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PHARMACOLOGICAL STUDIES OF MEDICINAL PLANT *CITRULLUS COLOCYNTHIS*: A REVIEW

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ABSTRACT: The medicinal plant *Citrullus colocynthis* is very significant for indigenous medicine. The pharmacological effects of root, fruits, seeds, leaves, and the whole *C. colocynthis* have been practiced for the treatment of diseases. Phytochemical screening of the fruits of *C. colocynthis* has observed several bioactive compounds. The glycosides, flavonoids, alkaloids, carbohydrates, fatty acids, and essential oils contain phenolic and flavonoids in the *C. colocynthis* fruit. In current research work, a review on pharmacological study of medicinal plant *C. colocynthis*. Many related research articles were checked and collected in Google Scholar, PubMed, Science direct, the scientific information Database, and Scopus. For the present study purpose, using the terms colocynthis, Indrayan, Garhtumba, and Kharatumba in the title of all articles published to 2021 were observed. This study suggests that the extract of *C. colocynthis* could offer cheaper herbal drugs. The finding of the present research work would be significant, help prepare less costly, eco-friendly herbal drugs to treat various diseases and infections to replace synthetic drugs.

INTRODUCTION: Medicinal plants are very beneficial, self-generating machinery, generating a wide range of valuable bioactive products. Herbal plants have as essential providers of the pharmaceutical, agriculture, and food industries. The crude aqueous and alcoholic extract of medicinal plants was used for *in-vitro* and *in-vivo* antifungal, antimicrobial and anthelmintic treatment against human pathogenic *Escherichia coli*, *Pseudomonas putida* (bacteria), and *Malassezia furfur* (fungus) by using the disc diffusion method.

A glimpse at the present literature discloses that the traditional knowledge alive in ethnomedicinal constitutes yet an untouched resource of potentially useful information for possible deployment in supportable animal health controlling systems in rural and peri-urban societies worldwide. Medicinal plant-based remedies have been used as an alternative to synthetic drugs. Medicinal plant *Citrullus colocynthis* served as a control to anthelmintic activity and various diseases. The present research work would be significant because it will help to prepare less costly, eco-friendly herbal drugs for the treatment of various diseases to replace the synthetic drugs which are currently in use.

1. Phytochemical constituents of *Citrullus colocynthis*: The main chemical constituents of fruit pulp colocynthin (14%), colocynthetin,

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colocynthin (resin), pectin gum. The seed contains albuminoids (6%) and fixed oil (17%)¹⁻³. The antimicrobial activity and antiulcer potential were reported in aqueous and ethanolic extracts of *Citrullus colocynthis*. The antiulcer properties of the *C. colocynthis* extracts may be attributed to the occurrence of phytochemicals like saponins, flavonoids, tannins, and alkaloids present in the medicinal plant extract with different biological activities^{4, 5}. The fruits of *C. colocynthis* are generally used in traditional herbal medicine due to their medicinal properties. The phytochemical analysis of *C. colocynthis* and its parts exposed the presence of alkaloids, Flavonoids, Phenols, Saponins, and Diterpenes. The crude oil from seeds of *C. colocynthis* fruit showed that the major ingredients were mainly free fatty acids, triglycerides, phospholipids, and sterols, along with other minor unidentified constituents⁶⁻¹².

2. Treatment of various diseases by *Citrullus colocynthis*:

The medicinal plant *Citrullus colocynthis* fruits are pungent, bitter, cooling use in treatment for purgative, anthelmintic, antipyretic, carminative, ascites, cures tumors, leucoderma, ulcers, asthma, jaundice, enlargement of spleen, bronchitis, urinary discharges, tuberculosis, dyspepsia, constipation, joints pain anemia, throat diseases, and elephantiasis. The medicinal plant *C. colocynthis* root is useful in urinary, jaundice diseases, ascites, rheumatism, and given in abdominal enlargements and cough and asthmatic attacks of children. The various parts such as fruit or roots of herbal plant *C. colocynthis* with or without nux-vomica are scrubbed into a paste mix with water and used on ulcers and pimples. The paste of the root is applied to the enlargement of the abdomen of children. Ethanol extract of *C. colocynthis* exhibited an antiandrogenic nature, thereby decrease alterable sterility in male albino rats¹³⁻¹⁵.

