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Review Article

Hidden Potential of Natural Herb *Carissa Carandas* (Karonda)

Reshu Virmani^{1*}, Tarun Virmani¹, Charan Singh¹, Geeta Sorout², Jyoti Gupta¹

¹School of Pharmaceutical Sciences, MVN University, Palwal, Haryana, INDIA

²CBS college of Pharmacy, Faridabad, Haryana, INDIA

ABSTRACT

Carissa carandas (F. Apocynaceae) is an important fruit commonly known as Karonda 'Christ's thorn' which grows wild in bushes. *Carissa carandas* is a useful food and medicinal plant of India, found to be widely distributed throughout subtropical and tropical regions. The plant has been used as a traditional medicinal plant over thousands of years in the Ayurvedic, Unani, and Homoeopathic system of medicine. 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, 16 β -hydroxybetulinic acid, α -amyrin, β -sitosterol glycoside, and des-N-methylnoracronycine, whereas leaves were reported to contain triterpenoid constituents 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. Traditionally the plant has been used in the treatment of scabies, intestinal worms, pruritus, biliousness and also used as antiscorbutic, anthelmintic. The notable biological activities reported are analgesic, anti-inflammatory, anti pyretic, cardiotoxic and histamine releasing. This review has been written to presents a detailed survey of the literature on phytochemistry, traditional and biologically evaluated medicinal uses of *C. carandas* to promote safe and effective herbal treatments to cure a number of diseases.

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*Correspondence to:

Reshu Virmani,

Email:

reshu.virmani@mvn.edu.in

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INTRODUCTION:

Carissa carandas belongs to the dogbane family Apocynaceae [1], found to be widely distributed throughout India. The shrub is commonly known as karonda 'Christ's thorn'. The scientific classification of plant is-

Classification

Kingdom: Plantae

Class: Angiosperms

Sub-class: Eudicots

Superorder: Asterids

Order: Gentianales

Family: Apocynaceae

Genus: *Carissa*

Species: *Carandas*

Karonda is an evergreen deciduous small to big shrub usually 2-4 m tall. The stem is rich in white latex and the branches contain sharp spines. Flowers are small,

measuring 3-5 cm in diameter, with white colors. The fruit is a berry, which is formed in clusters of 3-10 fruits. The fruit is globose to broad ovoid in shape and contains many seeds. Young fruits are pinkish white and become red to dark purple when ripe. Ripe fruit color varies from white, green and pinkish red depending on the genotype. Flowering starts in the month of January- February and fruits mature in May-June. Fruits are generally harvested at immature stage for vegetable purpose, fully ripen fruits are consumed [2].

Leaves: The leaves are oblong and conical, 4-6 inch long and 2-3 inch wide, green on the top and brown below. If the leaves or stems are injured, the white milky sap is seen, which is characteristic of this group of plants.

Flowers: White or yellowish flowers are found in groups.

Fruit: They are with 5-1 hard angles curving upwards, glabrous with five to seven wings, woody and fibrous.

Bark: The bark is smooth gray. The bark is thick, soft and of red color from inside [3].

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 [4]. 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 wide 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, anti scorbutic, 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 [5].

Cultivation & Collection:

C. carandas believed to be originated near the Himalayas, though some botanists place the fruit's origin to Java. The plant is found to be distributed in the Himalayas at elevations of 300-1800 m, in the Siwalik Hills, the Western Ghats, in Nepal, Afghanistan, India, Sri Lanka, Java, Malaysia, Myanmar, Pakistan, Australia, and South Africa. In India it is cultivated in the states of Maharashtra, Bihar, West Bengal, Chhattisgarh, Orissa, Gujarat, Madhya Pradesh, Rajasthan, and in the Western Ghats. In Maharashtra, the major area under this crop is scattered in submountain area like Kolhapur, Ratnagiri, and Pune district [6]. Some of the important cultivated *Carissa* species besides *C. carandas* L. includes: *Carissa grandiflora* DC, *Carissa bispinosa* Desf., *Carissa spinarum* DC, *Carissa ovata*, *Carissa edulis* Vahl., *Carissa inermis* Vahl. Syn., *Carissa macrophylla*, *Carissa paucinervia* D.C., and *C. spinarum* L. Syn., *Carissa diffusa*, *C. carandas* and *C. spinarum* are native to India (Index Kewensis, 1985-190) while *C. grandiflora* is native to South Africa [7]. In India, the fruit grows throughout several regions including the Siwalik Hills, Bihar, West Bengal, the Western Ghats, Karnataka and the Nilgiri hills. It thrives in tropical and subtropical regions without heavy

