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A REVIEW ON PHARMACOLOGICAL ACTIVITIES OF C*arissa carandas*

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ABSTRACT

Carissa carandas is a useful food and medicinal plant of India, found to be widely distributed throughout subtropical and topical regions. The plant has been used as a traditional medicinal plant over thousands of years in the Ayurvedic, Unani, and Homoeopathic system of medicine. Traditionally, whole plant and its parts were used in the treatment of various ailments. The major bioactive constituents, which impart medicinal value to the herb, are alkaloids, flavonoids, saponins and large amounts of cardiac glycosides, triterpenoids, phenolic compounds and tannins. Roots were reported to contain volatile principles including 2-acetyl phenol, lignan, carinol, sesquiterpenes (carissone, carindone), lupeol, β-sitosterol, 16β-hydroxybetulinic acid, α-amyrin, β-sitosterol glycoside, and des-Nmethylnoracronycine, whereas leaves were reported to contain triterpenoid constitutes as well as tannins. While, fruits have been reported to contain carisol, epimer of α-amyrin, linalool, β-caryophyllene, carissone, carissic acid, carindone, ursolic acid, carinol, ascorbic acid, lupeol, and β-sitosterol. Ethnopharmacological significance of the plant has been ascribed due to anti-cancer, anti-convulsant, anti-oxidant, analgesic, anti-inflammatoryAQ1, anti-ulcer, anthelmintic activity, cardiovascular, anti-nociceptive, anti-diabetic, antipyretic, hepatoprotective, neuropharmacological, and diuretic activities, antimicrobial activities and cytotoxic potentials, *in-vitro* anti-oxidant, and DNA damage inhibition, and constipation and diarrheal activities. The review also dealt with describing micropropagation strategies for effective conservation of this important food and medicinal plant. 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 carandas*, Karonda, Bioactive metabolites, Phytochemicals, Pharmacology, Conservation

INTRODUCTION

Carissa carandas Wight (syn. Carissa carandas Auct., formerly widely shown as C. carandas L.), belongs to the dogbane family Apocynaceae, found to be widely distributed throughout India. The shrub is commonly known as karonda (Devanagari), karamardaka (Sanskrit), Koromcha (Bengali), Bengal currant or Christ's thorn (South India), vakkay (Telugu), kilaakkaai (Tamil), and Karja tenga (Assam). Its fruits are berry-sized, which are commonly used as a condiment or additive to Indian pickles and spices. Karonda is good appetizer, and the fruit is pickled before it gets ripened. Ripe karonda fruit contains high amount of pectin therefore it is also used in making jelly, jam, squash, syrup, tarts and chutney, which are of great demand in international market. Karonda bushes are also suitable for hedging in the home gardens, and are sometimes grown as an ornamental plant due to its beautiful cherry-like fruits. The plant is a hardy, drought-tolerant in nature that can be grown in a wind range of soils. The species has been used as a traditional medicinal plant over thousands of years in the Ayurvedic, Unani, and Homoeopathic system of medicine. Traditionally, whole plant and its parts were used in the treatment of various ailments. Its fruits are eaten to treat liver dysfunction, to break fever, to counteract the putrefaction of blood while roots are used to improve digestion. Fruits are very rich source of iron and vitamin C, therefore, ethnomedically the fruits are used for curing anemia, as an astringent, antiscorbutic, and as a remedy for biliousness. Its leaf decoction is used against fever, diarrhea, and ear ache, whereas roots serve as a stomachic, vermifuge, remedy for itches, and insect repellent.

Classification:

Kingdom: Plantae
Class: Angiosperms
Sub-class: Eudicots
Superorder: Asterids
Order: Gentianales
Family: Apocynaceae
Genus: Carissa
Species: *Carandas*

MORPHOLOGY OF KARONDA FRUIT:

SIZE: Fruit length is 2.14cm, fruit weight 3.95g with 3.95seeds / fruit. It contains 88.28% flesh, TSS 3.92%, total titrable acidity 1.82% and yield 27kg per plant.