The *Citrullus colocynthis* leaves extract contains *Cucurbitacin glucosides* that are used in the treatment of human breast cancer cell growth¹⁶. *Cucurbitacin glucosides* display pleiotropic special effects on cells, apoptosis, and causing both cell cycle arrests. The therapeutic value of *Cucurbitacin glucosides* has an important role against breast cancer cells. The efficacy of medicinal plant *Citrullus colocynthis* extracts detected in lipid

profile on Rabbits. The tissue's lipids profiles of the liver and heart muscle displayed similar changes to those noticed in serum lipids. *Citrullus colocynthis* possesses active hyperlipidemic constituents. Medicinal plant *Citrullus colocynthis* scanned for their toxicity against the instar larvae of *Culexquinque fasciatus* (Diptera: culicidae)^{17, 18}.

Methanolic fruit extract of *C. colocynthis* was screened to assess its free radical scavenging effect. The petroleum ether extract of *C. colocynthis* and methanol extract of *M. charantia* was more effective than the other extracts. Various parts of *C. colocynthis* are generally used in the treatment of microbial infections, constipation, edema, cancer, and diabetes. Preliminary phytochemical screening of the plant exhibited the presence of large amounts of phenolic and flavonoids. The occurrence of phenolic compounds prompted us to evaluate their antioxidant activity. The medicinal herbal plant *C. colocynthis* beneficial for the treatment of tumors, diabetic patients, ascites, leucoderma, ulcers, asthma, urethrorrhea, dyspepsia, jaundice, bronchitis, constipation, elephantiasis, and splenomegaly. Fruit extract exhibits nematicidal properties¹⁹. A 2-month clinical trial was observed in 50 types of 11 diabetic patients using the powder of *C. colocynthis*. Diabetes mellitus disease found as one of the most widespread endocrine disorders throughout the world. *Citrullus colocynthis* is one of the most common traditional herbal plants used for diabetes mellitus^{20, 21}.

The herbal medicinal plant *Citrullus colocynthis* used in traditional medicine to treat numerous inflammation diseases. *In-vitro* microbial and anticandidal action observed aqueous and diluted acetone extracts of *C. colocynthis*. Inflammations and immune-related diseases including rheumatoid arthritis are exposed as widespread in the entire globe. The treatments of various diseases are mainly based on the use of synthetic or allopathic drugs in recent years. Experimental observations provide the scientific vision to utilize *Citrullus colocynthis* as an anti-inflammatory, analgesic agent and the anti-cancer effect of alkaloid-rich extract of *C. colocynthis* fruits²²⁻²⁵.

Scientists described depression as multifactorial characters, including brain-behavioral disorders, alteration in the cognitive psychomotor and

emotional process. Many people are worldwide suffering from many illnesses. All these diseases occur in all ages of men and women. This research tries to present a traditional medication in comparison with common chemical antidepressant drugs. This experiment was designed to assess probably the antidepressant effect of *Citrullus colocynthis* fruit extraction²⁶.

Antihyperglycemic activity of *C. colocynthis* fruit pulp was observed in streptozotocin-induced diabetic rats. The few herbal medicinal plant extract have been observed to increase the insulin levels at the same time intervals where there is the highest decrease of glucose. *C. colocynthis* fruit showed antioxidant, antimicrobial, antifungal, hypoglycemic activities, anti-diarrheal activity, and anti-diabetic activity. The leaves and pulp of *C. colocynthis* reduced the heart rate and the force of contraction in isolated rabbit hearts. Some pharmacological effects of an ethanol extract of leaves and the pulp were also evaluated. The effect of *C. colocynthis* seed extracts on glucose homeostasis was studied in normal and diabetic rats. Extracts of seeds had no effect on fasting glucose levels or in the oral glucose tolerance test in normal or diabetic rats. The ethanol extract of the leaves showed a secondary anti-inflammatory activity. At lower doses, however, no anti-inflammatory activity was detected. The mixture of the two plants *C. colocynthis* fruits and *R. stricta* leaves in Najdi sheep, was examined. The immunostimulating activity was tested in polysaccharide extracts of *Anacyclus pyrethrum* (L.), *C. colocynthis* (L.), Schrader, and *Alpinagalanga* (L.) in mice. The extract of *C. colocynthis* showed much weaker and variable immune-stimulating activity²⁷⁻³⁴.

