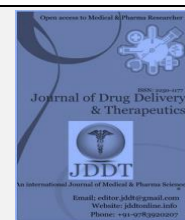
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Review Article

## A Review on *Carissa carandas*: Traditional Use, Phytochemical Constituents, and Pharmacological properties

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### Abstract

*Carissa carandas* L. (Karaunda) is a widely useful food and medicinal plant of India. Plant-based medicines play an important role in all cultures have been indispensable in maintaining health and combating diseases. Owing to the global trend towards better quality of life, there is a great claim for medicinal plants. *Carissa carandas* L. plant popularly used as a traditional medicinal plant over thousands of years in the Ayurvedic, Unani, and Homoeopathic system of medicine. The major bioactive elements, which impart the medicinal worth of herbs, are alkaloids, flavonoids, saponins, and huge amounts of cardiac glycosides, triterpenoids, phenolic compounds, and tannins. Traditionally, the whole plant and its parts were used in the treatment of various ailments. It contains several phytochemical constituents belonging to the terpenoids category. The root is attributed to bitter, stomachic; antidiarrheal, vermifuge, and ant helminthic properties. The medicinally unripe fruit is used as an astringent. The ripe fruit is taken as an antiscorbutic and therapy for nausea. The leaf decoction is appreciated in cases of alternating fever, diarrhea, oral inflammation, and earache. Also, *Carissa carandas* have showing a extensive range of evidence for its cardiogenic, hepatoprotective, free radical scavenging and xanthine oxidase inhibitory, histamine-releasing, antirheumatic, antibacterial, antiviral, and anticonvulsant activity. A higher gross heat value of this species indicates its higher potential to be used as a good fuel source.

**Keywords:** *Carissa carandas* , Phytochemical Constituents, Traditional Use, Pharmacological Properties.

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### 1. INTRODUCTION

*Carissa carandas* is a species of flowering plant in the dogbane family, Apocynaceae. It harvests berry-sized fruits that are commonly used as a condiment or preservative to Indian pickles and spices. The shrub Commonly name karonda (Devanagari: ) karamardaka(Sanskrit), Koromcha(Bengali), Christ's thorn (South India), vakkay (Telugu), kilaakkaai(Tamil) and Karja tenga(Asam).<sup>1</sup> Its botanical name was in recent years altered to *Carissa congesta* Wight (syn. *C. carandas* Auct formerly widely shown as *Carissa carandas*.<sup>2</sup> The famous biological activities reported are analgesic, anti-inflammatory, anti-pyretic, Cardiotonic, and histamine-releasing. The plant is also an alternative source of oil, hydrocarbon, and phytochemicals.<sup>3</sup>

#### 1.1 Description of Karaunda Tree: -

*Carissa carandas* Linn. Is a dichotomously pronged evergreen shrub with a short branch and strong thorns in pairs, *Carissa carandas* Linn is an evergreen diffuse and spiny shrub occurring through the country. The plant is very valued for the Indian System of medicine mainly Ayurveda. It

is used for alleviating Vata and pitta disorders.<sup>4</sup> Species is a rank-growing, usually growing to 10 or 15 ft (3-5 m) high, sometimes ascending to the tops of tall trees; and rich in white gummy latex. The branches, many and dispersal, forming dense masses, are set with sharp thorns, simple or forked, up to 2 in (5 cm) long, in pairs in the axils of the leaves. The leaves are evergreen, opposite, oval or egg-shaped, 1 to 3 in (2.5-7.5 cm) long; dark-green, leathery, glossy on the upper surface, lighter green, and dull on the underside. The fragrant flowers are cylindrical with 5 hairy lobes that are twisted to the left in the bud instead of to the right as in other species. They are white, regularly tinged with pink, and borne in terminal clusters of 2 to 12. The fruit, in clusters of 3 to 10, is oblong, broad-ovoid or round, 1/2 to 1 in (1.25-2.5 cm) long; has fairly thin but tough, purplish-red skin turning dark-purple or closely black when ripe; smooth, glossy; enclosing very acid to equally sweet, often bitter, juicy, red or pink, juicy pulp, radiating flecks of latex. There may be 2 to 8 small brown seeds. The Karanda is common throughout much of India, Burma, and Malacca and dry areas of Ceylon; is rather commonly cultivated in these

areas as a hedge and for its fruit, and the fruit is marketed in villages. The karanda was initial fruite in the Philippines in 1915.<sup>5</sup> Fruits are rich source of iron and vitamin C, therefore, ethnomedical the fruits are used for curing anemia, as an astringent, antiscorbutic, and as a remedy for

biliousness. Its leaf decoction is used in contradiction of fever, diarrhea, and earache, whereas roots help as a stomachic, vermifuge, remedy for itches, and insect repellent.<sup>6</sup>



