ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 8, Issue 3, 2015

ISSN - 0974-2441

Review Article

# A REVIEW ON *CARISSA CARANDAS* - PHYTOCHEMISTRY, ETHNO-PHARMACOLOGY, AND MICROPROPAGATION AS CONSERVATION STRATEGY

**AKANSHA SINGH*, GURSIMRAN KAUR UPPAL**

**National Facility for Biopharmaceuticals, GN Khalsa College of Arts, Science & Commerce, Matunga East, Mumbai - 400 019, Maharashtra, India. Email: akansha.iasbhu@gmail.com**

***Received: 01 March 2015, Revised and Accepted: 23 March 2015***

**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 congesta* Wight (syn. *Carissa carandas* Auct., formerly widely shown as *C. carandas* L.), belongs to the dogbane family Apocynaceae [1], found to be widely distributed throughout India. The shrub is commonly known as karonda (Devanagari: करोंदा), karamardaka (Sanskrit), Koromcha (Bengali), Bengal currant or Christ's thorn (South India), vakkay (Telugu), kilaakkaai (Tamil), and Karja tenga (Asam). 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 [2]. 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 [3].

### Classification

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

## PLANT DESCRIPTION

*Carissa carandas*, an evergreen deciduous, generally 2-4 m tall shrub of the dogbane family Apocynaceae. Its stem is rich in white latex, having sharp spines on branches. The leaves are oblong and conical, 4-6 inch long and 2-3 inch wide, green on the top and brown below. The plant produces white colored flowers, measuring 3-5 cm in diameter. The fruit is a berry, which is formed in clusters of 3-10 fruits, with 5-1 hard angles curving upwards, glabrous with five to seven wings, woody, and fibrous. The fruit shape is globose to broad ovoid consisting of several seeds. Young fruits are pinkish white, while ripe fruit became red to dark purple. Ripe fruit color varies from white, green and pinkish red depending on the genotype. Seed 3-5 per fruit, blackish brown, flat, eleptical, and light in weight. Flowering starts in the month of January-February and fruits mature in May June. Fruits are generally harvested at the immature stage for vegetable purpose, fully ripen fruits are consumed fresh or processed [4].

## ORIGIN AND DISTRIBUTION

*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 [5]. 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 [3].

**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 100 g of fresh fruit [6]. Whereas, Malik *et al*. [3], reported nutritional information of per 100 g of edible fruit is a source of: 42.5 kcal energy, 0.39-1.1 g protein (negligible), 2.5-4.63 g fat, 0.51-2.9 g carbohydrate, 0.62-1.81 g fiber, 21 mg calcium, 28 mg phosphorous, 1619 IU vitamin A, and 9-11 mg ascorbic acid.

**Phytochemical constituents**

Phytochemical screening of the root extract showed presence of small quantities of alkaloids, flavonoids, saponins and large amounts of cardiac glycosides, triterpenoids, phenolic compounds and tannins in crude extract [7]. Further, roots were 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-Nmethylnoracronycine, an acridone alkaloid [8-12].

Chemical analysis of stem showed the presence of sesquiterpene glucoside [13]. The leaves were reported to contain triterpenoid constitutes as well as tannins, and a new isomer of urosolic acid namely carissic acid triterpene carandinol, betulinic acid, β-sitosterol-3-O-β-d-glucopyranoside, oleanolic acid, ursolic acid, and 4-hydroxybenzoic acid [14-16]. Fruits of *C. carandas* 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 [17,18]. Further, Pino *et al*. [19] isolated the volatile flavor constituents of the karanda fruits; isoamyl alcohol, isobutanol, and β-caryophyllene being the major constituent.

**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*. [20] 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*. [21] demonstrated anti-diabetic potential of the plant by screening methanol extract, and its fractions in alloxan induced diabetic rats [21]. 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*. [7] 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.

**Analgesic, anti-inflammatory, and anti-pyretic activities**

Bhaskar and Balakrishnan [22], reported significant analgesic, anti-inflammatory and antipyretic activities of ethanol and aqueous extracts from *C. carandas* roots in rodent models. The ethanol and aqueous extracts from roots of *C. carandas* exhibited significant ($p<0.01$) analgesic, anti-inflammatory, and antipyretic activities at the doses of 100 and 200 mg/kg body weight. 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. Further, the ethanol and aqueous extracts of *C. carandas* reduced the formation of edema induced by carrageenan after 2 hrs, significantly.

Further, Hati *et al*. [23] evaluated anti-inflammatory, and anti-pyretic potentials of the methanol extract of *C. carandas* L. leaf. The extract at the 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 hrs with histamine, dextran and carrageenan induced rat paw edema respectively. The anti-pyretic activity was evaluated by Brewer's yeast induced pyrexia in albino rats. The extract at the dose of 100 and 200 mg/kg p.o. showed significant anti-pyretic activity.

