



A brief study of phytochemical profile and pharmacological applications of *Carissa carandas* (L.)

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Abstract

Carissa carandas is an important flowering herb, distributed widely in tropical and sub-tropical areas of the world. All plant parts are used traditionally as medicine to cure various diseases including pruritus, leprosy, myopathic spasms, nerve diseases, anorexia, etc. Major bioactive components, imparting medicinal value to this plant are flavonoids, triterpenoids, saponins, alkaloids, and cardiac glycosides. Furthermore, roots, fruits, stem, and leaves are rich in volatile components. Major ones are β -caryophyllene, luteol, β -sitosterol, carissic acid, and linalool. Major pharmacological properties are analgesic, anti-pyretic, anti-diabetic, anti-inflammatory, hepatoprotective, antioxidant, cardiovascular, anticancer, anti-malarial, anti-microbial, and anti-convulsant. Current review paper has an aim of providing detailed information of botany, chemistry, traditional and pharmacological uses of *Carissa carandas* to promote the use of herbs as natural medicines to cure a number of ailments.

Key words: Karaunda, pharmacology, bioactive constituents, anti-convulsant

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1. Botany

1.1. Introduction

Carissa carandas (Karonda) is a member of Apocynaceae family which consists of 300 genera and 1000 species. There are about 30 species in genus *Carissa* being native of tropics and subtropics of Asia, Africa and Australia and China. *Carissa carandas* is a rank-growing, woody shrub having climbing habit. Its fruits are berry-sized, which are used in Indian spices and pickles as an additive or condiment. The plant is found to be distributed in Afghanistan, Nepal, India, Sri-Lanka, Java, Malaysia, Myanmar, Australia, South Africa, and Pakistan [1]. Common names of *Carissa carandas* in different languages are as follows: craneberry (English), karonda (Urdu), vakkay (Telugu), karauna (Maithili), karaunda (Hindi) [2].

1.2. History

Carissa carandas is native to Malacca, Sri-Lanka, Myanmar, and Indian subcontinent. Later, it was introduced to Java, where it now runs wild [3].

1.3. Demography/Location

Karonda (hardy evergreen bush) grows well in subtropical and tropical climates. Waterlogged conditions and heavy rainfall are not favorable. A wide range of soils are favorable for its growth. It can grow well even on marginal and inferior land, where other fruits mostly fail to grow. Such properties making this plant a good candidate to

bring vast area of degraded/marginal lands under cultivation, particularly in arid/semiarid region [4-5]. It is found in Africa, Australia and Tropical Asia, particularly in Western Peninsula and dry tracts of India, Sri Lanka and Malaysia.

1.4. Botany, Morphology

Carissa carandas L. is a branched, large, ever green, spinous small tree which grows upto 4m in height. Its stem is rich in white latex, having sharp spines on branches. Its leaves are conical and oblong, 2-3 inch in width and 4-6 inch in length, brown from below and green on the top. Flowers are of white color having diameter of 3-5cm. The fruit (berry) is formed in clusters of about 3-10 fruits. Unripe fruits are pink, while, ripe fruits are green or purplish in color. The bark is soft, thick and gray in color [5].

2. Chemistry

Carissa carandas L. has engrossed more attention as a source of medicine because of presence of biologically active compounds including saponins, cardiac glycosides, phenolic components, flavonoids, alkaloids, and triterpenoids. Figure 1 shows structures of some important compounds found in *Carissa carandas* L. The roots contain cardiac glycosides and salicylic acid that cause a small decrease in the blood pressure. Roots also contain volatile compounds including 2-acetyl phenol, carinol, lignan, sesquiterpenes, luteol, β -hydroxybetulinic acid, β -sitosterol,

β -sitosterol glycoside, α -amyrinand des-N-methylnoracronycine, an acridone alkaloid [6-8]. Stem is rich in sesquiterpene glucoside [9]. Leaves were found to contain triterpenes and tannins. A new compound namely carrissic acid (isomer of urosolic acid) has also been reported in leaves [10]. Fruits contain mixture of volatile compounds including β -caryophyllene, carindone, linalool, lupeol, benzyl acetate, β -sitosterol, and ascorbic acid [11]. Furthermore, *Carissa carandas* contains polyphenols (7-8%), crude proteins (12-15%), free acid (25-30%), hydrocarbons (50-60%) and fixed oil (3-5%). GCMS analysis is generally used to find chemical composition of oil [12-16]. High gross heat values of this plant shows that it can be used as a source of fuel [11].

