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Phytochemical and Biological Activities of *Lagenaria siceraria*: An Overview

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Abstract

Lagenaria siceraria commonly known as bottle gourd, is a medicinal plant widely cultivated in African and Asian countries. It is official in Ayurvedic Pharmacopoeia. It is traditionally used as a nutritive agent having cardioprotective, cardiotonic, general tonic, diuretic, aphrodisiac, antidote to certain poisons, scorpion strings and alternative purgative. It cures pain, ulcers, fever and is used for pectoral cough, asthma and other bronchial disorders. It also has various biological activities such as: anthelmintic, hepatoprotective, antimicrobial, antihyperlipidemic, antihyperglycemic, analgesic and anti-inflammatory activity. Lagenaria siceraria contains a number of primary and secondary metabolites. It contains important terpenoids, sterols, flavonoids, alkaloids, phenolics and phenolic acids. The information in this review is retrieved from the database search including Egyptian Knowledge Bank (EKB), PubMed and Google scholar. From the literature, it was clearly revealed that L. siceraria showed a broad spectrum of biological and pharmacological activities due to the presence of various secondary metabolite. In the light of the above-mentioned multiple benefits of bottle gourd, the plant is regarded as a natural guard against diseases. L. siceraria possesses many important chemical constituents, which require further research to explore the medicinal value of this species.

Keywords: Lagenaria siceraria, Bottle gourd, Cucurbitaceae, Traditional use, Phytochemistry, Biological activities

1. Introduction

Cucurbit is the common name of the family Cucurbitaceae, which is usually called "the gourd, cucumber, melon, or pumpkin family". It is generally a medium size climbing plant family, including more than 118 genera and 825 species. These plants are widely distributed in warm places all over the world. Cucurbits are an outstanding source of secondary metabolites. Several genera of this family have received significant scientific interest due to their wide range of pharmacological activities and nutritional values [1]. Family Cucurbitaceae includes many vegetable gourds, such as Lagenaria siceraria (bottle gourd), Citrullus lanatus (watermelon), Cucumis sativus (cucumber), Cucumis melo (melon), Cucumis anguria (bur gherkin), Cucurbita (five species of squash & pumpkin), Momordica charantia (bitter melon), Momordica dioica (spine gourd), Sechium edule (chayote), Luffa acutangula (ridge gourd), Benincasa hispida (wax gourd), Trichosanthes anguina (snake gourd), Trichosanthes dioica (pointed gourd), Telfairia (two species of oyster nut), Sicana odorifera (casabanana), Coccinia grandis (ivy gourd), Praecitrullus fistulosus (tinda), Cyclanthera pedata (slipper gourd) and Cucumeropsis mannii (white-seeded melon) [2]. Among all the plants of the Cucurbitaceae family, the genus Lagenaria is the most common. Cucurbita (pumpkin) is one of the most common plants belonging to Cucurbitaceae family which was considered as a nutrient-dense food, helped Prophet Yunus to recover. L. siceraria (Mol.) Standl. (Family Cucurbitaceae), commonly known as bottle gourd, is a medicinal plant widely cultivated in African and Asian countries. It is official in Ayurvedic Pharmacopoeia. It is commonly known as lauki, Ghiya (Hindi), Kadoo (Marathi) and bottle gourd (English). The plant is considered an amazing medicinal plant [3]. Recently, L. siceraria has become widely cultivated in many countries for its culinary and medicinal uses. It may be considered a

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magical medicinal drug to mankind. The importance of L. siceraria has been increased worldwide. There is a great interest in the pharmacological activities and the corresponding bioactive constituents which has an amazing and significant ability for the treatment of various diseases.Most common bioactive compounds of L. siceraria include secondary metabolites such as alkaloids, phenolic compounds, plant growth factors, food grade pigments, antibiotics, and mycotoxins[4]**.** Many secondary metabolites that protect plants from pathogens, insects, and environmental stresses are also valuable to human health. Genus Lagenaria has six species. All six species are found in Africa. L. siceraria is the only cultivated species, the rest are wild [5]. L. siceraria is derived from the latin word lagena, which means bottle. It was often referred to as Lagenaria vulgaris or Lagenaria leucantha (white-flowered gourd), but nowadays, it is known as Lagenaria siceraria [6]. L. siceraria considered as a climbing perennial plant and cultivated in tropical countries (India, Japan and Thailand) as a vegetable crop. It is an annual plant, elliptical shaped fruit, climbing or tailing herb, dark green in color, bitter in taste and characteristic odor. Fruits vary widely in shape and size up to 25-60 cm long, mace or dumb-bell shaped fruits with a hard shell- like epicarp when ripe. Their external surface is smooth, pale green in color, the pulp is yellowish or pale brown, and Upon maturity it dries up, leaving a thick, hard hollow [7]. Flowers are stalked (female flower stalks shorter than male), axillary, solitary and unisexual. Both the male and female flowers open at the same time. The flowers are short lived. Leaves are simple, 5-lobed, cordate in shape, long petioled, pubescent, with softly hairy on both sides, undivided, angular, lobes rounded, margins are toothed, its odour is nonaromatic. Leaf stalks are up to 300 mm in long, thick, hollow, hairy dense, with two small lateral glands at the base of the leaf [8]. The seeds are numerous, embedded in a spongy pulp, pressed, with two flat facial ridges [8]. There are two types of fruits of this species, sweet and bitter [9].

