

# *Citrullus colocynthis* an Important Plant in Indian Traditional System of Medicine

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## ABSTRACT

*Citrullus colocynthis* (L.) Schrad, commonly known as Colocynth, a member of Cucurbitaceae is native to Mediterranean region and Asia. It is a wild, perennial, herbaceous, non-tough, harsh, angular vine with lobular tendrils, alternate leaves and small yellow monoecious flowers. Recently, various researches have been done to assess restorative capability of the plant. It contains various phytochemical constituents such as alkaloids, carbohydrates, flavonoids, tannins, triterpenoids, proteins, saponins and steroids along many pharmacological properties viz. diuretic, hypolipidemic, anti-cancerous, antioxidant, anti-microbial. This work is an endeavor to assemble and explore the various phytochemical and pharmacological properties announced till date.

**Key words:** *Citrullus colocynthis*, Colocynth, Cucurbitacins, Pharmacological activities, Vine of Sodom.

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## INTRODUCTION

*Citrullus colocynthis* (L.) Schrad, a valuable plant commonly known as Colocynth is member from Cucurbitaceae, reported among all parched, arid zones of world<sup>[1]</sup> however it is native to Mediterranean region and Asia.<sup>[2]</sup> Geographically it is distributed in deserts of North Africa, South Europe and whole of Asia,<sup>[3-6]</sup> extended up to Egypt.<sup>[3]</sup> In India, this drought tolerant plant species is usually dispersed among all hot arid areas.<sup>[1]</sup> It is the most commonly utilized plant in Indian traditional medicinal framework and easily propagated by vegetative and generative modes of reproduction in summers.<sup>[7]</sup> Local people use it to fix disorders like Boils, Pimples, Constipation, Inflammation of joints.<sup>[8]</sup> To reduce the glucose level,<sup>[9]</sup> joints aggravations, rheumatism, abdomen enlargement<sup>[10,11]</sup> *Citrullus* is being used. Plant species is additionally used to cure Urticaria, constipation, snake poison, stomach ache, Hepatitis<sup>[12,13]</sup> Malaria, Epilepsy and Bowel grievances.<sup>[14]</sup> Since all plant parts puts practically equivalent endeavors to the traditional medicinal system here is a survey of review giving updated information about phytochemical and therapeutic properties of plant.

## HISTORY

A colossal role of plant in man's life have been reported from ancient to present world.<sup>[15]</sup> Nearly 80% of word population rely on natural medicinal system for basic medical issues.<sup>[16]</sup> Diverse environmental conditions, physical factors and interesting geographic regions construct incredibly remarkable eco-systems, giving appropriate habitats

to a large number of species driving vegetation richness. That is the only reason, India is additionally called as the hub of wild medicinal plants. In Indian traditional medicinal framework namely; Ayurvedic, Siddha and Unani maximum number of medications are retrieved from plant species to cure ailments from ancestral period of time to nowadays and have been exploited expeditiously in the market as well.<sup>[17]</sup> Ethnic groups of specific terrains, have their very own cultures, food habits, customs, sacraments and so on where plants play considerable role. Such inhabitants have rich knowledge on customary remedial plants which can be used to fix different infirmities.<sup>[18]</sup> India ranks second after china in providing 80% of crude materials of restorative plant.<sup>[19]</sup> The worldwide production of medicinal plants, which amount to 1150 million USD in the year 2000 is foreseen to be of 5 trillion USD mark before 2050. The trade of medicinal plants in India has been evaluated to be US\$ 1 billion every year. It is assessed that the Indian export of the medicinal plants has doubled from 2010 to 2014.<sup>[20]</sup> Several evidences showed that in Indian subcontinent medical intercessions are being practiced since the time of 7000 BC. Archaeobotanical excavations directed the proof regarding the use of medicinal plants in the Middle Gangetic region of India and are still found in Ayurveda folk medicine. In the Indian medicinal systems namely; Ayurveda, Siddha, Unani, the herbal medicines have their eminent place. Ayurveda, is considered as the most established medicinal system mentioned in the four Vedas written in 500-1000 BC old Indian literature.<sup>[21]</sup> The Domestic trade of Ayurveda, Unani