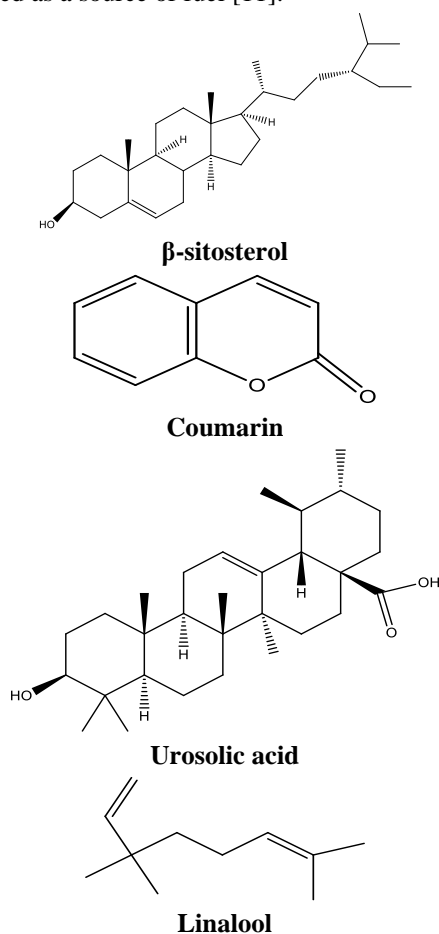


Fig. 1. Structures of important chemicals present in *Carissa carandas* L.

3. Post-harvest technology

Flowering and fruiting usually takes place twice in a year. Flowering usually starts in March-April and fruits get mature in August-September. The second flowering season is during October-November. Fruits get mature in approximately 100 days after fruit set. At this stage, natural color of fruit develops. Ripening of fruits takes place after 20-25 days of this stage. Fruits attain red or purple color and become soft. Harvested fruits are placed in shade. Blemished or undesirable fruits are separated out. Fresh fruits are then packed in special baskets for storage. Raw fruits are best for making pickle. While, dried fruit is

required for other applications involving jelly and candy formation. Fruits storage life is based upon the harvesting stage. Mature fruits can be stored at room temperature for one week, but, fully ripened fruits are very soft and can be stored at room temperature for 2-3 days. Fruit can be preserved for six months in solution of sulfur dioxide (2000 ppm).

4. Value addition

Various value added products can be prepared from *Carissa carandas*. Fruit pulp is a common ingredient in culinary preparations such as curries, condiments, and jams. Ripe fruit is used in the preparation of variety of jams, squash, and syrup etc. as it is rich in macro and micro nutrients. Unripe fruit is used in the preparation of chutney, pickle, candy, etc.

5. Traditional uses

Carissa carandas has been used traditionally to cure various diseases including fever, malaria, headache, cough, leprosy, colds, myopathic spasms, and nervous disorders. Ripe fruits are used to prevent scurvy and to treat burning sensation, anorexia, pruritus, and skin diseases [17]. The unripe fruits are rich in ascorbic acid and iron, and are used to cure anemia [18]. Root portion of this plant is used to reduce blood pressure, to cure stomach disorders, diabetes, intestinal worms, and to reduce blood pressure. Leaves are used in the treatment of fever, diarrhea, snake bite, and syphilitic pain [19-21].