rainfall. The drought-resistant nature of the plant enables the tribal areas of Madhya Pradesh, Rajasthan, Gujarat, and Bihar to grow the fruit on a limited scale. In fact, the Bhil tribe in Rajasthan sells karonda leaves for use as rolling tobacco paper to beedi manufacturers. Many of these groups also value the plant for its medicinal qualities. In the Jashpur district, for instance, the tree's roots kill the worms in the wounds of cattle, and the Munda tribe in Chota Nagpur uses the roots to treat rheumatism. Fruit harvest is august through october, though unripe fruits get plucked at the start of may through June. More specifically, harvest in the north occurs during the summer months of May through July, and some trees in the south bloom and yield fruit sporadically year-round.

Karonda's ripeness depends on its purpose. If intended for use as a vegetable, the fruits should be plucked while still under ripe, as apparent by the fruit's greenish white color. When fully ripe, the fruit bears no hint of white on its skin. These fruits are selected for canning, preserving and pickling. Some of the fruits turn red when fully ripe; others grow dark purple.

The sweet nectar from the shrub's flower has better taste than the karonda fruit itself. In its raw state, the fruit is sour and acidic with little sweetness. In its ripest state it becomes a bit sweeter, but only a few varieties become sweet enough to consume out of hand. However, karonda possesses several attributes that make it a highly desirable for culinary applications.

Karonda has 3 to 4 seeds per fruit requiring removal. Use a paring knife to cut in half and remove the seeds with the tip of knife. Also, expect plenty of gummy latex from the fruit when boiled: skim this from the surface periodically while cooking. Fruits keep for only three or four days at room temperature, and should instead be stored in the refrigerator. Even in a dry, chilled environment, the fruit will only last a week or so. The fruit, does, however, freeze well. Pack karondas loosely in a large freezer bag, or de-seed and boil in syrup beforehand.

Nutraceutical properties:

C. carandas fruits have been used as a dietary supplement or medicinal food for centuries and are of increasing importance to consumers (8, 9). A natural 'food colorant cum nutraceuticals supplement' was prepared from the ripe karonda fruits. The formulation had been named as 'Lalima'. 1 ml of this pigment suspension formulation is sufficient to give lovely red colour to one serving of any colourless beverage (100 ml) such as lemonade. One serve of

such supplemented beverage may in addition contain 469.2 µg anthocyanin, 12.7 mg flavonoids, 14.1 mg phenol, with total antioxidant activities to be 390 µM Trolox Equivalent (10). At present, many commercial fruit products are available in the market hence the present review will possibly act as bridge between nutraceutical food and industrial pharmaceutical potentials of *C. carandas*.

Processed product of *Carissa carandas*:

Carissa carandas fruit is full of calcium, iron, vitamin C, vitamin A, and other nutrients used as food and treatment of many ailments like anorexia, diarrhea, anemia, blood sugar stabilization etc. It freezes well and can also be kept in the fridge for long time or pickled in brine or canned with sugar.

Homemade fruit recipes

In north India fruits are made into condiment, pickles, syrups and jams. The tastes of fruit are extremely sour and make delicious by pickled with hot green chilies and garlic clove, both ingredients are packed with health benefits and increase the taste of the pickle. Karonda pickle is easy to prepare and ready to eat, this pickle can be made fresh or can be stored for at least four months.

It was found that chemical composition of the fresh and dried Karonda fruit showed that dried products contained substantially higher nutrient content than fresh one with the exception of vitamin C which was almost half of that present in fresh one. The plant fruit is rich in nutrients, vitamins and minerals such as protein, carbohydrate, calcium, iron, carotene, vitamin B1, B2, C etc. (Table 1).