COLOUR: The karonda cultivars can be categories as per their colour of fruits like PINK-WHITE, GREENISH PINK, AND REDDISH-PURPLE or based on utilization. The fruits of pink color varieties are white at the stage and turn to pink at maturity

SHAPE: The leaves are oblong and conical in shape, GREEN to BROWN in color, from which bloom small white flowers. Upon developing the unripe karonda fruit, a berry, is **globular** in shape with tiny seeds within occurring in clusters of 3 to 10 fruits.

TASTE: One such beneficial fruit is the karonda, as it is scientifically known, **sour and slightly acidic** in taste, it is a berry-sized fruit, commonly added to Indian pickles.

Fig: *Carissa carandas*

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, β-sitosterol, 16β-hydroxybetulinic acid, α-amyrin and β-sitosterol glycoside, and des-N methylnoracronycine, an acridone alkaloid [8, 9]. Fruits of *C.* carandas were stated to contain carisol, an epimer of α-amyrin, linalool, βcaryophyllene, carissone, carissic acid, carindone, ursolic acid, carinol, ascorbic acid, lupeol, and βsitostero 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 [11, 12]. flowers of C. carandas are volatile oil like myrcene, limonene, camphene, carene, dipentene, farnesol, nerolidol, α- terpeneol, citronellal, β-ionone, linalool, and geranyl acetate.

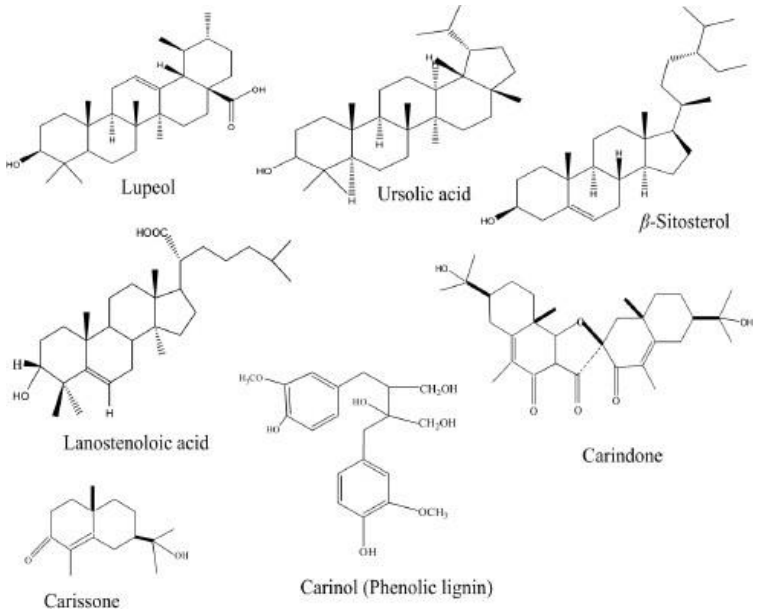

Fig: Phytochemical constituents of *C.* carandas.

Nutritional composition of karonda fruits:

C. carandas L. fruits were reported to contain 83.17-83.24 g of moisture, 0.39-0.66 g protein, 2.57-4.63 g fat, 0.51-0.94 g carbohydrates, 0.62-1.81 g fiber and 9-11 mg ascorbic acid per 100g of fresh fruit. Whereas,

Malik *et al*. reported nutritional information of per 100g of edible fruit is a source of: 42.5 kcal energy, 0.39-1.1 g protein (negligible), 2.5-4.63g fat, 0.51-2.9 g carbohydrate, 0.62-1.81 g fiber, 21mg calcium, 28mg phosphorous, 1619 IU vitamin A, and 9-11 mg ascorbic acid.