6. Pharmacological uses

6.1. Analgesic, anti-inflammatory, and antipyretic activities

In a study, aqueous and ethanolic extracts of *Carissa carandas* roots were examined for analgesic, antipyretic and anti-inflammatory activities in rodent models [21]. Significant ($p < 0.01$) analgesic, anti-inflammatory, and antipyretic activities were shown by the extracts at dose levels of 0.1 and 0.2g/Kg. Approximately, 72 percent inhibition of abdominal constriction was observed by *Carissa carandas* ethanol extract at concentration level of 0.1g/Kg. Furthermore, ethanol and aqueous extracts of *Carissa carandas* showed significant reduction in carrageenan induced edema. In another study, methanol extracts of leaves of *Carissa carandas* were examined [22]. The extract at dose level of 0.2g/kg showed maximum inhibitory effect against edema induced by dextran, carrageenan and histamine. Antipyretic effect of extracts was examined using diseased albino rats. Maximum antipyretic effect was shown by the extracts at concentrations of 0.1 and 0.2g/Kg. Methanol extracts of dried fruits exhibited significant anti-inflammatory effect against carrageenan induced edema in rats. In another study, anti-inflammatory action of methanol extract of *Carissa carandas* dried fruits was examined on carrageenan based edema in mice. Extracts were administered orally and significant ($p \leq 0.05$) anti-inflammatory action was observed [23].

6.2. Anti-cancer and anti-oxidant activities

The anti-cancerous activity of *Carissa carandas* leaves, the unripe and ripe fruits extract was evaluated against ovarian carcinoma and lung cancer cells using n-hexane, chloroform and methanol as the solvent systems [24]. Significant anti-cancer activity was shown by the extracts. In another study, antioxidant and anticancer activities of *Carissa carandas* leaf extracts (aqueous) were examined on cancer cell lines (MCF-7). Significant antioxidant action was observed by leaf extracts and cell death was prevented in MCF-7 line. The study concluded that, regular daily intake of fruits in diet reduces the risk of cancer and other infectious diseases [25].

6.3. Anti-diabetic activity

Anti-diabetic effect of *C. carandas* leaves aqueous extract was evaluated on alloxan induced and normoglycemic Wister rats. Extracts at concentration levels of 500 and 100 mg/kg significantly reduced glucose level of blood of alloxan induced diabetic rats at 4, 8, and 24 hrs. In another investigation, the anti-diabetic potential of *Carissa carandas* methanol extract and its fractions was examined in diabetic rats (alloxan induced). Significant reduction in blood glucose level was observed after oral administration of methanol extract and ethyl acetate soluble fraction (0.4g/Kg), when compared to control group. Anti-diabetic potential of ethyl acetate fraction was higher than methanol extract, and the reason was its partial purification gained by fractionation [26-27].

6.4. Hepatoprotective activity

In a study, the hepatoprotective activity of *Carissa carandas* extract (ethanolic) was examined against hepatotoxicity induced by paracetamol and CCl_4 . Extracts showed significant hepatoprotective activity at dose levels of 0.1, 0.2, and 0.4 g/kg by inhibiting the activities of serum marker enzymes (bilirubin and lipid peroxidase). Moreover, the levels of glutathione, dismutase, uric acid, and catalase were increased [28]. In another study, hepatoprotective effects of aqueous and ethanol extracts of *Carissa carandas* roots against ethanol induced hepatotoxicity in rats were studied. The ethanol and aqueous extracts at a dose level of 0.1g/kg and 0.2g/kg lowered the levels of serum transaminase, alkaline phosphate, bilirubin, and lipid peroxidase. Levels of liver glutathione, and serum protein were increased [2].

6.5. Cardiovascular activity

Cardiovascular disease comprises the large number of diseases; coronary based artery disease, heart failure, heart attack, stroke and high blood pressure that affect the heart and the blood vessels. According to World Health Organization, 30,000 victims of this disease die every day [29]. Plant as source of safe and effective treatment for cardiovascular diseases has been explored by researchers, who examined the effects of extracts of *Carissa carandas* on cardiovascular function of healthy mice [30]. *C. carandas* extract at dose levels of 5 to 45 mg/Kg, decreased the blood pressure of arteries, in mice. Significant reduction in

frequency of heart rate was noticed at dose level of 45mg/Kg. The results were comparable with standard drug (acetylcholine) [30].