Flowers of *Carissa carandas*

### 1.2. Cultivation: -

Karaunda is a very hardy and drought-tolerant plant, it thrives well throughout the tropical and subtropical climates. Heavy rainfall and waterlogged conditions are not desirable. It can be grown up on an extensive range of soils including saline and sodic soils. Karaunda is commonly grown from seeds. Vegetative methods—air-layering and stem (hardwood) cuttings are feasible but not very common. Fresh seeds are sown in the nursery during August – September. One-year old seedlings are transplanted. Air-layering is very successful in Karaunda. It can be performed at the beginning of the monsoon. Rooted cuttings can be separated 3 months after layering. Karaunda plants grown as a protective hedgerow are hardly fertilized. Manuring, however, is used as 10-15 kg well-rotten farmyard manure or compost/plant and should be applied before flowering. Irrigation: The water requirement of Karaunda is very low. Irrigation after planting and manuring is essential. Plantation once established does not need much water. The fruits grow from July to September in north India. Karaunda fruits mature 100-110 days after fruit set. At this stage, fruits develop their natural color. Fruits ripen after this stage, taking about 120 days (after fruit set) when they become soft and attain dark purple/maroon/red color. After the packing of fruits, they are kept in shade. Fruits collected at maturity can be stored for a week at room temperature. Fruits can be preserved/stored for 6 months in SO<sub>2</sub> solution (2,000 ppm).<sup>7</sup>