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and Siddha industry is near 80–90 billion rupees with the estimated export value of 110 billion rupees from medicinal plants and their related items from India.<sup>[22-24]</sup> Early literature shows that South African watermelon (*Citrullus lanatus*) and Linnaeus' watermelon (*Citrullus vulgaris* L.) was the nearest relative or begetter by *C. colocynthis*<sup>[25]</sup> yet herbarium test investigations led by<sup>[26]</sup> along molecular phylogenetic analyses revealed that in actual this was not possible. Besides, what was referred to as "Egusi" melon by<sup>[27-29]</sup> as *Colocynthis citrullus* L., was wrong inversion of the Latin name. Later on<sup>[30]</sup> proved that "Egusi" melon is *Citrullus mucospermus* a species in the past known as *C. lanatus* subsp. *Mucospermus*<sup>[31]</sup> supported by morphological, phonetic analyses<sup>[32]</sup> and genetic studies.<sup>[33]</sup> Jarret and Newman additionally indicated that *C. colocynthis* and *C. mucospermus* grouped independently using internal transcribed spacer (ITS) sequences.<sup>[34]</sup>

## BOTANY

### Taxonomic classification

Kingdom – Plantae  
 Sub kingdom- Tracheobionta  
 Super division- Spermatophyta  
 Division - Magnoliophyta  
 Class - Magnoliopsida  
 Sub- class - Dilleniidae  
 Order - Cucurbitales  
 Family - Cucurbitaceae  
 Genus – *Citrullus*  
 Species epithet- *Colocynthis* (L.) Schrad

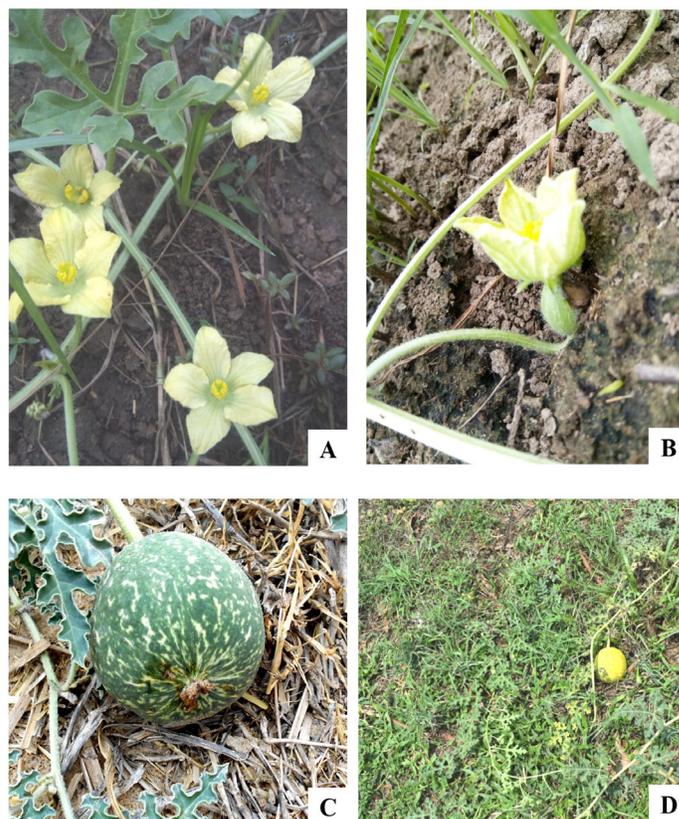
Vernacular Names of the plant in various languages and countries have been listed in Table 1.