Figure 1: Fruits of Lagenaria siceraria

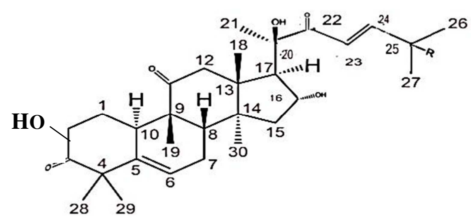
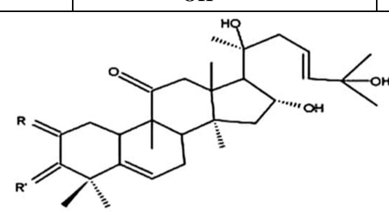
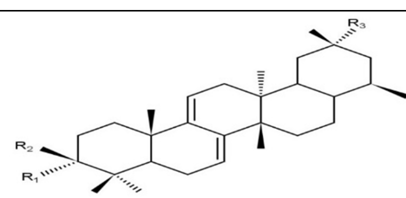
2. Materials and Methods

The information presented is retrieved from the database search including Egyptian Knowledge Bank (EKB), PubMed and Google scholar for “Lagenaria siceraria” or “bottle gourd” as keywords and full text were obtained from the respective publisher’s/journal’s website. Literature survey of genus lagenaria reveals the presence of different types of flavonoidal constituents, phenolic acids, fatty acids, amino acids, terpenoids and miscellaneous compounds. Many studies showed that tetracyclic triterpenoids (Cucurbitacin), a secondary metabolite found in L. siceraria and other Cucurbitaceae species, is responsible for the bitter flavor of cucurbits [10] and protects plants from herbivores, acting as an insecticide [11].

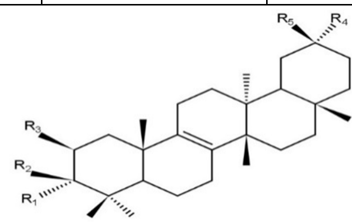
3. Results and Discussion

Current literature of Lagenaria proved that bitter fruits contain cucurbitacins B, D, G and H [12, 13]. The most common are cucurbitacin B, 22-deoxycucurbitacin-D and 22-deoxoisocucurbitacin-D [14]. These compounds are present in fruits as aglycones [15]. It is also reported that leaves contain cucurbitacins B, D and traces of curcubitacin E [15]. In addition to, cytotoxic triterpenes d:C-friedooleanane (5-13) were isolated from the methanol extract of the plant stems [16]. HPLC–ESI-Q-TOF-MS was used in the isolation of triterpene (Cucurbitacin I), tetranortriterpenoid (Swietenine) from the mesocarp of L. siceraria [17]. An antiallergic compound, was reported from callus culture of L. siceraria roots as Bryonolic acid [18]. L. siceraria contains steroids like Fucosterol, Campesterol, Avenasterol, Codisterol, Elesterol, Isofucasterol, Stigmasterol, Racemosol, Sitosterol, Compesterol and Spinasterol [19]. Moreover L. siceraria were found to contain flavone-C-glycosides such as isovitexin, isoorientin and saponarin [20-22]. A phenolic glycoside (E)-4-hydroxymethyl-phenyl-6-*O*-caffeoyl-*β*-D-glucopyranoside together with 1-(2-hydroxy-4-hydroxymethyl)-phenyl-6-*O*-caffeoyl-*β*-D-gluco-pyranoside, protocatechuic acid, gallic acid, caffeic acid and 3,4-dimethoxy cinnamic acid were isolated from fruits [23, 24]. In addition to, small amount of unidentified mono and dicaffeoylquinic acid derivative [25]. Another study succeeded in the isolation of alkaloids 1,4-Dideoxy-1,4-Imino-D Arabinitol and Cuscohygrine from the mesocarp of *L. siceraria* by HPLC–ESI-Q-TOF-MS [17, 26]. Fruits were reported to contain ascorbic acid and *β*-carotene, in addition to, vitamin B such as (thiamin, riboflavin, niacin, vitamin B6), pantothenic acid, vitamin E and pectin. Choline which is crucial for brain function was also detected [27, 28]. A water-soluble cytotoxic polysaccharide isolated from the fruits of *L. siceraria*, is composed of methyl-α-D-galactuoronate, 3-O-acetyl-methyl-α-D-galacuoronate, and β-D-galactose in a ratio 1:1:1. This polysaccharide exhibited a strong cytotoxic activity *in vitro* against human breast adenocarcinoma cell line (MCF-7) [29]. Some amino acids reported in fruits such as: leucines, phenylalanine, valine, tyrosine, alanine, threonine, glutamic acid, serine, aspartic acid, cystine, cysteine, arginine and proline [15]. It also contains glycine, histidine, lysine, methionine, tryptophan [30, 31]. Amino acids (Carnitine, 4-Hydroxy-L-threonine, Pantothenic acid) were also isolated from mesocarp of *L. siceraria* by using HPLC–ESI-Q-TOF-MS [17]. Fatty acids (Isovaleric acid, Isopalmitic acid, 13-methyl-pentadecanoic acid), Spingolipids (C16 Sphinganine, Phytosphingosine), Monoacylglycerols (1-Monopalmitin), Cardiac glycoside (Oleandrin), Fatty Alcohols (Avocadene) were also isolated from mesocarp extract of *L. siceraria* by HPLC–ESI-Q-TOF-MS [17]. The GC/MS analysis of the most active chloroform fraction showed the presence of hexadecanoic acid, methyl hexadecanoate, isopropyl palmitate, methyl 9,12-octadecadienate and methyl 9,12,15-octadecatrienoate [32]. In summary, a total of 66 compounds were identified, of which 14 belong to terpenoids, 10 belong to sterols, 12 belong to flavonoids, 28 belong to phenolics and the remaining two compounds belong to alkaloids. The compounds previously isolated from *L. siceraria* are listed in tables 1-5