### 1.3. Taxonomy

Kingdom: Plantae

Order: Gentianales

Class: Angiosperms

Family: Apocynaceae

Sub-class: Eudicots

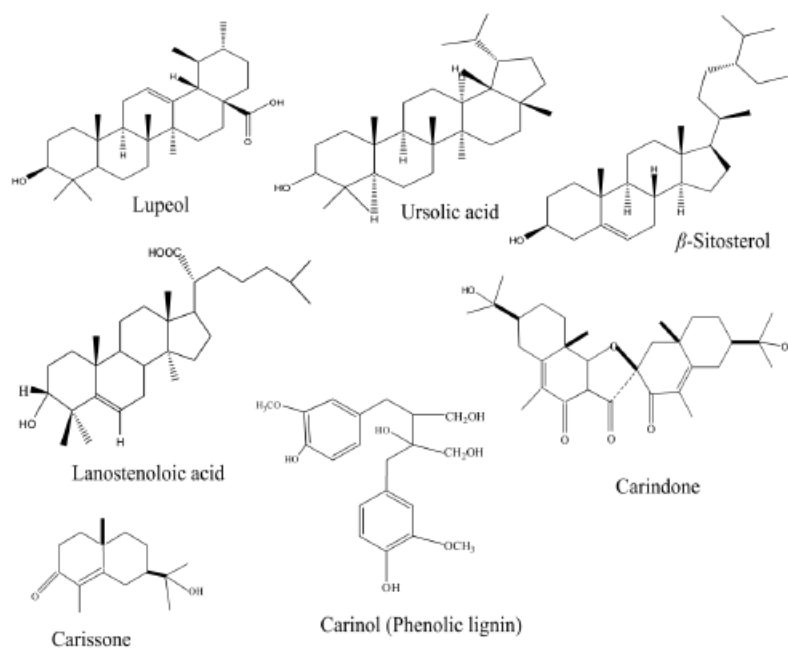
Superorder: Asterids

Genus: *Carissa*

Species: *carandas*

## 2. PHYTOCHEMICAL CONSTITUENTS

These activities of *C. carandas* were reported from the crude extract, their different fractions, and isolates from fruits, leaves, and roots. Roots also reported to contain volatile principles including 2-acetyl phenol, lignan, carinol, sesquiterpenes (carissone, carindone), lupeol,  $\beta$ -sitosterol, 16 $\beta$ -hydroxybetulinic acid,  $\alpha$ -amyrin and  $\beta$ -sitosterol glycoside, and des-N methylnoracronycine, an acridone alkaloid<sup>8, 9</sup>. Fruits of *C. carandas* were stated to contain carisol, an epimer of  $\alpha$ -amyrin, linalool,  $\beta$ caryophyllene, carissone, carissic acid, carindone, ursolic acid, carinol, ascorbic acid, lupeol, and  $\beta$ sitosterol<sup>11</sup> The crude methanolic extract of leaves of *Carissa carandas* was tested for its different chemical groups as alkaloids, flavonoids, gums, reducing sugars, saponins, steroids, and tannins<sup>11, 12</sup>. Flowers of *C. carandas* are volatile oil like myrcene, limonene, camphene, carene, dipentene, farnesol, nerolidol,  $\alpha$ -terpeneol, citronellal,  $\beta$ -ionone, linalool, and geranyl acetate.<sup>13</sup>



**Phytochemical constituents of *C. carandas*.**

### 3. TRADITIONAL USES

*Carissa carandas* has been used from immemorial time to yet traditionally to treat different human ailments. *C. carandas* is the best-known associate of the genus as it has been used as a old-style remedial shrub over thousands of centuries in the ayurvedic system of medicine as it is practiced on the Indian sub-continent. Thus, traditional uses of *C. carandas* are well established. The root is credited with bitter, stomachic, antidiarrhoeal, and antianthelmintic properties. The ripe fruits are utilized in curries, tarts, puddings, and chutney. When only slightly under-ripe, they are made into jelly.<sup>1</sup> Green, sour fruits are made into pickles in India. With skin and seeds removed and seasoned with sugar and cloves, they have been popular as a substitute for the apple in tarts. The unripe fruit is used therapeutically as an astringent. The ripe fruit is taken as an antiscorbutic and remedy for nausea. The fruits have been employed as agents in tanning and dyeing. British residents in India undoubtedly favored the karanda as being reminiscent of gooseberries. Karanda leaves have furnished food for the tussar silkworm. The leaf decoction is valued in cases of intermittent fever, diarrhea, oral inflammation, Antibacterial activity, and earache.<sup>14</sup> A paste of the pulverized roots serves as a fly repellent. The root is employed as a bitter stomachic and vermifuge and it is an ingredient in a remedy for itches. The roots of *Carissa carandas* contain salicylic acid and cardiac glycosides causing a slight decrease in blood pressure. The white or yellow wood is hard, smooth, and useful for molding spoons, combs, household utensils, and miscellaneous products of turnery. It is sometimes burned as fuel.<sup>5,15</sup>

### 4. PHARMACOLOGICAL ACTIVITIES

*Carissa carandas* are known to possess a wide range of phytochemicals in the plant parts (roots, leaves, stem, and fruit) that give the plant tremendous medicinal value. These active ingredients give the plant medicinal value. The pharmacological significance of the plant has been assessed by various workers through in vitro and in vivo approaches.

#### 4.1. Antioxidant and cytotoxic property: -

Yakut Bint-e-Sadek *et al* studied was to determine the

different phytochemical compounds of *Carissa carandas* leaf extracts, their antioxidant properties, antimicrobial activities, and cytotoxic potentials. Ethanolic and n-hexane extracts from the leaves of the *Carissa carandas* they were used. The results showed significant antioxidant activities compared to ascorbic acid and in DPPH eliminating free radicals with IC<sub>50</sub> of 1,292  $\mu$ g / ml and 1,824  $\mu$ g / ml of ethanolic extract and n-hexane extract. Extract H<sub>2</sub>O<sub>2</sub> removal activities were found to be better than the standard, which had higher IC<sub>50</sub> values than ascorbic acid. Total antioxidant activity and the total phenolic content was also determined. The leaf extracts showed no antimicrobial activity. through the disc diffusion method using extracts ranging from 0. 1 to 400  $\mu$ g / disc compared kanamycin disk 30  $\mu$ g / disk.<sup>2</sup>