Ethnopharmacological significance:

C. carandas is known to posses' wide range of phytochemicals in its plant parts (roots, leaves, stem, and fruits) that imparts immense medicinal value to the plant. These active constituents give medicinal value to the plant. Pharmacological significance of the plant has been evaluated by several workers through *in-vitro* and *in-vivo* approaches. The plant is used as ingredient in a number of ayurvedic formulations and preparation, which includes: Marma gutika, Hridya mahakashaya, Kalkantaka rasa, Kshudrakarvanda yoga, and Marichadi vati. We now review the ethnophamacological aspects of the plant.

Anti-diabetic activity:

Gaurav *et al*. evaluated the effect of the aqueous extract of *C. carandas* on alloxan induced and normoglycemic Wister rats, and found that the doses of 500 and 1000 mg/kg of the extract significantly ($p<0.05$) decreased the blood glucose levels of alloxan diabetic Wistar rats at 4, 8 and 24 hrs. The workers concluded that the plant extract doses had both significant ($p<0.05$) hypoglycemic as well as anti-hyperglycemic effects, Further, Itankar *et al*. demonstrated anti-diabetic potential of the plant by screening methanol extract, and its fractions in alloxan induced diabetic rats. The workers reported that the methanol extract and its ethyl acetate soluble fraction have significantly lowered the elevated blood glucose levels at dose level of 400 mg/kg per oral after 24 hrs, as compared to diabetic control. Polyphenol content of methanol extract and its ethyl acetate soluble fraction were found to be 15.8±1.2 mg and 18.55±0.34 mg (gallic acid equivalent/g extract), whereas, flavonoid content of both the extracts were 2.92±0.03 mg and 1.534±0.30 mg (rutin equivalent/g extract) respectively. The workers concluded that the anti-diabetic potential of ethyl acetate fraction over methanol extract is due to its partial purification achieved by fractionation which resulted in increase in degree of polymerization, and segregation of secondary metabolites.

Anti-convulsant activity:

Anti-convulsant effect of the ethanolic extract of *C. carandas* roots (100, 200 and 400 mg/kg, i.p.) has been investigated by Hegde *et al*. 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 had no effect on bicuculline-induced seizures. The authors concluded anti- convulsant effects of the ethanolic root extract of *C. carandas* via non- specific 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

Hepatoprotective activity:

Hegde and Joshi, demonstrated significant hepatoprotective activity of ethanolic extract of the roots of *C. carandas* (ERCC; 100, 200 and 400 mg/kg, p.o.) against CCl_4 and paracetamol induced hepatotoxicity by decreasing the activities of serum marker enzymes, bilirubin and lipid peroxidation, and significant increase in the levels of uric acid, glutathione, super oxide dismutase, catalase, and protein in a dose dependent manner that was confirmed by the decrease in the total weight of the liver and histopathological examination.

Whereas, Bhaskar and Balakrishnan reported hepatoprotective effects of the ethanol, and aqueous extracts of roots of *C. carandas* against ethanol induced hepatotoxicity in rats. The ethanol and aqueous extracts at a dose level of 100 mg/kg and 200 mg/kg produce significant hepatoprotection by decreasing serum transaminase (serum glutamic pyruvic transaminase and serum glutamic oxaloacetic transaminase), alkaline phosphate, bilirubin and lipid peroxidation, while significantly increased the levels of liver glutathione, and serum protein.

Neuropharmacological and diuretic activities:

Saha *et al*. evaluated methanolic extracts of *C. carandas* L. leaves for its neuropharmacological, and diuretic activities and reported significant neuropharmacological activity of the plant. While, diuretic activity of the extract was proved by the electrolyte loss ratio (Na^+/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).

