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A BRIEF REVIEW ON PHARMACOGNOSTIC, PHYTOCONSTITUENTS, PHARMACOLOGY AND TRADITIONAL USES OF *CARRISA SPINARUM* (APOCYNACEAE)

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ABSTRACT

Medicinal plants are the richest sources of phytoconstituents. Primary metabolites and secondary metabolites are synthesized in plants. These phytoconstituents are the source of traditional system of medicines, food supplements and nutraceuticals. Wild Karonda is a thorny bush which is known as *Carrisa spinarum* binomially, belonging to Apocynaceae family. They are drought resistant plants and it is grown in dry foothills. These bushes are found in dense forest of tropical or subtropical region of India. Traditionally it is used for treatment of various diseases like, inflammation, rheumatism, epilepsy, microbial and viral infection, cancer etc. Phytochemical studies revealed that glycosides, lignans, coumarins, fatty acids and volatile oils are present in this plants. Phytochemical investigation upon this plant researchers isolated 9 lignans compounds, 2 cardiac glycosides, one coumarins compound which of some are carinol, carissanol, nortrachelogenin, caeffic acid and stigmasterol. This plant exhibits positive pharmacological activities which are antioxidant, antiviral, antimicrobial, cytotoxic, Antiarthritic, anticancer, antipyretic, antiascaris, epilepsy, for pain, antirheumatic, liver disease, anticonvulsant, purgative etc. The aim of this review is more attention to researchers toward investigation of new phytochemical, pharmacological study scientifically drugs used traditionally and establishment of mode of action of drug.

KEYWORDS

Wild karonda, Jungli Karonda, *Carissa spinarum*, Traditional use, Phytochemicals and Pharmacological activities.

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INTRODUCTION

Herbal medicines in the view of therapeutic purpose it is now well-established and widely acknowledged to be safe, effective and easily available for human being. Herbal medicines include herbs, herbal preparation, herbal material and finished herbal products which are contained as active ingredients, parts of plants, or other plant materials, or combinations of plant materials. Many drugs

commonly used today in the developed and developing countries are of herbal origin and modern prescription drugs also contain at least one of the active ingredients derived from plant materials, either obtained from plant extracts or synthesized from natural plant compound[1]. World health organization (WHO) estimates about 80 percent of human beings of world population are still using herbal made medicines including plants and natural products derived from natural sources as their primary health care tools.

Carissa spinarum is a thorny shrub which is found as wild in hills of dry region like Punjab, Himalaya, Chhatisgarh, Madhya Pradesh, Jharkhand, Andaman etc in India[2]. It is wildly distributed in Africa, Southern Asia and Australia. It is drought resistant plant and grown in rocky, sandy and hill foot. Flowering and fruiting time of this plant is April to May. It bears white colored flowers and green fruit in unripe and black in ripe fruits which are edible[3]. Traditional as well as earlier studies are talked about its medicinal value. It is used for treatment of various diseases such as chronic inflammation, arthritis, hepatoprotective, cardio tonics, and antipyretics etc[4]. The present study deals a compiled literature review on Phytoconstituents, pharmacological activities, traditional as well as therapeutic uses of *Carissa spinarum.* This study would help the scientific base for investigators to provide information of traditional uses, earlier as well as current investigation on these plants. So that researcher can give more attention on investigation or innovation to validate scientific pharmacological activity and development of new phytoconstituents by analytical tools on *Carissa spinarum.*

MATERIAL AND METHODS

Literature survey was done from various journal, reference books, e books and web sites regarding *Carissa spinarum*. All information about phytoconstituents primary or secondary, isolated and identified by various analytical tools, their molecular structures, traditional uses as well as pharmacological activities are noted and compiled.

Plant profile

Synonyms

Wild Karonda, Jungli Karonda, Kavali, Karamdika, Chirukila, Vaka, Kalivi, Karamacha, Karmarda Karekayi, Garji, Kavali, Karanda, Karwant, Avighna, Kalakkay, Kalachedi[5].

Binomial classification[6]

Pharmacognostical characters of *Carissa spinarum*

Carissa spinarum is an erect thorny shrub 2 to 3 m high, having grey bark, hard wood with simple or forked spines which are rough or smooth 0.5 to 6.2 cm long brown to greenish at the base and deep brown towards the tips. Morphology and microscopy of this plant part is given in Table No.1[7].