Table 1: Structures of Terpenoids isolated from *L. siceraria*

#	Name	Structure			Reference
					
		R			
1.	**Cucurbitacin B**	**$COCH_3$**			**[33]**
2.	**Cucurbitacin D**	**OH**			**[33]**
					
		R1	**R2**		
3.	**22-Deoxocurcubitacin-D**	**H**	**O**		**[34]**
4.	**22-Deoxoisocurcubitacin-D**	**O**	**H**		**[34]**
	d: *C*- Friedo-oleanane-type Triterpenoids				
					
		R1	**R2**	**R3**	
5.	**3b -*O*-(E)-feruloyl-d:*C*-friedooleana-7,9(11)-dien-29-ol**	**H**	**O-(E)-feruloyl**	**CH_2OH**	**[34]**
6.	**3b-*O*-(E)-Coumaroyl-d:*C***				**[34]**

	friedooleana-7,9(11)-dien-29-ol	H	O-(E)-coumaroyl	CH$_2$OH	
7.	3b-*O*-(E)-coumaroyl d:*C* friedooleana-7,9(11)-dien-29-oic acid	H	O-(E)-coumaroyl	COOH	[34]
8.	3-Epikarounidiol	H	OH	CH$_2$OH	[34]
9.	3-Oxo-d:*C*-friedoolena-7, 9 (11)-dien- 29-oic acid	…	=O	COOH	[34]



		R1	R2	R3	R4	R5	
10.	Methyl 2b ,3b - dihydroxy-d:*C*-friedoolean-8-en-29-oate	H	OH	OH	COOCH$_3$	CH$_3$	[34]
11.	Bryonolol	H	OH	H	CH$_2$OH	CH$_3$	[34]
12.	Bryonolic acid	--	=O	H	COOH	CH$_3$	[34]
13.	20-Epibryonolic acid	H	OH	H	CH$_3$	CH$_3$	[34]

Tetranortriterpenoid

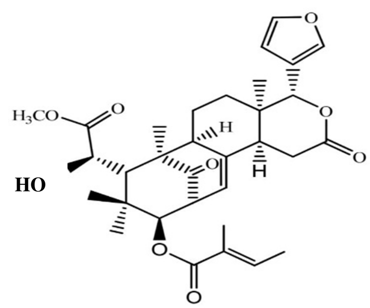
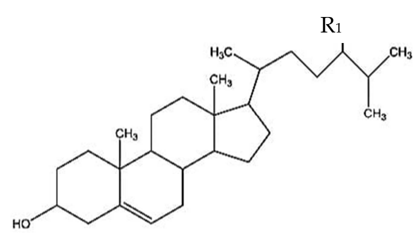
14.	Swietenine		[35]

Table 2: Structures of sterols isolated form *L. siceraria*

#	Name	Structure	Reference
			
		R1	
1.	Campesterol	CH$_3$	[36]
2.	*β*-sitosterol	C$_2$H$_5$	[37]
3.	Fucosterol	=CHCH$_3$	[20]

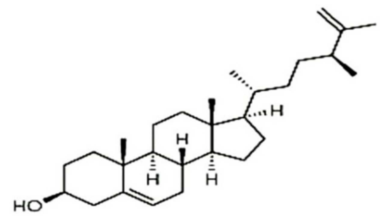
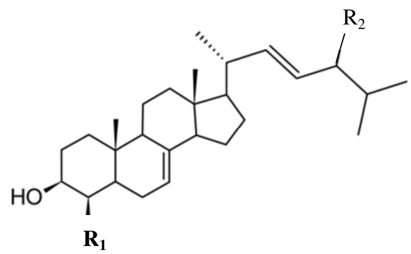
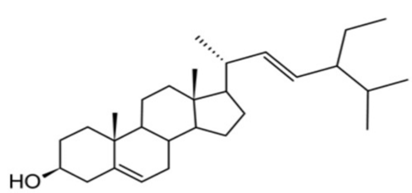
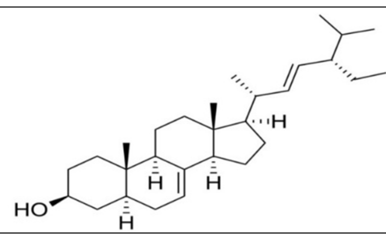
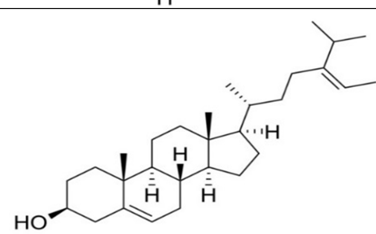
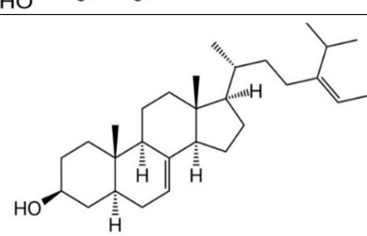
4.	**Codisterol**			**[38]**
				
