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Review Article

A BRIEF REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *CARISSA SPINARUM* L.

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ABSTRACT

Carissa spinarum L. belongs the Apocynaceae family, which officially itself has 94 synonyms and misspelled, misapplied, invalid, and illegitimate names. The plant is known as "Magic Shrub" in some of the African countries, as it is a source of treatment for various diseases and disorders. The plant contains certain major bioactive constituents such as acids, glycosides, terpenoids, alkaloids, tannins, and saponins which are responsible for medicinal value. Traditionally, the plant is used for treatment of malaria, chest complaints, stomach-ache, diarrhea, worms, a cough remedy, eye cataracts, gastric ulcers, polio, cancer, hypertension, kidney complication and for treating herpes, infertility, diabetes, asthma, rheumatism, and infections such as gonorrhea, syphilis, sickle-cell anemia, hernia, rabies, typhoid fever, jaundice, sexual asthenia in males, measles, and as a cough expectorant. Apart from this, the plant is evaluated for various pharmacological activities by employing the animal models. The review has been written with the aim to provide a direction for further clinical research to promote safe and effective herbal treatments to cure a number of diseases.

Keywords: *Carissa spinarum* L., Pharmacological activities, Medicinal properties, Traditional uses, *Carissa edulis.*

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INTRODUCTION

Carissa spinarum L., belongs to the dogbane family Apocynaceae [1], found to be widely distributed throughout tropical regions of Africa, Southern Asia, Australia, and various islands of the Indian Ocean. The shrub is commonly known as wild Karonda in India, referring to the related karanda (*Carissa carandas*). It is often misidentified as *C. carandas* due to similar appearance. Species in this family are significant in the food industry as well as in pharmacologically as traditional medicine. It is known as native currant or even blackcurrant in Australia; however, it is not related to *Prunus* or *Currant* species. In Africa, it is called as "enkeldoring-noemnoem" which means "simple-spine num-num" [2].

Carissa belongs to Apocynaceae family which contains 5 subspecies, 410 genera, and 5556 species. The Apocynaceae family has been known as one of the enormous flowering plant families. *Carissa* genus was listed more than 500 species, but most of them are relegated as synonyms. *C. spinarum* L. officially itself has 94 synonyms [3] and 7 misspelled, misapplied, invalid, and illegitimate names [4]. Some of these are shown in (Table 1).

As it is often misidentified as *C. carandas*, here is the difference between them [5]

C. carandas C. spinarum

1. Lateral veins of leaf 8 pairs	**1. Lateral veins of leaf 3–5 pairs**
2. Leaves 3.5–8 cm long	2. Leaves 2–5 cm long
3. Leaf apex rounded, emarginated	3. Leaf apex acute or acuminate to apiculate
4. Fruit ellipsoid, 15–25 mm long	4. Fruit subglobose, 5–12 mm
5. Ripe fruit reddish-purple	5. Ripe fruit shining black
6. Corolla tube 2–2.5 cm long	6. Corolla tube 1–1.5 cm long

1. Plant profile [6]
   - Family: Apocynaceae
   - Common names: Currant Bush, Conkerberry, Bush Plum, Burrum Bush, Wild Karaunda.
2. Taxonomical hierarchy
   - Kingdom: *Plantae*
   - Subkingdom: *Viridaeplantae*
   - Phylum: *Tracheophyta*
   - Class: *Magnoliopsida*
   - Subclass: *Asteridae*
   - Order: *Gentianales*
   - Family: *Apocynaceae*
   - Genus: *Carissa*
   - Species: *Spinarum.*
3. Vernacular names [7]
   - Maharashtra: *Karavada, Karanda, Karwant;*
   - Andhra Pradesh: *Vaka, Kalivi, Kalli;*
   - Bengal: *Karamacha;*
   - Gujarat: *Karmarda;*
   - Karnataka: Karekayi, Garji, Kavali;
   - Himachal Pradesh: *Karondhu, Garna, Kharnu;*
   - Hindi: *Karunda;*
   - Sanskrit: *Karamarda, Avighna;*
   - Tamil Nadu: *Kalakkay, Kalachedi.*

MORPHOLOGY [9]

1. Plant: Thorny shrub, with forked branches,
2. Height: 2–3 m
3. Wood: Very hard;
4. Bark: Light brown to green,
5. Thorns: 3.2 cm long, at the base brown to greenish and toward the tip deep brown colored,
6. Leaves: Ovate, 4.5 cm long, 2.5 cm broad, leathery; venation, reticulate pinnate; margin, entire; petiole 3 mm long; leaves exuding a white latex, when plucked from the stem,
7. Flowers: Short-stalked, sweetly scented, bisexual, complete, and white colored,
8. Fruit: An ovoid berry, 5–12 mm in length, 6 mm in diameter, green when unripe, and Shining black when completely ripe (Fig. 1).

PHYTOCHEMICAL TESTING OF VARIOUS PARTS OF PLANT

Leaves [10]
Phytochemical testing of leaves of C. spinarum L. are shown in (Table 3). And Phytochemical parameters of leaves of C. spinarum L. are shown in (Table 4).

Roots and root bark
Phytochemical testing of roots and root bark of C. spinarum L. are shown in (Table 5).

Fruit [15]
Phytochemical testing of fruit of C. spinarum L. are shown in (Table 6).

Stem and stem bark [16]
Phytochemical testing of stem and stem bark of C. spinarum L. are shown in (Table 7).

