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Citrullus colocynthis (Bitter-apple): a comprehensive review on general properties, biological activities, phenolic and chemical contents

Mustafa SEVINDIK[1,2], Imran UYSAL[3], Emre SEVINDIK[4]*, Tetiana KRUPODOROVA[5], Oğuzhan KOÇER[6], Orhan ÜNAL[7]

[1]*University of Osmaniye Korkut Ata, Faculty of Engineering and Natural Sciences, Department of Biology, Osmaniye, Türkiye; sevindik27@gmail.com*
[2]*Western Caspian University, Department of Life Sciences, Baku, Azerbaijan*
[3]*University of Osmaniye Korkut Ata, Bahçe Vocational School, Department of Food Processing, Osmaniye, Türkiye; imranuysal@osmaniye.edu.tr*
[4]*Department of Agricultural Biotechnology, Faculty of Agriculture, Aydın Adnan Menderes University, Aydın, Türkiye; ph.d-emre@hotmail.com (*corresponding author)*
[5]*Institute of Food Biotechnology and Genomics, National Academy of Sciences of Ukraine, Ukraine; krupoduorova_ta@nas.gov.ua*
[6]*Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Pharmacy Services, Osmaniye, Türkiye: oguzhankocer@osmaniye.edu.tr*
[7]*Akdeniz University, Faculty of Science, Department of Biology, Antalya, Türkiye; ounal@akdeniz.edu.tr*

Abstract

Plants display several biological activities as a result of the production of various chemicals inside their metabolic processes. In recent times, the growing prevalence of alternative medicine uses has elevated the significance of plants. The present work aimed to assess the biological activities, phenolic and chemical compositions, applicability, mineral composition, and overall characteristics of *Citrullus colocynthis* (L.) Schrad. as documented in existing literature. Literature study revealed that it possesses significant antioxidant, antibacterial, and anticancer properties. Furthermore, it has been observed that it may serve as a potential reservoir for the minerals documented inside its structure. It is also thought to be an important source, especially in terms of potassium. From this perspective, it became evident that the fruit components of the plant, in particular, could serve as a significant natural resource for promoting health.

Keywords: Abu Jahl's melon; antimicrobial; antioxidant; colocynth; medicinal plants; phenolics

Introduction

Throughout history, numerous plant species have emerged, each showcasing distinct traits. Plants have various functions for humans, including providing shelter, heat, tools and equipment, sustenance, and combating illnesses (Cedillo-Cortezano *et al*., 2024). They are highly regarded in people's dietary plans because of the abundance of nutrients they possess. Furthermore, the plants' aromatic characteristics render them essential in terms of preference (Uysal *et al*., 2023). Plants possess significant medicinal value in addition to

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their nutritional features, making them crucial natural resources. Various investigations have extensively recorded the diverse biological actions displayed by plants, encompassing their capacity to counteract cancer, combat germs, defend against oxidative damage, impede cell proliferation, diminish inflammation, protect liver health, and maintain DNA integrity (Doğan *et al*., 2023; Kalkan *et al*., 2023; El-Chaghaby *et al*., 2024; Kahraman and Çalışkan, 2024; Uysal *et al*., 2024). Plants possess certain characteristics that make them suitable for use in pharmacological research, making them natural substances of interest. The evaluation of the biological characteristics of plants is of great significance in this specific setting (Mohammed *et al*., 2022). We compiled the general features, mineral contents, chemical and phenolic contents, and biological activities of *C. colocynthis* in our study.