6.6. Anti-malarial activity

Malaria, an important parasitic disease, affects human health worldwide. Because of the increased drug resistance to malarial parasites, there is a need to search for new antimalarial drugs from plant sources. Therefore, *in-vitro* antimalarial activities of extracts (methanolic and aqueous) of three different parts including leaf, stem, and fruit of the plant *C. carandas* were tested against *Plasmodium falciparum* 3D7 strain. Methanolic extract exhibited promising antimalarial activity (IC_{50} ranged between 13.57 and 69.63 $\mu\text{g/ml}$) as compared to aqueous extracts (IC_{50} ranged between 41.52 and >100 $\mu\text{g/ml}$).

6.7. Anthelmintic activity

Anthelmintic effects of extracts (petroleum ether, ethanolic and chloroform) of unripe fruits of *Carissa carandas* were examined using earthworms. Time of paralysis and death of worms was determined at different concentrations of extracts. Piperazine citrate was used (15 mg/ml) as standard drug. It was concluded from the study that *C. carandas* unripe fruits extract causes earthworm paralysis, and also death, after some time. The shortest paralysis time observed at higher doses of ethanol, chloroform, and petroleum ether extracts (0.15g/ml) was 56.35 minutes, 40 minutes, and 22.35 minutes, respectively. Results showed that anti-helminthic potential of ethanol extract is greater than other two extracts [31].

6.8. Antimicrobial activity

The ethanolic extract of *Carissa carandas* fruit has powerful antibacterial activity against various strains of bacteria including *B. subtilis*, *E. coli*, *S. aureus*, *S. faecalis*, *P. aeruginosa* and *S. typhimurium* [32]. Moreover, ethanolic extract also showed antiviral effect against, polio Sindb virus, and herpes simplex virus at the concentration level of 3 $\mu\text{g/ml}$, 6 $\mu\text{g/ml}$ methanol, and pylorus ligation. All extracts increased the healing of acetic acid-induced chronic gastric ulcers ($p < 0.05$) [33].

6.9. Adaptogenic activity

A triterpenoid (lanostane) isolated from *C. carandas* fruit extract (ethanolic) was examined for adaptogenic activity against immune suppression induced by cyclophosphamide, swimming endurance, and anoxia stress tolerance model. The levels of red blood cells, white blood cells, hemoglobin, and body weight, suppressed by cyclophosphamide were evaluated [34].

6.10. Constipation and diarrhea

Researchers examined the pharmacological basis of *C. carandas* leaf crude extracts in diarrhea and constipation using *in-vivo* (mice) and *in-vitro* (isolated jejunum and ileum of rabbit) models. HPLC analysis of the extracts showed the presence of β -sitosterol, ursolic acid, oleanolic acid, and stigmasterol. Gut stimulatory action of crude extract of *C. carandas* leaf was due to its ability of

activation of histaminergic and muscarinic receptors. However, spasmolytic effect of extract was mediated by Ca²⁺ antagonist pathway. Thus, the study provides a clear evidence for the dual effectiveness of *C. carandas* in constipation and diarrhea [35].

6.11. Anticonvulsant activity

Anti-convulsant effect of *Carissa carandas* roots extract (ethanol) at dose levels of 0.1, 0.2 and 0.4 g/kg was investigated on chemically and electrically based seizures. The extract at concentration of 0.2 and 0.4 g/Kg significantly reduced the duration of seizures induced by electric shock in mice. The same doses protected the model animals from tonic seizures induced by pentylenetetrazole, N-methyl-dl-aspartic acid, and picrotoxin. There was no significant effect of extract on bicuculline based seizures. Researchers concluded that *C. carandas* root extracts possess anticonvulsant potential because extract reduced the time period of electrically induced seizures and delayed the latency of picrotoxin and pentylenetetrazole induced seizures [36].

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