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Review Article

PHYTOCHEMICAL AND PHARMACOLOGICAL ASPECTS OF *CARISSA EDULIS* VAHL: A REVIEW

[A] **HANAN M. AL-YOUSSEF AND** [B] **WAFAA H.B. HASSAN**

[a] department of pharmacognosy, faculty of pharmacy, King Saud University, Riyadh, Saudi Arabia
[b]Zagazig University, Faculty of Pharmacy, Pharmacognosy department, Zagazig, Egypt.

Corresponding Author: h_alyoussef@yahoo.com

Abstract

The scientific basis for the statement that plants and their active constituents play an important role in the prevention of chronic and degenerative diseases is continuously advancing. In fact the origin of many therapeutic substances is due to secondary metabolites in the plants. This article reviews the reported phytochemical and pharmacological properties of *Carissa edulis* vahl. (English name of the plant is Arabic num num, Arabic emir), the aerial parts and root are used in many parts of the world to make remedy. In folk medicine, the different extracts are used for the treatment of several complains, including high blood pressure, chest complains, rheumatism and diabetes mellitus. The pharmacological actions of the different extracts include *in vivo* and/or *in vitro* antihypertensive, anti-inflammatory, antiplasmodial, anticonvulsant and decrease blood glucose level. The consumption of *C. edulis* has resulted in significant increase in urinary excretion of sodium, potassium and chloride ions. In view of the reported nutritional and pharmacological properties and relative safety, *C. edulis* and compounds isolated from it (for example, flavonoids, sesquiterpenes and lignans) could be a source of therapeutically useful products.

Keywords: Carissa edulis, phytochemical, flavonoids, antimicrobial, antioxidants.

Introduction

In recent times, focus on plant research has increased all over the world, and a large body of evidence has been collected to show the immense potential of medicinal plants used in traditional systems. *Carissa edulis* belongs to the family Apocynaceae. This family consists of about 250 genera and 2000 species, which are closely allied to the Asclepiadaceae [Hutchinson and Dalziel 1963]. The plant is native in many countries such as Australia, Cambodia, Cameroon, Eritrea, Ethiopia, Ghana, Guinea, Japan, Kenya, Nigeria, Saudi Arabia, Senegal, South Africa, Sudan, Tanzania, Thailand, Uganda, Vietnam and Yemen. Many members are woody climbers found in the tropics and subtropics [Evans 2005]. It was formerly known as *C. pubescence* [Irvine 1961]. Family Apocyanaceae is represented in Saudi Arabia by seven genera among them genus *Carissa* including *Carissa edulis* [Atiqur Rahman, 2003; 2004]. Several classes of chemical constituents have been isolated from genus *Carissa* [Dharani 2010], such as, sesquiterpenes, cardiac glycosides, phenolic compounds and lignans [Kirira et al 2006; Pal et al 1975; Wang and Likhitwita 2009]. Chemical constituents isolated from *Carissa edulis* include 2-hydroxyacetophenone [Bentley et al 1984], phenolic compounds, insoluble proanthocyanidins, lignans; sesquiterpenes of the eudesmane and germacrane derivatives, sterols, tannins, cardiac glycosides and flavonoids have been isolated [Nedi et al, 2004; Achenbach et al, 1983, 1985]. In addition to, there were six volatile compounds from the root of *C. edulis* have been analyzed by GC/MS [Moudachirou et al 1998].

The Fruit (ripe and unripe), and flowers of *Carissa edulis* are edible. The plant is commonly known among Hausa people in Northern Nigeria as 'cizaki' and in Somalia as 'adishawel' [Gbile 1980, Oliver 1996].

The English name of the plant is Arabic num-num. other common names include; 'endelkoring-noeminoem' (Africana), 'agam' (Tigrigna and Amharic), 'emir' (Arabic) [Sofowora 1986]. *C. edulis* has many traditional uses, its fruit is edible, while its pungent root is used in Ethiopia for a variety of medicinal purposes. These include the treatment of chest complaints [Bentley et al 1984], rheumatism [Giday 2001], headache, gonorrhea, syphilis, rabies and as a diuretic [Abate et al, 1989; Addis et al 2001]. In traditional medicine an infusion of the root powder is administered once daily [Audu 1994, Nedi et al 2004]. *C. edulis* has been used in the Kenyan traditional medicine over the years for treatment of various ailments [Sofowora 1993]. It is commonly added to the meat soup to enhance taste [gachathi 1989]. Thus there are no adverse effects that have ever been reported on *C. edulis* herbal medicines. *C. edulis* is an indigenous plant naturally growing at different geographical localities in Kenya with a wide spread use in traditional medicine practice. The most utilized part of the plant are its roots which are usually boiled and given as an oral concoction at varying doses depending on age [kokwaro 1976]. The folkloric uses of *C. edulis* include fever, sickle cell aneamia and hernia [Yako 1992, Ibrahim 1997]. *C.edulis* is used as a source of dye [Banker and verma 1987, Irvine 1961, Omino 1993]. The use of local plants for the treatment of diabetes mellitus is quite common in the Middle Eastern countries. More than 400 local plant treatments for diabetes mellitus have been recommended by the traditional health care providers [Aigaonkar 1979; Bailey and day 1989; Ivorra et al, 1989]. *C. edulis* is a wild plant growing in different parts of south region of Saudi Arabia and Yemen, it has been used in different provinces as an oral hypoglycemic agent of folkloric credit [Bazeeb 1991].