CHEMICAL COMPOSITION [17-21]

Fruit
It consists of acids, sugars, reducing sugars, non-reducing sugars, tannins, pectin and Vitamin C. Carissol (an epimer of A-amyrin), lupeol, oxalic, tartaric, citric, malic, malonic and glycolic acids, glycine, alanine, phenyl alkaline, cerine, glucose, and galactose.

Root
The chemical compositions in root are carissone, carindone, carinol, odoroside H, digitoxigenin, glucose, and D- digitalose.

Seed
It consists of palmitic acid, stearic acid, oleic acid, arachidic acid, and linoleic acid.

Leave
It consists of triterpene alcohol and ursolic acid.

Flower
It consists of myrcene, limonene, camphene, canene, dipentene, farnesol, nerolidol, dihydrojasmone, A-terpeneol, citronellal, β-ionone, nerylacetate, linalool, and geranyl acetate.

TRADITIONAL USE

C. spinarum L. is a one of the main African ethnomedicine; it is one of the most prevalent traditional cures for a myriad of diseases. All the plant parts, roots, barks, leaves, and even the fruits are used to treat many diseases. As a multipurpose medicinal tree, some communities across Africa refer to *C. spinarum* as the "magic herb" [22] because it is used to cure several diseases including headache, chest complaints [23], rheumatism [23-25], gonorrhea, syphilis, rabies, herpes, malaria [26], sickle-cell anemia, hernia, edema, toothache, cough, ulcer, worm infestation [27] and as a diuretic, also for the treatment of typhoid fever, jaundice [28], sexual asthenias in males, measles, and as a cough expectorant [29]. The plant is also useful in the treatment of chickenpox and other skin diseases [30]. The decoction from the pounded root is also administered to treat epilepsy in some communities. In some cases, the patient is made to inhale the vapors coming from the root infusion to treat epilepsy. The traditional birth attendants use the decoction from dried leaves to increase labor and bring about quick child delivery especially during difficult labor.

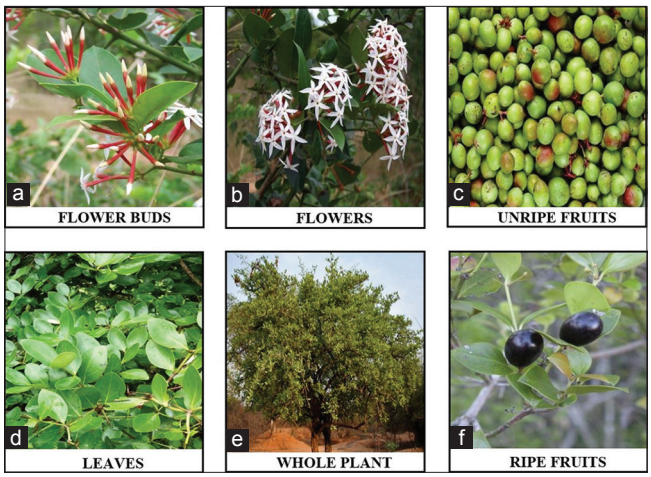

Fig. 1: Morphology of *Carissa spinarum* L., (a) flower buds (b) flowers (c) unripe fruits (d) leaves, (e) whole plant (f) ripe fruits

Like the roots, a decoction from the leaves and bark of *C. spinarum* is used in many societies in Africa in the treatment and management of breast cancer, headache, chest pains, gonorrhea, lowering blood pressure, rheumatism, syphilis, rabies, immune booster, fever, edema, cough, ulcer, malaria [31], and to relieve toothache. Roots and root bark are used as anti-venom and snake repellent [32, 33]. The ripe fruits are eaten as snacks to treat and manage dysentery.

Apart from the plant being used as one of the most valued traditional medicinal plants and fruit trees, it has also found many other applications in a number of communities. For instance, *C. spinarum* can be an ornamental plant due to its abundant branching habit and the presence of thorns that make it suitable as a protective hedge plant, while its fruits are gathered and eaten as food and for the processing of traditional natural dyes.

ETHNOPHARMACOLOGICAL SIGNIFICANCE
C. spinarum is known to possess an extensive range of phytochemicals in its leaves, roots, barks, as well as fruits that impart enormous medicinal value to the plant. These active constituents offer medicinal value to the plant. Pharmacological importance of the plant fruits has been evaluated by several researchers through *in vitro* and *in vivo* advances. These activities of *C. spinarum* have been reported from the crude extract and their different fractions and isolates from fruit, leave, and root.

PHARMACOLOGICAL ACTIVITIES

Anthelmintic activity
Anthelmintic activity was evaluated on adult Indian earthworm *Pheretima posthuma* by Harwansh *et al.* 2010. Earthworm was selected because of its anatomical and physiological resemblance with the intestinal roundworm parasites of human beings. The study was done at three different concentrations, each of crude extract of methanolic, aqueous, and chloroform (25, 50, and 100 mg/ml in distilled water) and Piperazine citrate served as standard drug. This study revealed that the methanolic (100 mg/ml) and chloroform extract (50 and 100 mg/ml) have equivalent potency compared to PC (10 mg/ml) in the time taken for both paralysis and death of *P. posthuma*. The possible mechanism was concluded as increased chloride ion conductance of worm muscle membrane produces hyperpolarization and reduced excitability that leads to muscle relaxation and flaccid paralysis [34].