		R1	**R2**	
5.	**Racemosol**	**H**	**C_3H_7**	**[20]**
6.	**Stigma-7,22-diene-3*β*,4*β*-diol**	**OH**	**C_2H_5**	**[20]**
7.	**Stigmasterol**			**[20]**
8.	**Spinasterol**			**[39]**
9.	**Isofucasterol**			**[40]**
10.	**Avenasterol**			**[41]**

Table 3: Structures of flavonoids isolated from *L. siceraria*

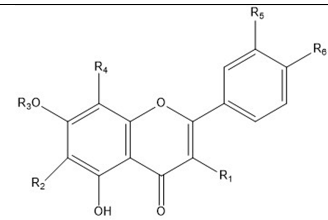
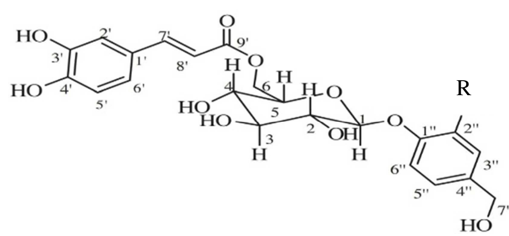
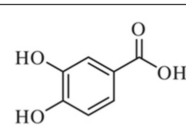
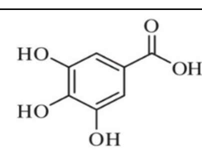
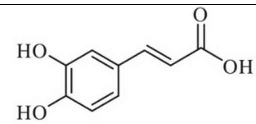
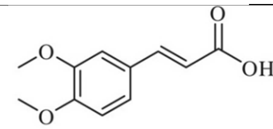
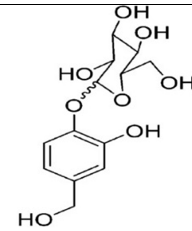
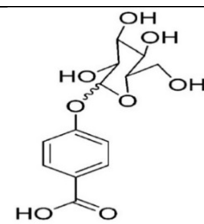
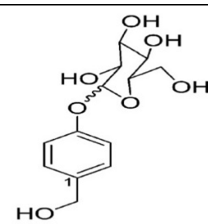
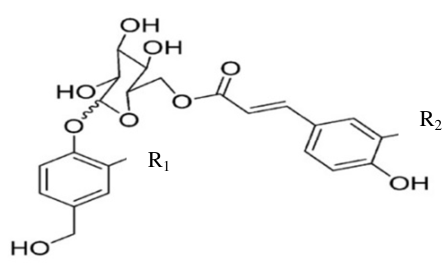
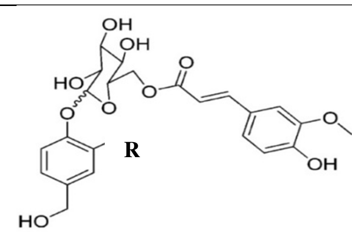
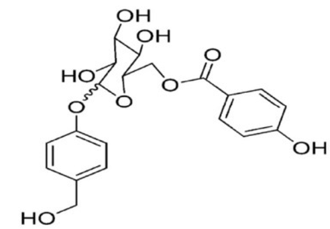
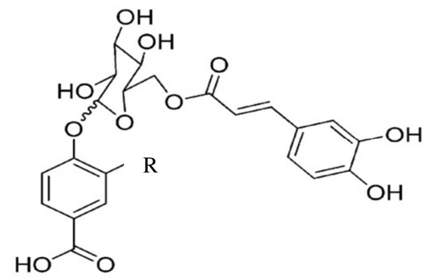
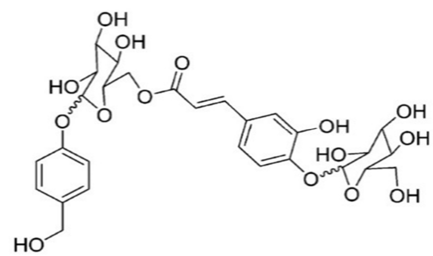
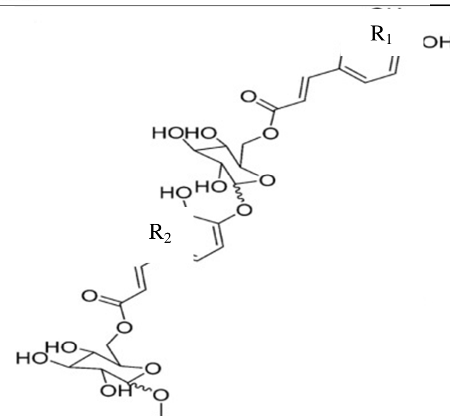
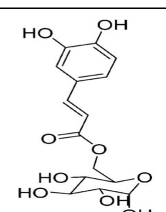
#	Name	Structure						Reference
								