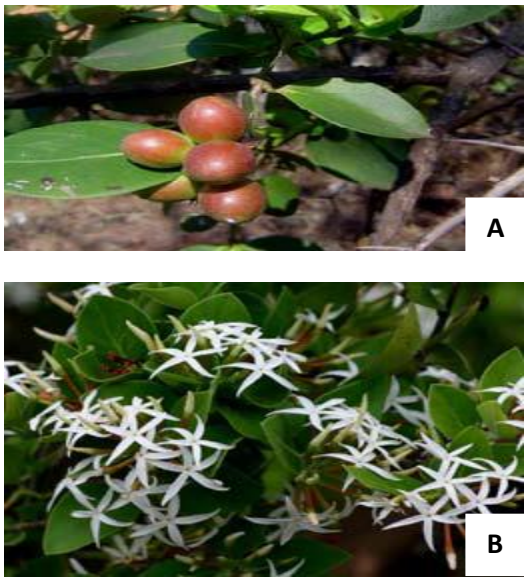


Figure 1. *Carissa edulis* A- fruit B- flowers

Constituents

Sesquiterpenes

Sesquiterpenes are class of compounds derived from farnesyl diphosphate, Figure 2, [Dewick 1999, 2002]. They are known to possess antimicrobial, antimalarial, anticancer and anti-inflammatory effects [Hettiarachchi, 2006]. Nine eudesmane -type sesquiterpenes were isolated from the methanolic extract of the root of *Carissa edulis* and are shown in Table 1, they include carissone (**1**), cryptomeridiol (**2**), *β*- eudesmol (**3**), 6*α*-carissanol (**4**), 6*β*-carissanol (**5**), 2*α*-carissanol (**6**), (**7**), 4-Epi-Aubergenone (**8**) and dehydrocarissone (**9**) [Sofowora 1986; Achenbach, 1983 and 1985]. From the same plant extract a germacrane-type sesquiterpene, germacrenol (**10**), was also obtained [Sofowora, 1986, Achenbach, 1985].

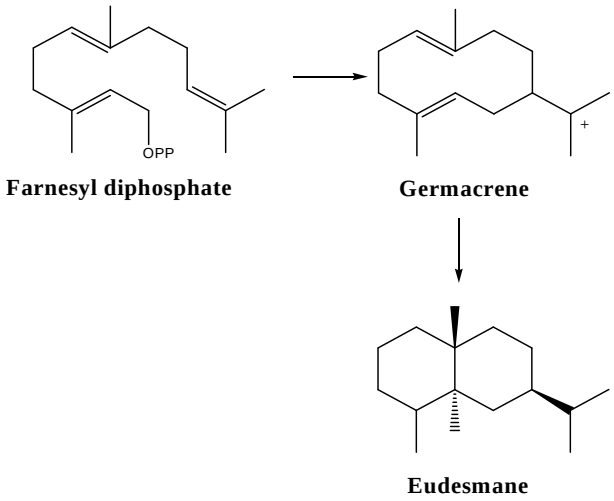
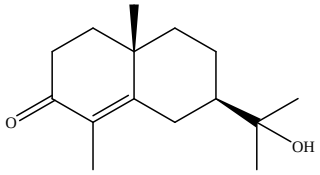
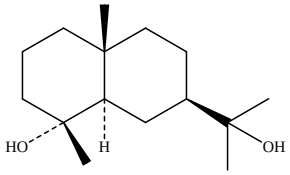
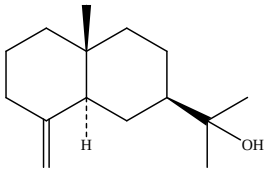
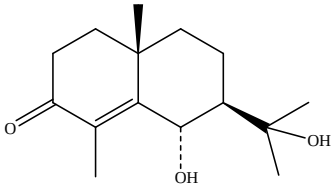
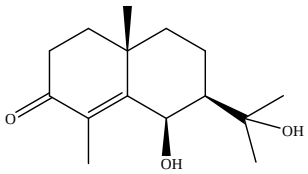
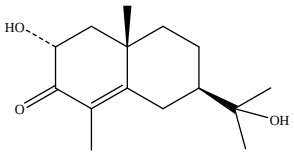
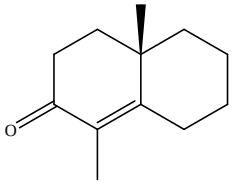
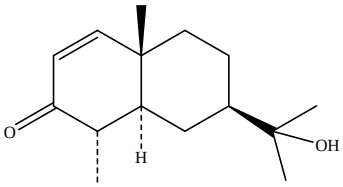
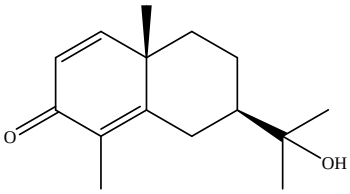
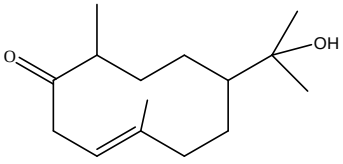


Figure 2. Biosynthesis pathway of eudesmane sesquiterpene

Lignans

In the plant world lignans are natural products which occupy quite a large area. They have been identified in some 70 families, many of which have been used in traditional medicine. Lignans, Table 2, have gained increasing attention due to their biological effects; antimitotic, antiviral, cathartic, allergenic and antitumor activities [Achenbach et al, 1983, 1985]. *Carissa edulis* has yielded six lignans (-)Nortrachelogenin (**11**), (+) lariciresinol (**12**) Secoisolaricirestinol (**13**), Carissanol (**14**), Carinol (**15**), (-) olivil (**16**), (Achenbach, 1985 and 1983). (-) Nortrachelogenin (**11**) was isolated from the methanolic extract of the root of *Carissa edulis* and it showed antiplasmodium activity at a dose of 14.50 µg/ml (Kebenei et al 2011; Achenbach, 1983).

Table 1: Sesquiterpens isolated from *Carissa edulis*

Sesquiterpenes		
		
Carissone (**1**)	Cryptomeridiol (**2**)	β- eudesmane (**3**)
		
6*α*-Carissanol (**4**)	6*β*-Carissanol (**5**)	2*α*-Carissanol (**6**)
		
(**7**)	4-Epi-Aubergenone (**8**)	Dehydrocarissone (**9**)
		
Germacrenol (**10**)		

Flavonoids

A flavonoid skeleton is composed of two aromatic rings known as A and B rings which are connected through a pyrone ring (C) as shown in Figure 3.

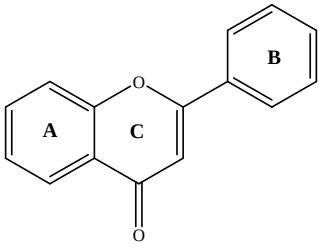
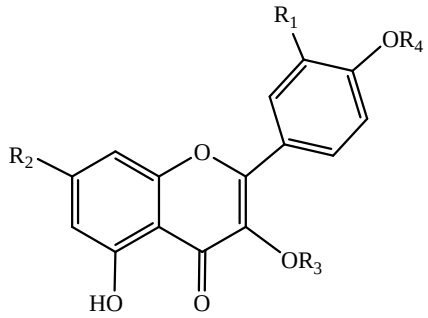


Figure 3: Flavone skeleton

Flavonoids present in *Carissa edulis* Table 3, present mainly in the form of their glycosyl derivatives. The most common sugar moieties include *β*-D-glucose and α-L-rhamnose and the glycosides are usually *–O*-glycosides in which the sugar moiety bound generally to the hydroxyl group of the aglycone at C-3. Aglycones (the forms lacking the sugar moieties) occur less frequently.