Furthermore, Anupama *et al*. [24] examined the anti-inflammatory effects of dried fruit methanol extract on carrageenan-induced hind paw edema in rats. *C. carandas* was defatted with petroleum ether, followed by methanol extraction. The methanol extracts of the dried fruits of *C. carandas* were given orally to the experimental rats and found significant activity ($p\leq0.05$) when compared with the control group.

**Hepatoprotective activity**

Hegde and Joshi [11], 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 [25] 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*. [26] 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 [27]. Plant as source for safe and effective treatment for cardiovascular diseases has been explored by Shamim and Ahmad in the year 2012 [28], 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-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 [29]. The result was comparable to the standard pain-killing drug; aspirin. The workers suggested anti-nociceptive activity of the plant leaves merit further scientific studies for isolation of anti-nociceptive components leading to the discovery of possibly novel and more efficacious pain-killing drugs. Standard pain-killing drugs like aspirin and paracetamol suffer from the problem of inducing gastric ulceration or hepatotoxicity from overdose or prolonged use. As such, newer and more efficacious painkillers can prove to be highly beneficial to human beings [29].

**Anti-cancerous activity and antioxidant potentials**

Sulaiman *et al*. [30] 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 [31] 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*. [32] 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 provide 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 [34] 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.

**Constipation and diarrhea**

Mehmood *et al*. [35] studied pharmacological basis 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 guinea-pig ileum preparations. The high-performance liquid chromatography fingerprints of the extract showed the presence of oleanolic acid, ursolic acid, stigmasterol and β-sitosterol. The workers concluded from the study 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. Thus, the study provides a clear evidence for the dual effectiveness of *C. carandas* in constipation and diarrhea.

**Anthelmintic activity**

Mishra *et al*. [36] evaluated *in-vitro* anthelmintic potency of the petroleum ether (60-80), chloroform and ethanolic unripe fruits extract of *C. carandas* L. on Indian earthworms (*Pheretima posthuma*). The various concentrations (50, 100, and 150 mg/ml) of the different solvent extract were tested in *in-vitro* for anthelmintic potency by the determination of time of paralysis and time of death of the worm. The workers used piperazine citrate (15 mg/ml) as standard drug. The workers concluded from the result of the study that the unripe fruits extract of *C. carandas* L. causes earthworm paralysis, and also its death after some time. The shortest time of paralysis was observed at higher dose (150 mg/ml) of ethanolic extract, chloroform extract, and petroleum ether extract, i.e., found to 56.35 minutes, 40 minutes, and 22.35 minutes, respectively, indicated that the ethanolic extract possess potent anthelmintic activity, than that of other solvent extracts due to the availability of some important phytoconstituents.

**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*. [37] 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 extract 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.

**Micropropagation as conservation strategy**

Conventionally, propagation of *C. carandas* is done via seeds, cuttings, grafting, air layering, and stooling [38-40]. However, these methods are season specific, and take long time to propagate. Whereas, micropropagation is a tissue culture method for producing thousands

of plantlets in a short span of time, through culturing explants in controlled laboratory environmental condition. Since concentration of phytochemicals vary from season to season, and developmental stages of the plant and continuous supply of healthy plant material for sustainable production of drugs in the pharmaceutical industry is required. Besides this, excessive collection from natural habitat, destructive harvesting techniques, coupled with poor seed germination with less viability [41], and low vegetative multiplication ratio of the *C. carandas* plant also necessitates to standardize the protocol for *in-vitro* micropropagation. Thus, in the year 2001, Rai [42] standardized the protocol for micropropagation of *C. carandas*. Further, in 2005 Rai and Mishra [43] demonstrated regeneration potential of "Pant Sudarshan" an elite cultivar of *C. carandas* through shoot tip culture on Murashige and Skoog's (MS) basal medium supplemented with benzyladenine and indolebutyric acid (IBA) during different seasons. The workers observed highest shoot proliferation on MS basal media supplemented with 3.0 mg/L IBA, whereas rooting of microshoots was observed in 1/2MS plus 0.8 mg/L IBA and 0.2 mg/L naphthalene acetic acid. The rooted plantlets were successfully acclimatized in vermiculite:sand:soil (1:1:1) potting mixture [43]. Furthermore, Imran and coworkers [44], developed protocol for *in-vitro* multiple shoot induction through node and shoot apex. The workers used adenine sulfate (Ads) as an experimental hormone for the production of multiple shoots. Maximum numbers of shoots from nodal explant were produced on MS medium supplemented with 1.5 mg/L benzyl aminopurine (BAP) + 1.0 mg/L kinetin (Kn) + 1.0 mg/L thidiazuron (TDZ) + 15 mg/L Ads. Same concentration i.e., 1.5 mg/L BAP + 1.0 mg/L Kn + 1.0 mg/L TDZ+ 15 mg/L Ads induced large number of shoots from shoot apex. Moreover, Hasmah *et al*. [45], developed micropropagation protocol for *C. carandas* using nodal segment as the explants.