### Synonyms

*Colocynthis vulgaris* Schrad.  
*Cucumis colocynthis* L. (basinonym)  
*Citrullus pseudocolocynthis* M. Roem.  
*Colocynthis officinalis* Schrad.<sup>[35]</sup>

### Taxonomic profile and Morphological Characteristics

The family comprises of around 118 genera and 825 species, including both cultivated and wild members<sup>[36]</sup> divided into two subfamilies; Zanonioideae (19 genera and 60 species) and Cucurbitoidae (111 genera and 740 species).<sup>[37]</sup> They are the excellent sources of secondary metabolites like Cucurbitacins, triterpenoids, imparting bitter flavor to the family and furthermore act as an attractant of pollinators like *Diabrotica*.<sup>[38]</sup> *C. colocynthis* is wild, perennial, herbaceous, non-tough, harsh, angular vine with lobular tendrils and is well adapted to the arid climatic conditions. Leaves are alternate, rough, hirsute with upper green and lower pale coloured surface with long petioles, 5-10 cm in length and 3-7 profound lobes. Flowers are monoecious (having subcomplanated five lobed, corolla and five parted calyx) solitary, yellow. Calyx of female flower is larger than that of male flower. Each plant contains 15 to 30 globoid fruits with smooth surface, indehiscent, diameter ranging from 5 to 7.5 cm, assorted with green and yellow strips turns yellow with maturity and ripening.<sup>[39]</sup> Seeds are small about 6 mm in size, brownish, smooth, and caramel when ripened. The plant has very delicate, fleshy and long tap roots.<sup>[40]</sup> About 75 % bulk of the *Citrullus colocynthis* fruit is found to be of seeds.<sup>[41]</sup> [Figure 1]



**Figure 1:** *Citrullus colocynthis* (L.) Schrad, A-B: Flowers; C-D: Fruits.

### Nutritional Value

Palmitic and Stearic acids are the main principle fatty acids found with concentrations ranging from 8.1-17.3% and 6.1-10.5% respectively. High content of essential monounsaturated fat linoleic acid i.e. 50.6–60.1 % in the oil of seed, acts as principle component for the restorative activities. Fat profile of unsaturated fatty acids exposes that the class of linoleic-oleic acid bear a close resemblance to few other vegetable oils. So, it is most likely going to have potential uses of cooking like some other cucurbit seed oils.<sup>[40]</sup> Seeds contain 13.19 g of protein, 18.59 g of fat, 4.91 g of moisture and 2 mg of ash per 100 g. Mineral present in the seeds contain 569 mg of Ca, 465 mg of K, 210 mg of Mg, 30.0 mg of P, 11.9 mg of Na, 11.6 mg of Fe, 5.1 mg of Cu and 1.1 mg of Zn.<sup>[41]</sup>

### Ethnobotanical importance

Most of the tribal areas and rural communities use entire plant but seeds are used to cure Bowel complaints<sup>[42]</sup> Blackness of grey hair<sup>[43]</sup> and;<sup>[8]</sup> Malaria.<sup>[44]</sup> Fruits are used to reduce stomach ache<sup>[45]</sup> Dropsy,<sup>[10]</sup> timely and easy delivery<sup>[46]</sup> Hepatitis,<sup>[12]</sup> Snake poison.<sup>[13]</sup> Roots are applied in the form of paste to enlarge the abdomen and to cure Rheumatism.<sup>[11,13]</sup> More knowledge about ethnobotanical importance of the various plant parts has been enlisted in Table 2.