General characteristics and uses of Citrullus colocynthis

The plant species *C. colocynthis* (Cucurbitaceae) is commonly referred to as "Abu Jahl's melon". *C. colocynthis* is also known by several other names such as bitter apple, colocynth, egusi, vine of Sodom, bitter cucumber, and wild vegetable. The distribution zones of this species encompass Central and Southern India, Arabia, Western Asia, Tropical Africa, and the Mediterranean regions. The vertical extent of *C. colocynthis* above the ground ranges from 2 to 3 metres. The roots of this plant are succulent and perennial, with an elongated taproot distribution. The leaves, bearing a striking resemblance to watermelon, are palmate, acute, and include three to seven segmented lobes. The blooms are transported on yellow, yellow-greenish flower stalks located in the axils of the leaves. Each flower has five lobes and a compound calyx consisting of five segments. As monoecious plants, the male and female reproductive organs are situated in distinct blooms on a single parent plant. The fruit has a smooth, spherical shape and the diameter range is between 5 and 10 cm. The seeds are of gray hue and have dimensions of around 5 mm in length and 3 mm in width (Levi *et al*., 2001; Amamou *et al*., 2011; Pravin *et al*., 2013; Al-Snafi, 2016; Rani *et al*., 2017). Numerous studies have documented the therapeutic properties of the fruit of *C. colocynthis* in treating ulcers, indigestion, joint problems, anthelmintic, asthma, laxative, antipyretic, jaundice, carminative, bronchitis, leukoderma, anemia, sore throat, constipation, enteric mucosa, intestinal peristalsis, and urinary infection (Katewa and Galav, 2005; Kirtikar and Basu, 2006; Upadhyay *et al*., 2007; Nadkarni, 2007). The root of *C. colocynthis* has been documented to have an impact on various health conditions such as amenorrhoea, boils, infertility, jaundice, carbuncles, hydrocele, enlarged abdomen, easy delivery, ophthalmia, chronic open wounds, bacterial infection, cough, asthma, worms, breast infection, rheumatism, urinary congestion, and abdominal discomfort (Tiwari *et al*., 2003; Kirtikar and Basu, 2006; Yadav *et al*., 2006; Nadkarni, 2007; Meena *et al*., 2014; Al-Snafi, 2016). Research has indicated that the seed of *C. colocynthis* has therapeutic properties against gall disease, toxic bites, intestinal problems, malaria, epilepsy, and hair care in animals. Additionally, it is utilized in culinary applications as a thickening and flavoring agent in soups (Singh and Pandey 1983; Badifu and Ogunsua 1991; Mohammed *et al*., 2004; Shah, 2005; Meena *et al*., 2014; Al- Snafi, 2016).

Mineral contents

Several mineral compounds present in natural products garner interest due to their nutritional qualities (Ahmad *et al*., 2023). Previous research in the literature have consistently shown a preference for analyzing the mineral content of the seed portion of the *C. colocynthis* plant. Table 1 displays the mineral compositions of *C. colocynthis* seed, as determined by literature study.

Table 1. Mineral contents of *Citrullus colocynthis*

Mineral compositions	Seed values (mg/g)	References
Mg	0.002-2.1	(Sawaya *et al*., 1983; Sawaya *et al*., 1986; Sadou *et al*., 2007; Akpambang *et al.,* 2008; Igwenyi *et al*., 2011; Ambi *et al*., 2017; QuratulAin *et al*., 2019; Falade *et al*., 2020)
K	0.028-6.84	
Na	0.017-1.68	
Fe	0.001-0.499	
Ca	0.019-5.69	
Zn	0.0009-0.030	
Cu	0.001-0.051	
Mn	0.0002-0.0974	

Potassium plays a crucial role in animal cells by regulating physiological fluid and electrolyte equilibrium. Furthermore, it contributes to muscular contraction and the transmission of nerve currents. In its deficiency, diarrhea, vomiting and worse hypokalemia can be seen. In addition, muscle weakness, heartbeat abnormalities and circulatory disorders, slow reflexes and difficulty in breathing, and weakness can be seen. Many plant foods such as cabbage, broccoli, dates, figs, avocados, apricots, and almonds are known as potassium sources (Abdel-Wahab *et al*., 1992; Manning 2010; Weaver, 2013). Upon reviewing literature data in our study, it is evident that the potassium (K) content in the seed section of *C. colocynthis* is greater than that of other minerals. Thus, it is believed that *C. colocynthis* can serve as a significant potassium reservoir.

Biological activity

The many biological activities of plants are attributed to the bioactive chemicals they synthesize inside their physiological systems (Mohammed *et al*., 2023). The present work involved the compilation of biological activity investigations of *C. colocynthis* from existing literature. The results are displayed in Table 2.