## 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.

## ACKNOWLEDGMENT

Authors are thankful to National Facility for Biopharmaceuticals Laboratory for providing basic support and infrastructural facility to carry out the literature search with respect to the manuscript.

## 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. Morton JF. Fruits of Warm Climates. Miami, FL: Creative Resource Systems, Inc. N.C.; 1987.
7. Hegde K, Thakker SP, Joshi AB, Shastry CS, Chandrashekhar KS. Anticonvulsant activity of *Carissa carandas* Linn. root extract in experimental mice. Trop J Pharm Res 2009;8:117-25.
8. Rastogi RC, Vohra MM, Rastogi RP, Dhar ML. Studies on *Carissa carandas* Linn. Part I. Isolation of the cardiac active principles. Indian J Chem 1966;4:132.
9. Singh B, Rastogi RP. The structure of carindone. Phytochemistry 1972;11(5):1797-801.
10. Pal R, Kulshreshtha DK, Rastogi RP. A new lignan from *Carissa carandas*. Phytochemistry 1975;14:2302-3.
11. Hegde K, Joshi AB. Hepatoprotective effect of *Carissa carandas* Linn root extract against CCl4 and paracetamol induced hepatic oxidative stress. Indian J Exp Biol 2009;47(8):660-7.
12. Ganapaty S, Bharath CH, Laatsch H. Des-N-Methylnoracronycine from the roots of *Carissa conjesta*. Wight. Int J Green Pharm 2010;4(3):186.
13. Wangteeraprasert R, Likhitwitayawuid K. Lignans and a sesquiterpene glucoside from *Carissa carandas* stem. Helv Chim Acta 2009;92(6):1217-23.
14. Naim Z, Khan MA, Nizami SS. Isolation of a new isomer of ursolic acid from fruits and leaves of *Carissa carandas*. Pak J Sci Ind Res 1988;31(11):753.
15. Siddiqui BS, Ghani U, Ali ST, Usmani SB, Begum S. Triterpenoidal constituents of the leaves of *Carissa carandas*. Nat Prod Res 2003;17(3):153-8.
16. Begum S, Syed SA, Siddiqui BS, Sattar SA, Choudhary MI. Carandinol: First isohopane triterpene from the leaves of *Carissa carandas* L. and its cytotoxicity against cancer cell lines. Phytochem Lett 2013;6(1):91-5.
17. Sharma A, Tiwari RK, Kaushik A, Tyagi LK, Shankar K, Virmani T, *et al*. Standardisation of *Carissa carandas* Linn: A drug used in Indian system of medicine as per WHO Guidelines. Cont J Pharm Sci 2007;1:9-14.
18. Devmurari V, Shivanand P, Goyani MB, Vaghani S, Jivani NP. A review: *Carissa congesta*: Phytochemical constituents, traditional use and pharmacological properties. Pharmacogn Rev 2009;3(6):375.
19. Pino JA, Marbot R, Vázquez C. Volatile flavor constituents of Karanda (*Carissa carandas* L.) fruit. J Essent Oil Res 2004;16(5):432-4.
20. Gaurav S, Navneet N, Sandeep R, Singh P, Amit P, Manisha N, *et al*. Effect of aqueous leaves extract of *Carissa carandas* linn. on blood glucose levels of normoglycemic & alloxan induced diabetic wister rats. Int J Curr Pharm Res 2010;2(3):65-7.
21. Itankar PR, Lokhande SJ, Verma PR, Arora SK, Sahu RA, Patil AT. Antidiabetic potential of unripe *Carissa carandas* Linn. fruit extract. J Ethnopharmacol 2011;135(2):430-3.
22. Bhaskar VH, Balakrishnan N. Analgesic, anti-inflammatory and antipyretic activities of *Pergularia daemia* and *Carissa carandas*. Daru J Pharm Sci 2009;17(3):168-74.
23. Hati M, Jena BK, Kar S, Nayak AK. Evaluation of anti-inflammatory and anti-pyretic activity of *Carissa carandas* L. leaf extract in rats. J Pharm Chem Biol Sci 2014;1(1):18-25.
24. Anupama N, Madhumitha G, Rajesh KS. Role of dried fruits of *Carissa carandas* as anti-inflammatory agents and the analysis of phytochemical constituents by GC-MS. Biomed Res Int 2014;2014:512369.
25. Bhaskar VH, Balakrishnan N. Hepatoprotective activity of laticiferous plant species (*Pergularia daemia* and *Carissa carandas*) from Western Ghats, Tamilnadu, India. Pharm Lett 2009;1(2):130-42.
26. Saha R, Hossain L, Bose U, Rahman AA. Europharmacological and diuretic activities of *Carissa carandas* linn. Leaf. Pharmacologyonline 2010;2:320-7.
27. Middlemiss D, Watson SP. A medicinal chemistry case study: An account of an angiotensin II antagonist drug discovery programme. Tetrahedron 1994;50:13049-80.
28. Shamim S, Ahmad SI. Pharmacodynamic study on acute hypotensive activities of *Carissa carandas* extract in normal rats. Pak J Pharm Sci 2012;25(3):577-82.
29. Islam MR, Rahman SM, Ahmed M, Das PR, Tabibul M, Islam MH, *et al*. Antinociceptive activity studies with methanol extract of *Annona reticulata* L.(Annonaceae) and *Carissa carandas* L.(Apocynaceae) leaves in Swiss albino mice. Adv Nat Appl Sci 2012;6(8):1313-8.
30. Sulaiman SF, Wong ST, Ooi KL, Yusof SR, Muhammad T, Sifzizul T. Anticancer study of *Carissa carandas* extracts. Anticancer study of *Carissa carandas* extracts. Project Report, Monograph Universiti Sains Malaysia; 2008. Available from: http://eprints.usm.my/180/1/Anticancer_study_of_Carissa_carandas_extracts.pdf. [Last accessed on 2015 May 01].
31. Dua D, Srivastav NS. Anti-cancerous and antioxidant potential of aqueous extracts of *Annona reticulata, Podophyllum peltatum, Psidium guajava, Ananas comosus, Carissa carandas* on MCF-7 cancer cell line. Int J Integr Sci Innov Technol Sec 2013;2(4):15-9.
32. Sadek YB, Choudhury N, Shahriar M. Biological investigations of the leaf extracts of *Carissa Carandas*. Int J Pharm Res Technol 2013;5(2):97-105.
33. Verma K, Shrivastava D, Kumar G. Antioxidant activity and DNA damage inhibition *in vitro* by a methanolic extract of *Carissa carandas* (Apocynaceae) leaves. J Taibah Univ Sci 2015;9(1):34-40.
34. Merai AH, Jadhav AG. Anti ulcer activity of *Carissa carandas* using root extract in albino rats. World J Pharm Pharm Sci 2014;3(4):1314-26.