### Phytochemical studies

Various important chemical constituents are elucidated from entire plant (root, stem, leaves, fruit and seeds) are documented in literature imparting medicinal value to the genus are carbohydrates, proteins, separated, amino acids, alkaloids, flavonoids, terpenoids. Fruits are the main source of drugs. *Citrullus colocynthis* have proved to have several active chemical constituents like colocynthin, colocynthetin, cucurbitacins, á-elaterin,<sup>[53]</sup> cucurbitacines,<sup>[54]</sup> cucurbitacin glycosides,<sup>[55-57]</sup> flavonoids and flavone glycosides.<sup>[57,58]</sup> The well-known bioactive compounds of fruit

**Table 1: Vernacular Names of *Citrullus colocynthis* in different languages.**

Language/ Country	Common Name
English	Colocynth or Vine-of-Sodom <sup>[2]</sup>
Sanskrit	Indravaruni or Brihadvani <sup>[2,7]</sup>
Hindi	Indrayan or Ghorumba <sup>[2,7]</sup>
Bengali	Makhal, Indrayan, Panjot, Indrabaruni <sup>[2,7]</sup>
Telugu	Eti-puchcha <sup>[2]</sup>
Gujarati	Indrayan <sup>[2]</sup>
Malayalam	Paikumatti <sup>[2]</sup>
Marathi	Kadu-indravani <sup>[2]</sup>
Tamil	Paedikari Attutummatti <sup>[2]</sup>
Punjabi	Kaudtumba
Kannada	Hamekkae, Hamekkikayi <sup>[7]</sup>
Urdu	Hanzal, Indyaran, Shahmehinzal <sup>[7]</sup>
Arabic	Handhal <sup>[35]</sup>
French	Coloquinte <sup>[35]</sup>
German	Bitter-melone or Koloquinte <sup>[35]</sup>
Portuguese	Colocintida <sup>[35]</sup>
Spanish	Alhandal or coloquintida <sup>[35]</sup>
Swedish	Kolokvint <sup>[35]</sup>

are cucurbitacins; cucurbitacins E (richly found from pulp), Phenolics, Flavonoids, Fatty Acids, Alcoholic and Ketonic alkyl chains.<sup>[59-61]</sup> These metabolites like phenols, tannins and flavonoids play very important role in defense mechanism against diseases caused by various bacteria and fungi. The major bioactive or principle compounds imparting medicinal values are group of Cucurbitacins i.e cucurbitacin (A, B, C, D, E, J and L) with some other compounds like alkaloids, terpenoids, tannins, saponins, anthranol, caffeic acid, cardiac glycoloids.<sup>[61]</sup> The active compounds such as saponins, sterols, steroids, terpene, flavonoids, tannins and alkaloids were reported from leaves, fruits and roots.<sup>[62]</sup> Alkaloids were found in all plant except roots, while flavonoids were only reported in seeds; steroids were present in all plant parts, while Gallic acid, tannins and cumarins were only reported in leaves. The presence of alkaloids, steroids glycosides and flavonoids were detected from seeds.<sup>[63]</sup> Cucurbitacins, the active compound of family was divided into 12 different classes. Cucurbitacin E was richly isolated from fruit pulp, while from fruit colocynthoside A and colocynthoside B were isolated. Colocynthoside compounds were isolated from methanolic extract of fruits. Various compounds of cucurbitacin i.e d, e, f, g and some flavonoids glucosides such as isovitixin, isorintin and isosapanorin were reported from fruit extracts (butanol).<sup>[40]</sup> Among the all compounds extracted from fruits, cucurbitacin and the glycosides were highly studied and nearly 20 of these were observed to be very highly oxygenated triterpenoides<sup>[41,56,64]</sup> Hydromethanolic extract were reported to shown the presence of alkaloids, tannins, saponins, flavonoids, unsaturated sterols, terpenes, sterols and steroids from fruits, leaves and roots. The amount of alkaloids, tannins, saponins and flavonoids were found to be in very low quantity from leaves.<sup>[62]</sup> The presence of alkaloids, glycosides, terpenoids, tannins, anthraquinol were observed in hexane, ethanol and methanol solvents, while reducing sugars were only present in hexane and ethanol. Flavonoids were only reported in ethanol. Ursolic acids, cucurbitacin E, 2-0-β-D-glycopyranoside, 4-methylqumoline<sup>[65]</sup> were extracted from methanolic extracts of fruits. The hydromethanolic extracts, ether extract, chloroform methanol (1:1) extract, butanol extract of fruits was