PHYTOCONSTITUENTS OF *CARRISA SPINARUM*

Phytoconstituents are the chemicals which are occur in plants naturally and derived from the plants, specifically secondary metabolic compounds. These phytoconstituents are protecting plants from various plant diseases and insect attack and also exhibit a number of protective functions for human consumers[8]. Phytochemicals are responsible for organoleptic properties and biological significance. There may be as many as 4,000 different phytochemical are found in plants[9]. In Carissa spinarum presence of phytochemical are alkaloid, tannin, carbohydrate, glycoside (Anthraquinones glycosides), saponins, terpenoids, flavonoids and steroids etc[10-12] and Table No.2[13].

Many researchers analysed phytoconstituents by using various analytical tools and reported which are following

It had analyzed characteristics and compositions of seeds and extracted oils of *Carissa spinarum* (Apocynaceae). The seeds of *Carissa spinarum* contained 22.4% oil and 10.1% protein. Fatty acid compositions are (area %) palmitic 12.6, stearic 7.6, oleic 72.7, linoleic 5.2, linolenic 0.9, and arachidic 1.0[14].

It had studied a new germacrane derivative; carenone was isolated from the stems of Carissa *spinarum* L. together with a new ester, 3′-(4″-

methoxyphenyl)-3′-oxo-propionyl hexadecanoate. Their structures had been established using by 1D, 2D, NMR spectroscopic and synthetic methods[15].

Six compounds were isolated namely stigmasterol, ursolic acid, lupeol, campesterol, 17-hydroxy-11-oxo-nor-β-amyrone and urs-12-ene-3β, 22β-diol-17-carboxylic acid from the petroleum ether extract of the roots of *Carissa spinarum* Linn (Apocynaceae) by using column chromatography. Their structures were characterized by melting point, IR, ^{1}HNMR, ^{13}CNMR and mass spectral data and reported the compounds are stigmasterol, campesterol, 17-hydroxy- 11-oxo-nor-β-amyrone and urs-12-ene-3β, 22β-diol-17-carboxylic acid[16].

Some bioactive compounds were isolated which are 9 lignans compounds, 2 cardiac glycosides, one coumarins compound. The lignans carinol, carissanol and nortrachelogenin were exhibited cytotoxic compounds[17]. Carinol belongs to the family of Dibenzylbutanediol lignans. Carissanol belongs to the family of Dibenzylbutyrolactols. The antitumor lignan Nortrachelogenin sensitizes prostate cancer cells to trail induced cell death by inhibition of the Akt pathway and growth factor signaling. Molecular structure of these lignan compounds are given below.

Caffeic acid (C9H8O4) was isolated from the root of Carissa spinarum. It is hydroxycinnamic acid which is found in many plants and foods[18].

Qualitative chemical analysis

Quantitative chemical analyses are the determination of the exact quantity or percentage of one or more constituents in a sample in numerical number[19]. Methods are used for experiments are volumetric, gravimetric and titrimeric analysis. The basic and important tool in all quantitative analyses is the analytical balance, which is used for the accurate weighing of samples and precipitates[20].

Pharmacological activities

Pharmacological evaluation involves the study of interactions of phytoconstituents with living system to understand the properties of drugs and their actions. It involves examining the different pharmacological classes of drugs used therapeutically and their roles in society for their healthcare [21].

Anthelmintic activity

Harwansh *et al*, (2010) investigated and reported positive antihelmintic activity of *C. spinarum.* Methanolic, aqueous and chloroform extracts of root of *C. spinarum* was evaluated on Indian earthworm *Pheretima posthuma*. Piperazine citrate (PC; 10 mg/ml) was taken as reference compound. Methanolic extract (100 mg/ml) and chloroform extract (50 and 100mg/ml) of *C. spinarum* exhibited equivalent potency of anthelmintic activity as compared to PC (10 mg/ml). But it took more time for causing paralysis and death of *Pheretima posthuma*[22].

Antioxidant activity

Hegde *et al*, (2010) investigated and reported ethanolic extract of the roots of *C. spinarum* for antioxidant activities in rats. CCl_4 induced and PCM model was used for evaluation. Silymarin was used as standard drug. Extracts have possibly attributed to its free radical scavenging properties[23]. Chloroform and aqueous fraction of extract of fruits of the plant exhibited strong antioxidant (DPPH) activity. And chloroform extract of plant stem exhibited strong antioxidant (DPPH) activity. Ascorbic acid was taken as standard drug. The antioxidant activity of major lignans was studied[24].