Table 2. Biological activities of *Citrullus colocynthis*

Biological activities	Solvents	Used parts	Geographic regions	References
Analgesic, anticancer, antiglycation, anti- anti-inflammatory, hyperglycemic, antidiabetic antimicrobial, antioxidant, cytotoxic, hepatoprotective, larvicidal activity	Methanol, chloroform, hexan, aqueous, butanolic, ethyl acetate, ethanol, hydroalcoholic, acetone, hydroethanolic, petroleum ether, crude, β-pyrazol-1-ylalanine, purified, essential oil	Fruit, leaves, seed, whole plant, root, pulp, peel	India, United Arab Emirates, Algeria, Saudi Arabia, Pakistan, Iran, Umman, Yemen, Tunusia, Egypt, Morocco, France	(Nmila *et al*., 2000; Rahuman *et al*., 2008; Priyavardhini *et al*., 2009; Gurudeeban *et al*., 2010; Ramanathan *et al*., 2010; Marzouk *et al*., 2013; Mohadjerani and Shokohsaljoghi, 2014; Nessa and Khan, 2014; Chekroun *et al*., 2015; Chawech *et al*., 2015; Eidi *et al*., 2015; Vakiloddin *et al*., 2015; Al-Malki, 2016; Gupta *et al*., 2018; Hassan and Sreea, 2019; Reddy *et al*., 2019; Ghauri *et al*., 2020; Bourhia *et al*., 2021; Fetni and Bertella, 2021; Mehmood *et al*., 2021; Perveen *et al*., 2021; Iftikhar *et al*., 2023; Mazher *et al*., 2023; Ranjbar *et al*., 2023; Thamer *et al*., 2023)

Antioxidant activity

Free radicals are extremely reactive molecules produced during essential metabolic processes and have the ability to induce oxidation of other substances. The cellular damage caused by exposure to high concentrations of these oxidizing chemicals can be significant. The antioxidant defence mechanism functions to neutralise the impact of oxidising species (Korkmaz *et al*., 2021). In certain cases, the antioxidant defence mechanism is insufficient in defending against powerful oxidizing agents. In this condition, oxidative stress is observed (Krupodorova and Sevindik, 2020). Oxidative stress can precipitate the onset of serious diseases in humans, such as malignancy, cardiovascular diseases, neurological disorders, diabetes, and metabolic syndrome. The usage of supplementary antioxidants can serve as a preventive measure to alleviate the adverse effects of oxidative stress (Eraslan *et al*., 2021; Krupodorova *et al*., 2024). Plants are essential natural resources with certain attributes. In this work, we consolidated the antioxidant activity results of *C. colocynthis* as reported in the literature. In this work conducted in India, the antioxidant potential of a methanol extract derived from the fruit and leaves of *C. colocynthis* was examined using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test. Furthermore, the IC_{50} value, which specifies the fatal concentration of the test employed, was calculated. The research findings revealed that the IC_{50} value for 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity in the fruit extract was 196.44 µg/mL, whereas in the leaf extract it was 413.33 µg/mL (Gupta *et al*., 2018). The present work investigated the lipid peroxidation and superoxide radical scavenging activities of four distinct solvent extracts (methanol, hexane, methanol-water, and chloroform) derived from the leaves of *C. colocynthis* in the United Arab Emirates. The 1,1-diphenyl-2-picrylhydrazyl (DPPH), β-carotene-linoleic acid model system was employed for this purpose. The investigation revealed that the chloroform extract had the highest 1,1-diphenyl-2-picrylhydrazyl (DPPH) finding of 2.76 mg/mL. Similarly, the methanol extract had the highest lipid peroxidation percentage of 82.24% when employing the β-carotene-linoleic acid model system. The optimal superoxide radical scavenging activity, when using an enzyme, was found to be 5.68 mg/mL in hexane extract. Conversely, the optimal superoxide radical scavenging activity, when using an enzyme, was 3.763 mg/mL in chloroform solvent (Nessa and Khan, 2014). In a separate study carried out in India, the antioxidant capacity of methanol extract derived from the fruit of *C. colocynthis* was examined by the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test. The laboratory findings indicated that the 1,1-diphenyl-2-picrylhydrazyl (DPPH) inhibition percentage ranged from 8.52% to 76.35% (Vakiloddin and colleagues, 2015). An investigation conducted in Algeria evaluated the antioxidant properties of aqueous and butanolic extracts obtained from the fruit of *C. colocynthis* using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test. The analysis resulted in an IC_{50} value of 61 µg/mL for the butanolic formulation and 241.25 µg/mL for the aqueous formulation (Chekroun *et al*., 2015). A study carried out in Saudi Arabia revealed that the ethyl acetate extract derived from the seed of *C. colocynthis* had the greatest hydroxyl radical scavenging percentage of 83.5% when measured at a concentration of 500 µg/mL (Al-Malki, 2016). The 1,1-diphenyl-2-picrylhydrazyl (DPPH) and reducing power tests were used to evaluate the antioxidant capabilities of methanol, ethanol, ethyl acetate, and water extracts obtained from the fruit and whole plant of *C. colocynthis* in Pakistan. The analysis showed that the water extract from the whole plant had the highest 1,1-diphenyl-2-picrylhydrazyl (DPPH) value of 77.5%, whereas the methanol extract from the same plant had a somewhat lower power value of 0.99 mg/mL (Mehmood *et al*., 2021). The 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, reducing power and overall antioxidant activities of a methanol extract obtained from the root and pulp of *C. colocynthis* in Iran were investigated. Therefore, the study reported that the activity of all the extracts was observed to have a positive correlation with the concentration in the conducted tests (Mohadjerani and Shokohsaljoghi, 2014). A separate study carried out in Pakistan revealed that the ethanol extract derived from the fruit of *C. colocynthis* exhibited an inhibition percentage of 92.31% when tested with the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test (Mazher *et al*., 2023). A separate study carried out in India examined the antioxidant properties of a methanol extract derived from the leaves and roots of *C. colocynthis* using 1,1-diphenyl-2-picrylhydrazyl (DPPH),