Cardiovascular activity:

Cardiovascular disease comprises the large number of diseases; coronary artery disease, heart attack, heart failure, high blood pressure and stroke, that affects the heart and the blood vessels both. The World Health Organization estimate reflects that the disease causes deaths of approximately 30,000 people each day. Plant as source for safe and effective treatment for cardiovascular diseases has been explored by Shamim and Ahmad in the year 2012, who evaluated the effect of *C. carandas* extract on cardiovascular function of normal rats. Intravenous bolus injection of this extract in the doses of 5-45 mg/kg, produced dose dependent reduction in arterial blood pressure ($p<0.001$). The 45 mg/kg dose caused significant (50.75%) decrease in mean arterial blood pressure. A significant reduction in heart rate frequency was observed after CC injection at a dose of 45 mg/kg ($p<0.001$). The results were comparable with acetylcholine 10^{-4} M. The workers concluded that the *C. carandas* ethanol extract possess potent acute hypotensive effect in normal rats. It stimulates the muscarinic receptors located on the endothelial cells of the vasculature. This stimulation results in the release of endothelial-derived relaxing factors or nitric oxide that diffuses to vasculature smooth muscles and causes their relaxation.

Anti-cancerous activity and antioxidant potentials:

Sulaiman *et al*. screened *C. carandas* leaves, the unripe and ripe fruits extract for their anti-cancer activity using n-hexane, chloroform and methanol as the solvent systems, a three-step extraction on the human ovarian carcinoma cells, and lung cancer cells. The extracts exhibited good anti-cancerous activity.

Further, Dua and Srivastav estimated anti-cancerous efficiencies, and antioxidant potentials of the aqueous leaf extracts of *C. carandas* by analyzing different antioxidant enzymes such as catalase, superoxide dismutase and glutathione-s-transferase, and non-enzymatic antioxidant, glutathione on MCF-7 cancer lines. This study showed significant antioxidant activity, and protection of cell death in MCF-7 cell line pretreated with *C. carandas*. The workers suggested the potential of this medicinal plant for future development of therapeutic drugs against breast cancer. Further, its fruits can be a good source of natural antioxidants for both pharmaceutical and dietary requirements and appears to be useful in relieving oxidative stress.

Furthermore, Sadek *et al*. evaluated antioxidant properties, antimicrobial activities, and cytotoxic potentials of ethanolic, and n-hexane leaf extracts of *C. carandas.* Results of this study showed significant antioxidant activities compared with ascorbic acid and butylated hydroxytoluene in 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging with inhibitory concentration (IC_{50}) of 1.292 µg/ml and 1.824 µg/ml of ethanolic extract and n-hexane extract. H_2O_2 scavenging activities of the extracts were found to be better than the standard, having IC_{50} values higher than ascorbic acid. Cytotoxic activities of the extractives were comparable to vincristine sulfate, having IC_{50} values of 2.818 and 1.995 of ethanolic extract and n-hexane

extract respectively, this provides evidence for antioxidant properties, and cytotoxic potentials of *C. carandas* leaves extract. Similarly, Verma *et al*. [33] investigated the antioxidant and DNA damage inhibition potential of methanolic extract of *C. carandas* leaves, which showed significant ($p<0.05$) dose-dependent DPPH radical scavenging activity (IC_{50}=73.12 µg/ml), total antioxidant activity, H_2O_2 scavenging activity (IC_{50}=84.03 µg/ml), and reducing power activity. Further, in DNA damage inhibition assay, extract exhibited complete protection of pBR322 plasmid DNA from free radicals mediated oxidative stress. The workers concluded that these activities could be attributed to the presence of high amount of phenolic compounds (84.00 mg GAE/g dry weight of the extract) in the extract.

Anti-ulcer activity:

Merai and Jadhav evaluated different *C. carandas* extracts, administered orally with the dose of 500 mg/kg on different models of gastric ulcer, such as acetic acid induce chronic gastric ulcer, pylorus ligation and ethanol induce acute gastric ulcer. All extracts increased the healing of acetic acid-induced chronic gastric ulcers ($p<0.05$). The workers concluded that the alcoholic extract of *C. carandas* exhibited highly significant anti-ulcer activity.