Hepatoprotective activity

Hegde *et al*, (2010) investigated and reported ethanolic extract of the roots of *C. spinarum* for hepato-protective activities in rats. Silymarin was used as standard drug. Oral pre-treatment with ethanolic extract (100, 200 and 400 mg/kg) showed significant hepatoprotective activity against CCl_4 and paracetamol- induced hepatotoxicity. Histopathological examination decreased the bilirubin and lipid peroxidase activities and increased levels of uric acid, glutathione, super oxide dismutase, catalase and proteins. It exhibited this according to the concentration of doses. This suggests that the hepatoprotective activity of *C. spinarum* is possibly attributed to its free radical scavenging properties [25].

Wound healing activity

Sanwal *et al*, (2011) studied and reported the effect of methanolic extract of *Carissa spinarum* root extracted by cold maceration on burn wound model in mice. Plain ointment base was taken for comparing the test sample. 1% and 2.5% (w/w) root extracts was exhibited wound contraction and epithelization. Histological study of the granulation tissue was carried out to know the extent of collagen formation in the wound tissue. The results showed that *Carissa spinarum* root extract has significant wound healing activity as evident from the rate of wound contraction and epithelization[26].

Antimicrobial activity

Sanwal *et al*, (2011) studied and reported the antimicrobial effect of methanolic extract of *Carissa spinarum* root against the bacterial and fungal strain using agar dilution method. Silver sulfadiazine was taken as standard drug. Methanolic extract exhibited significant antimicrobial activity against all the tested micro-organisms[26]. Rubaka *et al* 2014 were studied and reported antibacterial activity of leave extract of *Carissa spinarum* against *Escherichia coli* and *Staphylococcus aureus*. Plant extracts inhibited growth of the pathogens at different MIC values. The plant extracts with high activity against a particular organism usually gives low MIC value while the extracts with low activity gives high MIC value. The study demonstrated *C. spinarum* L. leaf petroleum ether extract and *C. spinarum* L. root methanolic extract have higher activity than other extracts when tested against S. *aureus*. Besides, *C. spinarum* L. root ethanolic and methanolic extracts demonstrated high activity when tested against E. coli. Bioactive compounds in the roots of *C. spinarum* L. have wide spectrum of antibacterial activity showed by low MIC values in both *E. coli* and *S. aureus* bacteria[27].

Cytotoxic activity

Seher *et al* 2011 reported the anti-cancer potential of *C. spinarum* stems aqueous extract (CSE) and its n-butanol fraction (CSF). Both inhibited cell proliferation of various human cancer cell lines. Leukaemia HL-60 cells treated with CSF showed maximum growth inhibition having an inhibitory concentration (IC (50) value of 34.58±0.91 µg/ml. CSF induced concentration-dependent apoptosis in HL-60 cells was measured by various end-points likes Annexin V binding, DNA laddering, apoptotic body formation and hypodiploidsubG0 DNA content. Translocation of Bax to mitochondria and Bcl-2 degradation were caused by persistent levels of reactive oxygen species. It might be due to loss of mitochondrial membrane potential and release of cytochrome c to the cytosol. These were happened by associating with significant activation of caspase-3, caspase-6 and caspase-9 leading to poly (ADP-ribose) polymerase cleavage. The cardiac glycoside evomonoside was found to be the only antiherpetic principle, showing moderate activity in the inactivation method against herpes simplex virus types I and II. Lignans which are found in this plants carinol, carissanol and nortrachelogenin exhibited cytotoxicities against breast (MCF7) and lung (A549) cancer cells[28].

Antipyretic activity

Hedae *et al*, (2010) investigated and reported the ethanolic extract of the roots of *Carissa spinarum* (ERCS) its phytochemical screening and antipyretic activity. Wistar albino rats were administered subcutaneous with Brewer's yeast (2 ml/kg) for pyrexia and elevation of body temperature. Ethanolic extract was treated at the dose of 100mg, 200mg and 400mg/kg. According to the concentration of the dose ethanolic extract reduced increased body temperature significantly ($P<0.05$). Phytoconstituents present in this plants glycosides, flavonoids, saponins, triterpenoids, steroids, phenolic compounds and tannins may attribute to the promising antipyretic activity of *Carissa spinarum* root extract[29].