Table. Food and nutritional value of *Carissa carandas* fruit

Components	Qty Present
Total acids	9 to 11 mg per 100 g.
Total Protein	0.39-0.66 g %
Total crude fat	2.57-4.63 g %
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Carbohydrate	0.51-0.94 g %
Sugar	7.35-11.58 g %
Iron	150 mg %
Calcium	115 mg %
Phosphorus	66 mg %
Energy (kcal/g)	338-342/lb calories (745-753/kg)
Ash	0.66-0.78 g %
Moisture	83.17-83.24 g %

Ayurvedic formulations

The plant *Carissa carandas* is used as ingredient in a number of ayurvedic formulations. Marmagutika used in the treatment of vital organs, like diseases related to brain, heart, urinary system. Hridayamahakashaya is employed in the treatment of heart disease. Kalkantaka rasa, 'juice' or 'essence' used for mental disease. Marichadivati used in the treatment of diseases of respiratory conditions and black pepper is the first ingredient of this medicine (11).

Traditional uses (12)

At industrial scale, Karonda is mainly used for making pickle, jelly, jam, squash, syrup and chutney. The ripe fruit emits gummy latex when it is cooked, but yields a rich red juice which becomes clear when it is cooled, so this is used as a refreshing cooling drink in summer. In many part of India fruits are commonly caring with green chilies to make a tasty dish taken with chapattis (13, 14). Unripe fruit is good appetizer; astringent, ant scorbutic, cooling, acidic, stomachic, anthelmintic and leaf decoctions are given in the commitment of remittent fever (15). Traditional healers of Chhattisgarh use the different plant parts to cover the cancerous wounds and to kill the maggots (16). In Konkan, India, root is pulverized with horse urine, lime-juice and camphor as a remedy for the itch (17). Two drops of plant oil is given with half cup of honey for controlling worms of minors (18).

Phytochemical constituents [19, 20]

Pino *et al.* isolated the volatile flavor constituents of the karonda fruits; isoamyl alcohol, isobutanol, and β -caryophyllene being the major constituent. Fruits were reported to contain a mixture of volatile constituents including 2-phenly ethanol, β -caryophylline, linalool, isoamyl alcohol, benzyl acetate and a novel tri terpenic alcohol, carissol. *C.congesta* contains crude protein 13%, polyphenols 7.8%, fixed oil 5.3 % hydrocarbons 58 % and free acid 31.4 %. Higher gross hest values of this species indicate that it can be used as fuel source. Essential oil from *C.congesta* was found to contain coumarin [21-23]. The roots of *C.congesta* have volatile principles including 2-acetyl phenol, Lignan, carinol from root of *C. congesta* sesquiterpenes, namely carissone and carindone. Triterpenoid constitutes as well as tannins, and a new isomer of urosolic acid namely carissic acid found in leaves. It has been reported that fresh leaves of *C.congesta* contain four pentacyclic triterpenoids including one new constituent carissin [24-27].

VARIOUS TEST OF CHEMICAL CONSTITUENTS FOUND IN CARRISA CARANDAS

The preliminary phytochemical studies were performed for testing the different chemical groups like alkaloids, carbohydrates, flavonoids, proteins, resins and saponins present in the drug. General screening of various extracts of the plant material was carried out for qualitative determination of the groups of organic compounds present in them (28)

ALKALOIDS

- **Dragendorff's test:**

A few mg of alcoholic or aq. extract of the drug was dissolved in 5 ml of distilled water, to which 2 N Hydrochloric acid was added until an acid reaction occurred, and then 1 ml of Dragendorff's reagent was added. An orange or orange red precipitate was considered positive test for alkaloids.

- **Hager's test:**

To 1 ml of alcoholic extract of the drug in a test tube, a few drops of Hager's reagent were added. Formation of yellow precipitate confirmed the presence of alkaloids.

- **Wagner's test:**

1 ml of alcoholic extract of the drug was acidified with 1.5% v/v of hydrochloric acid and a few drops of Wagner's reagent were added. A yellow or brown precipitate considered the presence of alkaloids.