Vijay Kumar *et al* demonstrated free radicals drilling capabilities of petroleum ether and methanolic extracts of seeds, fruits, and leaves. Phytochemical analysis of extractions of different parts of *C. Carandas* was performed followed by free radical extraction capacity using the frap method. The results of reducing the power capacity of different extracts were compared concerning each other through statistical analysis applying one-way ANOVA. Exploratory of phytochemical content in petroleum ether and methanolic extracts of leaves, fruits, and seeds of *Carissa carandas* extract found unicity of components including alkaloids, phenolics, flavonoids, oils and fats, saponins and tannins. Statistical analysis showed that the methanolic extract from the leaves was a strong free radical scavenger among all other extracts studied. The specific results that qualitative phytochemistry selection carried out in the petroleum ether and the methanolic extracts of leaves of *c. carandas*, fruits, and seed extract confirmed the presence of some bioactive compounds (alkaloids, phenolic compounds, flavonoids, tannins, saponins, oils, and fats) in its different parts. *Carissa's carandas* methanolic extract of the leaves had the highest free radical scavenging activity compared to the petroleum ether fruit extract and seed. The radical removal potential of plants compares highly to that of the standard, ascorbic acid. The methanolic extract from the leaves of *Carissa carandas* had the highest elimination of free radicals activity compared to the fruit and seed oil ether extract.<sup>16</sup>

Marina Khatun *et al* studied was designed to explore the antioxidant, cytotoxic and antineoplastic properties of the leaf extract of *Carissa carandas* Linn. a traditional medicinal plant. Methanol extract from *Carissa carandas* leaves (MELC) was applied in DPPH and ABTS experiments to determine its antioxidant activity. In vitro, the cytotoxic effect of MELC against colon adenocarcinoma cell lines (SW-480 and SW-48) while their antineoplastic property was tested in vivo against Ehrlich's carcinoma of ascites (EAC). The DPPH and ABTS tests revealed the antioxidant activity of MELC with IC50 10.5 ± 1.2 and 1.75 ± 0.3 µg / ml that was comparable to l-ascorbic acid. In vitro cytotoxic studied, MELC reduced the viability of adenocarcinoma cells in a dose-dependent manner, and in vivo administration of MELC (25 mg/kg) resulted in a significant decrease (p < 0.05) in the viable EAC cell count, thus increasing the lifespan of EAC cell-bearing mice. Restoration of hematological parameters such as red blood cells (RBC), hemoglobin, and white blood cells (WBC) was also observed at normal levels in MELC-treated mice. Further, treatment with MELC-induced apoptosis of EAC cells as seen in the DAPI fluorescence microscopic view (4, 6-diamidino-2-phenylindole) cells were stained and MELC-treated cells expression of p53 gene was also increased relative untreated EAC controlled. Furthermore, MELC was rich in polyphenol content and its GC-MS chromatogram confirmed the presence of some compounds, all of which showed anticancer and cytotoxic activities in previous studies. In a word, this studied supports the use of *Carissa carandas* in traditional medicine and highlights then they need to further explore the potentials of MELC as an antineoplastic agent.<sup>17</sup>

#### 4.2. Anti-inflammatory and antipyretic activity: -

Manoranjan Hati *et al* evaluated the anti-inflammatory and antipyretic activity of methanol extract of *C. carandas* l. leaf. The extract was evaluated by phytochemicals screening, which indicated the presence of steroids, glycosides, flavonoids, tannins, terpenoids, and carbohydrates the anti-inflammatory property was evaluated by using different models such as carrageenan, histamine, and dextran induced hind leg edema in Wister albino rats. Extract at a dose of 200 mg/kg. body weight exhibited maximum inhibition of inflammation, i. e. 72.10%, 71.90%, and 71.80% at the end of 3 hours with histamine, dextran, and carrageenan-induced rat paw edema respectively. The antipyretic activity was evaluated by brewer's yeast-induced pyrexia in albino rats. Extract at a dose of 100 and 200 mg/kg p. o., showed a significant reduction in yeast-induced elevated temperature at a dose-dependent manner, and the effect also lasted up to 4 hours after administration of the drug. The results of this studied. Indicated that the methanol extract from the leaves of *C. carandas* l. had important anti-inflammatory properties and antipyretic activities in rodent models.<sup>18</sup>

