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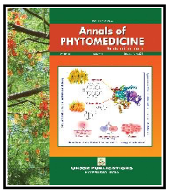

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Citrullus spp.: A treasure house of phytochemical, pharmaceutical potential and industrial applications

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Abstract

The *Citrullus* spp. includes seven species that have long served as essential food sources and hold significant value in folk medicine. This review examines their pharmacological potential, emphasizing active compounds like phenolic acids, flavonoids, and cucurbitacins, which offer diverse health benefits. These phytochemicals help prevent and treat conditions such as cancer, diabetes, and various gastrointestinal, respiratory, and urinary disorders. *Citrullus* extracts also display anti-inflammatory, antifertility, antigout, immunomodulatory, antioxidant, and antimicrobial properties, underscoring their therapeutic promise. Additionally, utilizing *Citrullus* waste supports eco-friendly, circular economy practices. This review synthesizes traditional and scientific research on *Citrullus* spp., analyzing their phytochemical profiles and bioactivities *in vivo* and *in vitro* to inform future medicinal applications.

1. Introduction

Cucurbitaceae family contains numerous genera native to Asia, Africa, and the Mediterranean region (Welbaum, 2015). A significant assemblage of plants encompasses more than 98 genera and 975 species (De Winter, 1990). Within this botanical family, the most extensively grown and consumed agricultural products globally include cucumbers, squash, gourds, and melons (Chomicki *et al*., 2020). Contemporary investigations into Cucurbitaceae have intensified, yielding fresh perspectives on their phytochemical composition, pharmacological properties, and biotechnological prospects (Tzortzakis *et al*., 2018).

In the modern Western world, the term alternative medicine has gained tremendous attention in society because of its natural remedies and therapeutic values with no side effects and its effective vital role in health (Yudharaj *et al*., 2016). Herbal plants are becoming a desirable source for developing drugs to treat various illnesses and their associated consequences. Hence, herbal medicines are thoroughly examined for their phytochemical content and pharmaceutical potential, aiming to develop industrial-scale treatments to cure various illnesses.

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Herbal medicines are classified into three categories based on their source of utilization: botanicals (where whole plants or plant parts are used), herbal preparations (extracts, tinctures, and infusions), and phytotherapeutic agents (isolated bioactive compounds) (Sivakrishnan, 2018). These herbal medicines have been accepted and used worldwide based on their region and availability.

2. Species of *Citrullus*

2.1 *Citrullus lanatus* Thunb.: Desert watermelon

Citrullus lanatus Thunb. (Desert watermelon) is a vining plant native to Asian and African deserts, widely grown in India for its sweetness, high water content, and health benefits (Chomicki *et al*., 2020). Melons from Sudan's Kordofan region are genetically closest to modern cultivated watermelons. The fruit, seeds, and rind hold significant medicinal value. It is a pepo berry and features a thick skin and juicy interior. Its phytochemical profile includes amino acids, fatty acids, and terpenes (Table 1), contributing to its pharmacological properties.

2.2 *Citrullus colocynthis* (L.) Schrad.: Bitter apple

Citrullus colocynthis (L.) Schrad., known as bitter apple, colocynth, bitter cucumber, vine of sodom, or wild gourd, is cultivated in India and Sri Lanka and is native to Arabia, Tropical Africa, Western Asia, and Mediterranean (Swarnakar *et al*., 2021). The bitter taste-producing substances in the colocynth are colocynthin and colocynthenin (Rezai *et al*., 2017). Rich in phytochemicals (Table

2), colocynth is traditionally used for purgative, anthelmintic, antipyretic, and carminative treatments. Despite its medicinal potential, it remains underutilized, warranting further pharmacological and ethnobotanical research.