- **Mayer's test:**

A few drops of Mayer's reagent were added to 1 ml of acidic aqueous extract of the drug. White or pale yellow precipitate was considered positive for the presence of alkaloids.

CARBOHYDRATES:

- **Benedict's test:**

0.5 ml of aqueous extract of the drug was added to 5 ml of Benedict's solution and boiled for 5 mins. Formation of a brick red coloured precipitate indicated the presence of carbohydrates.

- **Fehling's test:**

2 ml of aqueous extract of the drug was added to 1 ml of a mixture of equal parts of Fehling's solution 'A' and Fehling's solution 'B' and contents of the test tube were boiled for few mins. A red or brick red precipitate indicates the presence of carbohydrates.

- **Molisch's test:**

In a test tube containing 2 ml of aqueous extract of the drug 2 drops of a freshly prepared 20% alcoholic solution of b-naphthol was added and mixed and then 2 ml of conc. sulphuric acid was poured so as to form a layer below the mixture. Carbohydrates, if present, produce a red-violet ring, which disappears on the addition of an excess of alkali solution.

FLAVONOIDS

- **Shinoda's test:**

In a test tube containing 0.5 ml of alcoholic extract of the drug, 5-10 drops of dil. hydrochloric acid followed by a small piece of magnesium was added. In the presence of flavonoids a pink, reddish pink or brown colour indicated the presence of flavonoids.

- **Triterpenoids**

Liebermann-Burchard's test: 2 ml of acetic anhydride solution was added to 1 ml of petroleum ether extract of the drug in chloroform followed by 1 ml of conc. sulphuric acid.

A violet coloured ring indicated the presence of triterpenoids.

PROTEINS

- **Biuret's test:**

1 ml of hot aq extract of the drug was added and then 5-8 drops of 10% w/v sodium hydroxide solution was added followed by 1 to 2 drops of 3% w/v copper sulphate solution. A red or violet colour indicated the presence of protein.

- **Millon's test:**

Aqueous extract of the drug in 1 ml of distilled water was dissolved and 5-6 drops of Millon's reagent was added. A white precipitate which turns red on heating indicates the presence of protein.

RESINS

The extract was dissolved in acetone and the solution was poured into distilled water. Turbidity indicated the presence of resins.

SAPONINS

5 ml of an aqueous extract of the drug was taken in a test tube then a drop of sodium bicarbonate solution was added, the mixture was shaken vigorously and left for 3 mins. Honeycomb like froth showed the presence of saponins.

Standardization Procedure of Crude Drugs [29]

- **Determination of Foreign Matter**

100 g of the drug sample was examined, weighed and spread out in a thin layer. The foreign matter was detected by inspection with the naked eye. It was separated and weighed and the percentage was calculated. Drug which was undertaken for further study was free from moulds, insects, animal faecal matter and other contamination such as soil, stones and extraneous material.

- **Determination of Moisture Content**

The azeotropic distillation apparatus consisted of a glass flask connected by a tube to a cylindrical tube fitted with a graduated receiving tube and a reflux condenser. The receiving tube was graduated in 0.1ml division so that the error of reading does not exceed 0.05ml. Accurately weighed drug expected to give about 2-3ml of water and a few pieces of porous porcelain was placed in heating flask. When as the

boiling started initially the distillation rate was adjusted to the 2 drops per second was adjusted and then it was readjusted to a rate of 4 drops per second. As soon as the water was completely distilled, the inside of the condenser tube was rinsed with toluene. The receiving tube was allowed to cool at room temperature and the water droplets adhering to the walls of the receiving tube were dislodged by taping the tube. The layer of water and toluene layers were separated and the volume of water was measured. The percentage water content (%v/w) was calculated using the formula:

$$\% \text{ water content} = 100(N1-N)/w$$

Where w = the weight in g of the material being examined.

N = the number of ml of water obtained in the first distillation.

N1= the total number of ml of water obtained in both distillations.