		R1	R2	R3	R4	R5	R6	
1.	Vitexin	H	H	H	Glucose	H	OH	[42]
2.	Isovitexin	H	Glucose	H	H	H	OH	[34]
3.	Saponarin	H	Glucose	Glucose	H	H	OH	[34]
4.	Saponarin *C-O*-glucoside	H	Glucose	Glucose	H	Glucose	OH	[34]
5.	Saponarin Caffiec ester	H	Glucose	Caffeoyl glucose	H	H	OH	[42]
6.	Orientin	H	H	H	Glucose	OH	OH	[42]
7.	Isoorientin	H	Glucose	H	H	OH	OH	[34]
8.	Luteolin	H	H	H	H	OH	OH	[43]
9.	Lutonarin	H	Glucose	Glucose	H	OH	OH	[34]
10.	Quercitin	OH	H	H	H	OH	OH	[44]
11.	Isoquercitrin	O-Glucose	H	H	H	OH	OH	[45]
12.	Kaempferol	OH	H	H	H	H	OH	[46]

Table 4: Structures of phenolic compounds from *L. siceraria*

#	Name	Structure	Reference
1.	(E)-4-hydroxymethyl-phenyl-6-*O*-caffeoyl-*β*-D-glucopyranoside (R=H)		[25]
2.	1-(2-hydroxy-4-hydroxymethyl)-phenyl-6-*O*-caffeoyl-*β*-D-gluco-pyranoside (R=OH)		
3.	Protocatechuic acid		[25]
4.	Gallic acid		[25]

5.	**Caffeic acid**		**[25]**
6.	**3,4-dimethoxy cinnamic acid**		**[25]**
7.	**4-*O*-Glucosyl-3,4-dihydroxybenzyl alcohol.**		**[14]**
8.	**4-*O*-Glucosyl-4-hydroxybenzoic acid.**		**[14]**
9.	**4-*O*-Glucosyl-4-hydroxybenzyl alcohol.**		**[14]**
10.	**4-*O*-(6'-*O*-Glucosyl caffeoyl)-4-hydroxybenzyl alcohol. R1=H, R2=OH**		**[14]**
11.	**4-*O*-(6'-*O*-Glucosyl caffeoyl)-3,4-dihydroxybenzyl alcohol. R1=OH, R2=OH**		
12.	**4-*O*-(6'-*O*-Glucosyl p-coumaroyl)-4-hydroxybenzyl alcohol. R1=H, R2=H**		
13.	**4-*O*-(6'-*O*-Glucosyl 4''-hydroxybenzoyl)-4-hydroxybenzyl alcohol.**		**[14]**

14.	**4-*O*-(6'-*O*-Glucosyl feruloyl)-3,4-dihydroxybenzyl alcohol.** **(R=OH)**		**[14]**
15.	**4-*O*-(6'-*O*-Glucosyl feruloyl)-4-hydroxybenzyl alcohol.** **(R=H)**		
16.	**4-*O*-(6'-*O*-Glucosyl caffeoyl)-4-hydroxybenzoic acid.** **R=H**		**[14]**
17.	**4-*O*-(6'-*O*-Glucosyl caffeoyl)-3,4-dihydroxybenzoic acid.** **R=OH**		
18.	**4-*O*-(6′-*O*-glucosylcaffeoylglucosyl)-4-hydroxybenzyl alcohol**		**[14]**
19.	**4-*O*-(6'-*O*-Glucosyl caffeoyl-glucosyl-caffeoyl)-4-hydroxybenzyl alcohol.** **R1=OH, R2= OH**		**[14]**
20.	**4-*O*-(6'-*O*-Glucosyl caffeoyl-glucosyl-p-coumaroyl)-4-hydroxybenzyl alcohol.** **R1=H, R2= OH**		
21.	**4-*O*-(6'-*O*-Glucosyl caffeoyl-glucosyl-feruloyl)-4-hydroxybenzyl alcohol.** **R1=OCH_3, R2= OH**		
22.	**4-*O*-(6'-*O*-Glucosyl feruloyl-glucosyl-caffeoyl)-4-hydroxybenzyl alcohol.** **R1=OH, R2= OCH_3,**		
23.	**6-*O*-Caffeoyl-*α*-glucose.**		**[14]**

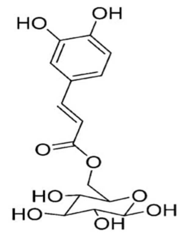
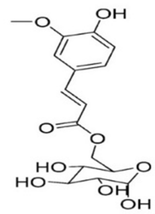
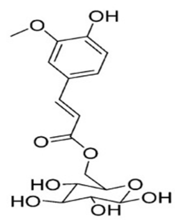
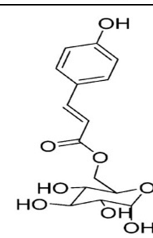
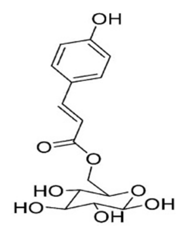
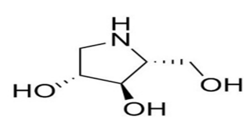
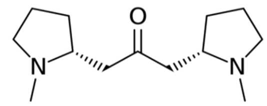
24.	**6-*O*-Caffeoyl-*β*-glucose.**		**[14]**
25.	**6-*O*-Feruloyl-*α*-glucose.**		**[14]**
26.	**6-*O*-Feruloyl-*β*-glucose.**		**[14]**
27.	**6-*O*-p-Coumaroyl-*α*- glucose.**		**[14]**
28.	**6-*O*-p-Coumaroyl-*β*-glucose.**		**[14]**