Antidiabetic activity

Acetone extract of leaves of *Carissa spinarum* exhibited significant antidiabetic activity on Alloxan -induced diabetic rats. Acetone extract treatment on diabetic rats increases significantly cholesterol, triglyceride, LDL and VLDL level whereas HDL level decreased[30].

Antihyperlipidaemic effects

Acetone extract of leaves of *Carissa spinarum* on diabetic rats increase significantly cholesterol, triglyceride, LDL and VLDL level whereas HDL

level decreased. Acetone extract showed significant antihyperlipidaemic activity[30].

Anticonvulsant activity

Hegde *et al* 2011 studied and reported positive anticonvulsant activity of ethanolic extract of root on MES, PTZ, and PC induced seizures. Test dose was taken 100,200, 400 mg/kg and diazepam and phenobarbitone was taken as standard drug[31].

Proteomic activity

Zang *et al*, (2010) studied and reported *Carissa spinarum* is one of the secondary advantage plants grown in dry-hot valleys in China, which can survive under stress conditions of high temperature and extreme low humidity. They had studied the physiological and proteomic changes of *C. spinarum* in response to 42 degrees C heat stress treatment in combination with drought stress. Dynamic changes in the leaf proteome were analysed at four time points during the stress treatment and recovery stages. Approximately, 650 protein spots were reproducibly detected in each gel. Heat and drought treatment were carried out upon plants, forty nine spots were changed in their expression levels. Thirty proteins were identified by MS and 2-D Western blot. These proteins such as HSP, photosynthesis - related proteins, RNA - processing proteins etc were involved in metabolism and energy production[32].

Antinociceptive activity

Mworia *et al* 2015 studied and reported positive antinociceptive activity of acetone extract of leave of *Carissa spinarum* in formalin induced animal model in Swiss albino rats. 50 and 100 mg/ kg of extracts sample were given in sub planner region of rat left hind paw. Different dose levels were lowered paw licking time in dose dependent manner[33].

Traditional medicinal uses of *Carrisa spinarum*

Medicinal values of *Carissa spinarum* Linn are reported in many ancient literatures. Roots are ground and put into the wounds of cattle to kill worms. In combination with the roots of some other medicinal plants are used for treatment of rheumatism by the Mundas (a tribe) of Chhota Nagpur (Kirtikar and Basu, 1938). Roots are used in the treatment of glandular inflammation, venereal disease, chest complaints, cough remedy, tonic, abortifacient etc.

A root-decoction, combined with pimento, is used as an anthelmintic, especially against Taenia. The roots contain an active ingredient, 'carissin', that may prove useful in the treatment of cancer. The root-bark is mixed with spices and used as an enema for lumbago and other pains. The root is chewed and saliva swallowed, the root-sap being considered tonic and restorative of virility. A paste of the grounded roots serves as a fly repellant, snake repellant.

The plants are also used as ‘bitters’, macerated in rum, gin, etc, and as an expectorant[34]. It is a strong purgative and is used as one of the ingredients in some purgative preparations. The unripe fruit is rich in tannins and is used medicinally as an astringent. The ripe fruit is taken as an antiscorbutic and remedy for biliousness. The fruits are a source of tannins, and have been used in dyeing and as an expectorant.

S.No	Domain	Eukaryota
1	Regnum	Plantae
2	Clade	Angiosperms
3	Order	Gentianales
4	Family	Apocynaceae
5	Subfamily	Rauvolfioideae
6	Tribus	Carisseae
7	Genus	Carissa
8	Species	*Carissa spinarum* L.

Table No.1: Pharmacognostical characters of *Carissa spinarum*[7]