hydroxyl radical scavenging, and nitrite radical scavenging tests. The investigation revealed that the tests employed yielded results of 88.21%, 71.4%, and 61.3% for the leaf, respectively. Furthermore, the root extract was shown to lack hydroxyl radical scavenging capacity, with 1,1-diphenyl-2-picrylhydrazyl (DPPH) and nitrite radical scavenging assays yielding scores of 89.13% and 86.4%, respectively (Ramanathan *et al*., 2010). A separate study carried out in Algeria revealed that the ethanol extract derived from the fruit of *C. colocynthis* displayed a significant ability to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals (IC50 value 6.31 µg/mL), as well as a potent ferric reducing antioxidant power (IC_{50} value 27.94 µg/ml) and robust antioxidant activity against Hydroxyl radicals (OH) radicals (IC_{50} value 67.13 µg/mL) (Fetni and Bertella, 2021). The present investigation in Oman aimed to assess the 1,1-diphenyl-2-picrylhydrazyl (DPPH) and hydrogen peroxide scavenging effectiveness of ethanol and methanol extracts derived from the seeds, leaves, and peel components of *C. colocynthis*. The investigation revealed that the methanol extract of the peel achieved the highest result in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test, with a reported value of 95.42%. Moreover, the methanol extract of the leaf achieved the highest outcome in the hydrogen peroxide cleaning test, reaching 91.6% (Reddy *et al*., 2019). A study was carried out in Yemen to examine the antioxidant capabilities of the extract derived from the pulp and seed sections of *C. colocynthis* using Ferric-Bipyridine Reducing Capacity of total antioxidants (FBRC) and Ferric Reducing Antioxidant Power (FRAP) tests. The investigation revealed that the FBRC test yielded a result of 0.30 g AAE/g for pulp, while the Ferric Reducing Antioxidant Power (FRAP) test result was 0.45 g AAE/g. Furthermore, the FBRC test yielded a result of 0.13 g AAE/g for the seed, while the Ferric Reducing Antioxidant Power (FRAP) test result was 0.16 g AAE/g (Thamer et al. 2023). An investigation was carried out in Egypt to examine the antioxidant potential of an aqueous extract derived from the fruit of *C. colocynthis* using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test. The optimal IC50 value for the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test was determined to be 715.939 µg/mL (Hassan and Sreea, 2019). A further study carried out in Pakistan revealed that the 1,1-diphenyl-2-picrylhydrazyl (DPPH) test yielded results ranging from 5.0 to 115.9 µg/mL for various extract fractions derived from the fruit of *C. colocynthis*. The ABTS test resulted in values ranging from 31.2 to 9782 µg/mL, while the inhibition value of linoleic acid peroxidation ranged from 26.1 to 89.8% (Iftikhar et al. 2023). An investigation carried out in Morocco revealed that the hexane extract derived from the seed of *C. colocynthis* had an IC_{50} value of 2.22 mg/mL for the β-carotene bleaching test and a 1,1-diphenyl-2-picrylhydrazyl (DPPH) test result of 8.98 mg/mL (Bourhia *et al*., 2021). Considering the antioxidant activity data documented in the literature, it is evident that *C. colocynthis* possesses a substantial antioxidant capacity. Within this particular framework, it was observed that some components of *C. colocynthis* have the potential to serve as natural sources of antioxidants.