Antiarthritic activity
Hegde *et al*. 2010 evaluated antiarthritic activity of ethanolic extract of *C. spinarum* root in freund's adjuvant-induced polyarthritis in rats. Arthritis was induced by injecting 0.1 ml of Freund's adjuvant in sub-plantar region. Treatments were given as 100 mg/kg of phenylbutazone as a standard and 100, 200, and 400 mg/kg doses of ethanolic extract of *C. spinarum* root. The study concluded that the plant extract doses had significant ($p<0.05$) dose-dependent antiarthritic activity [35].

Anticonvulsant activity
Ya'u *et al.* 2008 demonstrated significant anticonvulsant activity of hydroala coholic extract of root bark of *C. spinarum* in pentylenetetrazole

(PTZ)-induced convulsion in mice as well as maximal electroshock-induced convulsion in chicks. For anticonvulsant screening 5, 10, and 20 mg/kg of hydroalcoholic extract was given through IP route. Naloxone and diazepam were standard drugs in PTZ-induced convulsion, and phenytoin was standard drug in MEST-induced convulsion [36].

Table 1: List of some synonyms of *C. spinarum* L. [4]

Carissa abyssinica R.Br.	*Carissa inermis* Vahl
Carissa Africana A.DC.	*Carissa lanceolate* R.Br.
Carissa axillaris Roxb.	*Carissa laxiflora* Benth.
Carissa brownie F. Muell.	*Carissa macrophylla* Wall.
Carissa campenonii (Drake) Palacky	*Carissa madagascariensis* Thouars ex Poir.
Carissa candolleana Jaub. and Spach	*Carissa obovate* Markgr.
C. carandas var. *congesta* (Wight) Bedd.	*Carissa oleoides* Markgr.
C. carandas var. *paucinervia* (A.DC.) Bedd.	*Carissa ovata* R.Br.
Carissa cochinchinensis Pierre ex Pit.	*Carissa paucinervia* A.DC.
Carissa comorensis (Pichon) Markgr.	*Carissa pilosa* Schinz
Carissa congesta Wight	*Carissa pubescens* A.DC.
Carissa coriacea Wall.	*Carissa revolute* Scott-Elliot
Carissa cornifolia Jaub. and Spach	*Carissa richardiana* Jaub. and Spach
Carissa dalzellii Bedd.	*Carissa scabra* R.Br.
Carissa densiflora Baker	*Carissa sechellensis* Baker
Carissa diffusa Roxb.	*Carissa suavissima* Bedd. ex Hook.f.
Carissa dulcis Schumach. and Thonn.	*Carissa tomentosa* A.Rich.
Carissa edulis (Forssk.) Vahl	*Carissa villosa* Roxb.
Carissa hirsute Roth	*Carissa xylopicron* Thouars
Carissa horrida Pichon	*Carissa yunnanensis* Tsiang P.T.Li

C. spinarum: Carissa spinarum

Table 2: Uses of different parts of the plant [8]

Description	Parts	Use
Medicinal uses		
Roots	Root extract	Purgative, wounds in animals
All parts	Glycosidal extract	Cardio tonic
Commercial uses		
Leaves and fruits	Fresh	Garlands
Fruit	Raw	Pickles
	Ripe	Syrup, jelly, preserves
Leaf	Green leaves	Fodder for goats, fodder for sheep
	Dried leaves	Tanning industry
Plant	Whole plant	Hedge plant, fragrant flower, cover crop in dry rocky areas
Other uses	Fresh flowers	Personal adornment

Antidiabetic activity

EI-Fiky *et al*. 1995 studied the effects of ethanolic extract of leaves of C. spinarum in streptozotocin-induced diabetes in adult male albino rats. 2000mg/kg extract was given orally after to giving 40 mg/kg streptozotocin by ip route. Blood was collected at 0, 1, 2, and 3 h from each rat and evaluated for blood glucose levels. The extract showed significant antidiabetic activity on comparison with the reference drugs, which were metformin and glibenclamide [37].

Anti-inflammatory activity

Beck and Namdeo 2016 evaluated anti-inflammatory activity in petroleum ether, chloroform, alcoholic, and aqueous extracts of leaves of *C. spinarum* at a dose of 200 mg/kg, each given by oral route to albino rats. Formalin was used as an inducer for the inflammation, while analgin (30 mg/kg) acts as a standard drug. The result of the study shows the percentage of inhibition in standard drug (33.87%), aqueous extract (17.04%), alcoholic extract (6.93%), chloroform extract (6.93%), and petroleum ether extract (4.76%). Thus, it was concluded that *C. spinarum* leaves have significant ($p<0.01$) anti-inflammatory activity at a dose of 200 mg/kg [38].

Carrageenan-induced paw edema in chicks was used by Woode *et al.* 2007, to evaluate the extract of root powder with 70% ethanol for anti-inflammatory activity. The results of this study suggested that extract inhibits acute edema induced by carrageenan in the chick foot [39].

Antioxidant activity

The results of Sahreen *et al*. 2010 show considerable antioxidant activities of chloroform and aqueous fractions of *C. spinarum* fruits. The activity of these fractions is attributed to the phenolic and flavonoid contents. Consequently, the results suggested that the extracts can be utilized as an effective and safe antioxidant source, although the antioxidant activities of chloroform and aqueous fractions were lower than that of ascorbic acid and rutin. This research was done extraction by n-hexane, ethyl acetate, chloroform, butanol, methanol, and water [40].

Rao et al. in 2006 isolated carenone and formulated its synthetic derivatives. All compounds show potent antioxidant activity [41].