**Table 2: Ethnobotanical importance of *Citrullus colocynthis*.**

Uses	Plant part used
To reduce acute stomachache <sup>[45]</sup>	Seed and Fruit
Antibacterial activity <sup>[47]</sup>	Fruit
Abortifacient <sup>[47]</sup>	Fruit
Ascites <sup>[13]</sup>	Roots
Abdominal pain <sup>[47]</sup>	Roots
Amenorrhoea <sup>[47]</sup>	Roots
Boils and carbuncles <sup>[47]</sup>	Roots and raw fruit
Chronic open wounds <sup>[47]</sup>	Roots
To cure biliousness in animals <sup>[48]</sup>	Seeds
To treat bowel Complaints <sup>[45]</sup>	Seeds
Bacterial Infection <sup>[51]</sup>	Roots
Boils and pimple <sup>[11]</sup>	Fruit and root
Cooking purpose <sup>[49]</sup>	Seeds
Cancer <sup>[51]</sup>	Fruit
Constipation <sup>[47]</sup>	Fruit
Cure Bilious <sup>[50]</sup>	Fruit
Constipation and Toxemia <sup>[50]</sup>	Fruit
To cure epilepsy <sup>[14]</sup>	Seeds
Deafness <sup>[47]</sup>	Fruit
Dental caries <sup>[47]</sup>	Fruit
Dropsy <sup>[10]</sup>	Fruit
Diabetes <sup>[51]</sup>	Fruit
Dyspepsia <sup>[47]</sup>	Fruit
Enlarged Abdomen <sup>[11]</sup>	Roots
Easy delivery <sup>[52]</sup>	Roots
Flatulence <sup>[47]</sup>	Fruits
Fever <sup>[51]</sup>	Fruit
Hair growth and blackness of grey hairs <sup>[43]</sup>	Seeds
Hydrocele <sup>[47]</sup>	Roots
Indurations of liver <sup>[47]</sup>	Whole plant
Infertility <sup>[47]</sup>	Roots and ripe fruit pulp
Inflammation of breast <sup>[8]</sup>	Roots
Inflammation of joints <sup>[8]</sup>	8Roots
Jaundice <sup>[47]</sup>	Roots
Leucoderma <sup>[47]</sup>	Leafs
Malaria <sup>[47]</sup>	Seeds
Oedema <sup>[51]</sup>	Fruit
Ophthalmia <sup>[51]</sup>	Roots
Poisonous bites <sup>[51]</sup>	Seeds
Piles <sup>[47]</sup>	Fruit pulp
Rheumatism <sup>[47]</sup>	Roots
Scarcity <sup>[47]</sup>	Seeds
Soup thickening and Flavorings agent <sup>[51]</sup>	Seeds
Syphilis <sup>[47]</sup>	Seeds
Timely and easy delivery <sup>[46]</sup>	Fruit
Urinary Disease <sup>[51]</sup>	Roots
Worms <sup>[51]</sup>	Roots

reported to isolate 3'-O-methyl ether, cucurbitacin glycoside,<sup>[66]</sup> elatericin B, tetrahydroelatericin B, elaterinidell<sup>[67]</sup> cucurbitacin E, I and E, while the chloroform extracts of whole plant constitute compounds cucurbitacin E, cucurbitacin I and cucurbitacin L.<sup>[68]</sup>