Antimicrobial activity

Microbial diseases have shown a notable surge in prevalence in recent years. Antimicrobial medications are obtained by individuals to treat illnesses resulting from microbial infections (Mohammed *et al*., 2019). Nevertheless, the prevalence of antibiotic-resistant bacteria is rapidly rising as a result of the unintentional use of antibiotics. The current scenario renders the efficacy of the antimicrobial medications employed inadequate (Krupodorova *et al*., 2022). Consequently, researchers are now focusing on the identification of novel antimicrobial medications. The preference for natural antimicrobial medications is driven by the potential adverse effects associated with synthetic antibiotics (Baba *et al*., 2020). Plants serve as significant reservoirs of antibacterial action. Our work involved the compilation of antibiotic activity investigations of *C. colocynthis* as described in the relevant literature. In a study conducted in Saudi Arabia, the antimicrobial activity of ethyl acetate extract obtained from the seed of *C. colocynthis* against *Staphylococcus aureus, S. epidermidis, Bacillus subtilis, Enterococcus faecalis, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeroginosa, Aspergillus flavus, Alternaria alternata, A. niger, Botyritis cinerea, Curvularia maculans, C. lunata, Candida albicans, Epidermophyton floccosum, Fusarium oxysporum* and *Penicillium citrinum* was investigated. The research

findings indicated that the bacteria *E. faecalis* had the highest Minimum Inhibitory Concentration (MIC) value of 200 µg/mL, while the fungus *B. cinerea* and *A. alternata* had the highest MIC values of 200 µg/mL (Al-Malki, 2016). In Pakistan, a study was undertaken to examine the antibacterial properties of methanol, ethanol, ethyl acetate, and water extracts derived from the fruit of *C. colocynthis* and the entire plant against *P. aeruginosa, E. coli, S. aureus*, *B. subtilis*, and *Salmonella typhi*. The research findings indicated that the ethanol extract of the fruit exhibited the highest inhibition percentage of 47.37% against *S. aureus* (Mehmood *et al*., 2021). A separate study carried out in Pakistan revealed that the ethanol extract derived from the fruit of *C. colocynthis* exhibited outstanding efficacy against *Micrococcus luteus* (activity index 1.11; inhibition zone 29.1 mm) and *P. pickettii* (activity index 1.14; inhibition zone 32.4 mm) (Mazher *et al*., 2023). The present work aimed to examine the antibacterial properties of ethanol and methanol extracts derived from the seeds, leaves, and peel of *C. colocynthis* against *Bacillus circulans, Micrococcus lutein, S. aureus, Salmonella enterica,* and *E. coli* in Oman. The research findings indicated that the peel ethanol extract exhibited the highest inhibition zone value of 22.6 mm against *B. circulans* (Reddy *et al*., 2019). An investigation was carried out in Tunisia to assess the antibacterial properties of hexane, ethyl acetate, and methanol extracts derived from the root and leaf of *C. colocynthis* against *Bacillus cereus, E. faecalis, Salmonella enteritidis, E. coli, S. aureus,* and *P. aeruginosa*. The research findings indicated that the leaf part exhibited the highest inhibition zone value of 29.5 mm in the ethyl acetate extract against *E. faecalis,* while the root part displayed the highest inhibition zone value of 30.0 mm in the hexane extract against *S. aureus* (Chawech *et al*., 2015). The present work was undertaken in Egypt to examine the antibacterial properties of an aqueous extract derived from the fruit of *C. colocynthis* against *B. cereus, E. coli, S. aureus*, and *Clostridium perfringens*. The research findings indicated that *B. cereus* had the highest inhibition zone value of 20 mm (Hassan and Sreea, 2019). The present work was undertaken in Morocco to examine the antibacterial properties of a hexane extract derived from the seed of *C. colocynthis* against *Listeria monocytogenes, E. faecalis, P. aeruginosa, E. coli, S. aureus*, and *Salmonella typhimurium*. The study findings indicated that the most distinct inhibition zone seen was 3 mm against *E. faecalis* (Bourhia *et al*., 2021). In another study conducted in India, the antimicrobial activity of aqueous and methanol extracts obtained from the leaves of *C. colocynthis* was investigated against *S. aureus, Streptococcus faecalis, S. pyogenes, B. subtilis, E. coli, Klebseilla pneumoniae, Proteus mirabilis, P. vulgaris, S. typhi, Vibrio cholerae, Aspergillus flavus, A. fumigatus, Mucor* sp., *Penicillium s*p., *Rhizopus* sp., and *C. albicans.* The research findings indicated that the most effective inhibition zone value for bacterial strains was 14 mm against *E. coli*, while for fungal strains it was 10 mm against *A. fumigatus* (Gurudeeban *et al*., 2010). An investigation was carried out in Iran to assess the antibacterial properties of a hydroalcoholic extract derived from the fruit of *C. colocynthis* against *Candida guilliermondii, C. albicans, C. parapsilosis, C. tropicalis, C. kreusei, C. glabrata, C. dubliniensis, Aspergillus fumigatus, A. niger,* and *A. flavus*. The research findings indicated that the most effective inhibition zone value was seen against *A. fumigatus*, measuring 6 mm (Eidi *et al*., 2015). A separate study carried out in India found that the acetone extract derived from the leaves of *C. colocynthis* generated an inhibition zone measuring 14.0 mm against *P. aeruginosa*. However, the chloroform leaf extract showed no antibacterial activity against *S. aureus*. The minimum inhibitory concentration of the chloroform extract was 4.0 mm for *E. coli* (Priyavardhini *et al*., 2009). Based on the antimicrobial activity tests of *C. colocynthis* documented in the literature, it was established that the plant possesses antibacterial properties against the specified strains. Within this particular framework, it is widely believed that *C. colocynthis* holds potential as a natural antibacterial agent.