Flavone glycosides found in *C. edulis* are generally -3-*O*-glucoside in addition to 3-*O*-rutinoside. Flavones glycosides and aglycone are summarized in Table 3, they include kampferol-3-*O*-*β*-D-glucopyranoside (**17**),quercetin3-*O*-*β*- D -glucopyranoside (**18**), isorhamnetin 3-*O*-*β*- D -glucopyranoside (**19**), rhamnetin-3-*O*-*β*- D -glucopyranoside (**20**), isorhamnetin-3-*O*-rutinoside (**21**), rutin (**22**), quercetin-3-*O*-*β*-D-
glucopyranoside-7, 3‘, 4‘ trimethyl ether (**23**), and kaempferol (**24**) [Al-Youssef and Hassan 2010].

Other phenolic and aromatic compounds

Phenylpropanoids and phenylethanoids

Phenylpropanoids and phenylethanoids belong to the largest group of secondary metabolites produced by plants, mainly, in response to biotic or abiotic stresses such as infections, wounding, UV irradiation, exposure to ozone, pollutants and other hostile environmental conditions. Last few years, much interest has been attracted to natural and synthetic phenyl propanoids for medicinal use as antioxidant, UV screens, anticancer, antivirus, anti-inflammatory, wound healing and antibacterial activities [Johns 1999]. The root of *Carissa edulis* was found to contain phenolic compounds Table 4, [Bentley et al, 1984].

Chlorogenic acid derivatives

Caffeoylquinic acids with the most well known compound being chlorogenic acid (5-caffeoylquinic acid, Table 5), are a group of natural products found in many medicinal and dietary plants. They are potent antioxidants and might contribute to the prevention of Type II diabetes mellitus, cardiovascular disease and certain aging related diseases [Chao-Mei Ma et al 2010].

Sterols and triterpenes

Triterpenes: they are isolated from *C. edulis* which have possess a hepatoprotective, anti-inflamatory, anti-HIV and anti-hyperlipidemic activities, Table 6 [Gupta et al., 1980; Hettiarachchi, 2006].

Coumarins

Coumarins and their derivatives exert anti-coagulant, anti-tumor, anti-viral, anti-inflammatory and antioxidant effects, as well as anti-microbial and enzyme inhibition properties [Pakrashi 1968]. Two coumarins have been isolated from *Carissa edulis* as shown in Table 7.

Cardiac glycosides

Cardiac glycosides occur naturally in certain plants species. Cardiac glycosides have effects on the heart, stomach, intestines, and nervous system. These are the active ingredient in many different heart medicines in clinical use and they are the major class of medications used to treat heart failure. The cardiotonic activity and prolonged blood pressure lowering effect of *Carissa edulis* was previously reported (Vohra & De, 1963). The cardiac activity of water-soluble fraction has been
attributed to the presence of the odoroside glucosides including odoroside H and F, Table 8 [Burkill 1985].

Miscellaneous compounds

Many other compounds were isolated from C. edulis such as Butyl rhamnose (47), Ononitol (48) and Caredulis (49) [Al youssef and Wafaa, 2014].

Table 2: Lignans isolated from *Carissa edulis*

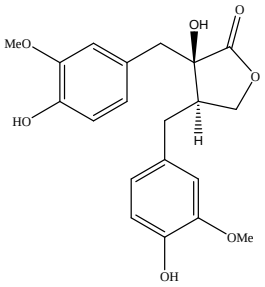
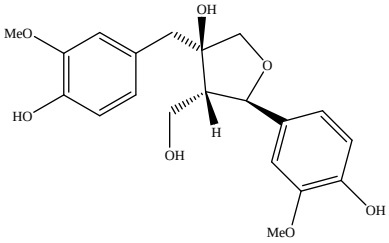
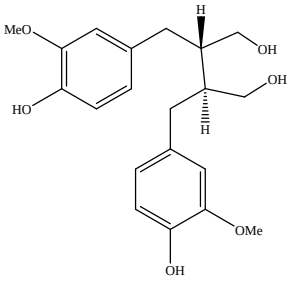
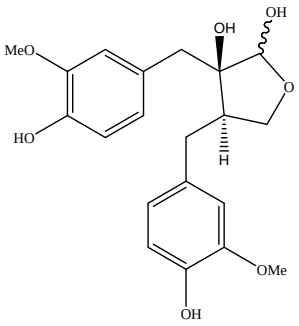
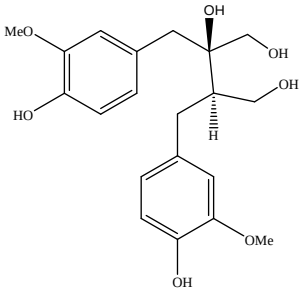
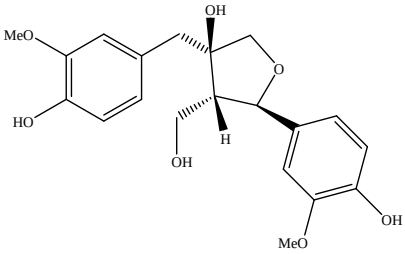
Lignans		
		
(-) Nortrachelogenin (**11**)	(+) Lariciresinol (**12**)	Secoisolaricirestinol (**13**)
		
Carissanol (**14**)	Carinol (**15**)	(-) Olivil (**16**)

Table 3. Flavone and flavones glycosides present in *C. edulis*

Compound No.	**R_1**	**R_2**	**R_3**	**R_4**
17	H	OH	Glu	H
18	OH	OH	Glu	H
19	OMe	OH	Glu	H
20	OH	OMe	Glu	H
21	OMe	OH	Glu (2---1)Rha	H
22	OH	OH	Glu (6---1)Rha	H
23	OMe	OMe	Glu	Me
24	H	OH	H	H