Table 1: The compounds isolated from different parts of *C. lanatus*

S. No.	Parts	Compound	Molecular formula	References
	Amino acids			
1.	Fruit	a-Citrulline	$C_6H_{13}N_3O_3$	Deshmukh *et al.*, 2015
2.	Fruit	b-Glutamine	$C_5H_{10}N_2O_3$	Deshmukh *et al.*, 2015
3.	Fruit	C-Aspartic acid	$C_4H_7NO_4$	Deshmukh *et al.*, 2015
	Pigments			
4.	Fruit flesh	Lycopene and β-carotene	$C_{40}H_{56}$	Adetutu *et al.*, 2015
	Fatty acids			
5.	Seeds and peel	Linoleic acid	$C_{18}H_{32}O_2$	Shah *et al.*, 2023
6.	Seeds	Linolenic acid	$C_{18}H_{30}O_2$	Shah *et al.*, 2023
7.	Seeds	Methyl palmitate	$C_{17}H_{34}O_2$	Oloyede and Aderibigbe, 2018
8.	Seeds	Oleic acid, methyl ester	$C_{19}H_{34}O_2$	Oloyede and Aderibigbe, 2018
	Terpenes			
9.	Pulp and leaves	Cucurbitacin B	$C_{32}H_{46}O_8$	Jebir and Mustafa, 2022
10.	Pulp and leaves	Cucurbitacin C	$C_{32}H_{48}O_8$	Jebir and Mustafa, 2022
11.	Pulp and leaves	Cucurbitacin D	$C_{30}H_{44}O_7$	Jebir and Mustafa, 2022

Table 2: The compounds isolated from different parts of *C. colocynthis*

S. No.	Parts	Compound	Molecular formula	References
	Amino acids			
1.	Seed, pulp and rind	Alanine and tyrosine	$C_3H_7NO_2$ and $C_9H_{11}NO_3$	Abudayeh *et al.*, 2016
2.	Seed, pulp and rind	Glycine and proline	$C_2H_5NO_2$ and $C_5H_9NO_2$	Abudayeh *et al.*, 2016
	Pigments			
3.	Leaves	Rhodoxanthin	$C_{40}H_{50}O_2$	Selvaraj and Mosses, 2016
4.	Leaves	Lycopene	$C_{40}H_{56}$	Owoade *et al.*, 2018
	Fatty acids			
5.	Whole plant	Succinic acid	$C_4H_6O_4$	Gupta *et al.*, 2018
	Steroids			
6.	Seeds	Ergosterol	$C_{28}H_{44}O$	Selvaraj and Mosses, 2016
7.	Leaves	p-hydroxybenzoic acid	$C_7H_6O_3$	Jing *et al.*, 2012
8.	Fruit	Vanillic acid	$C_8H_8O_4$	Kumar *et al.*, 2008
	Terpenes			
9.	Leaves	Cucurbitacin A	$C_{32}H_{46}O_9$	Chawech *et al.*, 2015
10.	Fruit	Cucurbitacin C	$C_{32}H_{48}O_8$	Lavie *et al.*, 1964
11.	Fruit	Cucurbitacin K	$C_{30}H_{44}O_8$	Masayuki *et al.*, 2007
12.	Fruit and seed	Colocynthoside A	$C_{38}H_{54}O_{14}$	Rezai *et al.*, 2017
13.	Fruit and seed	Colocynthoside B	$C_{42}H_{62}O_{15}$	Rezai *et al.*, 2017

2.3 *Citrullus mucosospermus* Fursa: Egusi melon

Citrullus mucosospermus Fursa, or Egusi melon, native to West Africa, is a type of watermelon grown in Nigeria and its bordering nations. The fruit is oval-shaped with glossy green skin and white seeds (Achigan-Dako *et al.*, 2015). It is a major crop in West Africa that is used for food purposes, and its seed oil has a high protein content. It is also used in folklore medicine because of its significant phytochemical constituents (Table 3) and is utilized for numerous conditions, including fever and digestive problems.

Table 3: The compounds isolated from different parts of *C. mucosospermus*

S. No.	Parts	Compound	Molecular formula	References
1.	Pulp	Cucurbitacin E	$C_{32}H_{44}O_8$	Park *et al.*, 2024
2.	Pulp	Cucurbitacin E-2-O-glucoside	$C_{40}H_{56}0_{13}$	Park *et al.*, 2024

2.4 *Citrullus naudinianus* Sond. Hook. f.: Gemsbok cucumber

Citrullus naudinianus Sond. Hook. f. is known as the gemsbok cucumber, is a vining plant native to southern Africa, especially Namibia, that grows in sandy or rocky soils. Indigenous communities have long used it as a food source and in folk medicine (Bisognin, 2002). The plant features large, carrot-like root tubers up to one meter in length, from which most bioactive compounds are isolated (Table 4). Their stems are heavily covered with hairs, and rootings are observed in the nodes of the stems. The species is considered vulnerable in Zimbabwe due to habitat fragmentation from agriculture and development (Golding, 2002).