Anticancer activity

The current trend is a continuous increase in the occurrence of cancer. Among the proven therapeutic methods, radiation and chemotherapy are frequently used. Moreover, supplementary natural products possess

a vital function as anticancer agents (Sevindik *et al*., 2024). The intrinsic qualities of plants make them noteworthy natural commodities that attract considerable attention. The objective of this study was to gather the verified anticancer properties of *C. colocynthis* as reported in the body of literature. This study conducted in Algeria investigated the cytotoxic effects of an ethanol extract obtained from the fruit of *C. colocynthis* on multiple human cancer cell lines, including HepG2, SH-SY5Y, and Raw 264.7. The study produced IC50 values of 15.69, 4.82, and 10.72 µg/mL for the cell lines under examination (Fetni and Bertella, 2021). A cytotoxicity study was conducted in Egypt to evaluate the effects of an aqueous extract obtained from the fruit of *C. colocynthis* on the Ti-38 human normal fetal lung cell line and the Vero normal adult African green monkey kidney cell line. The study results revealed that the concentration of Wi-38 was 313.43 micrograms per milliliter and Vero was 515.84 micrograms per milliliter (Hassan and Sreea, 2019). The present inquiry analyzes the anticancer activities of hexane extract produced from the seed of *C. colocynthis* on two human cell lines: HT-29 human colorectal adenocarcinoma and MDA MB 231 human breast adenocarcinoma. Upon research, it was determined that the IC_{50} values for MDA-MB-231 and HT-29 cancer cells were 86.89 and 242.1 µg/mL, respectively (Bourhia *et al*., 2021). The study carried out in Pakistan demonstrated that the methanol extract obtained from the leaves of *C. colocynthis* significantly decreased the proliferation and growth capacity, as well as the cell cycle, of the MCF-7 human breast cancer cell line. By substantially upregulating the expression of cyclin-CDK inhibitors (p21 and p27), this effect was attained (Perveen *et al*., 2021). Using nanoemulsion and nanogel formulations, an experiment was conducted in Iran to evaluate the impact of the essential oil obtained from *C. colocynthis* on A-375 human melanoma cells. The study found that the intermediate concentration (IC50) values of the nanoemulsion and nanogel against A-375 cells were 369.6 and 127.2 µg/mL, respectively (Ranjbar et al. 2023). Within this specific framework, it was observed that *C. colocynthis* exhibits significant anticancer characteristics against cell lines as reported in current literature.

