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Phytochemical analysis and pharmacological spectrum of *Citrullus colocynthis* (L.) Schrad. (Cucurbitaceae)

Prashant Kumar Dhakad, Pramod Kumar Sharma, Sokindra Kumar

INTRODUCTION

Ethno medicinal studies play a major role to highlight the endemic plant species notably for the invention of recent crude medicine. Documentation of native medicinal information of ancient plant species has resulted in development of variety of recent medicine [1]. Medicinal plants are found through varied habitats and landscapes. Rajasthan state is understood for a fashionable floral diversity with 1911 wild species including 780 genera and 154 families. The most skillfully accustomed herbal medicines used by tribes of Rajasthan are plants of Fabaceae, Euphorbiaceae, Asteraceae, Apiaceae, Cucurbitaceae, Acanthaceae, Papaveraceae, Capparidaceae and Solanaceae families [2].

Chemical constituents of plants are of utmost importance for the discovery of therapeutic agents and in establishing the medicinal value of traditional plants [3]. *Citrullus colocynthis* (L.) is a member of family Cucurbitaceae, a xerophyte with huge medicative importance and a decent supply of valuable oil. It is cosmopolitan throughout Asia as well as India. It is normally referred to as bitter apple, or colosynth is employed as an abortifacient, cathartic, purgative and vermifuge, and for the treatment of fever, cancer, amenorrhea, jaundice, leukemia, rheumatism, neoplasm and as an insectifuge. It additionally act as a conventional medicines for inflammatory disease, diabetes, inflammatory disorders, and gastralgia [4].

Citrullus colocynthis is annual or perennial (in wild), herbaceous, bearing monoecious type flowers, pepo fruit and numerous seed. Its fruits are used as robust laxative [5]. This plant produces fruits known as as colocynth apples that are the same as the common *Citrullus vulgaris* and tastes bitter. It possesses solitary sterile flowers and an oversized, fleshy perennial root, that rises to from slender, tough, angular, vine-like stems and branched tendrils [6].

Aqueous pulp extract of *Citrullus colocynthis* fruits is used for treatment of kidney, liver related diseases. Isolated phenolic compounds have antioxidative and antineoplastic properties by absorption and neutralization of free radicals [7]. *Citrullus colocynthis* fruits are known for pain relieving, cathartic, anti-inflammatory, antioxidative, anti-diabetic effects. Cucurbitacins are reported to be the main constituent of fruits of this plant [8]. Infusion prepared from the seed as well as fruit of this plant are indeed recommended to diabetic patients. Since this plant has promising effect on diabetic patients and it is known that antidiabetic plants contains alkaloids, polyphenols, polysaccharides, gums and glycans [9].

This literature survey involves the documentation of data from 1950–2017 from authenticated sources like Google scholar, ScienceDirect and PubMed regarding phytochemical studies and pharmacological activities of various parts of *Citrullus colocynthis* plant. Figure 1 shows the fruits and leaves of *Citrullus colocynthis* lying in desert region while Figure 2 shows the dried fruits and seeds portion of *Citrullus colocynthis* plant.

PHYTOCHEMICAL STUDIES

Isolated compounds ursolic acid and cucurbitacin E 2-O-β-D-glucopyranoside in the methanolic fruit extract of *Citrullus colocynthis* showed antimicrobial activity. In

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an experimentation isolated compounds, cucurbitacin and colocynthis from the ethanolic root extract of this species proved to be hepatoprotective against carbontetra chloride induced toxicity in experimental animals [10].

In an investigation identified with *Citrullus colocynthis* leaf extract two new triterpene glycosides were isolated from an ethyl acetic acid derivation concentrate of leaves of this plant alongside four known cucurbitacins. Compound structures were designed through spectroscopic information utilizing NMR and mass spectrometry. Two new cucurbitacins isolated were-25-p-coumaroyl-3′-acetyl-2-O-β-D-glucocucurbitacin I and 6′-acetyl-2-O-β-D-glucocucurbitacin E. The later coumaroyl cucurbitacin subordinate demonstrated huge particular cytotoxic action towards colorectal cell lines [11].

In an experimental study, the methanolic extract of the *Citrullus colocynthis* plant was divided into fractions soluble in hexane, chloroform, ethyl acetate, butanol, and water. Column chromatography of the ethyl acetic acid soluble fraction showed three new bitter principles named colocynthis A, B and C along with β-sitosterol, 3-O-β-D-glucopyranoside, elaterinide, and bryoamaride, respectively. New compounds were glycosides gave positive Molisch test result, as well as Salkowski and Liebermann–Burchard color reactions for triterpenes.