Bhaskar and Balakrishnan *et al* reported pain relievers, significant anti-inflammatories, and antipyretic activities of ethanol and aqueous extracts of roots of *C. Carandas* in rodent models. Ethanol and aqueous *C. carandas* root extracts exhibited a significant (p < 0.01) analgesic, anti-inflammatory, and antipyretic activities at doses 100 and 200 mg/kg of body weight. Observed higher inhibition percentage of abdominal constriction (72.67%) ethanol *C. carandas* extracts at a dose of 100 mg/kg body weight in pain reliever exercise. Besides, ethanol and aqueous extracts of *C. carandas* reduced the formation of carrageenan-induced edema after 2 hours.<sup>19</sup>

#### 4.3. Anti-diabetic activity: -

Prakash R. Itankar *et al.* evaluated the anti-diabetic potential of the plant by screening methanol extracts and their

fractions in alloxan Diabetic rats. He reported that methanol extract and its ethyl acetate soluble fraction is significantly reduced Blood glucose levels per oral dose of 400 mg/kg after 24 hours Compared with diabetes control. Polyphenol content of methanol extract the ethyl acetate soluble fraction was found to be 15.8 ± 1.2 mg, 18.55 ± 0.34 mg (gallate equivalent / g extract), while flavonoids contents of the two extracts are 2.92 ± 0.03 mg and 1.534 ± 0.30 mg (Rutin equivalent / g extract). Concluded that the anti-diabetic potential of ethyl acetate fraction for methanol extract is partly purified by fractional distillation, Leading to an increased degree of polymerization, and Secondary metabolites.<sup>20</sup>

Gaurav et al. evaluated the effects of aqueous extracts of *Carissa carandas* on alloxan-induced and normoglycemic Wister rats. Three doses of extract (250 mg / kg; oral 500 mg / kg and 1000 mg / kg.) and found that 250 mg / kg extract of *Carissa carandas* line. did not show any major changes in blood glucose levels compared to untreated controls. The doses of 500 and 1000 mg/kg extract showed a significant (p < 0.05) reduction in blood glucose levels after 4, 8, and 24 hours. In rats with normal blood sugar, the dose of the extract was significant at 1000 mg/kg (p < 0.05) 8-hour and 24-hour blood glucose levels. The dosage of the extract had shown significant (p < 0.05) hypoglycemic and antihyperglycemic effects in Wister rats.<sup>21</sup>

#### 4.4. Anti-convulsant activity: -

Hegde *et al.* Anti-convulsant effect of the ethanolic extract of *C. carandas* roots (100, 200, and 400 mg/kg, i.p.) has been investigated on electrically, and chemically induced seizures. The extract (100-400 mg/kg) significantly reduced the duration of seizures induced by maximal electroshock. However, only 200 and 400 mg/kg of the extract conferred protection (25% and 50%, respectively) on the mice. The same doses also protected animals from pentylenetetrazole induced tonic seizures and significantly delayed the onset of tonic seizures produced by picrotoxin and N-methyl-dl-aspartic acid. The extract did not affect bicuculline-induced seizures. Observed the anticonvulsant effects of the ethanolic root extract of *C. carandas* via nonspecific mechanisms since the extract reduced the duration of seizures produced by maximal electroshock as well as delayed the latency of seizures produced by pentylenetetrazole, and picrotoxin.<sup>8</sup>

#### 4.5. Anti-cancerous activity and antioxidant potentials: -

David M and Karekalammanavar G *et al:* Fruit extracts of *C. carandas* in chloroform, n-hexane, and methanol were tested for their anticancer activity in lung cancer cells and human ovarian carcinoma cells. All the extracts showed excellent anticancer activity. Besides, the anticancer and antioxidant potentials of the extracts. were analyzed for unusual antioxidant enzymes such as catalase, dismutase, superoxide, glutathione-s-transferase, and glutathione in MCF-7 cancer lines. This study exhibited important antioxidant activity and fortification of cell death in the MCF-7 cell line pretreated with *C. carandas* extracts. Researchers suggested the anticancer potential value of this medicinal plant fruit for the future development of therapeutic drugs<sup>22</sup>. Furthermore, in vitro anti Cancer studies showed that aqueous ethanolic fruit extract (ESA) induces cytotoxicity at 800 µg / ml in HeLa cancer cells maintained in Dulbecco's modified Eagle's medium (DMEM). The study concluded that regular daily intake Suggested Diet Fruits with Reduced Risk of Infection diseases and cancer.<sup>23</sup>