Table 4. phenolic and aromatic compounds present in *C. edulis*

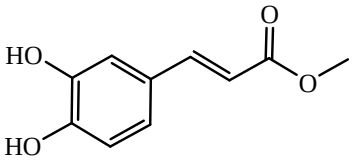
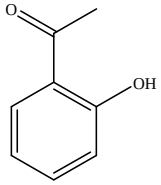
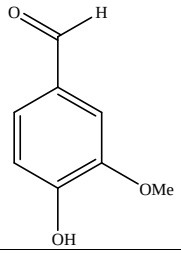
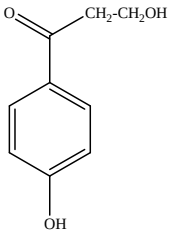
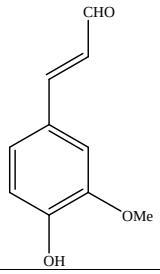
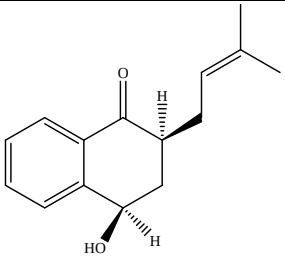
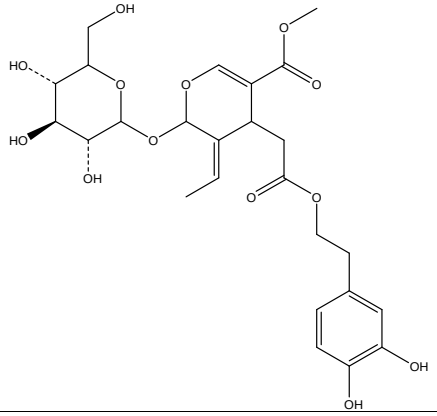
Other phenolic and aromatic compounds		
		
		
4-Hydroxy—(3-hydroxypropionyl)-benzene (**28**)	Coniferaldehyde (**29**)	Catalponol (**30**)
		
Oleuropein (**31**)		

Table 5 Chlorogenic acid derivatives isolated from *Carissa edulis*

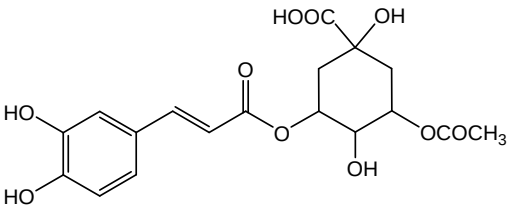
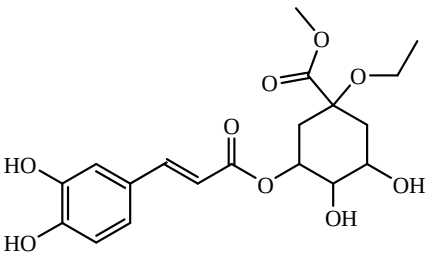
Chlorogenic acid derivatives	
	
Acetyl chlorogenic acid (**32**)	Chlorogenic acid-1-methylester-1-ethyl ether (**33**)

Table 6. Sterols and triterpenes isolated from *Carissa edulis*

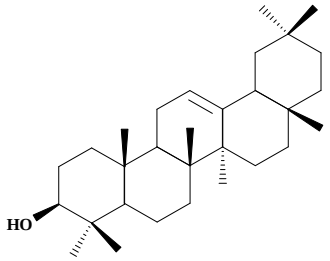
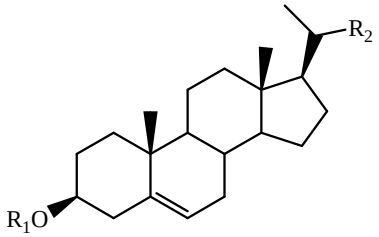
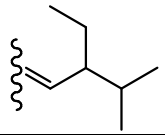
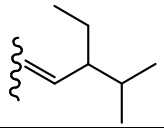
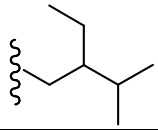
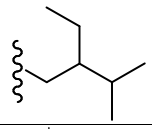
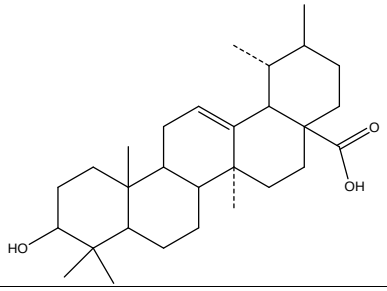
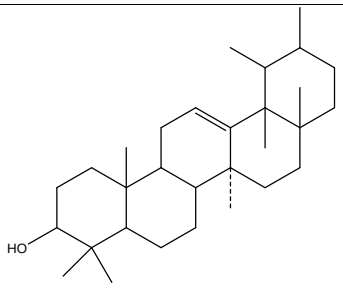
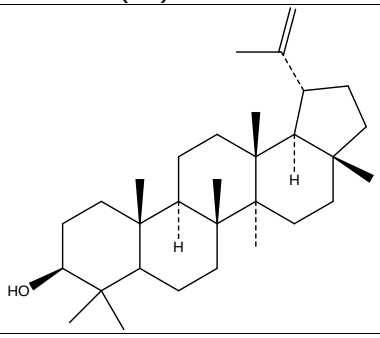
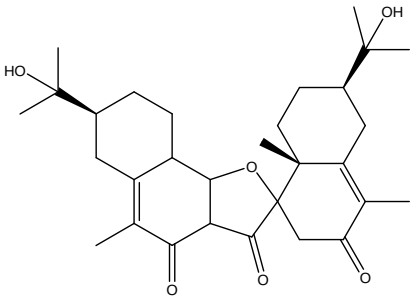
Sterols and triterpenes isolated from *Carissa edulis*	
	
(**34**) β-amyrin	
(**35**) β-sitosterol	R1 = H R2 = 
(**36**) β-sitosterol glucoside	R1 = Glu R2 = 
(**37**) Stigmasterol	R1 = H R2 = 
(**38**) Stigmasterol glucoside	R1 = Glu R2 = 
	
Urosolic acid (**39**)	Carissol (**40**)
	
Lupeol (**41**)	Carindone (**42**)

Table 7 . Coumarins isolated from *Carissa edulis*

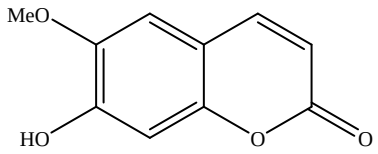
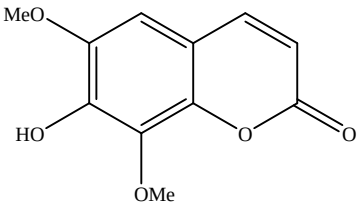
Coumarins	
	