- **Determination of Total Ash and Acid Insoluble Ash**

2.0g of powdered drug was incinerated in a tarred silica dish at a temperature not exceeding 450°C until free carbon was left, then it was cooled and the final weight was taken. The percentage of ash with reference to the air dried drug was calculated (PASF 1987).

The ash obtained by above method was boiled for 5 minutes with 25 ml of dilute hydrochloric acid and the insoluble matter was collected on an ash-less filter paper, washed with hot water and ignited to constant weight. The percentage of acid-insoluble ash with reference to the air dried drug was calculated (30).

- **Determination of Extractable Matter :**

For Hot Extraction Method, 4.0 g of coarsely powdered air-dried drug was placed in a thumble and refluxed with various organic solvents over soxhlet extraction. The successive extraction was carried out in the order of solvent Petroleum ether, alcohol and water. After recovery of solvents under vacuum and drying in desiccator, the percentage extractable matter was calculated. Whereas for *Cold Maceration Method* 4.0 g of coarsely powdered air dried material was taken in a glass stoppered conical flask and macerated for 6 hours with 100ml of the specified solvent, shaking frequently and then allowed to stand for 18 hours. It was then filtered rapidly taking care not to lose any solvent in the process. The extracted matter was dried at 105°C for 6 hours, cooled in a desiccator for 30 minutes and then weighed. The percentage extractable matter was calculated.

- **Determination of Volatile Oils**

The steam distillate of 20-40g of coarsely powdered air dried material was collected in a graduate tube, using xylene. The aqueous phase was allowed to re-circulate into the distillation flask for all determinations and the rate of distillation was read from the marks engraved on the apparatus. The increase in the volume of xylene was noted and the difference in initial and final value of xylene was used to calculate the volatile oil content of the drug.

- **Determination of Swelling Index**

4.0 g of fine powdered material was taken in a 25ml glass stoppered measuring cylinder. 25 ml of water was added and the mixture was thoroughly shaken for every 10 minutes for an hour and kept for 3 hours at room temperature. After 3 hours the volume in ml occupied by the plant material, including any sticky mucilage was measured. The mean value of the individual determination, related to 1.0g of plant material was calculated.

- **Determination of Foaming Index**

1.0 g of a coarse powder of the drug was placed into a 500ml conical flask containing 100ml of boiling water and moderate boiling was maintained for 30 minutes. Then it was cooled and filtered into a 100 ml volumetric flask and the volume was made up to the mark with distilled water. The decoction was then poured into 10 stoppered test tubes in successive portions of 1ml, 2ml, 3ml etc. up to 10ml, and adjusted the volume of the liquid in each tube with water to 10ml. The tubes were stoppered and shaken in a length wise motion for 15 seconds, two shakes per second. After 15 minutes, the height of the foam were measured. The results are assessed as follows.

1. If the height of the foam in every tube is less than 1 cm, the foaming index is less than 100 &
2. If a height of foam 1 cm was measured in any tube, the volume of the plant material decoction in this tube (a) was used to determine the index. If this tube is the first or second tube in a series, an intermediate dilution was prepared in a similar manner to obtain a more precise result.
3. If the height of the foam was more than 1 cm in every tube, the foaming index was over 1000. In this case the determination was repeated using a new series of dilution of the decoction in order to obtain a precise result.

$$\text{Foaming index} = 1000/a$$

Where a = the volume in ml of the decoction used for preparing the dilution in the tube where foaming to a height of 1cm was observed.

- **Determination of Pesticide Residues**

Organo chloride pesticides were extracted from powdered drug of *Carissa carandas* adopting the procedures mentioned in WHO guidelines (31). The organochloride pesticides standard and the sample extract were applied on to GLC (Nucon 5767) under the following conditions. Column 6"x1/8" (ID) glass column filled with 80- 100 mesh gas chromatography

coated with mixture of 1.5% OV- 17 and 1.95 OV 210, temperature 190°C, Detector: Ni63 ECD, 250°C, Injector: temp. 250°C. Carrier gas IOLAR grade Nitrogen, flow rate 60 ml/min. Using the above mentioned analytical condition the level of the detection (LOD) and level of the quantitation (LOQ) of the organochlorine pesticide were in the range of 0.1-0.5µg/L and 1-3µg/L, respectively.

