop a natural drugs from traditionally used plants.

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