Figure 1: *Citrullus colocynthis* plant with leaves and fruits in the desert region.

Figure 2: Dried fruits and seeds of *Citrullus colocynthis* plant.

The compound colocynthin A was obtained as grayish indistinct amorphous solid and infrared spectrum showed bands for OH (3400 cm^{-1}), C¼O (1715 cm^{-1}), conjugated C¼O (1680 cm^{-1}), and olefinic (1610–1650 cm^{-1}) functionalities. The HR-FAB-MS (positive-ion mode) gave a $[M+H]^+$ crest at m/z 659.3422, showing the atomic recipe $C_{36}H_{50}O_{11}$, and also a fragment ion $[M-162+H]^+$ at m/z 497.2832 because of the loss of the glucose moiety. Colocynthin B also obtained as grayish formless strong compound. The HR-FAB-MS of Colocynthin B gave signal at 691.3681 $[M+H]^+$, and in conjunction with the ^{13}C-NMR information, the sub-atomic formula decided as $C_{37}H_{54}O_{12}$. Colocynthin C was obtained as a grayish nebulous strong. The atomic equation got as $C_{37}H_{54}O_{11}$ by HR-FAB-MS in the positive-particle mode, which gave an $[M+H]^+$ peak at m/z 675.3732 ($C_{37}H_{55}O^+_{11}$; calc. 675.3744) [12].

In a study conducted in the chloroform portion of the methanol concentrate of *C. colocynthis* natural products, dynamic constituent was isolated by silica gel segment chromatography and preparative HPLC. Structural analysis was done using spectroscopy including EI/MS, ^1H NMR, ^{13}C NMR, COSY, DEPT, and HMQC NMR and then by direct comparison with an authentic reference compound. The dynamic compound segregated was 4-methylquinoline. Spectroscopy detailed around 4-methylquinoline ($C_{10}H_9N$); EI/MS (70 eV) m/z M^+ 143 (100, base peak), 135 (40), 105 (39), 107 (40), 79 (46), 51 (13); ^1H NMR (CD_3 OD, 600 MHz) δ 2.61 (s), 7.26–7.27 (d, J = 6.7 Hz), 7.42–7.43 (t, J = 6.9 Hz), 7.63–7.75 (t, J = 83.1 Hz), 8.00–8.05 (d, J = 35.7 Hz), 8.09–8.11 (d, J = 7.3 Hz), 8.42– 8.43 (d, J = 1.6 Hz); ^{13}C NMR (CD_3OD, 150 MHz) δ 150.6, 148.2, 135.5, 130.0, 128.5, 128.1, 126.5, 124.4, 122.9, 19.6 [13].

Amid the examination of *Citrullus colocynthis* in vivo (leaf, stem, fruit and root) and in vitro callus a flavonoid quercetin was obtained. Rf value (0.82) of quercetin separated from extract samples resembles the Rf value of standard quercetin and in addition characteristic infrared spectral peaks were superimposable with individual standard reference mixes of quercetin. The HPLC parameter showed retention time of 3.475 min which matched with that of standard quercetin. Quercetin was present both in vivo and in vitro samples of *Citrullus colocynthis* [14].

In an investigation the reversed-phase preparative investigation of the butanol portion of the methanol concentrate of *C. colocynthis* fruits gave three flavonoid glycosides, isosaponarin, isovitexin and isoorientin 3'-O-methyl ether and two cucurbitacin glucosides, 2-O-β-D-glucopyranosylcucurbitacin L and 2-O-β-D-gluco-pyranosylcucurbitacin I. An ESIMS mass spectrum of isosaponarin showed [M+H]+ (positive ion mode) ion peak at m/z 595, M_r = 594 and obtained molecular formula as $C_{27}H_{30}O_{15}$. An ESIMS mass spectrum of isovitexin obtained as $[M+H]^+$ ion peak at m/z 433, M_r = 432 and $C_{21}H_{20}O_{10}$. An ESIMS mass range of isoorientin 3'-O-methyl ether demonstrated $[M+H]^+$ ion peak at m/z

463, M_r = 462 and $C_{22}H_{22}O_{11}$. While ESIMS mass range of 2-O-β-D-gluco-pyranosylcucurbitacin I gave $[M+H]^+$ (positive ion mode) particle peak at m/z 677, suggesting M_r = 676 and understanding for $C_{36}H_{52}O_{12}$ and ESIMS mass spectrum of 2-O-β-D-glucopyranosylcucurbitacin L demonstrated $[M+H]^+$ (positive ion mode) ion peak at m/z 679,Mr = 678 and $C_{36}H_{54}O_{12}$ [15].