Antimalarial 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 source. Therefore, with the aforementioned aim Bapna *et al*. analyzed, *in-vitro* antimalarial activity of three different parts (leaf, stem bark and fruit) of the plant *C. carandas*, tested against *Plasmodium falciparum* 3D7 strain. Of the two solvent extracts tested, methanolic extract exhibited promising antimalarial activity (IC_{50} ranged between
13.57 and 69.63 µg/mL) as compared to aqueous extracts (IC_{50} ranged between 41.52 and >100 µg/mL). While, the host cell cytotoxicity was also analyzed on Madin-Darby canine kidney cell line using the MTT test that revealed no cytotoxicity in maximum dose tested.

CONCLUSION:

C. carandas, an evergreen, deciduous shrub with immense medicinal value has been reviewed with the aim to provide a reference source for biology, phytochemistry, ethnopharmacology, and conservation strategy for further research on the plant. Ethnopharmacological studies strengthen the concept for utilizing *C. carandas* plant as a source to facilitate safe and effective herbal treatments for biological problems. Furthermore, the review aims to provide a direction for further clinical research.

REFERENCES

1. Jain SK. Dictionary of Indian Folk Medicine and Ethnobotany. New Delhi: Deep Publications; 1991.
2. Wani RA, Prasad VM, Hakeem SA, Sheema S, Angchuk S, Dixit A. Shelf life of Karonda jams (*Carissa carandas* L.) under ambient temperature. Afr J Agric Res 2013;8(21):2447-9.
3. Malik SK, Chaudhury R, Dhariwaln OP, Bhandari DC. Genetic Resources of Tropical Underutilized Fruits in India. New Delhi: NBPGR; 2010. p. 178.
4. Maheshwari R, Sharma A, Verma D. Phyto-therapeutic Significance of Karaunda. Bull Environ Pharmacol Life Sci 2012; 1:34-6.
5. Sawant RB, Desai UT, Ranpise SA, More TA, Sawant SV. Genotypic and phenotypic variability in Karonda (*Carissa carandas* L.,). J Maharashtra Agric Univ 2002;27(3):266-8.
6. Singh A, Uppl GK, A Review on *Carissa carandas* - phytochemical, ethno-Pharmacology and Micropropagation as conservation stratergy, Asian Journal of Pharmaceutical and Clinical Research,

2015; 8(3):54-60.
7. Bint-e-sadek Y, Choudhary N and Shahriar M, Biological Investigation of the leaf extract of *Carissa carandas*, International Journal of Pharmacy Research and Technology, 2013; 5(2):97-105
8. Maheshwari R, Sharma A, and Verma D, Phyto-therapeutic significance of karaunda, Bulletin of Environment, Pharmacology and Life Science, 2012; 1(12):34-36.
9. Sawant RS, Comparative studies of Phytochemical screening of *Carissa carandas* liin., Asian Journal of Plant Science and Research, 2013; 3(1):21-25
10. Devmurari V, Shivanand P, Goyani MB, Vaghani S, Jivani NP, A Review: *Carissa Congesta* Phytochemical constituents, Traditional Use and Pharmacological propertices, Pharmacological Review, 2009; 3(6):375-377.
11. Alikeramat SS, Malek MA, Islam K, Salamatullah K, "The food values of indigenous foods Institute of food and Nutrition, Dhaka University, Bangladesh, 1977 :15.
12. Mishra CK, Sasmal D, Shrivastava B, An *in vitro* evaluation of the anthelmintic activity of unripe fruits extract of *Carissa carandas* Linn, International Journal of Drug Development and Research, 2012; 4(4):393-7.
13. Verma S, Chaudhary HS, Effect of Carissa carandas against Clinically Pathogenic bacterial strains, Journal of Pharmacy Research. 2011; 4: 3769–3771.
14. Saha R, Hossain L, Neuropharmacological and Diuretic activity of *Carissa carandas* Linn. Leaf, Pharmacology online, 2010; 2: 320- 327.
15. Bapna S, Ramaiya M, Chowdhary A, Antimalarial activity of *Carissa carandas* Linn. against *Plasmodium falciparum*, Journal of Antimicrobial Photon, 2013; 128: 246-50.