The aqueous extract of *C. colocynthis* fruit was examined for its antimicrobial activity against certain pathogenic fungal and bacterial isolates using the agar well diffusion method. The inhibitory effect of *C. colocynthis* fruit aqueous extract may attribute to active compounds present in the extract³⁵.

The herbal medicinal plant *C. colocynthis* used in the treatment of diabetic disease as a hypoglycemic agent, and it has also been found to use in the treatment of gastrointestinal complaints. *C.*

colocynthis pulps with the seeds were examined for the activity on the lipid profile of hyperlipidemic in the New Zealand rabbits. Hyperlipidemia is a well-known risk factor for numerous illnesses, including atherosclerosis, heart stroke, and vascular diseases^{36, 37}.

Researchers investigated the antimicrobial efficiency of *C. colocynthis* against seven bacteria *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Salmonella typhi*, and *Staphylococcus aureus*. All extracts showed considerably less effectiveness on *Klebsiella pneumoniae* and *Salmonella typhi*. The steroidal compound isolated in petroleum ether extract of *C. colocynthis* Schrader (Cucurbitaceae) fruits. *C. colocynthis* shows antibacterial and anti-candidal properties. All extracts showed activity against all strains. *C. colocynthis* fruit aqueous extracts against *Candida albicans*, *Candida glabrata*, *Escherichia coli*, and *Pseudomonas aeruginosa*^{38, 39}.

The Fruits of *Citrullus colocynthis* L. contain seventeen compounds broadly recognized and divided into five classes: ketones, alcohols, epoxy compounds, hydrocarbons, and an acid. The *C. colocynthis* Schrader fruit is assessed for hair growth activity in androgen-induced alopecia and showed broad-spectrum antimicrobial, anti-inflammatory, anti-diabetic activity, and hepatoprotective activity⁴⁰⁻⁵⁰.

The molluscicidal effect of *Punica granatum* and three wild plants, *Calotropis procera*, *Citrullus colocynthis*, and *Solanum incanum*, were observed on *Biomphalaria arabica*, the intermediate host of *Schistosoma mansoni*, in Saudi Arabia⁵¹.

Citrullus colocynthis was used in the treatment of ophthalmic, neuralgia, migraine, bronchitis, abortifacient, cathartic, purgative, and for the treatment of fever, cancer, amenorrhea, jaundice, leukemia, rheumatism, and tumor. Ethanol and aqueous extract show comparable anthelmintic activity with standard drug albendazole⁵².

The antihelminthic and anti-haemonchosis effects were observed in the *Citrullus colocynthis* fruit and the seed of *Peganum harmala*⁵³. The acaricidal effects of the aqueous - methanolic extracts of *Curcuma longarhizome*, *C. colocynthis* fruit, and

Peganum harmala seed were observed on *Rhipicephalus microplus*. *In-vitro* acaricidal activity of plant *C. longa*, *C. colocynthis*, and *P. harmala* extracts were evaluated against *Rhipicephalus microplus*. Crude aqueous methanol extracts of the three plants *C. longa*, *C. colocynthis*, and *P. harmala* combination were found effective against larvae of ticks⁵⁴.

Based on the ethnobotanical survey, the utilization of herbal medicinal plants by the tribal peoples has been gained importance in the recent past all over the world. In India, a lot of research work has been done at the national and regional levels. Rajasthan is the largest state in India, and this state is rich in ethnic diversity, which shows it the ideal place to work on ethnobotanical work. *C. colocynthis* is a very significant indigenous medicinal plant that is used by different tribes for the treatment of many diseases in Rajasthan. Many recipes of medicinal plant *C. colocynthis* are very important, which are based on the root, fruits, seeds, leaf, and the whole plant are used for the treatment of many diseases. Gallic acid was the first report compound in *Citrullus colocynthis* plant⁵⁵⁻⁵⁷. The effects of aqueous and alcoholic fruit extract of *C. colocynthis* exposed on amphistome *Orthocoelium scoliocoelium* and reported plant-based anthelmintics for their safety and eco-friendly properties. The study discovered that aqueous and alcoholic extracts of *Citrullus colocynthis* were found to be potential sources for novel anthelmintic and justify their ethnoveterinary uses⁵⁸.