Woode *et al.* 2007 evaluated the extract of root powder with 70% ethanol for antioxidant and anti-inflammatory activity. The antioxidant study was conducted on the basis of total phenolic content, reducing power, 2,2-diphenyl-1-picryl-hydrazyl-hydrate assay, and lipid peroxidation. The extract shows significant antioxidant activity though it is not as potent as standard drugs [39].

Antimicrobial activity

Ibrahim et al., 2005 and 2010, in their research on aqueous extracts of fruit and leaves of *C. spinarum* L. showed the extracts to be more active on the Gram-positive organisms (*Bacillus subtilis and Staphylococcus*

Table 3: Phytochemical testing of leaves of *C. spinarum* L.

Sr. No.	Test for	Petroleum ether extract	Chloroform extract	Ethanolic extract	Aqueous extract
1	Alkaloids	−	−	+	+
2	Tannins	−	+	+	+
3	Flavonoids	−	−	+	+
4	Saponins	−	−	+	−
5	Glycosides	−	+	+	−
6	Terpenoids	−	−	+	−
7	Carbohydrate and sugars	−	−	+	+
8	Fats and fixed oil	+	−	−	−
9	Protein and amino acid	−	−	−	−
10	Steroids	−	−	+	+
11	Gums and mucilages	−	−	−	+

C. spinarum: Carissa spinarum

aureus) compared to Gram-negative organisms (*Escherichia coli* and *Pseudomonas aeruginosa*). The aqueous extract of leaves shows more significant antimicrobial activity than fruit extract. Both extracts proved their activity at up to the 1/10000 dilution, which is probably occurs due to the secondary metabolites present in the plant which are tannins, saponins, and flavonoids. As the extract seems more active in Gram-negative bacteria than Gram-positive might be due to the structural difference between them [42,43].

Shahada *et al.,* 2014, prepared extract by making and combining powder of various plant parts and extracted with various solvents by cold maceration method. These extracts were subjected to testing against *S. aureus* and *E. coli*. The result of this study also showed that the activity of the extract was found to be more efficacious in Gram-positive bacteria than Gram-negative [14].

Chandra *et al.* 2011 evaluated various extracts of fruit of *C. spinarum* L. at different concentrations (10 and 50 mg/ml) for antimicrobial activity. Ethanolic extract was found to be having highest efficacy, followed by acetone, aqueous, and ethyl acetate extract, respectively. The degree of inhibition was found highest in *Streptococcus pyogenes, S. aures* and *Bacillus cereus* [15].

Another antimicrobial study was conducted by Ngulde *et al.* 2013 on various strains of microorganisms of ethanolic extract of root bark of *C. spinarum* L. at doses of 25, 50, 100, and 200 mg/ml with tetracycline (250 mg/ml) as a standard. In this study, the extract failed to provide action against *S. aureus, B. subtilis, E. coli,* and *P. aeruginosa* but showed significant activity at doses of 100 and 200 mg/ml on *Salmonella typhi, Shigella dysenteriae,* and *S. pyogenes* [44].

Antileishmanial activity

A study done by Njau *et al.* 2016 evaluated preliminary antileishmanial screening of *C. spinarum* extracts performed on the promastigote form of *Leishmania major* showed that their activity against promastigotes is not in relation to their polarity. The less polar petroleum ether, polar total methanol, and successive methanol extracts recorded moderate activity while the water and less polar extracts (dichloromethane and ethyl acetate) recorded weak activity. The activity of these extracts against the amastigote form of *L. major* was seen to be dose-dependent. Higher concentrations of *C. spinarum* extracts seemed to reduce the infection rate of macrophages. The polar extracts (water, total methanol, successive methanol, and ethyl acetate) were found to be more active than less polar extracts (petroleum ether and dichloromethane). At their highest concentrations (200 µg/ml) all extracts, except petroleum ether, had IR values not significantly different to the standard reference drug pentostam at concentration 50 µg/ml ($p>0.05$) [16].

Table 4: Phytochemical parameters of leaves of *C. spinarum* L.

Sr. No.	Analytical parameter Leaves	% w/w
1	Total ash	14
2	Acid-insoluble ash	5.3
3	Water-insoluble ash	6.6
4	Sulfated ash	10.3
5	Alcohol soluble extractive	4.56
6	Water-soluble extractive value	15.62
7	Chloroform soluble extractive value	4.3
8	Loss on drying	3.62

C. spinarum: Carissa spinarum

Antinociceptive activity

Maina *et al.* 2015 designed a study to bioscreen the dichloromethane: Methanolic extract of the leaf and root bark of *C. spinarum* for antinociceptive potential. The method utilizes formalin induces pain for evaluation of antinociceptive screening. 30 min after dosing with standard and reference drugs, all the animals were injected intraperitoneally with 0.1 ml of 2.50% formalin in the subplantar region of the left hind paw to induce nociceptive behavior of lifting, licking, and biting. The time that the rats spent lifting, licking, or biting the injected paw was, hence, recorded. The responses were divided into two phases, early phase (0–5 min) and late phase (15–30 min). The dichloromethane: Methanolic leaf and root bark extracts of *C. spinarum*, produced non-dose dependent analgesic activity. The highest analgesic effect determined by percent licking inhibition of leaf extracts was by 47.19% and 84.93% in the early and late phases, respectively, while by root bark extracts were by 41.89% and 90.62% in the early and late phases, respectively [45].