Other activities

Prior research has established that *C. colocynthis* demonstrates additional activities beyond its characteristic antioxidant, antibacterial, and anticancer characteristics. The present investigation conducted in India aimed to assess the hepatoprotective effects of the methanol extract obtained from the fruit of *C. colocynthis* in rats that were made hepatotoxic by the injection of paracetamol. Analysis revealed a significant increase in the levels of total bilirubin (TB), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and alkaline phosphatase (ALP) in group II who were administered paracetamol. Moreover, it was demonstrated that the extract was given to rats as a pre-treatment at an oral dosage of 300 mg/kg for this procedure (Vakiloddin *et al*., 2015). An investigation carried out in Pakistan found that methanol, ethanol, ethyl acetate, and water extract derived from the fruit and whole plant of *C. colocynthis* had antiglycation and anti-inflammatory properties. The investigation revealed that the water extract of the fruit had the highest percentage of 35.8% for inhibiting edema caused by ethyl phenylpropiolate (EPP) in rat ear, while the highest percentage for antiglycation was 46.21% in the ethyl acetate extract of the whole plant (Mehmood *et al*., 2021). An investigation carried out in Tunisia revealed that chloroform fractions derived from the seed portion of *C. colocynthis* exhibited analgesic properties (Marzouk and colleagues, 2013). A separate study carried out in Pakistan examined the anti-hyperglycemic properties of the hydroethanolic extract derived from the seed of *C. colocynthis*. The research findings indicated a time-dependent reduction in blood glucose levels from 351.3 to 258 m/kg (Ghauri *et al*., 2020). In an independent investigation carried out in India, the larvicidal activity of acetone, hexane, ethyl acetate, methanol, and petroleum ether extracts derived from *C. colocynthis* was examined. The analysis revealed that the maximum IC_{50} value recorded was 18.20 ppm, whereas the LC_{90} value attained was 96.33 ppm on *Aedes aegypti*. The highest IC_{50} value recorded on *Anopheles stephensi* was 11.49 ppm, with an LC_{90} value of 47.35 ppm. On *Culex quinquefasciatus*, the highest IC_{50} value detected was 27.24 ppm, with an LC_{90} value of 70.38 ppm (Rahuman and colleagues, 2008). An investigation

was carried out in France to assess the antidiabetic properties of crude, hydro-alcoholic, purified, and β-pyrazol-1-ylalanine extracts derived from the fruit of *C. colocynthis*. The study revealed that all examined extracts, when administered at a concentration of 0.1 mg/mL for a duration of 20 minutes, promptly and significantly enhanced the secretion of insulin in a temporary manner. Furthermore, the purified extract effectively increased the release of insulin from isolated islets in a dose-dependent manner (Nmila *et al*., 2000).

Chemical and phenolic contents

Plants synthesise bioactive chemicals with distinct characteristics from their own physical structures. Although lacking nutritional qualities, these bioactive molecules are considered medically significant secondary metabolites (Şabik *et al*., 2024). The chemical compositions of *C. colocynthis* tissue documented in the literature are presented in Table 3 of our investigation.

Table 3. Chemical contents of *Citrullus colocynthis*

Geographic regions	Used parts	Chemical contents (%)	References
Morocco, Saudi Arabia, Iraq	Seeds	Undecane (2.04), 2,4-nonadienal (2.34), tetradecane (3.29), hexadienol (3.6-5.47), hexanal (3.79-4.54), 2,4-decadienal (7.79-11.49), hexadecane (1.27-14.76), ethyl2-octynoate (1.66), linalool propanoate (14.29), pentadecane (7.15-21.7), nonadienal (15.39), tetrachloroethylene (3.94), 2-heptenal (6.09-6.25), 2,4,6,8-tetramethyl-1-undecene (8.43), dodecane (9.85-19.2), 2-decenal (10.76), germacrene-D (12.36), heptadecane (12.45-20.4), 2-dodecanol (16.84), 2,6-nonadienal (22), α-pinene (3.25-30.6), isopropyl butanoate (10.4), δ3-Carene (5.1), o-methylacetophenone (10.8), thymol (3.0-37.2), methyl hexadecanoate (5.6-18.3), limonene (5.11), camphene (2.59), carvacrol (4.11), camphor (9.25), p-cymene (6.25), terpinene (12.14), sabinen (6.25)	(Bourhia *et al*., 2020; Bourhia *et al*., 2021; Bilal and Khorsheed, 2023; Khan *et al*., 2023)
India, Iraq	Fruits	2-methyl, 4-heptanone (48), 3-methyl, 2-heptanone (12.88), trimethylsilyl methanol (9.08), 1-propoxy pentane (6.49), α-pinene (5.58), limonene (7.12), camphene (3.65), carvacrol (5.44), camphor (12.25), p-cymene (8.46), terpinene (16.58), sabinen (9.58)	(Gurudeeban *et al*., 2011; Bilal and Khorsheed, 2023)
China	Leaves	Cyclotrisiloxane (3.57), triamterene (1.53), octasiloxane (1.25-7.06), tetrasiloxane (1.10), heptasiloxane (21.3), 5-methyl-2-phenylindolizine (17.9)	(Ahmed *et al*., 2020)