The effect of foliar application of amino acid and NAA on the growth, yield, and some phytoconstituents of melon *C. colocynthis*, *Physalis alkekengi*, and *Solanum nigrum* showed strong *in-vitro* antimalarial effects. The presence of anthelmintic and antiplasmodial combinations was discovered in *C. colocynthis* plant extracts⁵⁹⁻⁶². The *in-vitro* anthelmintic effect of alcoholic fruit extract of *Citrullus colocynthis* and albendazole were observed against *Fasciola gigantica* parasites. The research work discovered that alcoholic fruit extracts of *C. colocynthis* are potential sources for innovative anthelmintic and defend their ethnoveterinary uses⁶³. The effectiveness of crude aqueous methanol extracts of *C. colocynthis* fruits elucidate in opposing benzimidazole-resistant gastrointestinal nematode, *Haemonchus contortus*.

The egg hatching assay (EHA) showed that *C. colocynthis* fruit can inhibit egg hatching but not embryonations⁶⁴. The anthelmintic effect of *C. colocynthis* was described on the tegument of *Cotylophoron cotylophorum* by light microscope. The above research work suggests that the herbal medicinal plant *C. colocynthis* could offer cheaper and suitable alternative herbal drugs against various diseases, and anthelmintic drugs in comparison to synthetic drugs. The results of this study will help to prepare the eco-friendly, less costly anthelmintic veterinary drug and socio-economic upliftment of cattle farmers^{65,66}.

Keeping the view of the above-said literature, which has been majorly found, remains silent on the anthelmintic effect of herbal drugs on helminth parasites. Finding the research gaps encouraged me to undertake the current research work on "A review of Pharmacological study of Medicinal plant *Citrullus colocynthis* against various diseases".

The above review of literature proves the importance of natural products, especially plant-derived test substances, in the treatment of various diseased conditions. Despite the rich biodiversity in India and the traditional knowledge available through Ayurveda, Unani, and Homeopathy, the pharmacological exploitation of these medicinal plants has still been limited. However, some of the plants have been extensively investigated; others await thorough investigation. In the present study, the medicinal plant *Citrullus colocynthis* has been screened for various diseases such as anthelmintic effects against paramphistomiasis.

METHODS: The present review was conducted in 2021 by reviewing from international and national search web sides of Google Scholar, Pub Med and Science Direct, scientific information database, and Scopus and collected all full-text research papers published in the English language on the effect of *Citrullus colocynthis* on various diseases, infections, and helminth parasites.

The plant *C. colocynthis* with fruits were collected from the Barmer (Rajasthan). The plant was identified and authenticated by Dr. Asha Arora, Associate Professor, Department of Botany, B. N. University, Udaipur (Rajasthan). The herbarium sheet was prepared and deposited in the department

for future reference and an accession number BNC/11-12/021123 was assigned.

RESULTS: The current research work on pharmacological studies of medicinal plant *Citrullus colocynthis* were revealed on the basis of reviewing full research articles on the *C. colocynthis*.

Distribution of *Citrullus colocynthis*: The *Citrullus colocynthis* Wild and cultivated also found throughout India and Ceylon. It is also indigenous in Arabia, tropical Africa, the Mediterranean region, and West Asia.

Vernacular Names of *Citrullus colocynthis* in India: Sanskrit - Indravaruni, Hindi - Indrayan, English - Colocynth, Bengali - Makhal, Gujarati - Indrayan, Marathi - Kadu- indravani, Telugu - Eti-puchcha, Tamil - Paedikari and Attutummatti, Malayalam - Paikummatti, and Punjabi - Ghurunba.

Ayurveda and Siddha Action: As per Ayurveda and Siddha's system of medicine, *Citrullus colocynthis* is Tikta-rasam, Katuvipakam, Ushnaveeryam, purgative, diuretic, Lagu, kaphaharam, puerperal disorders, abortifacient,

ascites, and dropsy. Oil of seeds is useful for hair growth.