Mworia *et al.* 2015 conducted a study of acetone extract of *C. spinarum* in Swiss albino mice by formalin-induced pain (paw licking) and acetic acid-induced writing. In this study, the significant antinociceptive effect is observed by reducing formalin paw- licking time in both phases and acetic acid-induced writhing, with more potent activity in the second phase. This suggests both central and peripheral antinociceptive effects [46].

Antioxidant activity

Hegde and Joshi 2010 evaluated ethanolic extracts of *C. spinarum* roots for in chloroform (CCl_4)-induced as well as paracetamol (PCM)-induced hepatotoxicity. The livers were processed after sacrificing animals and tested for antioxidant activity for reduced glutathione (GSH) estimation, superoxide dismutase (SOD), catalase (CAT) activity, and lipid peroxidation of malondialdehyde (MDA). The results were found to as decreased levels of GSH and MDA, as well as a significant rise in hepatic SOD and CAT activities. These changes contribute to its overall antioxidant activity [47].

Antiplasmodial activity

Kebenei *et al.* 2011 evaluated antiplasmodial activity of nortrachelogenin, a compound which is isolated from the root bark of *C. spinarum L.* and found that the compound has potential to be the cheap antimalarial drug, and also proves the ethnopharmacological use of the plant [48]. Ayuko *et al.* 2009 screens the root bark extract and stem bark extract on CQ-sensitive and CQ-resistant strains of *Plasmodium falciparum.* The result of this study shows that the plant has mild antimalarial activity [49].

Antiviral activity

Tolo *et al.* 2006 demonstrated the antiviral activity of aqueous extract of root bark of *C. spinarum* against herpes simplex virus (HSV) for *in vitro* and *in vivo* anti-HSV activity, at different parameters such as plaque inhibition assay, cell cytotoxicity assay, virus yield reduction assay, and against Balb/C mice cutaneously infected with HSV. In plaque inhibition assay, the result shows that the resistant strains of the virus were more

Table 5: Phytochemical testing of roots and root bark of *C. spinarum* L.

Sr. No.	Test for	ROOTS [11-13]				Root bark [14]
		Aqueous extract	n-butanol extract	Petroleum ether extract	Ethanolic extract	Methanolic extract
1	Tannins	+	+	+	+	+
2	Saponins	+	+	+	−	+
3	Flavonoids	−	−	−	−	+
4	Terpenoids	+	−	−	+	+
5	Cardiac glycosides	−	+	+	+	+

C. spinarum: Carissa spinarum

susceptible to the extract than the wild-type strains. In yield reduction, assay 200g/ml dose of the extract significantly reduced the virus yields of APr HSV-1 by 100%, HSV-2 by 99.5%, HSV-1 by 97.8%, and TK- HSV-1 by 96.3%. In the animal experiments using Balb/C mice cutaneously infected with wild-type strains of HSV-1 or HSV-2 at 1×10^6 PFU/mouse, all the infected untreated mice ultimately died, whereas animals treated orally with the extract provided some protection [50].

Cytotoxicity studies

In vitro cytotoxicity studies on *C. spinarum* extracts by sulforhodamine-B assay method were evaluated by Doshi and Une 2015. *C. spinarum* extract showed equivalent activity comparable to the standard compound ADR for human breast cancer cell line MCF7, and also showed mild progressive activity on other two selected cell lines, i.e. human colon cancer cell line HCT15 and human leukemia cell line MOLT4 [51].

Diuretic activity

Nedi *et al.* 2004 evaluated the diuretic effect of the root bark and root wood of the plant in albino Wistar rats with 80% methanol. The extract used in this study was root bark maceration extract, root bark Soxhlet extract, root wood maceration extract, and root wood Soxhlet extract. For the study, all extracts were used at concentration of 50, 125, 250, 500, and 1000 mg/kg, while hydrochlorothiazide 10 mg/kg acts as a standard drug. The root bark maceration extract failed to show anti significant diuretic activity, but root bark Soxhlet extract showed the significant diuretic activity. Similarly, the root wood maceration extract showed significant activity even at a dose of 50 mg/kg on electrolytes. The Soxhlet extract of root wood extract showed diuretic activity till 500 mg/kg, but then at more than 500 mg/kg test drug failed to produce the diuretic activity. As shown in this study, the extract did not produce a dose-dependent increase in activity, thus giving only mediate diuretic effect [52].

Similar study was conducted by Kebamo *et al.* 2015. The study was conducted on different solvent fractions of methanol extract of *C. spinarum* root bark. The study showed that the aqueous fraction of the methanol Soxhlet extract of the root bark of the plant has a significant diuretic activity while the petroleum ether and n-butanol fractions of the extract did not show significant diuresis at the tested doses in rats [11].

Erythropoietic effect

Koffuor *et al.* 2012 used the ethanolic root extract of *C. spinarum* against phenylhydrazine-induced anemia in Sprague Dawley rats at doses of 100, 300, and 1000 mg/kg, while 0.23 ml/kg bioferon acts as a reference drug. *C. spinarum* at doses of 300 and 100 mg/kg was able to reverse very significantly anemia caused by phenylhydrazine after 45 days of treatment without anisocytosis, thus concluding that the extract has erythropoietic activity with normocytosis [53].

Hepatoprotective activity

Hegde and Joshi 2010 evaluated ethanolic extracts of *C. spinarum* roots in chloroform (CCl_4)-induced as well as PCM-induced hepatotoxicity. The significant elevation in the levels of serum marker enzymes in control group such as SGOT, SGPT, and SALP content of CCl_4/PCM shows degree of hepatotoxicity. Animals pre-treated with extract (100, 200, and 400 mg/kg) as well as a standard drug (silymarin) demonstrated significant hepatoprotection by decreasing serum marker enzymes in a dose-dependent manner [47].