Scopoletin (**43**)	Isofraxidin (**44**)

Table 8 Cardiac glycosides isolated from *Carissa edulis*

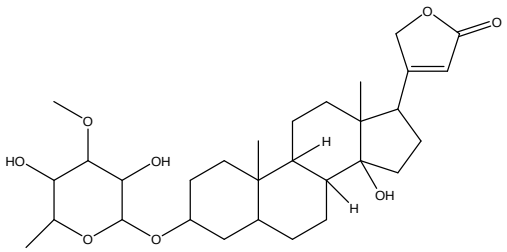
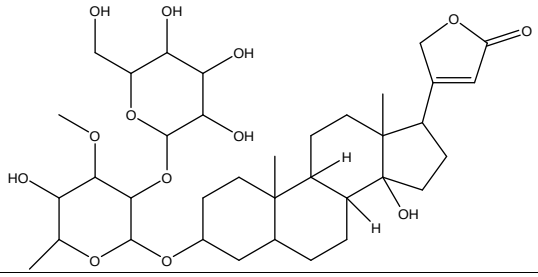
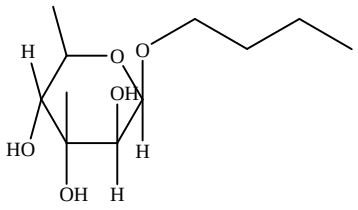
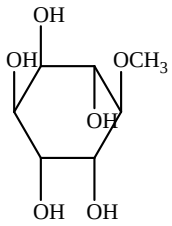
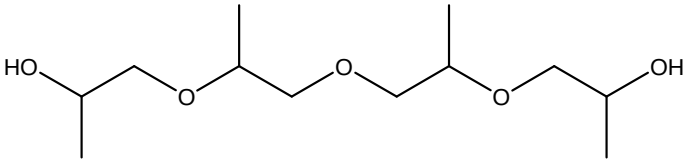
Cardiac glycosides	
	
Odoroside H (**45**)	Odoroside F(**46**)

Table Miscellaneous compounds

Miscellaneous compounds	
	
Butyl rhamnose (47)	**Ononitol(48)**
	
Caredulis (49)	

Volatil oil of *Carissa edulis*

The root oil of *Carissa edulis* from Benin was analyzed by GC/MS and six components were identified. The main constituent was 2-acetylphenol (92.7%) with lesser amounts of limonene (1.2%), γ-eudesmol (1.2%), α-pinene (0.3%), sabinene (0.3%) and myrcene (0.8%) (Moudachirou et al, 1998).

Pharmacological properties

Effect on blood pressure and cardiovascular

Most of the cardiovascular depressant activity has been found in petroleum ether, ethyl acetate and aqueous extracts of *Carissa edulis*. These extracts, at a dose of 0.05g/kg, produced a perceptible fall in arterial pressure by 27.2, 27 and 9.1 mmHg respectively. Increasing the dose to 0.1g/kg produced more depression of blood pressure by 36.3, 34.5 and 32.7 mm Hg respectively. At a higher dose, 0.2g/kg, there was a severe and profound fall of blood pressure by 52.7 and 63.7 mmHg in case of petroleum ether and aqueous extracts respectively. The butanol extract, at doses 0.1 and 0.2 g/kg caused a decrease in arterial pressure by 27.2 mmHg. Also, the percentage decrease in heart rate was more pronounced in petroleum ether than aqueous extract at a dose dependent manner. On the other hand, the ethyl acetate and butanol extracts have not shown any change in heart rate. Most of the cardio-depressant activity seemed to be contained in the petroleum ether, ethyl acetate and aqueous extracts at a dose dependent manner while butanol extract has not shown any significant decrease in arterial pressure at higher dose. The petroleum ether, ethyl acetate and aqueous extracts of *Carissa edulis* possess a marked potency for lowering the blood pressure in rats at a dose dependent manner [Al-Youssef and Hassan 2010].

Electrocardiogram (ECG)

ECG is a record of the electric currents (voltages, potentials) produced by the heart obtained by means of metal electrodes placed on the surface of the body. The percentage decrease in conduction velocity of heart has been shown by petroleum ether, chloroform and ethyl acetate which was more pronounced in petroleum ether by 33% at 1.0 g/kg where as 25% for chloroform and 14.3% for ethyl acetate at a dose of 0.4 and 1.0 g/kg respectively after 20 minutes. Also, the force of conduction was decreased by 50% and 66% after 10 and 20 minutes respectively in petroleum. Ether extract. However, the butanol and aqueous extracts did not show any change in force of conduction, however may possess effects of direct cardiac depressant drugs like anti-fibrillation drugs, general anesthetics drugs, etc., which causes slow conduction in the myocardium, reduce the arterial pressure as well as decrease in heart rate [Al-Youssef and Hassan 2010].

Anti-inflammatory and antioxidant effects

Root extracts of *Carissa edulis* (Forsk.) Vahl (Apocynaceae) are used for the treatment several pathological states including inflammatory disorders. Oral administration of CEE (30-300 mg kg-1 p.o.) significantly inhibited carrageenan-induced foot oedemas with a maximal inhibition of 53.8±8.2%. Similarly, the NSAID diclofenac (10-100 mg kg-1, i.p.) and the steroidal anti-inflammatory agent dexamethasone (0.3-3 mg kg-1, i.p) reduced the total oedema with a maximal inhibition of 62.7±9.1% and 66.4±7.8% respectively. The extract also scavenged DPPH and prevented lipid peroxidation in rat brain homogenates. These results suggest that alcoholic extract of *C. edulis* exerts *in vivo* antiinflammatory activity after oral administration and also has antioxidant properties which may contribute to its activity [Woode et al 2007].

Antiplasmodial activity

Kebenei, J. S., et al., 2011 have been studied the anti-plasmoidal activity of the root bark of *C.edulis*. They have been shown that the total methanolic extract of *C.edulis* has a significant antimalarial activity of 1.95 mg/ml and the most active compound isolated from *C.edulis* is nortrachelogenin with IC_{50} of 14.53 mg/ml. Therefore, the crude extract of *C.edulis* has high potential of being developed into anti-malarial drug which is cheap and available to the community [Kebenei et al 2011]. Also, these results have confirmed the correlation between the ethnoanti-malarial bioactivity of *C.edulis* [Kebenei et al 2011].