The chloroform concentrate of the defatted *Citrullus colocynthis* plant was fractionated to result four glycosides as, 2-O-β-D-glucopyranosyl-cucurbitacin E, 2-O-β-D-glucopyranosyl-cucurbitacin I as the major product, 2-O-β-D-glucopyranosyl-cucurbitacin L and a novel glycoside 2-O-β-D-glucopyranosyl-(22-27)-hexanorcucurbitacin I. Structural studies of cucurbitacins were done using ^{1}H and ^{13}CNMR spectra. The NMR spectra of first three compounds resemble with free aglycones while EIMS spectra for same compounds did not deliver noticeable parent particles. But FABMS showed observable parent ions either: as $[M+1]^+$ or $[M + Na]^+$ ions. The spectral evidence lead to the structural assignment of 2-O-B-D-glucopyranosyl-(22-27)-hexanorcucurbitacin I, which was the only degraded cucurbitacin glycoside reported till 1988. This compound was isolated as an amorphous powder, and investigation demonstrated a sub-atomic particle crest at m/z 585 $[M (C_{30}H_{42}O_{10}) + Na]^+$ in the FAB mass spectrum, and ketonic carbonyl absorption (1690 cm^{-1}) in the infrared spectrum [16].

In this study alcoholic concentrate of *Citrullus colocynthis* was extracted with chloroform and the product of this extraction after maintaining the pH 5.2–5.4 and addition of elaterase enzyme showed the formation of elaterin in the sediment. Further experimental studies segregated a white crystalline substance distinguished as Elatericin B (II) (cucurbitacin I). Thereafter two more compounds were isolated as dihydroelatericin B (III) and tetrahydroelatericin B (IV) with petroleum ether and ether. A yellow substance solidified out of from ether solution distinguished as the glycoside elaterinide ll [17].

During the gas chromatography-mass spectrometry spectral investigation of methanolic extract of *Citrullus colocynthis* 33 bioactive phytochemical compounds were obtained by investigating the retention time molecular weight, peak area and molecular formula. Spectral analysis of *C. colocynthis* revealed the existence of the methyl 6-oxoheptanoate, hexanoic acid, 2-isopropyl-2-methyl-5-oxo-, methyl ester, dodecanoic acid, 3-hydroxy, benzofuran,2,3-dihydro, 1,1-cyclopropanedimethanol, 2-methyl-α-phenyl, 1,1-cyclopropanedimethanol, 2-methyl-α-phenyl, 12,15-octadecadiynoic acid, methyl ester, (5ß)pregnane-3,20ß-diol, 14α,18α- [4-methyl-3-oxo-(1-oxa-4-azabutan, 3-N,Ndimethyllaurylammonio) propanesulfonate, 2H-1-benzopyran-3,4-diol,2-(3,4-dimethoxyphenyl)-3,4dihydro-6-met, 11,13-dihydroxy-tetradec-5-ynoic acid, methyl ester, cyclopenta [1,3] cyclopropa [1,2] cycloheptan-3(3aH)-one,1,2,3b,6,7, 4-(2,4,4-trimethyl-cyclohexa-1,5-dienyl)-but-3-en-2-one, 1-tetradecanamine,N,N-dimethyl, α-D-glucopyranoside, O-α-D-glucopyranosyl-(1,fwdarw.3)-ß-D-fructo, acetamide, N-methyl-N-[4-(3-hydroxypyrrolidinyl)-2-butynyl]-,9-octadecenamide,(z)-,butyrophenone,2´,3,4´,6´-tetramethyl-,ethyl 5,8,11,14,-eicosatetraenoate, 9,12,15-octadecatrienoic acid, 2,3,-dihydroxypropyl ester, (Z,Z,Z)-,1H-cyclopropa [3, 4] benz [1,2-e] ezulene-5,7b,9,9a 476.241018tetrol,1a,1b,4,4a, 9,12,15-octadecatrienoic acid, 9,10-Secocholesta-5,7,10(19)-triene-3,24,25,-triol,(3ß,5Z,7E)-,9,12,15-octadecatrienoic acid, 2,3-dihydroxypropyl ester, (Z,Z,Z)-, triazido-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-german, ethyl iso-allocholate, α-N-Normethadol, octadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester, phthalic acid, decyl oct-3-yl ester, 1,2-benzenedicarboxylic acid, bis-(8-methylnonyl)ester, phthalic acid, di(6-ethyl-3-octyl) ester, y-tocopherol, 1,4-ethanonaphthalene -6,9(4H)-dione,1,4a,5,8a-tetrahydro-4,5,7,10 and vitamin E [6].