Similar studies were conducted by Sahreen *et al*. 2011, but instead of roots, leaves were selected for screening of potential hepatoprotective activity. Phytochemical analysis of methanolic extract confirmed the presence of alkaloids, anthraquinones, cardiac glycosides, coumarins, flavonoids, saponins, phlobatannins, tannins, and terpenoids, which all are closely related to compounds useful in protection of liver in various mechanisms. CCl_4 decreases the activities of hepatic antioxidant enzymes increases the activity of serum marker enzymes, and also significantly increases the hepatic thiobarbituric acid reactive substances (TBARS) and H_2O_2 level whereas significantly decreased the GSH and protein content. The result of animals pre-treated with 200 mg/kg of methanolic extract of Carissa leaves showed reduction in serum marker enzyme activity, increased activity of hepatic antioxidant enzymes and also prevents alteration in TBARS, H_2O_2, GSH, and protein content [54].

Wound healing

Sanwal and Chaudhary, 2011, prepared ointment of the methanolic extract of *C. spinarum* root, which exhibited significant pro-healing activity when topically applied on mice by affecting various stages of healing process, significant amelioration potential by root extract evident by the rate of wound contraction and epithelization, suggesting that the plant has significant wound healing activity [55].

Table 6: Phytochemical testing of fruit of *C. spinarum* L.

Sr. No.	Test for	Unripe fruit		Ripe fruit
		Petroleum ether extract	Methanol extract	
1	Carbohydrates	+	+	+
2	Alkaloids	–	+	+
3	Flavonoid	–	+	+
4	Tannins and phenolic	–	+	+
5	Steroids	+	+	+
6	Terpenoids	–	+	+

C. spinarum: Carissa spinarum

CONCLUSION

The evergreen shrub of *C. spinarum* has enormous medicinal and cultural value. The plant has a variety of use in day to day life, as well as pharmacological activities. These activities are present due to the presence of a variety of phytochemicals present in the plant. All plant parts have medicinal as well as nutritional value and used for the same traditionally throughout the world especially in African countries. Ethnopharmacological studies of the plant strengthen the concept for utilizing *C. spinarum* plant as a source to facilitate safe and effective herbal treatments for biological problems.

C. spinarum, similar to *C. carandas* has various medicinal properties [56]. All the plant parts have significant therapeutic activities. Carissa species have shown the presence of phytoconstituents such as alkaloids, flavonoids, glycosides, reducing sugar, steroids, terpenoids, tannins, and saponins, which mostly attributed for the pharmacological activity of the plant [57].

This review is prepared with the aim to provide a reference source for biology, phytochemistry, ethnopharmacology, and research done on the *C. spinarum* for aid in research of future researchers. The traditional and

Table 7: Phytochemical testing of stem and stem bark of *C. spinarum* L.

Sr. No.	Test For	Aqueous	Methanolic	Petroleum Ether	Dichloromethane	Ethyl Acetate	Successive methanol
1	Alkaloids	+	–	+	+	+	–
2	Terpenoids	+	+	+	+	+	+
3	Phenols	+	+	+	+	–	+
4	Anthraquinones	+	+	+	+	+	+
5	Saponins	+	–	–	+	–	–

C. spinarum: Carissa spinarum

ethnomedicinal literatures showed that the plant is very effective and safe for medicinal uses. Using the reverse pharmacological approaches in natural drug discovery a potent and safe drug can be investigated from the plant for various chronic diseases.

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AUTHOR'S CONTRIBUTION

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Mr. Diptesh T. Patil collected the data and analyzed the data and prepared the manuscript. Mr. Imtiyaz Ansariproof-read the whole manuscript, and suggested the necessary changes, and helps in designing manuscript.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