The chemical contents of the seeds, fruits and leaves of *C. colocynthis* have been reported in the literature. When we look at the studies, the major components in the seed part are hexadecane, linalool propanoate, pentadecane, nonadienal, dodecane, heptadecane, germacren-D, 2 -dodecanol, 2,6-nonadienal, α-pinene, thymol and terpinene were found. It was observed that the major components in the fruit part were 2-methyl, 4-heptanone, 2-heptanone, camphor and terpinene, while the major components in the leaf part were heptasiloxane and 5-methyl-2-phenylindolizine.

In our study, the phenolic content of *C. colocynthis* tissues reported in the literature is shown in Table 4 as mg/100 g.

Table 4. Phenolic contents of *Citrullus colocynthis*

Used parts	Phenolic contents (mg/100 g)	References
Root	Gallic acid (3.71), p-hydroxy-benzoic acid (0.02-1.85), chlorogenic acid (0.08-2.06), caffeic acid (0.05-2.79), vanillic acid (0.02-1.53), p-coumaric acid (0.96), sinapic acid (0.20), ferulic acid (1.55), catechin (0.11-65.31), myricetin (0.05-25.81), quercetin (0.10-7.05), kaempferol (0.07-6.79)	(Hussain *et al*., 2013)
Leaves, Fruit, Seed	Gallic acid (0.16- 13.3), p-hydroxy-benzoic acid (0.04-10.57), chlorogenic acid (0.20- 16.3), caffeic acid (0.04-13.37), vanillic acid (0.19-13.78), p-coumaric acid (1.26-12.91), sinapic acid (3.38-12.98), ferulic acid (2.10-193.8), catechin (0.59-95.45), myricetin (0.16-381.7), quercetin (0.62-579.9), kaempferol (0.20-5.95), protocatchuic acid (6.9), ellagic acid (16.7-18.1), luteolin (4.1)	(Ibrahim *et al*., 2010; Hussain *et al*., 2013; Bilal and Khorsheed, 2022)

Conclusions

C. colocynthis is a botanical species whose fruits are extensively ingested in contemporary times. Numerous components of the plant find application in traditional medicinal treatments. Distinct components of the plant are ingested to counteract various ailments. The present work involved the compilation of phenolic and chemical contents, general characteristics, mineral contents, and biological activities of *C. colocynthis* as documented in existing literature. The literature study revealed that *C. colocynthis* shown potent antioxidant, antibacterial, and anticancer properties. Furthermore, it has been observed that it may serve as a significant reservoir of potassium. Furthermore, it was established that it may be a natural origin based on the specific phenolic and chemical constituents documented in it. Consequently, it was concluded that the *C. colocynthis* plant has the potential to be a significant natural resource in the development of pharmaceutical formulations.

Authors' Contributions

Conceptualization: M.S.; Formal analysis: M.S.; E.S.; Investigation and Methodology: M.S.; I.U.; E.S.; T.K.; O.K.; O.Ü.; Project administration: M.S.; I.U.; E.S.; Resources: M.S.; I.U.; E.S.; T.K.; O.K.; O.Ü.; Supervision: M.S.; I.U.; E.S.; T.K.; O.K.; O.Ü.; Validation: M.S.; I.U.; E.S.; T.K.; O.K.; O.Ü.; Writing - original draft: M.; I.U.; E.S.; T.K.; O.K.; O.Ü.; Writing - review and editing: M.S.; E.S.; T.K.

All authors read and approved the final manuscript.

Ethical approval (for researches involving animals or humans)

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Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

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