Table 4: The compounds isolated from different parts of *C. naudinianus*

S. No.	Parts	Compound	Molecular formula	References
1.	Tuber	Cucurbitacin G	$C_{30}H_{46}O_8$	Moritz *et al.*, 2023
2.	Tuber	Cucurbitacin J	$C_{30}H_{44}O_8$	Moritz *et al.*, 2023
3.	Tuber	Cucurbitacin I	$C_{30}H_{42}O_7$	Moritz *et al.*, 2023
4.	Tuber	23,24-Dihydro-cucurbitacin E	$C_{32}H_{46}O_8$	Moritz *et al.*, 2023

2.5 *Citrullus ecirrhosus* Cogn.: Tendril-less melon

Citrullus ecirrhosus Cogn. or tendril-less melon, is a water melon species native to South Africa (Meeuse, 1962). Its fruit is a pepo berry with a green exterior and red or pink interior containing black seeds. The seeds are analysed for their nutritional composition to be a source of protein (Table 5). Researchers have hybridized *C. ecirrhosus* with *C. lanatus* to develop water melon cultivars with improved resistance to white flies (*Bemisia tabaci*), although complete resistance was not achieved, hybrids still out performed conventional varieties (Simmons *et al.*, 2019). Similar breeding studies in the Cucurbitaceae family indicate that variations in cultivar growth and production may result from differences in graft compatibility and growth traits (Pranitha *et al.*, 2024).

Table 5: The compounds isolated from different parts of *C. ecirrhosus*

S. No.	Parts	Compound	Molecular formula	References
1.	Seeds	Glutamic acid	$C_5H_9NO_4$	Umar *et al.*, 2013
2.	Seeds	Arginine	$C_6H_{14}N_4O_2$	Umar *et al.*, 2013
3.	Seeds	Leucine	$C_6H_{13}NO_2$	Umar *et al.*, 2013
4.	Seeds	Histidine	$C_6H_9N_3O_2$	Umar *et al.*, 2013
5.	Seeds	Serine	$C_3H_7NO_3$	Umar *et al.*, 2013

2.6 *Citrullus amarus* Schrad.: Citron melon

Citrullus amarus Schrad. or citron melon, is a lesser-known species in the Cucurbitaceae family native to Africa, probably the Kalahari Desert, where it grows profusely. The fruits, seeds, and rinds of this underrated crop have a long-standing use in herbal medicine throughout history (Kirtikar and Basu, 1975) to cure various illnesses, like fever, rheumatism, anti-influenza (Morimoto and Isegawa, 2023) and stomach problems (Nkoana *et al.*, 2022). The fruit is analysed for its quality traits (Table 6) to use this species in resistance breeding programs.

Table 6: The compounds isolated from different parts of *C. amarus*

S. No.	Parts	Compound	Molecular formula	References
1.	Fruit flesh	β-Carotene	$C_{40}H_{56}$	Maragal *et al.*, 2019
2.	Fruit flesh	Zeaxanthin	$C_{40}H_{56}O_2$	Maragal *et al.*, 2019
3.	Fruit flesh	Phytoene	$C_{40}H_{64}$	Maragal *et al.*, 2019
4.	Fruit flesh	Violaxanthin	$C_{40}H_{56}O_4$	Maragal *et al.*, 2019

2.7 *Citrullus rehmii* De Winter: Namib desert melon

Citrullus rehmii, commonly known as the Namib melon native to Namibia (De Winter, 1990). *C. rehmii* contains cucurbitacin E and traces of cucurbitacin B and I (Table 7). The fruit was observed to have a dark grey rind with randomly scattered light brown-orange spots. The fruits are inedible and are used as ornamental plants because they differ in morphology from other species (Guo *et al.*, 2019).