Table 5: Structures of alkaloids isolated from *L. siceraria*

#	Name	Structure	Reference
1.	**1,4-Dideoxy-1,4-Imino-D Arabinitol**		**[17, 26]**

2.	**Cuscohygrine**		**[17,26]**

3.1. TRADITIONAL USES

Crushed leaves of *L. siceraria* are used as an alternative purgative. Probably, the purgative property is due to the bitter principle found in the wild bottle gourds [47]. In Curacao, flatulence is treated with a leaf decoction [48]. Also, leaves of *L. siceraria* are used as an emetic in the form of juice or decoction and are used for Jaundice [49]. *L. siceraria* fruits are consumed in India as a major component of weight reducing diet. Indian pharmacopoeia highly recommended fruits for diabetic patients and young children, due to fiber and low-fat content. In Punjab, the pulp is used for treatment of burning feet [50]. It was observed that flowers had antidote activity to certain types of poisons. Stem bark and rind of the fruit are used as diuretic [47]. Pulverized seeds are used as vermifuge to treat tapeworm infections in children [51]. Seed oil had a cooling effect and can be used in migraine type headache. A poultice of boiled seeds is used in the treatment of boils. Also, seeds are used as a dental remedy [6]. Studies showed that *L. siceraria* juice is the best for dehydration cases caused by diarrhea and diabetes as it prevented the excessive loss of sodium and gives a cooling effect [52]. Ayurveda also recommended the juice as a sedative for epilepsy, insomnia and other nervous diseases, and it also helped in dissolving calculus (stones) in the body [53]. A mixture of juice of *L. siceraria* leaves and sesame oil was applied on the scalp by the Gutti Koya tribals as it gives beneficial results in baldness (Hair loss) [47]. In China, roots of *L. siceraria* have been used as a single treatment for diabetes mellitus and as emetic in a dose of 3g / day [54]. Bottle gourd juice is rich in magnesium, zinc, iron, vitamin C and thiamin thus helping in better health [15].

3.2. Commercial applications

Commercially the domestic utensils were prepared from the dry hard shells of bottle gourd fruits by tribal communities as (Koyas, Gutti Koyas, and Lambadas) and It is also used for decorative purposes [55].

3.3. Biological activities

Anthelmintic activity: Crude methanol and benzene extracts of seeds and leaves of L. siceraria significantly demonstrated paralysis and death of adult Indian earthworm, Pheretima posthuma [56]. While, ethanoic extract of L. siceraria seeds exhibited a powerful activity against Hymenolepis nana (tape worm) infections [57]. Sterols content could possess a significant anthelmintic and antimicrobial activities [58].

Antigiardial Activity: Elhadi *et al*., (2013) evaluated the antigiardial activity of *L. siceraria*. The result showed that petroleum ether extract of *L. siceraria* exhibited 100% mortality within 72 hrs with IC50 (95.65 ppm). This result would approve that *L. siceraria* is a potential drug in treating *Giardia lambelia* which agreed with the traditional claims. The antigiardial of *L. siceraria* may be enhanced due to the presence of triterpenes (Cucurbitacins) and fatty acids like: myristic, stearic, palmitic, linolenic and arachidic acid [59].

Antioxidant activity: *L. siceraria* fruits contain phytochemicals such as polyphenols, carotenoids, vitamins C and E which are believed to act as antioxidants [60-62]**.** The acetone extract of *L. siceraria* epicarp showed significant antioxidant activity. This may be due to the presence of ellagitannins [63]. Seeds also can be used as an excellent natural antioxidant [64]. Moreover, the methanolic extract of *L. siceraria* peel, aerial part and leaves were found to scavenge DPPH in a concentration dependent manner [65], this is due to the high phenolic contents (E)-4-hydroxymethyl-phenyl-6-O-caffeoyl-β-D-glucopyranoside) and the presence of flavonoids and flavanols [66]. *L. siceraria* phytochemicals can be considered as a source of natural antioxidants for food and nutraceutical products [24, 67]. In addition, the no-solvent, cold-pressed, bottle gourd extract exhibited potent free radical scavenging activity [68].

Hepatoprotective activity: The experimental results revealed that *L. siceraria* fruits extract and their different fractions possess significant hepatoprotective activity [69]. Later, Panchal, C., *et al*., (2013) studied the evaluation of hepatoprotective effect of *L. siceraria* fruits against paracetamol induced heptotoxicity. Both petroleum ether and ethanolic extracts exhibited a significant hepatoprotective and antioxidant activities [70]. In addition, the methanolic extract of mesocarp of *L. siceraria* showed significant protection of liver from free radical mediated damage in an oral dose of (200 mg/kg). This hepatoprotective activity may be attributed to phenolics and flavonoids [68].

Anti-inflammatory activity: Ghule *et al.,* (2006) investigated the *in vivo* anti-inflammatory effects of *L. siceraria* fruits juice extract in rats and mice [71]. It inhibited albumin-induced paw edema over a period of 90 min. *L. siceraria* juice extract might have inhibitory effects on the release and/or synthesis of inflammatory mediators, especially lipooxinase and cyclooxygenase [72]. It was also observed that the alcoholic extract of *L. siceraria* seeds possessed a good therapeutic potential against inflammation and pain [73].

Analgesic activity: Different extracts of *L. siceraria* leaves were evaluated. The results proved that petroleum ether extract have the maximum analgesic activity among them [74]. The methanolic and aqueous extracts of *L. siceraria* showed moderate analgesic effect which coincides with its folkloric medicinal use [75, 76].