Anticonvulsant activity

Ya'u et al., 2008 have been investigated the anticonvulsant activity of root bark extract of *C. edulis*. The results of this study showed that the *C. edulis* produced 40% and 20% protection against convulsion at 5 and 20 mg/kg respectively, compared with 100% protection with benzodiazepine. *C. edulis* exhibited dose-dependent inhibition of the convulsion include by maximal electroshock (MEST) with 20mg/kg providing 90% protection while phenytoin (20 mg/kg) produced 100% protection. These results suggest that *C. edulis* possesses biologically active constituent(s) that have anticonvulsant activity which supports the ethnomedicinal claims of the use of the plant in the

management of epilepsy [Ya'u et al 2008]. The result of this study have shown that *C.edulis* possessed anticonvulsant activity on the animal models investigated and this provides a rational for its use in traditional medicine for the management of epilepsy [Ya'u et al 2008].

Antiviral activity

It has been reported on an aqueous medicinal plant extract from the root bark of *C. edulis* that has shown significant anti-HSV activity *in vitro* and *in vivo.* The plant *C. edulis* is reputed in traditional medicine as a good source of medicine for treatment of skin infections, acotoparasitic diseases, abdominal problems, headache and sexually transmitted diseases [Omino 1993].

The dried total aqueous extract from the root bark of *C. edulis* has been evaluated for *in vitro* and *in vivo* anti-herpes simplex virus (HSV) activity. It has been shown that both the wild and resistant strains of HSV were sensitive to the aqueous extract. The resistant strains were even more sensitive to the extract than the wild strains [Tolo et al 2006]. The extract appeared to have synergestic effects on the resistant strains and this may explain why the virus was not responsive to a cyclovir [Tolo et al 2006]. The mortality rate for mice treated with extract was significantly reduced by 70-90% as compared with the infected untreated mice that exhibited 100% mortality [Tolo et al 2006].

The extract significantly inhibited formation of plaques in Vero E_6 cells infected with 100 PFU of wild type stains of HSV or resistant strains of HSV by 100% at 50 mg/ml *in vitro* with minimal cell cytotoxicity (CC_{50}=480 mg/ml). Also, the extract at an oral dose of 250 mg/kg significantly delayed the onset of HSV infections by over 50% and increased the mean survival time of treated infected mice by 28-35% relative to the infected untreated mice [Tolo et al 2006]. These results suggest that this herbal extract has potent anti-viral agents.

Antimicrobial effects

The antimicrobial studies of the water ad methanolic extracts of *Carissa edulis* plant were carried out on standard organisms, *Staphylococcus aureus,* (ATCC13709), *Streptococcus pyogenes,* (NCTC 8198), *Escherichia coli,* (NCTC 10418), *Pseudomonas aeruginosa,* (NCTC 6570), *Candida albicans* (NCTC3151A) *and clinical isolates (P, aeruginosa. P. putrefaciens),* using cup-plate method on solid media [Sakke, 1971]. The results have shown that the leaves of *C. Edulis* to possess a wide range of antimicrobial activity against both Gram positive (*Staph. aureus, Srept. Pyogenes*, *B. subtilis*) or Gram negative (*E. colis Ps. Arruginosa*) and yeast (*C. albicans*). Also the leaves have wider spectrum of activity than that of Ampicillin which was not effective against *B. subtilis and C. albicans*. (Cold water seems to be a better solvent for extracting the active constituents responsible for the inhibitory activity of the leaves of *C. edulis* since it gave higher zones of inhibition and the organisms were more sensitive to the extracts obtained using cold water the cold water used by the herbalist is justified. The organisms tested are known to cause chest or venereal infections and other ailments. Therefore the results justify the use of the leaves in ethnomedicine [Ibrahim et al 2005].

Renal effects

Nedi et al., 2004 have been studied the diuretic activity of different extracts of *C. edulis* in a dose range of 50-1000 mg/kg orally in rats using hydrochlorothiazide as a standard drug. The root bark maceration extract showed no effect on the urine output up to a dose of 1000 mg/kg, while the root bark soxhlet extract produced a significant increase in urine output at a dose of 1000 mg/kg. the root wood maceration and root wood soxhlet extracts produced a significant increase in urine output at a dose of 50 mg/kg. Urinary electrolyte excretion was also affected by the extracts, the root bark soxhlet extract increased urinary excretion of sodium, potassium and chloride ions; root wood maceration extract increased extraction of sodium and potassium, while root wood soxhlet extract increased excretion of potassium ion [Nedi et al 2004]. The results of this study indicated that *C .edulis* extracts contained compound(s) that mediate diuretic effect by increasing the rate of urine output as well as increasing excretion of electrolytes, sodium, potassium and chloride ions [Nedi et al 2004]. These results support the ethnomedical use of *C.edulis* as a diuretic agent [Nedi et al 2004].

The diuretic activity of different extracts of the aerial parts of *C. edulis* in a dose of 1g/kg i.p. has been studied in comparison with a control group using normal saline in rats. The petroleum ether and ethyl acetate extracts showed slightly effect on the urine output by 9.1% and 12.7% respectively. While chloroform and aqueous extracts produced a significant increase in urine output by 54.5% and 45.4% at a dose of 1g/kg respectively. The results of this study indicated that *C. edulis* extracts contain compound (s) that mediate effect by increasing in blood flow in the kidneys and increasing in the glomerular filtration rate resulting in increase urine output and act as a diuretic action. The present results support the ethnomedical and traditional use of *Carissa edulis* as a diuretic agent. Also a previous

study has been proved that this plant has a significant effect on urine output. However, this study also showed a decreased in urine output in butanol extract only at a dose of 1g/kg i.p. by 45.4% when comparison to control group. Further experimentation is needed in order to understand the precise mechanism of action from the diuretic effect of the different extracts [Al-Youssef and Hassan 2010].

Effect on blood glucose level

Worker studied the decreases in blood glucose level that follow the consumption of ethanolic extract (leaves) of *Carissa edulis* both in normal and streptozotocin (STZ) diabetic rats. This work indicated that consumption of ethanolic extract (2g/kg body weight) resulted in significant decreases in the blood glucose level in STZ diabetic rats during the first three hours of treatment by 89.36 mg/dl in comparison with glibenclamide by 67.36 mg/dl. On the other hand, in normal rats, ethanolic extract of *C. edulis* treatment produced insignificant changes in blood glucose levels compared to glibenclamide treatment [El-Fiky, 1996]. This plant contain some hypoglycaemic principles which act probably by initiating the release of insulin from the pancreatic B-cells of normal animals, sulfonylurea like effect [Akhtar et al 1984].