Table 7: The compounds isolated from different parts of *C. rehmii*

S. No.	Parts	Compound	Molecular formula	References
1.	Fruit	Cucurbitacin E	$C_{32}H_{44}O_8$	De Winter, 1990
2.	Fruit	Cucurbitacin B	$C_{32}H_{46}O_8$	De Winter, 1990
3.	Fruit	Cucurbitacin I	$C_{30}H_{42}O_7$	De Winter, 1990

3. Physiological and genomic variation in the *Citrullus* spp.

The *Citrullus* spp. shows significant genomic and physiological variation, which reflects the effects of domestication and adaptation to various habitats. Studies have shown that various *Citrullus* spp. and cultivars respond physiologically differently to abiotic challenges like drought, with notable variations in photosynthetic efficiency, water-use strategies, and gene expression profiles under stress (Erez *et al*., 2020). High genetic diversity and structural dynamism are indicated by recent super-pangenome analyses that include both wild and cultivated species (*C. lanatus, C. mucosospermus, C. amarus, and C. colocynthis*). These analyses have revealed a relatively low proportion of core genes throughout the *Citrullus* spp. large inter-chromosomal rearrangements and extensive gene variation (Wu *et al*., 2023). Domestication has resulted in the loss of certain resistance genes in cultivated lines and selection sweeps in areas governing important fruit quality features, including sugar buildup, flesh color, and disease resistance. After fruit loses its bitterness, it is difficult to determine whether the domestication syndrome includes concurrent ripening, lycopene accumulation, fruit size, rind thickness, flesh softening, and sucrose synthesis (Nimmakayala *et al*., 2022). These integrated physiological and genomic insights provide a complete understanding of the adaptive strategies, evolutionary past, and breeding potential within the *Citrullus* spp.

4. Ethnobotanical importance of *Citrullus* spp.

C. colocynthis is traditionally used to treat a wide range of problems, including digestive issues, joint pain, acting as a diuretic, anticancerous, antihypolipidemic and supporting immune functions (Figure 1). The fruit is a strong purgative and laxative due to its high concentration of cucurbitacins. Seed oil is used for hair growth, bowel movement, and malaria (Kapoor *et al*., 2021). Watermelon is used as a laxative and to cure rheumatism, gout, burns, and swelling in Northern Sudan (Erhirhie and Ekene, 2013). The fruit is used as a purgative in Senegal and as a remedy for gonorrhea and diarrhea in Nigeria (Naz *et al*., 2014). The rind has been demonstrated to help treat alcohol intoxication and diabetes. It can be consumed as a vegetable, given to cattle, or fermented into juice (Njoya, 2019).

C. naudinianus is used to alleviate thirst, while different plant structures are employed in folk medicine (Abubakar *et al*., 2023). Plant parts including leaves, roots, stems, and tubers, have traditional medicinal uses for treating sores and wounds, inflammation, carcinoma, and gonorrhoea. *C. amarus* acts as a hydration and nutrition source in desert areas. It is consumed either raw or cooked (Bush, 1978). The ethnobotanical uses of *C. ecirrhosus* (tendril-less melon), *C. mucosospermus* (Egusi melon), and *C. rehmii* (Namib desert melon) are not extensively documented, but they are used as food and water sources in desert areas (Chomicki *et al*., 2020).