Medicinal Plant *Citrullus colocynthis*: *Citrullus colocynthis* is perennial herbs normally found wild in the sandy lands of North West, Punjab, Sind and Rajasthan, Central and Southern region of India. Also found native in Arabia, Tropical Africa, West Asia, and the Mediterranean region. The scientific name of this medicinal plant is initially Colocynthis Citrullus but is currently classified as *Citrullus colocynthis*. Tendrils are simple, 2-3 fits slender and hairy. Leaves are very variable in size. The length of *C. colocynthis* leaf is 3.8 to 6.3 cm and width is 2.5 cm whereas, the medicinal plant is cultivated in are in large numbers. The Leaf is the pale green color on the above side and ashy color on the beneath side; deltoid margin and scab ride on both surfaces with 5-7 lobed are found. *Citrullus colocynthis* shows the presence of female and male flowers. Fruit are bulbous, slightly depressed; size is 5-7.5 cm in diameter, green in color, and gets white glabrous when ripe. The fruit has dry, spongy and bitter pulp. The size of seeds is 4-6 mm long and pale brown (Fig. 1: A, B, C, and D).

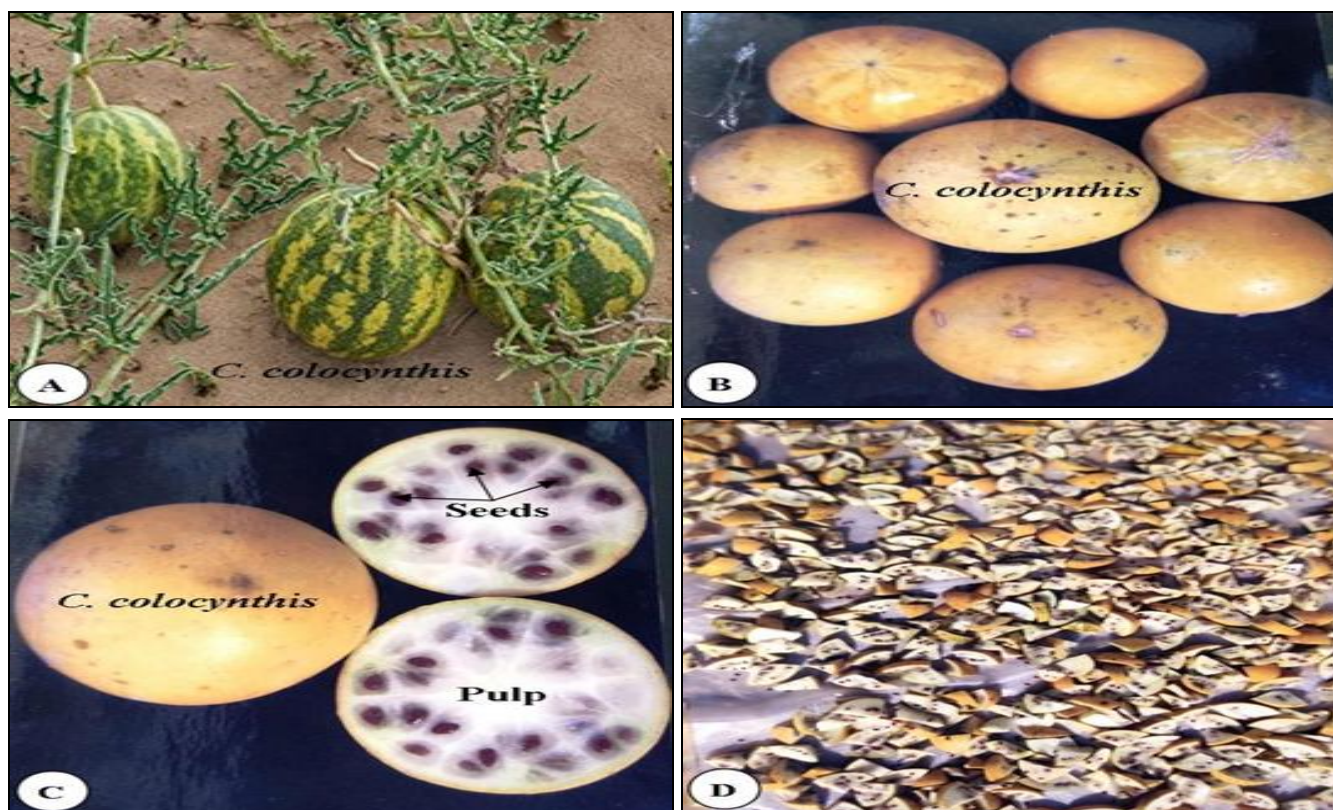


FIG. 1: A - VINE WITH FRUITS OF *CITRULLUS COLOCYNTHIS*., B - FRUITS OF *CITRULLUS COLOCYNTHIS*, C - FRUITS OF *CITRULLUS COLOCYNTHIS* SHOWING PULP AND SEEDS, D - PIECES OF *CITRULLUS COLOCYNTHIS*

Classification of *Citrullus colocynthis* (Bitter Apple):

Kingdom	-	Plantae
Phylum	-	Embryophyta
Class	-	Dicotyledoneae
Order	-	Cucurbitales
Family	-	Cucurbitaceae
Genus	-	<i>Citrullus</i>
Species	-	<i>colocynthis</i>
Local name	-	Indrayan, Garhtumba and Kharatumba

Botanical Description:

Leaf: The leaves have a triangular shape with many clefts. The leaves have a rough, hairy texture with open sinuses. The upper surface of the leaves is fine green in color and the lower surface is comparatively pale. The angular leaves are alternately located on long petioles. The size of each leaf is almost 5 to 10 centimeters in length and has nearby 3 to 7 lobes. Sometimes the middle lobe might have an ovate structure.

Fruit: The ripe fruits are yellow and characterized by a thin but stiff rind. The fruits have soft and white pulp with numerous ovate compressed seeds. Each *Citrullus colocynthis* (bitter apple) plant harvests around 15 to 30 spherical fruits with a diameter of around 7 to 10 centimeters. The outer surface of the fruit is surrounded by green skin with yellow stripes.