REFERENCES

1. Tropicos.org. Tropicos Name-*Carissa spinarum* L; 2018. Available from: http://www.tropicos.org/name/1800028. [Last accessed on 2018 Apr 29].
2. Worldagroforestry.org. *Carissa edulis*; 2018. Available from: Available from: http://www.worldagroforestry.org/treedb2/speciesprofile.php?Spid=443. [Last accessed on 2018 Jan 28].
3. Govaerts, R. *Carissa spinarum* L., Mant. Pl 2018;2:559. World Checklist of Selected Plant Families. Available from: http://www.wcsp.science.kew.org/synonomy.do?name_id=34226. [Last accessed on 2018 Jan 28].
4. Theplantlist.org. *Carissa spinarum* L.—The Plant List; 2018. Available from: http://www.theplantlist.org/tpl1.1/record/kew-34226. [Last accessed on 2018 Jan 28].
5. Sites.google.com. *Carissa spinarum*-efloraofindia; 2018. Available from: https://www.sites.google.com/site/efloraofindia/species/a---l/a/apocynaceae/carissa/carissa-congesta. [Last accessed on 2018 Jan 28].
6. Uniprot.org. *Carissa spinarum*; 2018. Available from: http://www.uniprot.org/taxonomy/429256. [Last accessed on 2018 May 01].
7. Kirtikar K, Basu B. Indian Medicinal Plants. Vol. II. Allahabad: Lalit Mohan Basu; 1980. p. 1548-9.
8. Fatima A, Singh P, Agarwal P, Irchhaiya R, Alok S, Verma A. Treatment of various diseases by *Carissa spinarum* L.: A promising shrub. Int J Pharm Sci Res 2013;4:2489-95.
9. Parmar C, Kaushal M. Wild Fruits of the Sub-Himalayan Region. New Delhi: Kalyani; 1982. p. 15-8.
10. Beck N, Namdeo K. Preliminary phytochemical and pharmacognostical evaluation of *Carissa spinarum* leaves. Asian J Pharm Technol 2013;3:30-3.
11. Kebamo S. Evaluation of diuretic activity of different solvent fractions of methanol extract of *Carissa edulis* root bark in rats. Med Chem 2015;5:472-8.
12. Onotu C, Musa U, Fajinmi A, Mazadu M, Shaida S. Physiochemical evaluation of ethanolic root extract of *Carissa Spinarum* (Wild Karanda) on *Trypanosoma brucei* Brucei (Federe Strain) infected mice. Int J Pharm Sci Invent 2013;2:18-26.
13. Hegde K, Joshi A. Preliminary phytochemical screening and antipyretic activity of *Carissa Spinarum* root extract. Pharm Lett 2010;2:255-60.
14. Shahada F, Rubaka C, Ndakidemi P, Malebo H. Analysis of phytochemical and antibacterial activity of *Carissa spinarum* Linn crude extracts. Eur J Med Plants 2014;4:937-45.
15. Chandra S, Saklani S, Kandri A. Nutritional evaluation, antimicrobial activity and phytochemical screening of wild edible fruit (*Carissa opaca*). Int Res J Pharm 2011;2:217-21.
16. Njau V, Maina E, Anjili C, Ingonga J, Koech J, Kariuki H, *et al*. *In vitro* antileishmanial activity and phytochemical analysis of *Carissa edulis* against Leishmania major. Afr J Pharmacol Ther 2016;5:253-62.
17. Dennis T, Sharma P, Yelne M. Database on medicinal plants used in Ayurveda. 3rd ed. New Delhi: Central Council for Research in Ayurveda & Siddha; 2005. p. 369-77.
18. Al-Youssef H, Hassan W. Chemical constituents of *Carissa edulis* Vahl. Arab J Chem 2017;10:109-13.
19. Bentley M, Brackett S, Chapya A. 2-Hydroxyacetophenone: Principal root volatile of the east African medicinal plant, *Carissa edulis*. J Natl Prod 1984;47:1056-7.
20. Achenbach H, Waibel R, Addae-Mensah I. Sesquiterpenes from *carissa edulis*. Phytochemistry 1985;24:2325-8.
21. Achenbach H, Waibel R, Addae-Mensah I. Lignans and other constituents from *Carissa edulis*. Phytochemistry 1983;22:749-53.
22. Komakech R, Omujal F. *Carissa Spinarum*: The Magic Herb-News and Views from Emerging Countries SouthWorld; 2016. Available from: http://www.southworld.net/carissa-spinarum-the-magic-herb/. [Last accessed on 2018 Jan 28].
23. Bussmann R, Gilbreath G, Solio J, Lutura M, Lutuluo R, Kunguru K, *et al*. Plant use of the maasai of sekenani Valley, Maasai Mara, Kenya. J Ethnobiol Ethnomed 2006;2:22.
24. Giday M, Asfaw Z, Elmqvist T, Woldu Z. An ethnobotanical study of medicinal plants used by the Zay people in Ethiopia. J Ethnopharmacol 2003;85:43-52.
25. Wambugu SN, Mathiu PM, Gakuya DW, Kanui TI, Kabasa JD, Kiama SG, *et al.* Medicinal plants used in the management of chronic joint pains in Machakos and Makueni counties, Kenya. J Ethnopharmacol 2011;137:945-55.
26. Addis G, Abebe D, Urga K. A survey of traditional medicinal plants in Shirka District, Arsi Zone, Ethiopia. Ethiop Pharm J 2018;19:30-47.
27. Burkill H, Dalziel J, Hutchinson J. The Useful Plants of West Tropical Africa. Kew: Royal Botanic Gardens; 1985.
28. Zafar M, Abbasi A, Khan M, Ahmad M, Khan H, Muhammad N, *et al*. Medicinal plants used for the treatment of jaundice and hepatitis based on socio-economic documentation. Afr J Biotechnol 2009;8:1643-50.
29. Wutthamawech W. Encyclopaedia of Medicinal Plants. Bangkok: Odeonstore Publishing; 1997. p. 473.
30. Gradé J, Tabuti J, Van Damme P. Ethnoveterinary knowledge in pastoral Karamoja, Uganda. J Ethnopharmacol 2009;122:273-93.
31. Kokwaro J. Medicinal plants of East Africa. 2nd ed. Nairobi: East African Literature Bureau; 1976. p. 26.
32. Pakrashi S, Datta S, Ghosh-Dastidar P. Indian medicinal plants—XVII.3 phytochemical examination of *Carissa* SPP. Phytochemistry 1968;7:495-6.
33. Chopra R, Nayar S, Chopra I. Glossary of Indian Medicinal Plants. New Delhi: Council of Scientific and Industrial Research; 1956. p. 52.
34. Harwansh R, Garabadu D, Rahman M, Garabadu P. *In vitro* anthelmintic activity of different extracts of root of *Carissa spinarum*. Int J Pharm Sci Res 2010;1:84-8.
35. Hegde K, Issac C, Joshi A. Antiarthritic activity of *Carissa spinarum* root extract in freund's adjuvant induced polyarthritis in rats. Pharmacologyonline 2010;2:713-8.
36. Ya'u J, Yaro A, Abubakar M, Anuka J, Hussaini I. Anticonvulsant activity of *Carissa edulis* (Vahl) (*Apocynaceae*) root bark extract. J Ethnopharmacol 2008;120:255-8.
37. El-Fiky F, Abou-Karam M, Afify E. Effect of *Luffa aegyptiaca* (seeds) and *Carissa edulis* (leaves) extracts on blood glucose level of normal and streptozotocin diabetic rats. J Ethnopharmacol 1996;50:43-7.
38. Beck N, Namdeo K. Evaluation of *in-vivo* anti-inflammatory activity of leaves Extract of *Carissa spinarum* on formalin induced paw edema in albino rats. UK J Pharm Biosci 2016;4:36-40.
39. Woode E, Ansah C, Ainooson G, Abotsi W, Mensah A, Duweijua M. Anti-inflammatory and antioxidant properties of the root extract of *Carissa edulis* (forsk.) Vahl (*Apocynaceae*). J Sci Technol (Ghana) 2008;27:5-15.
40. Sahreen S, Khan M, Khan R. Evaluation of antioxidant activities of various solvent extracts of *Carissa opaca* fruits. Food Chem 2010;122:1205-11.
41. Rao RJ, Kumar US, Reddy SV, Tiwari A, Rao JM. Antioxidants and a new germacrane sesquiterpene from *Carissa spinarum*. Natl Prod Res 2005;19:763-9.
42. Ibrahim H, Bolaji R, Abdurrahman E, Shok M, Ilyas N, Habib A. Preliminary phytochemical and antimicrobial studies of the leaves of *Carissa edulis* VAHL. Chem Class J 2005;2:15-8.
43. Ibrahim H, Oyi R, Ehinmidu J, Musa K, Bright N. Antimicrobial activity of the water extracts of the leaves and fruits of *Carissa edulis* Vahl (*Apocynaceae*). J Med Plants Res 2010;4:1028-32.
44. Ngulde S, Sandabe U, Tijjani M, Barkindo A, Hussaini I. Phytochemical constituents, antimicrobial screening and acute toxicity studies of the ethanol extract of *Carissa edulis* Vahl. root bark in rats and mice. Am J