Phytochemicals viz. carbohydrates, alkaloids, fatty acids, glycosides, flavonoids and essential oils, have been expounded in the fruit of *Citrullus colocynthis* by various researchers so far. The most widely reported phytochemical is Cucurbitacins, in the family Cucurbitaceae. The property of cytotoxicity of Cucurbitacins appear to take up an essential part in drug discovery, specifically as anti-cancer drug recovery. Cucurbitacin E (compound a) out of all cucurbitacins was exposed abundantly in the extract of fruit pulp, while other major principle compounds like Colocynthiside A (compound b) and Colocynthiside B (compound c), were elucidated in methanol fruit extracts. Other compounds of Cucurbitacins secluded from butanolic extracts were enlisted as; Cucurbitacin L 2-O- $\beta$ -D-glucopyranoside (compound d), hexanocucurbitacin I 2-O- $\beta$ -D-glucopyranoside (compound e), cucurbitacin K 2-O- $\beta$ -D-glucopyranoside (compound f) and khekadaengoside E (compound g), cucurbitacin J 2-O- $\beta$ -D-glucopyranoside (compound h), cucurbitacin I 2-O- $\beta$ -D-glucopyranoside (compound i). The butanol fractions of extracts of whole plant parts of methanol reveals the presence of certain flavonoid glycosides compounds e.g., isoorientin 30-O-methyl ether (compound j), isovitexin (compound k) and isosaponarin (compound l) along two Cucurbitacin glycosides compounds named as 2-O- $\beta$ -D-glucopyranosyl cucurbitacin L and 2-O- $\beta$ -D-glucopyranosyl cucurbitacin I.<sup>[40]</sup> Similarly, the compounds of flavone glucosides and Cucurbitacin glucosides were isolated from the fruit extracts.<sup>[66]</sup>

### Pharmacological activities

The species has shown wide range of activities<sup>[51]</sup> like antioxidant activity<sup>[17]</sup> of phenolic, anti-hyperlipidemic effects of saponins<sup>[69]</sup> anti-fertility by decrease in level of cholesterol<sup>[70]</sup> anti-ulcer activity of flavonoids, saponins, alkaloids and tannins,<sup>[71]</sup> anti-microbial of alkaloids, tannins and flavonoids<sup>[11]</sup> antibacterial by tannins, steroids, flavonoids, alkaloids, irridoids<sup>[72]</sup> and antidiabetic effects by saponins, flavonoids and glycosides.<sup>[73]</sup> The fruit extracts of this plant had  $88.0 \pm 2.7$  % free radical scavenging activity on DPPH radical at a concentration of 2500 mg/mL.<sup>[17]</sup> The pulp and seed extracts of *Citrullus colocynthis* were responsible for reduction of LDL-C in rabbits which had significant reduction ( $p < 0.05$ ). Aqueous extracts of *Citrullus colocynthis* provide antibacterial properties against *E. coli* and *Staphylococcus aureus* and mild effects on *Klebsiella pneumonia* and *Bacillus subtilis*. However, the antibacterial action of methanolic extracts were better against *Bacillus subtilis*, *Salmonella typhi* and *Streptococcus pyogenes*.<sup>[74]</sup> Inhibitory effect of ethanolic extracts were observed against *Staphylococcus aureus*, which is significantly more in comparison to aqueous extracts.<sup>[60]</sup>

### Side effects and toxicity

The teratogenicity of pulp extract of *Citrullus colocynthis* was studied in rats and 20<sup>th</sup> day anatomical perceptions shown maximum percentage of minor size, resorbed or less weight of fetuses. Coccygeal vertebrae, metacarpal, carpal and metatarsal, tarsal bones were reported to be absent and it was supposed that extract of pulp, may develop teratogenic effects at the beginning period of pregnancy.<sup>[75]</sup>

Similarly, Rabbits were also treated with (100 or 200 mg/kg/day) pulp or seed extract. One month later, observations revealed zero animal survival with treatment of 200 mg/kg/day of pulp extract. The specimens treated with 100 mg/kg/day of pulp extract were than sacrificed and organs like small intestine, kidney and liver were studied morphologically and severe lesions were detected reveals the effect of seed and pulp extracts on

rabbits which can be fatal. Interestingly, creatures treated with either 100 or 200 mg/kg/day of seed extract showed just minor intestinal affront. In contrast to seed extract, pulp extract of *Citrullus colocynthis* could be fatal to rabbit.<sup>[76]</sup> Due to the principle secondary metabolite Cucurbitacin glycoside, the drug is extremely noxious and strongly effects the mucous membrane by irritation or pain. Overdose leads to vomiting, bloody diarrhea, colic, kidney irritation and sometimes excessive production of urine move forward to failure of kidney to produce urine. Lethal dosages usually associated with convulsions, paralysis and circulatory collapse follows the intake starting at 2 g.<sup>[77]</sup>