In this study the chromatographic purification obtained from *C. colocynthis* fruits extract resulted in cucurbitacin E and cucurbitacin I glycosides. These compounds demonstrated promising outcomes against in vitro cytotoxic action against hepatoma cell line (HepG2) and mice-bearing tumor of Ehrlich's ascites carcinoma (EAC). The in vivo study showed the tendency of both compounds prolonging the survival time, life span and normalize the biochemical parameters of the infected mice with EAC. The two compounds had strong inhibitory effect onHepG2 with IC50 3.5 and 2.8 nmol/ml individually [18].

During investigation of *Citrullus colocynthis* fruits using different solvents (n-hexane, methylene chloride, chloroform and ethanol) showed the presence of six compounds, and the most bottomless of them had retention time (Rt.) 4.8 min. (69.3%). This compound was purified by utilizing Florisil® column section stepwise eluted with various blends of methanol: chloroform. Mass examination of the compound demonstrated the atomic particle peak at m/z 719. The elemental analysis demonstrated molecular recipe to be $C_{38}H_{55}O_{13}$ and I.R., proton and ^{13}C NMR analysis recognized the compound as 2-O-β-D-glucopyranosylcucurbitacin E [19].

PHARMACOLOGICAL ACTIVITIES

Traditional uses

Citrullus colocynthis (Linn.) Schrad is an imperative therapeutic plant of Cucurbitaceae family. It is recognized plant in the ethnical medicine and was utilized by individuals in country zones as a laxative, anti-diabetic and bug spray. *Citrullus colocynthis* has a valuable impact in sciatica and gout. It is valuable as douche during colic, sciatica, spinal pain, and loss of motion distresses. *C. colocynthis* oil obtained by boiling pulp with sesame or olive oil is externally used for ear pains, tinnitus, toothache, and male pattern baldness. The leaf of *C.*

colocynthis has laxative impact and furthermore utilized as a part of epilepsy. External application of leaf of this plant is useful in treating inflammation and bleeding. The root goes about as a powerful antitoxin for scorpion and snail nibbles. The most popular traditional use of *C. colocynthis* fruits and seeds is in diabetes treatment [20].

Antioxidant activity

Methanolic fruit extract of *Citrullus colocynthis* showed the total phenolic content as 0.74% of gallic acid equivalents of phenolic and the total flavonoid content as 0.13% of catechin equivalents. The free radical scavenging effect of fruit extract of this plant on the 2,2-diphenyl-1-picrylhydrazyl radical found to be 88.0±2.7% ($p < 0.005$), at concentration of 2500 $mgmL^{-1}$ while scavenging effects of ascorbic acid, BHA and α-tocopherol found to be 50 $mgmL^{-1}$ of 89.5±1.1, 83.2±1.1 and 67.5±0.8% ($p < 0.05$) respectively. The level of H_2O_2 scavenging action of was observed to be 62.7±3.5 ($p < 0.001$) at 2500 mg mL^{-1}, and antioxidant activity of BHA and α-tocopherol was 89.3±3.1% ($p < 0.05$) and 94.5±2.5% ($p < 0.05$), respectively with concentration 50 mg mL^{-1}. The most astounding antioxidative and free radical scavenging capacity of the fruit extract was seen at 2500 mg mL^{-1} concentration [21].

Antihyperlipidemic effect

Citrullus colocynthis pulp and the seeds were investigated for the antihyperlipidemic effects on New Zealand rabbits. The hypercholesterolemic regimen of *Citrullus colocynthis* essentially expanded the measure of LDL-C, blood cholesterol, triglyceride, HDL-C and glucose ($p<0.05$). The reduction of low density lipoprotein-cholesterol in the groups administered with pulp extracts and 100 mg/kg of seed extract found significant ($p<0.05$). High density lipoprotein-cholesterol decrease was found in the groups administered with diet containing the standard regimen, along with cholesterol (0.5%) and 100 mg/kg of *Citrullus* pulp extract as well as with diet having standard treatment, with cholesterol (0.5%) and 100 mg/kg of *Citrullus* seed extract. The impact of *C. colocynthis* on the blood lipid profile in rabbits might be because of high measures of saponins in *C. colocynthis* which diminished cholesterol levels by lessening the ingestion of cholesterol, expanding the repulse of feces estriol, and looseness of the bowels because of expanded peristalsis. In this trial, the utilization of *C. colocynthis* came about huge diminishment of total serum cholesterol and LDL-C in groups administered with extracts [22].