Analgesic effect

The analgesic activity of the water extracts (50,100 and150 mg/Kg body weight) of the root bark, stem bark, leaves, fruits and seeds of *Carissa edulis* showed that the plant was found to have analgesic activity. The fruits having the highest activity, followed by the leaves, seeds, root bark and stem bark respectively. The activity of the 100 mg extracts is comparable to 150 mg acetylsalicylic acid. [Ibrahim et al 2007]. These result justified the use of the plant in the treatment of toothache, lumbago, oedema and chest complaints by the traditional medical practitioners [Ibrahim et al 2007].

Antioxidant effect

Woode et al 2007 indicated that the antioxidants activities of the alcoholic extract of *C. edulis* is due to the presence of many active constituents such as phenolic compounds [Woode et al 2007]. Phenolic antioxidants are potent free radical terminators [Shahidi et al., 1992]. The high potential of phenolic compounds to scavenge radicals may be explained by their phenolic hydroxyl groups [Sawa et al, 1999]. The author have been evaluated the antioxidant activities by four different assays: the total phenolic content, reducing power, DPPH scavenging ability and lipid peroxidation inhibition [Woode et al 2007].

Conclusion

In conclusion, the *C. edulis* different extracts contain potential agents with activities against many diseases. Some of these agents are isolated and we need to isolate, identify and screen for many possible agents that may cure against many diseases. Such agents could be developed as drugs or provide a template for the synthesis of a new agents.

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References

Abate, G., 1989. Etse Debdabe (Ethiopian Traditional Medicine). Addis Ababa University, Addis Ababa (in Amharic).

Achenbach, H., Weibal., R and Addac-mensah., I (1985). Sesquiterpenes from *Carissa edulis,* Phytochemistry, **24**: 1056-1067.

Achenbach, H., Weibal., R and Addac-mensah., I (1983). Lignins from *Carissa edulis.* Phytochemistry, **24**: 2325-2328.

Addis, G., Abebe D., Urga, K., 2001. A survey of traditional medicinal plants in Shirka district, Arsi Zone, Ethiopia. Ethiopian Pharmaceutical Journal 19, 30-47.

Ajgaonkar, S. S. (1979) Herbal drugs in the treatment of diabetes, a review. IDF Bulletin 24, 10-17.

Akhtar, M. S., Khan, Q. M. and Khaliq, T. (1984) Effects of *Euphorbia prostrate* and *Fumaria parviflora* in normoglycaemic and alloxan-treated hyperglycaemic rabbits. Planta Medica 50, 138-142.

Al-youssef, H. and Hassan, W. 2010. Phytochemical and biological studies of the aerial parts of *Carissa edulis* growing in Saudi Arabia Biosciences, Biotechnology Research Asia, 7(2), 635-646.

Al-youssef, H. and Hassan, W., 2014. Chemical constituents of *Carissa edulis* Vahl. Arabian Journal of Chemistry, V (1), in press.

Atiqur Rahman M., Mossa J. S., Al-Said M.S. and Al-yahya M.A., 2003. Saudi J. Biol. Sci., 10(2): 158-67.

Atiqur Rahman M., Mossa J.S., Al-Said M.S. and Al-Yahya M.A., 2004. Fitoterapia, 75: 149-161.

Audu., B (1994). *Traditional Medicinal Uses of Carissa edulis.* (Oral Communication).Department of Pharmacognosy and Drug Development, Ahmadu Belo University, Zaria

Bailey, C. J. and Day, C. (1989) Traditional plant medications as treatment for diabetes. Diabetic Care 12, 553-564.

Banker, G. J., Verma, S. K., 1987. Preliminary studies of flowering and fruiting in Bentley, M. D., Brackett, S. R., Chapya, A., 1984. 2-Hydroxyacetophenone, Principal root volatile of the East African Medicinal Plant. *Carissa edulis*, Journal of natural products 47, 1056-1057.

Bazeeb, A. S. (1991) The medicinal plants in Yemen, 1st edn. Pub. (in Arabic), El-Ershad Press, Sana'a, Yemen.

Bentley MD, Brackett SR (1984) 2-hydroxyaceto phenol ne: principal root volatile of the East African medicinal plant, *Carissa edulis.* J. Nat. Prod., 47, 1056-1057.

Burkill., H. M., (1985). *The Useful Plants of West Africa*. Second Edition. Vol. 1. Families A-D. Royal Botanical Gardens. Kew. Pp 145-146.

Chao-Mei Ma, Takuya Kawahata b, Masao Hattori a,*, Toru Otake b, Lili Wangc, Mohsen Daneshtalab. Synthesis, anti-HIV and anti-oxidant activities of caffeoyl 5,6-anhydroquinic acid derivatives. Bioorganic & Medicinal Chemistry 18 (2010) 863–869.

Dharani N and Yenesew A (2010) Medicinal plants of East Africa: An illustrated guide. Publisher – Najma Dharani; in association with Drongo Editing & Publishing. ISBN 978-9966-05-167-168.

Dewick, P.M. (2002). The biosynthesis of C-5-C-25 terpenoid compounds. *Nat.Prod.Rep.*19: 181-222.

Dewick, P.M., 1999. The biosynthesis of C-5-C-25 terpenoid compounds. Nat. Prod. Rep. 16, 97–130.

El-Fiky, F. K. (1996) Effect of *Luffa aegyptiaca* (seeds) and *Carissa edulis* (leaves) extracts on blood glucose level of normal and streptozotocin diabetic rats. Journal of Ethnopharmacology 50, 43-47.

Evans, W. C., 2005. Trease and Evans Pharmacognosy, 15th ed. W. B Saunders, London.

Gachathi, F. N., 1989. Kikuyu Botanical Dictinary of plant names and uses. Printing Department, AMREF, Nairobi, Kenya, p. 80.

Gbile., Z (1980). *Vernacular Names of Nigeria Plants* (Hausa). Printed by the Federal Department of Forestry, Lagos. Pp 7.