Flowers: Flowers are Monoecious; the pistils and stamens are present in different flowers of the same plant. They have long peduncles. Each flower is also comprised of yellow campanulas. The corolla has five lobes, and the calyx is parted five ways. The female flowers are easily identified from the males by their villous and hairy ovaries.

Seed: The seeds are present in the pulp of the fruit, and they are light yellowish-orange to dark brown. The seeds are smooth, compressed, and ovoid-shaped, and the size of seeds is around 6 mm.

Root and Stem: The Bitter Apple plant has a large perennial root that sends out long and slender, angular, hard, rough vine-like stems. The stems are generally spread on the ground and tend to climb over herbs and shrubs by their axillary branching tendrils.

DISCUSSION: Phytochemical screening of the fruits of *Citrullus colocynthis* observed several bioactive compounds. *C. colocynthis* fruit has been grouped as glycosides, flavonoids, alkaloids, carbohydrates, fatty acids, and essential oils exhibited the presence of large amounts of phenolic and flavonoids. The presence of phenolic compounds prompted us to evaluate their antioxidant activity. The fruit extract of *C. colocynthis* has been used for the treatment of elephantiasis, cancer, diabetes, inflammation, jaundice, leucoderma, microbial, edema, ulcer, and urinary diseases^{8, 11, 12, 31, 29, 62-74}.

This study suggests that the extract of fruit pulp of *C. colocynthis* could offer a suitable, eco-friendly, and cheaper herbal drug for treating various diseases and infections such as microbial and antihelminthic compared to synthetic drugs. Consequently, it might help to reduce the occurrence of the parasite in the host environment after treatments. This study will help to socio-economic upliftment of cattle farmers and scientific documentation of traditional veterinary practices.

CONCLUSION: The use of *Citrullus colocynthis* extract offers a new aspect and potential for control of such an ignored infectious disease in ruminants at a time when paramphistomiasis has arisen as an important cause of economic loss. Thus plant-based medicines such as *C. colocynthis* could be used as an efficient anthelmintic in the treatment of paramphistomiasis and various diseases. Thus there is an urgent need to develop new and eco-friendly medicine from the medicinal plant *C. colocynthis* to cure and control the antihelminthic, paramphistomiasis, various diseases, and infections.

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