Antifertility effects

The present investigation of *C. colocynthis* 50% ethanolic extract suppresses sperm density and motility and fertility of rats. But fruit extract administration showed a serious and reversible restraint of sperm fertility and density. The sperm density approached to around 10 million/mm^3 in all treatment groups as compared to 46.5 million/mm^3 in the vehicle-treated group. The weights of testicles, epididymis, original vesicles, and ventral prostate extraordinarily decreased after *C. colocynthis* treatment in the different groups due to the antiandrogenic nature of the drug recommending androgen imbalance and inhibition of the androgen generation by the testicles. Hence 50% ethanol extract of *C. colocynthis* fruit actuated reversible antifertility activity in male rats because of antiandrogenic nature [23].

Antiulcer activity

The present examination explored the antiulcer capability of ethanolic and aqueous extracts of *Citrullus colocynthis* plant. Ethanolic and aqueous extracts at 400 mg/kg indicated noteworthy ($p<0.001$) diminish in the total acidity, free acidity and gastric volume. The pH of the gastric juice significantly ($p<0.001$) ascended at the dose of 400 mg/kg. It indicated additionally significant ($p<0.001$) diminish in number of ulcer score index & ulcers using pylorus ligation ulceration model. *Citrullus colocynthis* fruit extracts exhibited a significant antiulcer activity in experimental male Wistar rats. Ethanolic extract indicated preferable hostile than aqueous extract [24].

Anticonvulsant activity

This examination researched the *Citrullus colocynthis* fruit extract as anticonvulsive in the treatment of seizures. Pentylenetetrazole induced convulsions were made in albino mice pretreated with fruits extract of 10, 25, 50, and 100 mg/kg dose. 25 and 50 mg/kg of hydroalcoholic extract delayed the beginning of seizures and diminished the duration in comparison to control group. *Citrullus colocynthis* pulp extract demonstrated a measurable significant reduction in the seizures term and increment in latency period of seizures instigated by pentylenetetrazole in mice. Anticonvulsive effect increased dose dependently with following doses 10, 25, and 50 mg/kg. The primary activity of the pentylenetetrazole-instigated seizure is diminishing Ɣ-aminobutyric acid level in the cortex [8].

Antimicrobial effect

Antimicrobial effect of aqueous extract of the *Citrullus colocynthis* demonstrated high antibacterial action against *Staphylococcus aureus* and *E. coli* and significantly less impact against *Klebsiella pneumoniae* and *Bacillus subtilis*. While, methanolic extracts of this plant showed significant antibacterial action against *Bacillus subtilis*, *Streptococcus pyogenes*, *Salmonella typhi*, considerably less activity against Streptococcus faecalis and there was no impact against *Proteus vulgaris*, *Vibrio cholera* and *Proteus mirabilis*. The methanolic extract also indicated high antifungal activity against

Aspergillus fumigatus, *Mucor* sp., and *Aspergillus flavus*, *Candida albicans*, *Penicillium* sp., and *Rhizopus* sp. did not demonstrated any antifungal action. The outcomes acquired in the investigation propose the antimicrobial role of *Citrullus colocynthis* in treating diseases caused by the test organisms [25].

Antifungal activity

The study assessed the antifungal action of hydroalcoholic extract of *Citrullus colocynthis* fruits against various *Aspergillus* and *Candida* strains. Activity was determined utilizing broth of macrodilution and disc diffusion methods. All tested parasitic strains indicated sensitivity to the extract. The growth restraint value of the fruits extract indicated high antifungal action against *A. niger* and *A. fumigatus* and a lesser impact against *C. krusei* and *C. guilliermondii*. The minimum fungicidal concentration (MFC) and minimal inhibitory concentration (MIC) values ranged from 3.125–25 mg/ml and 1.56–12.5 mg/ml respectively [26].