PHARMACOLOGICAL ACTIVITIES

C. carandas have a wide range of pharmacological activities due to presence of phytochemicals. Pharmacological importance of the plant fruits has been evaluated by several researchers through *in vitro* and *in vivo* advances. The roots of *C. carandas* are anthelmintic, stomachic, antiscorbutic and, intestinal worms, scabies, diabetic ulcer and pruritus. The unripe fruit is constipating, appetiser, antipyretic and useful in hyperdipsia, anorexia, diarrhea, disease of brain, nematocidal and intermittent fevers. Decoction of leaves is given at the commencement of remittent fever. Various plant parts are reported to be used in dropsy, anasarca, madness, rheumatism, emeplegia, epilepsy, convulsions, postnatal complaints, sores and bite of rabid jackal or dog. (32)

Analgesic, anti-inflammatory, and Anti-pyretic activities: Analgesic, anti-inflammatory and antipyretic activities of ethanol and aqueous extracts from *C. carandas* roots in rodent models were reported by Bhaskar and Balakrishnan [33]. The workers observed highest percentage of inhibition of abdominal constriction (72.67%) ethanol extracts of *C. carandas* at a dose of 100 mg/kg body weight in analgesic activity. Whereas methanolic extract of *C. carandas* leaves reduced the edema induced by histamine, carrageenan and dextran in rat hind paw at the dose of 200 mg/kg b.w. It exhibited maximum inhibition of inflammation, i.e., 72.10 %, 71.80 and % 71.90 % at the end of 3 hrs with histamine, carrageenan and dextran induced rat paw edema respectively. [34, 35].

Anticancer activity: Anti-cancer activity was shown in the extracts of *C. carandas* fruits in chloroform, n-hexane and methanol on the lung cancer cells and human ovarian carcinoma cells. (36). Further, anti-cancer and antioxidant potentials of the extracts were analyzed by unusual antioxidant enzymes such as catalase, dismutase, superoxide, glutathione-s-transferase and glutathione on MCF-7 cancer lines. This study exhibited significant antioxidant activity, and fortification of cell death in MCF-7cell line pretreated with *C. carandas* extracts (37). Sadek *et al.* [38] 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 hydroxyl toluene in 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging with inhibitory concentration (IC₅₀) of 1.292 µg/ml and 1.824 µg/ml of ethanolic extract and n-hexane extract. H₂O₂ scavenging activities of the extracts were found to be better than the standard, having IC₅₀ values higher than ascorbic acid. Similarly, Verma *et al.* [39] 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 (IC₅₀=73.12 µg/ml), total antioxidant activity, H₂O₂ scavenging activity (IC₅₀=84.03 µg/ml), and reducing power activity.

Anti-diabetic activity: Anti-diabetic activity of aqueous extract of *C. carandas* leaves are evaluated by Gaurav *et al.* [40] on alloxan induced and normoglycemic Wister rats, and it was found that the doses of 500 and 1000 mg/kg of the drug significantly (P<0.05) reduced the blood glucose level of alloxan induced diabetic rats at 4, 8 and 24 hrs. Plant extract had significant (P<0.05) hypoglycemic as well as anti-hyperglycemic property on both doses. Further, methanolic extract and its fraction of fruits were evaluated for anti-diabetic activity in alloxan induced diabetic rats by Itankar *et al.* [41]. It is reported that the methanol extract and its ethyl acetate soluble fraction have significantly lowered the increased blood glucose levels at dose level of 400 mg/ kg p.o. after 24 hrs, as compared to diabetic control. The researchers accomplished that the anti-diabetic potential of ethyl acetate portion over methanol extract is due to its partial purification achieved by fractionation which resulted increase the polymerization, and separation of secondary metabolites flavonoids and phenolic compounds.

Cardiovascular activity: Coronary artery disease, heart attack, heart failure, high blood pressure and stroke, that affects the heart and the blood vessels come under Cardiovascular disease. The World Health Organization estimate reflects that the disease causes deaths of approximately 30,000 people each day [42].