Giday, M., 2001. An ethnobotanical study of medicinal plants used by the Zay people in Ethiopia. CMB: Skriftserie 3, 81-99.

Gupta, M.B., Nath, R., Srivastava, N., Shanker, K., Kishor, K., Bhargava, K.P., 1980. Anti-inflammatory and antipyretic activities of beta-sitosterol. Planta Medica 39, 157-163.

Hettiarachchi, D. S., 2006. Isolation, identification, and characterization of antimicrobial compounds from Carissa lanceolata R.Br. root. M.Pharm. Thesis, Curtin University of technology.Hutchinson., J and Dalziel., J. M., (1963). *Flora of West Africa*. Vol. II Crown Agents for Oversea Governments and Administration, Millbank, London S.W. 1. Pp 51-54.

Ibrahim, H., 1997. Pharmacognostic and biological (analgesic activity) studies of Carissa edulis Vahl. PHD. Thesis. Ahmadu Bello University, Zaria, Nigeria, pp. 232.

Ibrahim, H., R.O. Bolaji., E.M Abdurahman1, M. Shok1, N. Ilyas1and A.G. Habib, 2005. Preliminary phytochemical and antimicrobial studies of the leaves of *Carissa edulis* VAHL. *ChemClass Journal, ,*V (2), 15-18.

Irvine., F. R., (1961). *Woody Plants of Ghana*. Oxford University Press. London. pp 616-618.

Ivorra, M. D., Paya, M. and Villar, A. (1989) A review of natural plant products and plants as potential antidiabetic drugs. Journal of Ethnopharmacology 27, 243-275.

Johns T., Mahunnah, R. L. A., Sanaya, P., Chapman, L., and Ticktin, T., 1999.

Saponins and phenolic content in plant dietary additives of a traditional subsistence community, the Batemi of Ngorongoro District, Tanzania. Journal of Ethnopharmacology 66, 1-10.

Kebenei, J. S., Ndalut, P.K., Sabah, A. O., 2011. Anti-plasmoidal activity ofNortrachelogenin from the root bark of C.edulis (vahl). International Journal of Applied Research in Natural Products. 4(3), 1-5.

Kirira P.G., Rukungo G.M., Wanyonyi A.W., Gathinwa J.W., Muthaura C.N., Omar S.A., Tolo F., Mungai G.M. and Ndiege I.O., 2006. Anti-plasmodial activity and toxicity of extracts of plants used in traditional malaria therapy in Meru and Kilifi Districts of Kenya . J. Ethnopharmacol., 106: 403-407.

Kokwaro, J. O., 1976. Medicinal plants of east Africa. East African Literature Bureau, Nairobi, Kenya, pp. 1-8, 25-26.

Moudachirou, M., Abel Ayedoun, M., Gbenou, J. D., Garneau, F. X., Gagnon, H., Jean, F. I., 1998. Essential oil of *Carissa edulis* Vahl. From Benin. Journal of Essential Oil Research, 10(2), 195-196.

Nedi, T., Mekonnen, N., and Urga, K., 2004. Diuretic effect of the crude extracts of Carissa edulis in rats. Journal of Ethnopharmacology 95, 57-61.

B. Oliver (1996). *Medicinal Plants in Nigeria*. Published as private edition by the Nigeria College of Arts, Science and Technology. pp 52,

Omino, E. A., Kokwaro, J. O., 1993. Ethnobotany of Apocyanaceae species in Kenya. Journal of Ethno-pharmacology 40, 167-180.

Pal R., Kulshreshtha D. and Rastoqi R.P., 1975. Phytochemistry, 14: 2302-3.

Pakrashi, S. C., Datta, S and Ghosh-Dastidar, PP., 1968. Indian medicinal plants- XVII.3 Phytochemical examination of Carissa SPP. Phytochemistry 7 (3), 495-6.

Sawa , T., Nakao, M., Akaike, T., Ono, K., and Macda, H., 1999. Alkyl phenoxyl radical scavenging activity of various flavonoids and other phenolic compounds: implications for the anti tumor promoter effect of vegetables. Journal Agric. Food. Chem., 47, 397-402.

Shahidi, F., and Wana sundara, P. K., 1992. Phenolic antioxidants. Crit. Rev. Food Sci. Nutr., 32, 67-103.

Sakke., A. J., (1971). Fundamental Principles of bacteriology. Seventh edition. McGraw-Hill Book Company. New York. pp. 223, 17.

Seema Patel, Food, pharmaceutical and industrial potential of *Carissa* genus: an overview, Rev Environ Sci Biotechnol 2012. 9306.

Sofowora., A., (1986). The State of medicinal Plants Research In Nigeria. 1st Edition. University Press Ltd Ife Nigeria. pp 338.

Sofowora., A., (1993). Medicinal Plants and Traditional Medicine Africa. Second edition. Spectrum Book Ltd. Ibadan, pp 145,148.

Tolo, F. M., Rukuga, G. M., Muli, F. W., Nijagi, E. N. M., Njue, W., Kumon, K., Mungai, G. M., Muthaura, C.N., Muli, J. M., Keter, L. K., Oishi, E., Kofi-Tsekpo, M.W., 2006. Anti-viral activity of the extracts of a Kenyan medicinal plant *Carissa edulis* against herpes simplex virus. Journal of Ethnopharmacology 104, 92-99.

Wang T. R. and Likhitwita Y.K., 2009. Helvetica Chemica Acta, 92: 1217-23.

Woode., E, Ansah., C, Ainooson., G.K., Abotsi., W.M. K., Mensah, . A.Y., and Duwiejua, M., 2007. Anti-inflammatory and antioxidant properties of the root extract of *carissa edulis* (forsk.) vahl (apocynaceae). journal of science and technology, vol. 27, no. 3, december**.**

Vohra, M.M.& De, N.N., 1963. Comparative cardiotonic activity of *Carissa carandas* and Carissa spinarum. Indian J Med Res. 51, 937-40.

Ya'u, J., Yaro, A. H., Abubakar, M S., Anuka, J. A., Hussaini, I.M., 2008. Anticonvulsant activity of C.edulis (Vahl) (Apocynaceae) root bark extract, Journal of ethnopharmacology 120, 255-258.

Yako, H. Y., (1992). Medicinal Treatment of Sickle Cell Anaemia. (Oral Communication). Department of Pharmacognosy and Drug Development, Ahmadu Bello University, Zaria.