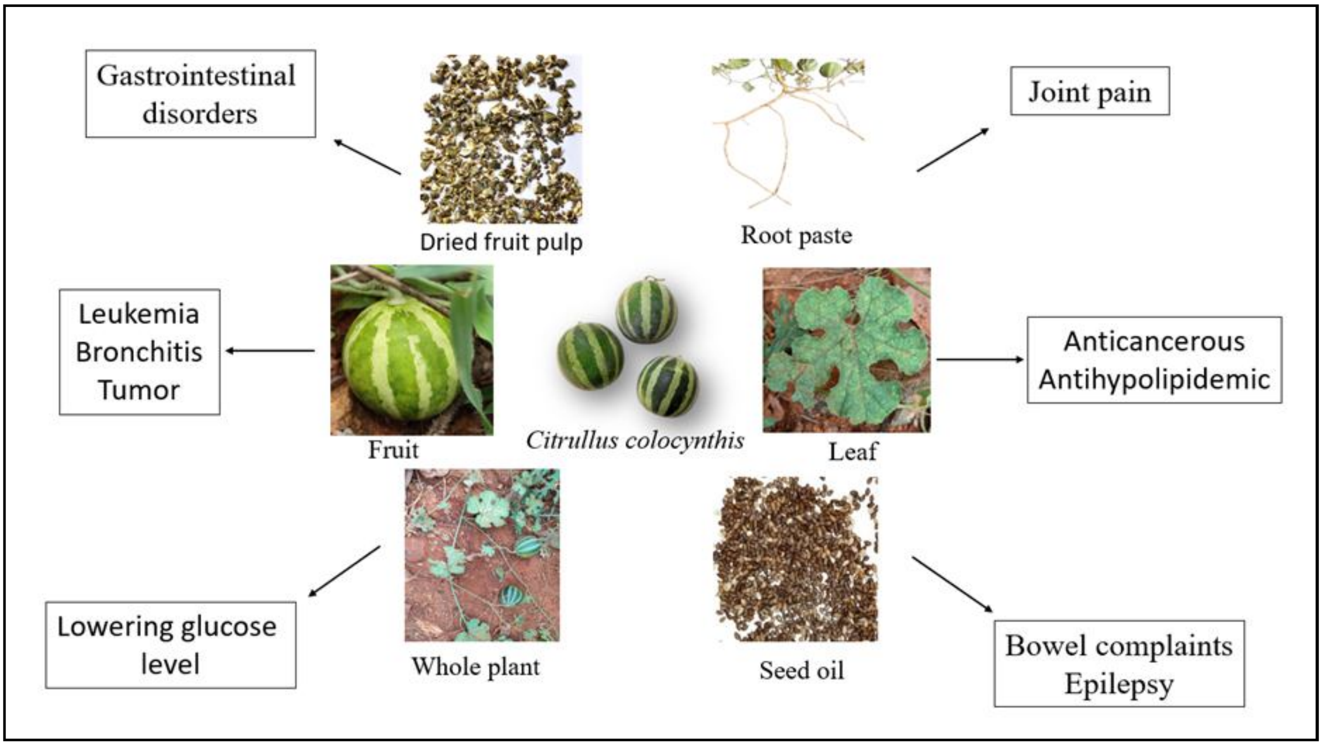

Figure 1: Ethnobotanical uses of *C. colocynthis.*

5. Pharmacological activity of *Citrullus* spp.

Citrullus spp. were found to possess various therapeutic activities because of the existence of biologically active substances, and they are known to treat various ailments and have applications in medicine, pharmaceuticals, cosmetics, and folk remedies (Kapoor *et al*., 2021). The pharmacological activities of *Citrullus* are due to the existence of bioactive chemical constituents, one of the key components is cucurbitacin, which is responsible for functions including antihyperglycemic, anti-inflammatory, antifertility and antimicrobial properties in *C. colocynthis* (Table 8). The flavonoids such as quercetin, kaempferol, and rutin are responsible for cardiovascular and anti-inflammatory properties (Amsa *et al*., 2024) and have various health benefits. Colocynth antihyperglycemic effects are demonstrated through the inhibition of glucosidase enzymes, reduction of fasting blood glucose, and significant lowering of HbA1c levels (Figure 2). *C. lanatus* seeds, fruit and pulp have exhibited antimicrobial, antiulcer, antioxidant and laxative properties. The pharmacological activity like immunomo-dulatory, anticancer and HIV inhibition is exhibited by *C. naudinianus*.

Table 8: Pharmacological activities of *Citrullus* spp.