Effect on central nervous system: Jayashree *et al*., (2010) observed that the methanolic extract of *L. siceraria* reduced the spontaneous motor activity at higher doses and exerted a sedative effect and potentiated the effect of pentobarbitone [74]. Another studies revealed that extract of *L. siceraria* fruits possessed a significant antidepressant activity [77].

Antistress, adaptogenic and Anti-anorectic activity: The antistress effect of alcoholic extract of *L. siceraria* fruits was evaluated. It prolonged the onset of clonic convulsion, swimming time and ameliorated stress induced. Steroids, saponins, flavonoids, cucurbitans, triterpenes and glycosides were responsible for this activity [78, 79]. In addition, the ethanolic fruit extract possessed anti-anorectic activity in stress and lipopolysaccharide (LPS) induced anorexic rats and the required dose dependently reduced the physical stress & LPS induced anorexia in female rats [80].

Diuretic activity: *L. siceraria* fruits extract exhibited higher urine volume and increased in excretion of electrolytes when compared with its respective control in a manner of dose dependent. This observation supported the folkloric consideration of this fruit as diuretic [81].

Anticancer and cytotoxic activity: The Japanese dietary fiber from *L. siceraria* (yugao-melon) showed a great suppression of the bile acid concentration in the colon of 1,2 dimethylhydrazine (DMH) induced colonic carcinogenesis in mice [82]. Two D:C-friedooleanane triterpenes were isolated from the methanolic extract of *L. siceraria* stems and showed a significant cytotoxic activity against the SK-Hep 1 cell line (human hepatoma) of IC50 4.8 and 2.1 μg/ml, respectively [16]. Experimental results revealed a significant anticancer effect of *L. siceraria* methanolic extract against Ehrlich Ascites carcinoma (EAC) model in mice [83]. On the other hand, the observed results of *L. siceraria* fruits and flowers showed that Human breast adenocarcinoma cell lines (MCF-7) were reduced in cytotoxicity level [29, 84, 85]. It also showed a significant antimutagenicity [86].

Radioprotective effect: Sharma *et al*., (2016) discovered the radioprotective potential of *L. siceraria* extract against radiation-induced gastrointestinal injury. Results showed that the administration of *L. siceraria* countered the radiation effects [87].

Antiulcer activity: It was found that *L. siceraria* possessed a good antiulcer property [88].

Obesity control and antihyperlipidemic effect: Bottle gourd is considered one of the best foods for weight loss; it has been proven by using a model that studied the lipase inhibitory activity of extracts and fractions using numerous concentrations. Ghule *et al.,* (2006) estimated the antihyperlipidemic effect of different extracts of *L. siceraria* fruits in Triton-induced hyperlipidemic rats. Results proved that chloroform and ethanolic extracts significantly lowered the total cholesterol (TC), triglyceride (TG) and low-density lipoprotein (LDL) along with an increase in high-density lipoprotein (HDL) level as compared to other. This effect was due to presence of sterols (campesterol and fucosterol) [89]. It was also proved that *L. siceraria* fruits have a capacity to increase the excretion of bile salts [90]. On the other hand, Nainwal *et al.,* (2011) detected that juice of fresh fruits of *L. siceraria* effectively decreased the blood cholesterol level and change the serum biochemistry which may suggest that the juice extract has a tonic effect on kidneys, liver and organs and playing central role in drug metabolism. The low blood cholesterol levels and reduction of morbidity and mortality from coronary artery disease are due to the presence of sterol ester in *L. siceraria* fruit juice [91]. In addition, it was proved that fractions of stems and leaves of *L. siceraria* were potentially useful for the treatment of hyperlipidaemia and atherosclerosis [92]. Also, *L. siceraria* fruits ethanolic extract induced the lipoprotein lipase activity and amazingly decreased cholesterogenesis in liver by reducing HMG-CoA reductase activity in hypercholeaterolemic rats. Fatty acids and their esters may play role as lipase inhibitors [32].

Cardioprotective activity: It was investigated that the antioxidant and anti-inflammatory activities of *L. siceraria* fruits powder extract contributed to the cardioprotective effects in both doxorubicin and isoprenaline-induced cardiotoxicity, where markers of cardiotoxicity i.e CK-MB (Creatine kinase), low-density lipoprotein (LDL) and lactate dehydrogenase (LDH) were significantly reduced [93]. A significant relief could be achieved by cardiac patients through consuming the fresh fruit juice of *L. siceraria* daily [94]. An increasing in force of contraction and a decreasing in rate of contraction have been showed by the ethanolic extract of the fruits [60]. These effects might be due to the high concentration of polyphenolic components in fruits [95].

Antihypertensive activity: It was proved that *L. siceraria* pretreatment partially reversed dexamethasone induced hypertension while the mean arterial blood pressure and heart rate were reduced [96]. Also, Mali *et al*., (2012) detected that the antioxidants orientin and isoorientin in *L. siceraria* fruits reduced myocardial inflammation and necrosis, in addition to, isoflavones (vitexin) showed strong antihypertensive and cardioprotective activities [97].

Immunomodulatory activity: Oral administration of different fractions of *L. siceraria* fruits extract significantly inhibited delayed-type hypersensitivity reaction in rats [98]. Similarly, hot aqueous extract of *L. siceraria* stems showed significant immunomodulatory [99]. Sathaye *et al.,* (2011) evaluated the immunomodulatory effect of fresh juice from *L. siceraria* fruits against Pyrogallol-induced immunosuppression in mice. Results showed an increasing effect on the count of neutrophils and total leukocyte, which could be responsible for stimulation of non-specific immunity [100].