Antibacterial activity

In the present examination, the antibacterial effect of *Citrullus colocynthis* was studied. The antibacterial activity of *Citrullus colocynthis* fruits and leaves extracts against standard (ATCC 25923) and isolated strains of *Staphylococcus aureus* from novobiocin treatment patients were assessed utilizing disc diffusion method. The inhibitory impacts of these extracts were compared to novobiocin (standard antibiotic). The ethanolic extract indicated inhibitory activity as compared to aqueous extract against *S. aureus*. 5 mg/mL fruits ethanolic extract demonstrated comparative inhibitory impact with novobiocin against standard strain. The present research proposed that one of the concoction segments in ethanolic concentrate, for example, alkaloids, flavonoids and glycosides had an intense antibacterial impact significantly more than novobiocin, particularly against hospital isolated strains [27].

Insecticidal activity

A glycoside Cucurbitacin E separated from *Citrullus colocynthis* was examined for insecticidal activity against *Aphis craccivora* with extraction with extraction acquired from various solvents like methylene chloride, chloroform 50, ethanol and *n*-hexane. The ethanolic extract demonstrated the most noteworthy insecticidal effect (LC 11003 ppm) against *A. craccivora*. After further extraction of the deposit staying after vanishing of ethanolic extract with nine solvents, the butanol portion demonstrated the most noteworthy insecticidal effect (LC3123.10 ppm). This insecticidal strength of *C. colocynthis* extract is because of the presence of active ingredients like glycosides, saponin, and alkaloids. Overall analysis, conclude that this compound showed an insecticidal effect against *Aphis craccivora* [19].

Antibacterial and anticandidal activity

Citrullus colocynthis aqueous and diluted acetone extracts of stems, roots, leaves and maturation stages of its seeds and fruit) demonstrated activity against every single microbial strain such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Escherichia coli* and different *Candida* spp. i.e., *Candida krusei*, *Candida parapsilosis*, *Candida albicans* and *Candida glabrata*. The most elevated minimum inhibitory concentration (MICs) and minimum bactericidal concentration (MBCs) were obtained from the fruit aqueous extracts (MIC 0.20 mg/ml against *Escherichia coli* and *Pseudomonas aeruginosa* and 0.10 mg/ml against *Candida albicans* and *Candida glabrata*) and obtained lowest activity from the plant root extracts [28].

Hypoglycemic activity

A study showed presence of saponin glycosides, triterpenoids, alkaloids, flavonoids and resins in aqueous extract of roots of *Citrullus colocynthis* which lessened the glucose level (58.70%) when compared with ethanolic (36.60%) and chloroform (34.72%) extracts ($p< 0.01$). Assumed mechanism behind the lessening in the blood glucose levels of diabetic rats treated with the extracts is due to stimulation of residual pancreatic mechanism or by increment in fringe use of glucose. The water extracts of *Citrullus colocynthis* enhanced the parameters like serum urea, body weight, serum creatinine and serum protein additionally lipid profile and furthermore reestablished the serum level of bilirubin add up to serum glutamate oxaloacetate transaminase (SGOT), conjugated bilirubin, serum glutamate pyruvate transaminase (SGPT) and antacid phosphatase [29].

Antihyperglycaemic effect

Oral dosage of aqueous extract of *Citrullus colocynthis* (300 mg/kg) in normal rabbits produced noteworthy decrease in plasma glucose after 1 h and exceptionally huge after 2, 3 and 6 h. The hypoglycemic impacts of tertiary and quaternary alkaloids, glycoside and saponin segments introduce in this plant at a measurements (50 mg/kg p.o) were studied in normoglycemic rabbits. The alkaloidal extract did not essentially bring down the blood glucose levels while the glycosidic extract fundamentally brought down the fasting glucose levels after 2 and 3 h and exceptionally huge after 6 h. The action was more articulated with saponin extract which decreased the glucose levels (fasting) after 1 and 2 h and significantly ($p<0.001$) after 3 and 6 h [30].

Antidiabetic activity

Antidiabetic action of petroleum ether fruits extract of *Citrullus colocynthis* against Streptozotocin initiated hyperglycemic rats was assessed after oral administration of two distinct doses (300 and 500 mg/

kg) of *Citrullus colocynthis*. Additionally subacute impact i.e., antihyperglycemic effect was seen on seventh and in addition day-14 of the analysis. Administration of petroleum ether extract of *Citrullus colocynthis* fundamentally enhanced body weight of diabetic rats in a dose and time dependent manner. The total hemoglobin and glycosylated hemoglobin levels ($p < 0.01$) was also restored by administration of extracts. The investigation reported that petroleum ether extract of *Citrullus colocynthis* demonstrated critical pharmacological action towards bringing down blood glucose in diabetes [31].