S.No	Plant parts	Pharmacognostical characters
1	Leaves	Leaves are ovate, 4.5 cm long, 2.5 cm broad, Petiolated, petiole 0.5-6 mm long; ovate shaped or elliptic or orbicular. Apex acute or rounded at the apex and rounded at the base entire margin and reticulate pinnate venation. Surface of leaves are glabrous or pubescent. Leaves exuding white latex, when plucked from the stem.
2	Inflorescence	Inflorescence terminal or occasionally axillary, dense-flowered cymes.
3	Flowers	Flowers are short-stalked, fragrant, bisexual, bracteates, cyclic and actinomorphic. Colour of flower is between white and rose. Calyx is polysepalous, with 5 sepals, green, 2 to 3 mm, long. Corolla is tubular at the base of flower and dilated at the top, five-lobed, glabrous and white in colour. Androecium, with 5 stamens, each 2 to 3 mm long which is inserted near the neck of the tubular portion of the corolla. Gynoecium is in superior with a spindle-shaped stigma, which is 7 to 8 mm long.
4	Fruits	Fruits are red to black in colour, globose or ellipsoidal shape, 5-25 mm long and 3-20mm wide.
5	Seeds	Lanceolate, black colored, 5 to 6 mm in length, 4 mm in diameter.

Table No.2: Phytochemical composition of different plant parts[13]

S.No	Plant parts	Phytochemical Contents
1	Leaves	Triterpene, alcohol, ursolic acid
2	Roots	Carissone, Carindone, Carinol, Odoroside H, digitoxigenin, glucose and D- digitalose
3	Flowers	Myrcene, limonene, linalool, camphene, canine, dipentene, farnesol, α terpeneol, nerolidol, dihydrojasmone, citronellal, geranyle acetate, nerylacetate.
4	Fruits	Reducing and non reducing sugar, glucose, galactose, glycine, alanine, Phenylalanine, vitamin C, Pectin, Carissol, Lupeol, cerine, malonic acid, oxalic acid, tartaric acid, malic acid, glycolic acid and citric acid.
5	Seeds	Fatty acids – palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, and arachidic acid.

Table No.3: Quantitive chemical analysis of plant extracts

S.No	Quantitive analysis	Quantitive value	References
1	Iodine values of volatile oil	70.1	Rao *et al*, (1984)
2	Saponification values of volatile oil	186	Rao *et al*, (1984)
3	Unsaponifiable matter of volatile oil	5.2	Rao *et al*, (1984)
4	Moisture content	64 %	Rao *et al* 2005
5	Total soluble solids of the fruit-juice	25.8 %	Rao *et al* 2005
6	Acids	1.51 g	Rao *et al* 2005
7	Total sugars	10.80 g	Rao *et al* 2005
8	Reducing sugar	10.77 g	Rao *et al* 2005
9	Non-reducing sugars	0.03 g	Rao *et al* 2005
10	Tannins	0.42 g	Rao *et al* 2005
11	Pectin	1.39 g	Rao *et al* 2005
12	Vitamin C	1.83 mg	Rao *et al* 2005
13	Protein content	4.09 %	Rao *et al* 2005
14	Mineral content	1.621 %	Rao *et al* 2005
15	Phosphorus	0.057	Rao *et al* 2005
16	Potassium	0.504	Rao *et al* 2005
17	Calcium	0.051	Rao *et al* 2005
18	Magnesium	0.052	Rao *et al* 2005
19	Iron	0.007	Rao *et al* 2005
20	P^H range of extract	4.0 to 7.5	Maobe *et al*, (2013)