35. Mehmood MH, Anila N, Begum S, Syed SA, Siddiqui BS, Gilani AH. Pharmacological basis for the medicinal use of *Carissa carandas* in constipation and diarrhea. J Ethnopharmacol 2014;153(2):359-67.
36. Mishra CK, Sasmal D, Shrivastava B. An *in vitro* evaluation of the anthelmintic activity of unripe fruits extract of *Carissa carandas* Linn. Int J Drug Dev Res 2012;4(4):393-7.
37. Bapna S, Ramaiya M, Chowdhary A. Antimalarial activity of *Carissa carandas* Linn. against *Plasmodium falciparum*. J Antimicrob (Photon) 2013;128:246-50.
38. Misra KK, Jaiswal HR. Effect of growth regulators on rooting of stool layers of karonda (*Carissa carandas* L.). Indian J Forestry 1993;16(2):181-2.
39. Misra KK, Singh R. Effect of growth regulators on rooting and survival of air layers of karonda (*Carissa carandas* L.). Ann Agric Res 1990;11(2):208-10.
40. Tyagi S, Misra KK, Jaiswal HR. Effect of auxins on rooting of softwood stem cuttings of *Carissa* under mist. Sci Hortic 1999;6:37-43.
41. Kumar D, Pandey V, Nath V. Karonda (*Carissa congesta*) – An Underutilized fruit crop. In: Peter KV, editor. Underutilized and Underexploited Horticulture Crops. Vol. I. New Delhi: Pitam Pura; 2007. p. 313-25.
42. Rai R. Standardization of micropropagation technique in *Carissa* Spp. Diss. Pantnagar: Govind Ballabh Pant University of Agriculture and Technology; 2001.
43. Rai R, Misra KK. Micropropagation of karonda (*Carissa carandas*) through shoot multiplication. Sci Hortic 2005;103:227-32.
44. Imran MA, Begum G, Sujatha K, Mallaiah B. Effect of adenine sulphate (ads) with cytokinins on multiple shoot production in *Carissa carandas* (l.). Int J Pharma Bio Sci 2012;3(1):473-80.
45. Hasmah SN, Bhatt A, Keng CL. Micropropagation of Asam Karanda (*Carissa carandas* Linn). Pertanika J Trop Agric Sci 2013;36(1):89-98.