### Anti-microbial activity

Anti-microbial activity of the leaf extract was studied against sixteen bacteria and six fungal strains was correlated with standards (Gentamicin 10 $\mu$ g/disc and piperacillin 100 $\mu$ g/disc). The extracts of water have excessive action against bacterial strain of *Staphylococcus aureus* and *E. coli* on the other hand strains like *Klebsiella pneumoniae* and *Bacillus subtilis* shows a smaller amount of antibacterial action. Best antibacterial actions were found on the extracts of methanol against bacterial strains of *Bacillus subtilis*, *Streptococcus pyogenes*, *Salmonella typhi*.<sup>[1]</sup> The extracts of acetone, ethanol, methanol and water exhibited excessive antimicrobial activity against *E. coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Shigella shigella*, the bacterial strains and *Candida albicans* a fungus. On the other hand, petroleum ether extracts are very less active on all above strains.<sup>[78]</sup> Antifungal activity of hydroalcoholic extracts against *Aspergillus* strains were studied by disc diffusion and broth macrodilution methods indicated sensitivity to the extract. Antifungal activity of *A. niger* and *A. fumigatus* was informed to be very high when compared along the activity of *C. krusei* and *C. guilliermondii*.<sup>[79]</sup>

### Effect on hair growth

Ethanol and petroleum ether plant extracts were smeared on the denuded skin of albino mouse's to observe the growth of hairs and time required for initiation of hair growth. The growth cycle was observed with the use of 2% of Minoxidil solution which was served as standard. Better quantity of hair follicles was observed successfully using extracts as compare to the standards.<sup>[80]</sup>

### Anti-inflammatory and analgesic activities immature fruit and seed

The aqueous extracts of roots, stems, fruits and seeds at several stages of maturation revealed a large number of analgesic and anti-inflammatory activities. Carrageenan-induced paw edema assay and Acetic acid writhing test in mice and rats respectively, were used to detect the pharmacological activities like analgesic and anti-inflammatory from fruit and seed where stem and root extracts of plant have very less inhibitory activity.<sup>[81,82]</sup>

### Hypolipidemic

The examination on the hypolipidemic impact of *C. colocynthis* beyond the hypoglycemic effect on human was considered. It was reported that intake of powdered form of seeds (300 mg per day) by non-diabetic hyperlipidemia patients is very beneficial in reducing triglyceride and cholesterol level.<sup>[83]</sup>

### Mosquito larvicidal activity

The plant shows significant noxious properties against mosquito larvae (*Culex quinquefasciatus*). After twenty-four hours Rahuman observed the death rate of larvae. The maximum death rate was reported by using petroleum ether as a solvent in whole plant. It was reported that Oleic and Linoleic acids were observed potent up to certain extent against

fourth instar larvae of *Anopheles stephensi*, *Aedes aegypti* L. and *Culex quinquefasciatus*.<sup>[84]</sup>

## CONCLUSION

This review supports the remedial capability of the plant. However, these outcomes must be additionally assessed and revalidated by clinical preliminaries experiments. It provides novel ideas to explore all those major principle components responsible for the various significant activities along restorative properties.

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## CONFLICT OF INTEREST

Authors declare that they have no conflict of interest regarding the publication of this research. The research did not involve any human participants and/or animals.

## ABBREVIATIONS

**DPPH:**  $\alpha$ ,  $\alpha$ -diphenyl- $\beta$ -picrylhydrazyl; **LDL-C:** Low-density lipoprotein-cholesterol.

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