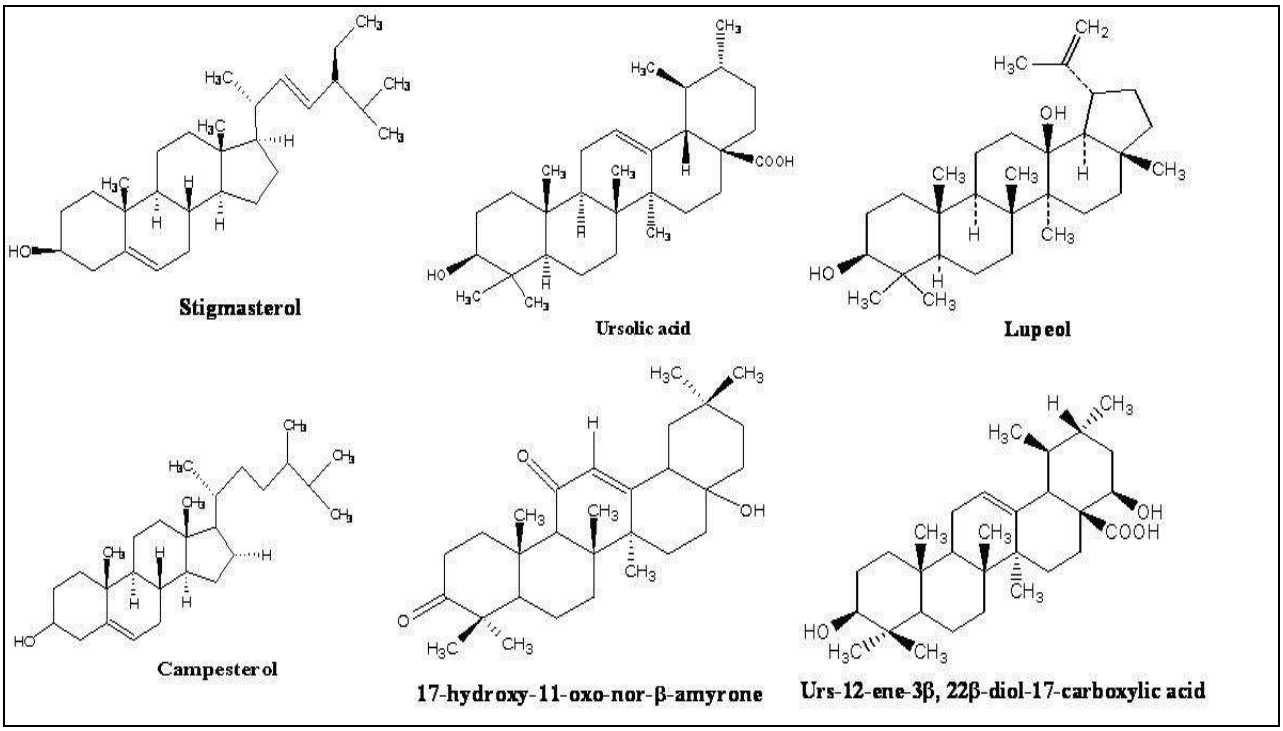
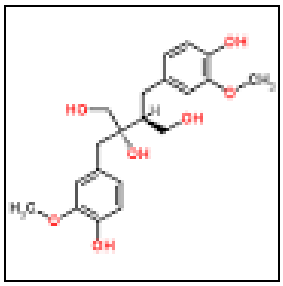
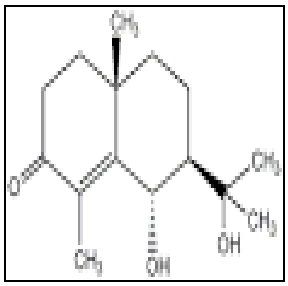


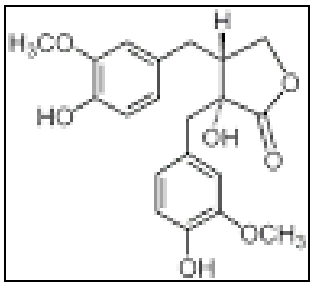
Figure No.1: Phytoconstituents of *C. spinarum*



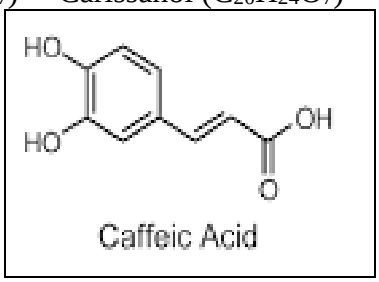
Carinol ($C_{20}H_{26}O_7$)



Carissanol ($C_{20}H_{24}O_7$)



Nortrachelogenin



Caffeic Acid

CONCLUSION

Current scenario natural products are widely used in the world population for the treatment of their healthcare. *Carissa spinarum* is potent medicinal drug and used traditionally for the treatment of various diseases like glandular inflammation, venereal disease, chest complaints, cough remedy, tonic, and abortifacient, fly repellent and snake repellent etc. Literature revealed that presences of phyto constituent are alkaloid, tannin, carbohydrate, glycosides, saponins, terpenoids, flavonoids and steroids. It has been reported after evaluation of various pharmacological activities, this plant exhibited anthelmintic, antinociceptive, proteomic, anticonvulsant, antihyperlipidaemic, wound healing, antidiabetic activity, antipyretic, hepatoprotective and antioxidant. Because of more medicinal value of this plant need to more attention toward expansion of further research on pharmacological activity, mechanism of action and discovery of new phytoconstituents of *Carrissa spinarum*.

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CONFLICT OF INTEREST

I declare that I have no Conflict of interest.

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