S. No.	Plant part	Extract	Pharmacological activity	References
	C. colocynthis			
1.	Rind	Aqueous	Hypoglycaemic	Abdel-Hassan *et al.*, 2000
2.	Fruit	Petroleum ether	Anticancer	Abdulridha *et al*., 2020
3.	Fruits	Ethanolic	Lymphocytes inhibition	Stein *et al*., 2024
4.	Fruits	Ethanolic	Antiulcer	Reddy *et al*., 2012
5.	Seed	Methanolic	Antioxidant and antiulcer	Gill *et al*., 2011
6.	Leaves	Methanolic	Cytotoxic to breast cancer cells	Perveen *et al*., 2021
7.	Fruit, seed, and root	Ethanolic	Antibacterial and antifungal	Hameed *et al*., 2020
8.	Fruits and seeds	Aqueous	Antineurodegenerative damage	Chen *et al*., 2019
9.	Fruit	Dried fruit powder	Antiarthritic	Raziani *et al*., 2023
10.	Fruits	Ethanolic	Antioxidant and antigout	Karunakaran and Hari, 2022
11.	Fruit pulp and seeds	Hydromethanolic	Antihyperlipidaemia	Zamani *et al*., 2007
12.	Fruits	Aqueous and ethanolic	Antihypertensive	Iftikhar *et al*., 2023
13.	Fruits	Ethanol	Antifertility	Chaturvedi *et al*., 2003
	C. lanatus			
14.	Seed	Chloroform, methanol and distilled water	Antimicrobial	Adunola *et al.*, 2015
15.	Seed oil	n-hexane	Hepatoprotective activity	Madhavi *et al*., 2012
16.	Seeds	Methanolic	Antiulcer activity in wistar rats	Bhardwaj *et al*., 2012
17.	Fruit pulp	Aqueous	Laxative activity	Sharma *et al*., 2011
18.	Seeds	Chloroform, ethyl acetate, and methanol	tiulcerative potential in rats	Singh *et al*., 2011
19.	Peel	Methanolic	Antioxidant activity	Saiharini and Padmaja, 2022
	C. naudinianus			
20.	Tubers	Methanol and ethyl acetate	Immunomodulatory	Du Preez *et al*., 2020
21.	Tubers	Dichloromethane and methanol	HIV-1 RT inhibition activities	Hedimbi, 2015
22.	Tubers	Aqueous and ethanol	Anticancer	Stuurmann, 2016