#### 4.6. Hepatoprotective activity: -

Hegde K, Joshi A B *et al.* : Ethanolic extract of roots of *C.*

carandas (100, 200 and 400 mg/kg, p.o.) showed significant hepatoprotective activity against paracetamol-induced and carbon tetrachloride hepatotoxicity by declining the activities of serum marker lipid peroxidation and bilirubin and significantly amplifying the levels of glutathione, uric acid, superoxide dismutase and protein. *Carissa carandas* root extract shows Hepatoprotective activity.<sup>24</sup>

#### 4.7. Cardiovascular activity: -

Vohra M M and De N N *et al.*: The ethanolic extract of roots of *C. carandas* exhibited cardiotoxic activity and lowered the blood pressure. The cardiac activity of the plant has been recognized as the presence of water-soluble glucosides known as odoroside. The dose 45 mg/kg, i.p. caused a significant (50.75%) decrease in arterial blood pressure ( $P < 0.001$ ), and the frequency of heart rate was also reduced significantly. It was also found that the ethanol extract of the plant possess a potent hypotensive effect in normal rats.<sup>25</sup>

#### 4.8. Antimicrobial activity:

The ethanolic extract of the fruit has powerful antibacterial action against different test bacteria like *B. subtilis*, *S. aureus*, *E. coli*, *S. faecalis*, *S. Typhimurium*, and *P. aeruginosa*. Moreover, the ethanolic extract has also shown extensive anticandidal action.<sup>26</sup>

#### 4.9. Anthelmintic activity: -

Mishra C K *et al.*: The different concentrations (50, 100, and 150 mg/ml) of fruits extract *C. carandas* in solvent petroleum ether (60-80), ethanol and chloroform were evaluated in vitro anthelmintic potency on *Pheretimap osthuma* by determination of time of paralysis and time of death of the worm. The Piperazine citrate (15 mg/ml) was used as the standard drug. It was concluded that the fruits extract of *C. carandas* causes earthworm paralysis and also its death after some time.<sup>27</sup>

#### 4.10. Antibacterial activity: -

S. Verma, H.S. Chaudhary *et al.*: The dichloromethane and toluene extract of the leaves of *C. carandas* showed better results against *Staphylococcus aureus* and *Klebsiella pneumoniae*. The fruit extract of *C. carandas* in dichloromethane exhibited high antibacterial activity against *E. coli*. The fruit extract in ethyl acetate showed the best result against all the strains of bacteria.<sup>28</sup>

#### 4.11. Neuropharmacological and diuretic activities: -

Ripan Saha *et al.*: The crude methanolic extracts of leaves of *Carissa carandas* Linn. were evaluated for its neuropharmacological and diuretic activities. The extract of *Carissa carandas* leaves also potentiated the pentobarbital-induced sleeping time in mice and decreased the open field score in the open field test, decreased the number of holes crossed from one chamber in the hole cross test, and decreased the head dip responses in hole board test. The diuretic activity was proved by the electrolyte loss ratio ( $\text{Na}^+/\text{K}^+$  excretion ratio was 1.46 and 1.43 at the doses of 200 and 400 mg/kg respectively) as that of the standard diuretic furosemide (1.48).<sup>29</sup>

#### 4.12. Antimalarial activity: -

Bapna S *et al.*: Methanolic and aqueous extracts of leaf, stem bark, and fruit of the plant *C. carandas*, tested against *Plasmodium falciparum* 3D7 strain. Both aqueous and methanolic extract exhibited promising antimalarial activity (IC50 ranged between 41.52 and 100  $\mu\text{g}/\text{mL}$ ) and (IC50 ranged between 13.57 and 69.63  $\mu\text{g}/\text{mL}$ ). The cytotoxicity of the host cell was also analyzed on the Madin-Darby canine

kidney cell line utilizing the MTT test that exposed no cytotoxicity in the maximum dose tested.<sup>30</sup>

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