Res Commun 2013;1:99-110.
45. Maina GS, Kelvin JK, Maina MB, Muriithi NJ, Kiambi MJ, Kelvin JK. Antinociceptive properties of dichloromethane: Methanolic leaf and root bark extracts of *Carissa edulis* in rats. J Phytopharmacol 2015;4:106-12.
46. Mworia JK, Gitahi SM, Juma KK, Njagi JM, Mwangi BM, Aliyu U, *et al*. Antinociceptive activities of acetone leaves extracts of *Carissa Spinarum* in mice. Med Aromat Plants 2015;s1:1-4.
47. Hegde K, Joshi AB. Hepatoprotective and antioxidant effect of *Carissa spinarum* root extract against CCl4 and paracetamol-induced hepatic damage in rats. Bangladesh J Pharmacol 2010;5:73-6.
48. Kebenei J, Ndalut P, Sabah A. Anti-plasmodial activity of Nortrachelogenin from the root bark of *Carissa edulis* (vahl). Int J Appl Res Natl Prod 2011;4:1-5.
49. Ayuko T, Njau R, Cornelius W, Leah N, Ndiege I. *In vitro* antiplasmodial activity and toxicity assessment of plant extracts used in traditional malaria therapy in the Lake Victoria Region. Mem Inst Oswaldo Cruz 2009;104:689-94.
50. Tolo FM, Rukunga GM, Muli FW, Njagi EN, Njue W, Kumon K, *et al*. Anti-viral activity of the extracts of a Kenyan medicinal plant *Carissa edulis* against herpes simplex virus. J Ethnopharmacol 2006;104:92-9.
51. Doshi G, Une H. *In vitro* cytotoxicity studies on *Carissa congesta*, *Polyalthia longifolia*, and *Benincasa hispida* extracts by Sulforhodamine B assay method. Int J Green Pharm 2015;9:157.
52. Nedi T, Mekonnen N, Urga K. Diuretic effect of the crude extracts of *Carissa edulis* in rats. J Ethnopharmacol 2004;95:57-61.
53. Koffuor GA, Sam GH, Dadzeasah PE, Owiafe EO, Asante-Gyapong A. Erythropoietic effect of the ethanolic root bark extract of *Carissa edulis* in Phenylhydrazine-induced anemic Sprague-Dawley rats. Res J Pharmacol 2012;6:20-4.
54. Sahreen S, Khan MR, Khan RA. Hepatoprotective effects of methanol extract of *Carissa opaca* leaves on CCl4-induced damage in rat. BMC Complementary Altern Med 2011;11:8.
55. Sanwal R, Chaudhary A. Wound healing and antimicrobial potential of *Carissa spinarum* Linn. in albino mice. J Ethnopharmacol 2011;135:792-6.
56. Alam F, Shahriar M, Bhuiyan MA. *In-vivo* pharmacological investigations of bark extracts of *Carissa carandas*. Int J Pharm Pharm Sci 2014;6:180-5.
57. Mishra CK, Shrivastava B, Sasmal D. Pharmacognostical standarization and phytochemical identification of fruit and root of *Carissa carandas* Linn. Int J Pharm Pharm Sci 2013;5 Suppl 3:347-50.