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Keywords: Cucurbitaceae family, Cucurbitacins, Phytochemistry, Pharmacological activites

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Guarantor
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Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES

1. Mahmood A, Mahmood A, Malik RN, Shinwari ZK. Indigenous knowledge of medicinal plants from Gujranwala district, Pakistan. J Ethnopharmacol 2013 Jul 9;148(2):714–23.
2. Upadhyay B, Parveen, Dhaker AK, Kumar A. Ethnomedicinal and ethnopharmaco-statistical studies of Eastern Rajasthan, India. J Ethnopharmacol 2010 May 4;129(1):64–86.
3. Uma C, Sekar KG. Phytochemical analysis of a folklore medicinal plant *Citrullus colocynthis* L (bitter apple). Journal of Pharmacognosy Phytochemistry 2014;2(6):195–202.
4. Khatri T, Pada R, Vijay R, Khokhani K, Viresh Shah V. Tracking bioactive Content in butanol extract of *Citrullus colocynthis* L. fruit pulp by GC/MS. International Journal of Pharmaceutical Research & Analysis 2013;3(2):67–70.
5. Dar AI, Saxena RC, Bansal SK. Hepatoprotection: A hallmark of *Citrullus colocynthis* L. against paracetamol induced hepatotoxicity in swiss albino rats. IJPS 2012;3:1022–7.
6. Idan SA, Al-marzoqi AH, Hameed IH. Spectral analysis and anti-bacterial activity of methanolic fruit extract of *Citrullus colocynthis* using gas chromatography-mass spectrometry. Afr J Biotechnol 2015;14(46):3131–58.
7. Salama HMH. Alkaloids and flavonoids from the air dried aerial parts of *Citrullus colocynthis*. J Med Plants Res 2012;6(38):5150–5.
8. Mehrzadi S, Shojaii A, Pur SA, Motevalian M. Anticonvulsant activity of hydroalcoholic extract of *Citrullus colocynthis* fruit: Involvement of benzodiazepine and opioid receptors. J Evid Based Complementary Altern Med 2016 Oct;21(4):NP31–5.
9. Shawkey AM, Rabeh MA, Abdellatif AO. Biofunctional molecules from *Citrullus colocynthis*: An HPLC/MS analysis in correlation to antimicrobial and anticancer activities. Advances in Life Science and Technology 2014;17:51–61.
10. Jamuna S, Karthika K, Paulsamy S. Phytochemical and pharmacological properties of certain medicinally important species of Cucurbitaceae family: A review. J Res Biol 2015;5(6):1835–49.