Shamim and Ahmad in the year 2012 [43], 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 stimulates the muscarinic receptors located on the endothelial cells of the vasculature. By this there is release of endothelial-derived relaxing factors or nitric oxide that diffuses to vasculature smooth muscles and causes their relaxation.

Hepatoprotective activity: Hegde and Joshi [44], reported significant hepatoprotective activity of ethanolic extract of the roots of *C. carandas* (ERCC; 100, 200 and 400 mg/kg, p.o.) against CCl₄ and paracetamol induced hepatotoxicity. It decreases 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. Bhaskar and Balakrishnan [45] 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 hepato protection by decreasing serum transaminase, alkaline phosphate, bilirubin and lipid peroxidation while significantly increased the levels of liver glutathione, and serum protein.

Anti-convulsant activity: Hegde *et al.* [46] investigated anti-convulsant effect of the ethanolic extract of *C. carandas* roots (100, 200 and 400 mg/kg, i.p.). 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 pentylene tetrazole-induced tonic seizures and significantly delayed the onset of tonic seizures produced by picrotoxin, and N-methyl-dl-aspartic acid.

Neuropharmacological and diuretic activities: A significant neuropharmacological activity evaluated on methanolic extracts of *C. carandas* L. leaves by Saha *et al.* [47]. 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.

Adaptogenic activity: The ethanolic fruit extract and lanostane triterpenoid isolated from the *C. Carandas* were screened for adaptogenic activity using swimming endurance, anoxia stress tolerance and cyclophosphamide induced immunosuppression model. The levels of RBC, Hb, WBC, organ weight and body weight suppressed by cyclophosphamide were estimated. It was observed that extract and lanostane triterpenoid significantly increased the swimming endurance, anoxia stress tolerance and

normalized the RBC, Hb, WBC, changed organ and body weight suppressed by cyclophosphamide demonstrate that extract and isolated compound showed significant adaptogenic activity (48).

Anti-nociceptive activity: Methanolic extract of *C. carandas* leaves exhibited dose-dependent and significant anti-nociceptive activity, and decreased the number of writhings induced by intraperitoneal administration of acetic acid in acetic acid-induced gastric pain model in Swiss albino mice [49]. The result was comparable to the standard pain-killing drug; aspirin.

Anti-ulcer activity: Merai and Jadhav [50] observed that the alcoholic extract of *C. carandas* exhibited highly significant anti-ulcer activity. They 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.

Constipation and diarrhea: Pharmacological use of crude extract of the leaves of *C. carandas* in constipation and diarrhea via *in-vivo* on mice, and *in-vitro* experiments on isolated rabbit jejunum, and guineapig ileum preparations was studied by Mehmood *et al.* [51]. The extract had the oleanolic acid, ursolic acid, stigmasterol and β -sitosterol which were shown by HPLC. Thus they concluded that the crude extract of *C. carandas* possesses a gut-stimulatory effect mediated primarily through the activation of muscarinic and histaminergic receptors while its spasmolytic effect was mediated possibly through Ca⁺⁺ antagonist pathway.

Antimalarial activity Bapna *et al.* [52] analyzed, 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 extract tested, methanolic extract exhibited promising antimalarial activity (IC₅₀ ranged between 13.57 and 69.63 μ g/mL) as compared to aqueous extracts (IC₅₀ ranged between 41.52 and >100 μ g/mL).

Anthelmintic activity: The various concentrations (50, 100, and 150 mg/ml) of the different solvent extracts of *C. carandas* (petroleum ether (60-80), chloroform and ethanolic unripe fruits extract) were tested in *in-vitro* for anthelmintic potency by the determination of time of paralysis and time of death of the worm [53]. The workers used piperazine citrate (15 mg/ml) as standard drug and they concluded from that the unripe fruits extract of *C. carandas* L. causes earthworm paralysis, and also its death after some

time. The result indicated that the ethanolic extract possess potent anthelmintic activity, than that of other solvent extracts due to the availability of some important phyto constituents.

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