Antithrombotic potential: *Lagenaria* may be considered as a thrombolytic agent which improve the health of patients with atherothrombotic disease as it was proved that *L. siceraria* fruits lyses fibrin clots *in vitro* [101]. Major phytoconstituents presented in fruits of *L. siceraria* such as flavonoid, Saponins and fatty oils may be responsible for its antithrombotic activity through the ability of *L. siceraria* ethanolic extract to expand the time required for blood coagulation in plasma [28].

Carbonic Anhydrase Inhibitor: Chanda, J., *et al.,* detected that carbonic anhydrase inhibition, which could play a useful role in the management of oedema, hypertension, obesity and related metabolic disorders, was due to the major contributors of phenolic compounds of *L. siceraria* [102].

Antidiabetic activity: The methanolic extract of aerial part of the *L. siceraria* possessed both a potent anti-hyperglycemic activity of Streptozotocin induced diabetic rats [103] and decreased glucose level without toxicity in chronic and acute toxicity model in mice [104]. Findings clearly found that *L. siceraria* pulp (LSPE) and *L. siceraria* seed extracts (LSSE) preserved the pancreatic cell integrity in diabetes [105]. *L. siceraria* juice can be used as an alternative and additive treatment in disorders associated with carbohydrate and lipid metabolism as it exhibited a significant reduction in blood glucose and cholesterol level [106] clinically. Hydroalcoholic extract of *L. siceraria* (LHA) was effective against sorbitol accumulation due to its antioxidant and antiglycation potential [20].

Antimicrobial activity: Different extracts of *L. siceraria* exhibited antimicrobial activity against *Pseudomonas aeruginosa* and *Streptococcus pyogenes* in addition to, moderate antifungal action [58, 107]. In other study the ethanolic and chloroform extracts (100 µ/ml) inhibited the growth of *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Klebisella* species in comparison with the standard streptomycin and amikacin [108]. The n-hexane extract of *L. siceraria* reduced the microbial growth of Escherichia coli (17.25 mm) and *Salmonella typhi* (17.80 mm) [109]. Also, *L. siceraria* seeds extract exhibited potent antibacterial and antifungal activities against selected pathogens (*Staphylococcus aureus, Pseudomonas especially Escherichia coli, Bacillus subtilis, Candida sp.* and *Aspergillus niger*) using agar well diffusion method [110]. It was found that seed protein hydrolysates showed outstanding antimicrobial activity against all tested Gram-negative bacteria which could be added as food preservative for the prevention of bacterial growth in food. Also, it could be applied as natural antibiotics for treatment of various infectious diseases [111]. Also, the pedicles of *L. siceraria* fruits could be a potential source for new antibiotics against a variety of microorganisms [112]. *L. siceraria* leaves extract was established in green synthesis of iron oxide nanoparticles (Fe_3O_4-NPs). The antimicrobial property of synthesized Fe_3O_4-NPs was evaluated against Gram positive, Staphylococcus aureus, Gram negative, *Escherchia coli*. The zone of inhibition was found to be 10 mm and 8 mm, respectively. So that, this naturally stabilized herbal Fe3O4-NPs could be used in various biological applications [113].

Anti-asthmatic and anti-allergic activity: *Lagenaria siceraria* leaves are used traditionally for cough, bronchitis and asthma. The aqueous extract of *L. siceraria* leaf revealed strong bronchodilator activity at doses of 150 and 300 mg/kg [114]. It was reported that the triterpene bryonolic acid that isolated from callus culture of *L. siceraria* roots is a potent anti-allergic compound [115, 116].

4. Conclusion

There is an increasing interest worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases. Numerous drugs have entered the international market through exploration of ethnopharmacology and traditional medicine. *Lagenaria siceraria* commonly known as bottle gourd, is a medicinal plant widely cultivated in countries of African and Asian origin. From the literature, it was clearly revealed that *L. siceraria* showed a broad spectrum of pharmacological activities such as antioxidant, antiulcer, antidiabetic, cardioprotective, immune modulatory, diuretic, hepatoprotective, anti-inflammatory, anti-helminthic, cardiotonic, cytotoxic, adaptogenic, anti-hyperlipidaemic, analgesic, hyperthyroidism, hyperglycaemia and lipid peroxidation effects due to the presence of various secondary metabolite such as; alkaloids, glycosides, carbohydrates, proteins and minerals present in large amount. Bottle gourd makes an excellent diet, rich in vitamins, iron and minerals. It has the highest content of choline, which serves as the precursor of neurotransmitter acetylcholine, which in turn is crucial for retaining and enhancing memory, among all the vegetables known to man till date. Furthermore, *Lagenaria siceraria* juice helps to control blood pressure of hypertensive patients, because of its high potassium content. It helps in losing weight quickly, because of its high dietary fiber and low fat and cholesterol content. In the light of the above-mentioned multiple benefits of bottle gourd, it may be regarded as a natural guard against diseases. *L. siceraria* possesses many important chemical constituents, which require further research to explore the medicinal value of this species. Efforts are therefore needed to establish and validate evidence regarding safety and practices of Ayurvedic medicines.

5. Conflict of interests

The authors declare that they have no conflict of interests.

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