11. Chawech R, Jarraya R, Girardi C, et al. Cucurbitacins from the leaves of *Citrullus colocynthis* (L.) Schrad. Molecules 2015;20(10):18001–15.
12. Taylor P, Nayab D, Ali D, Arshad N, Malik A, Choudhary MI, Ahmed Z. Cucurbitacin glucosides from *Citrullus colocynthis*. Natural Product Research 2006;20(5):409–13.
13. Jeon JH, Lee HS. Biofunctional constituent isolated from *Citrullus colocynthis* fruits and structure-activity relationships of its analogues show acaricidal and insecticidal efficacy. J Agric Food Chem 2014 Aug 27;62(34):8663–7.
14. Meena MC, Patni V. Isolation and identification of flavonoid "Quercetin" from *Citrullus colocynthis* (Linn.) Schrad. Assin J Exp Sci 2008;22:137–42.
15. Delazar A, Gibbons S, Kosari AR, et al. Flavone C-glycosides and cucurbitacin glycosides from *Citrullus colocynthis*. DARU 2006;14(3):109–14.
16. Hatam NAR, Whiting DA, Yousf NJ. Cucurbitacin glycosides from *Citrullus colocynthis*. Phytochemistry 1989;28(4):1268–71.
17. Lavie D, Will D, Merenlender Z. Constituents of *Citrullus colocyinthis* (L.) Schrad. Phytochemistry 1964;3(1):51-6.
18. Ayyad SE, Abdel-Lateff A, Alarif WM, Patacchioli FR, Badria FA, Ezmirly ST. In vitro and in vivo study of cucurbitacins-type triterpene glucoside from *Citrullus colocynthis* growing in Saudi Arabia against hepatocellular carcinoma. Environ Toxicol Pharmacol 2012 Mar;33(2):245–51.
19. Torkey HM, Azeiz AZA. Insecticidal effect of cucurbitacin E glycoside isolated from *Citrullus colocynthis* against *Aphis craccivora*. Australian Journal of Basic and Applied Sciences 2009;3(4):4060–6.
20. Rahimi R, Amin G, Reza M, Ardekani S. A Review on *Citrullus colocynthis* Schrad: From traditional Iranian medicine to modern phytotherapy. The Journal of Alternative and Complementary Medicine 2012;18(6):551–4.
21. Kumar S, Kumar D, Manjusha, Saroha K, Singh N, Vashishta B. Antioxidant and free radical scavenging potential of *Citrullus colocynthis* (L.) Schrad. methanolic fruit extract. Acta Pharm 2008;58(2):215–20.
22. Zamani M, Rahimi AO, Mahdavi R, et al. Assessment of anti-hyperlipidemic effect of *Citrullus colocynthis*. Rev Bras Farmacogn 2007;17(4):492–6.
23. Chaturvedi M, Mali PC, Ansari AS. Induction of reversible antifertility with a crude ethanol extract of *Citrullus colocynthis* Schrad fruit in male rats. Pharmacology 2003;68(1):38–48.
24. Reddy VP, Sudheshna G, Afsar SK, et al. Evaluation of anti-ulcer activity of *Citrullus colocynthis* fruit against pylorus ligation induced ulcers in male wistar rats. Int J Pharm Pharm Sci 2012;4(2):446–51.
25. Gurudeeban S, Rajamanickam E, Ramanathan T, Satyavani K. Antimicrobial activity of *Citrullus colocynthis* in gulf of mannar. Int J Curr Res 2010;2:78–81.
26. Eidi S, Azadi HG, Rahbar N, Mehmannavaz HR. Evaluation of antifungal activity of hydroalcoholic extracts of *Citrullus colocynthis* fruit. J Herb Med 2015;5(1):36–40.
27. Najafi S, Sanadgol N, Nejad BS, Beiragi MA, Sanadgol E. Phytochemical screening and antibacterial activity of *Citrullus colocynthis* (Linn.) Schrad against *Staphylococcus aureus*. J Med Plants Res 2010;4(22):2321–5.
28. Marzouk B, Marzouk Z, Décor R, et al. Antibacterial and anticandidal screening of Tunisian *Citrullus colocynthis* Schrad. J Ethnopharmacol 2009 Sep 7;125(2):344–9.
29. Agarwal V, Sharma AK, Upadhyay A, Singh G, Gupta R. Hypoglycemic effects of *Citrullus colocynthis* roots. Acta Pol Pharm 2012 Jan–Feb;69(1):75–9.
30. Abdel-Hassan IA, Abdel-Barry JA, Tariq Mohammeda S. The hypoglycaemic and antihyperglycaemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. J Ethnopharmacol 2000 Jul;71(1–2):325–30.
31. Jayaraman R, Arihara Shivakumar A, Anitha T, Joshi VD, Palei NN. Antidiabetic effect of petroleum ether extract of *Citrullus colocynthis* fruits against streptozotocin-induced hyperglycemic rats. Rom J Biol-Plant Biol 2009;54:127–34.

SUGGESTED READING

- Amnon L, Claude ET, Anthony PK, Todd C. Wehner. Genetic diversity among watermelon (*Citrullus lanatus* and *Citrullus colocynthis*) accessions. Genetic Resources and Crop Evolution 2001;48:559–66.
- Boulos L. Flora of Egypt, volume two. Cairo, Egypt: Al Hadara Publishing; 2000. p. 140.
- Dafni A, Yaniv Z, Palevitch D. Ethnobotanical survey of medicinal plants in Northern Israel. J Ethnopharmacol 1984;10:295–310.
- Mahla HR, Singh JP, Roy MM. Seed Purpose Watermelon in Arid Zone. Central Arid Zone Research Institute, Jodhpur. 2014:44.
- Shah AH, Qureshi S, Tariq M, Ageel AM. Toxicity studies on six plants used in the traditional Arab system of medicine. Phytotherapy Research 1989;3(1):25–9.
- Soliman MA, El Sawy AA, Fadel HM, Osman F, Gad AM. Volatile components of roasted *Citrullus colocynthis* var. colocynthoides. Agr Biol Chem Tokyo 1985;49:269–75.