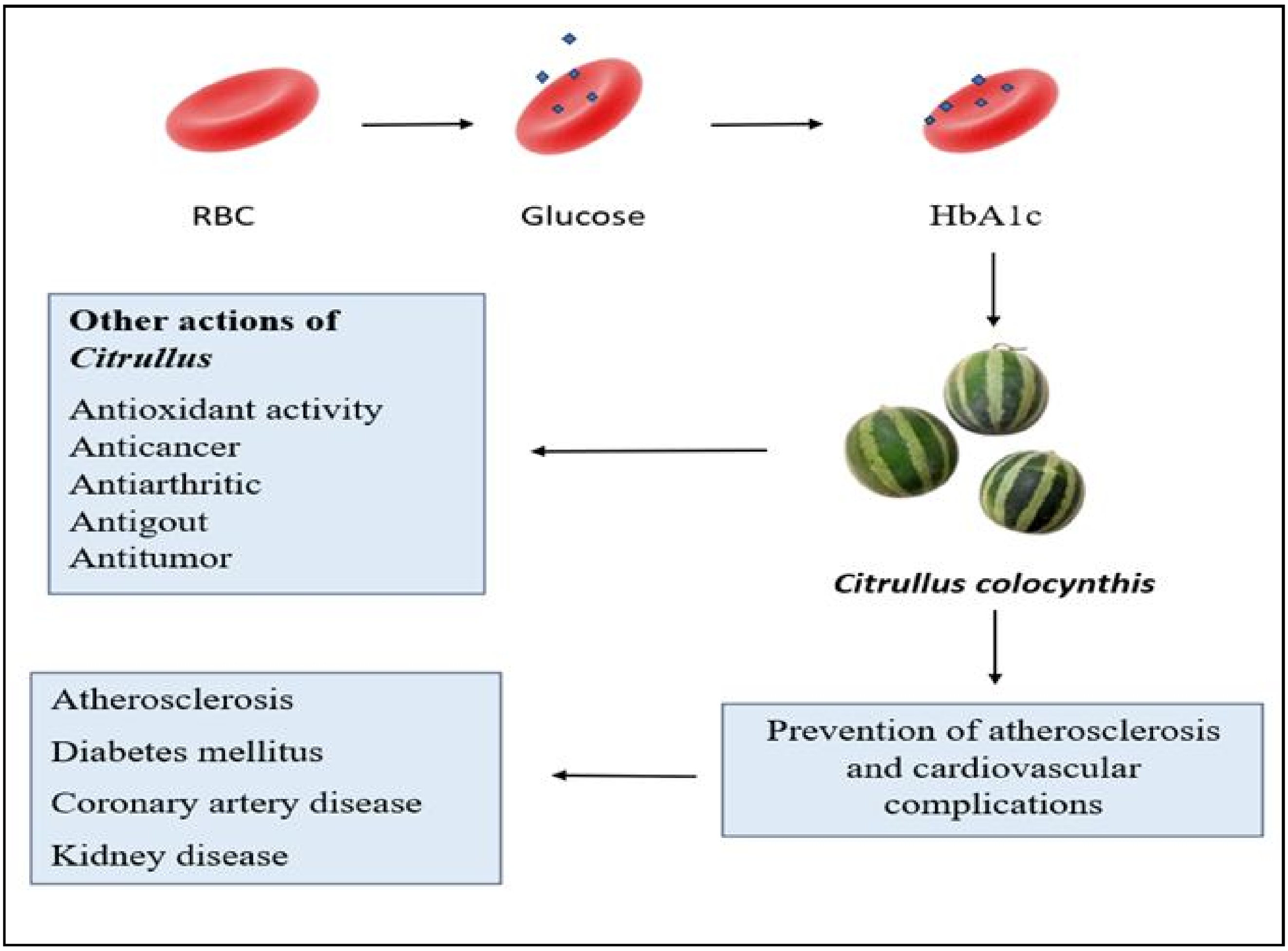

Figure 2: Pharmacological activity of *C. colocynthis*.

6. Therapeutic potential of *Citrullus* spp.

The *Citrullus* spp., are rich in phytochemical constituents that offer impressive health benefits. Among these, gallic acid stands out for its antioxidant and anti-inflammatory properties (Kroes *et al*., 1992). Cucurbitacin B is known for its anticancer effects (Mandour *et al*., 2023). Vanillic acid contributes to both antioxidant and antimicrobial activities, making it a valuable component for fighting infections (Al-Nablsi *et al*., 2022). Lycopene and citrulline content, which contribute to cardiovascular protection, metabolic regulation, and the management of hypertension and diabetes. Additionally, cucurbitacin L has shown promise in managing diabetes and reducing inflammation, and colocynthosides A may help address metabolic disorders (Khatri *et al*., 2021). Likewise, *Citrullus* spp. contain various bioactive substances which are used to treat a wide range of illnesses as discussed below.

6.1 Antimicrobial activity of *Citrullus* spp.

Citrullus spp. have been traditionally used in folk medicine to treat various infections. Recent studies have demonstrated their antimicrobial properties against fungi and bacteria, highlighting them as natural sources against pathogens. Research on *C. colocynthis* revealed that ethanolic extracts from its fleshy core, seeds, and roots showed significant antibacterial activity, with the fleshy core extract being most effective against Gram-positive bacteria of *Staphylococcus aureus* and *Bacillus subtilis* (Hameed *et al.,* 2020). Similarly, aqueous and ethanolic extracts of *C. lanatus* exhibited antibacterial effects, with the aqueous extract at 50 mg/ml displaying the highest inhibition (8 mm) against *Pseudomonas aeruginosa* (Bello *et al.,* 2016).

Fungal infections pose a significant health risk, particularly to immunocompromised individuals (Garnacho-Montero *et al.,* 2024). The emergence of drug-resistant strains has driven the search for new antifungal agents. *C. colocynthis*, known for its medicinal properties, has demonstrated antifungal activity (Idan *et al.,* 2015). Studies revealed that methanolic extracts of *C. lanatus* seeds exhibited strong antifungal effects against various fungi, including *Aspergillus flavus*, *Aspergillus niger*, *Penicillium notatum*, *Trichophytonmen tagrophytes*, and *Candida albicans* (Gautam *et al.,* 2023). Additionally, hydroalcoholic extracts of *C. colocynthis* fruits showed significant antifungal activity against *Aspergillus* and *Candida* strains, particularly *A. niger* and *A. fumigatus*, indicating its potential as an effective antifungal agent (Dhakad *et al.,* 2017).

6.2 Anticancerous activity

Studies have demonstrated that extracts from *C. colocynthis and C. naudinianus* possess significant anticancer properties. The phytochemicals present, including flavonoids, alkaloids, and phenolic compounds, exhibit inhibitory effects on cancer cell proliferation and induce apoptosis in cancerous cells (Stuurmann, 2016; Perveen *et al*., 2021). The anticancer methods are complex and include downregulating important signaling pathways like Wnt/β-catenin and STAT3, suppressing metastatic activity, inhibiting cell growth, and inducing apoptosis (Mandour *et al*., 2023). The seeds and fruit extracts from *C. colocynthis* and *C. naudinianus* are particularly effective against breast, liver, and colorectal cancers due to their antioxidant-rich profile and cytotoxic activities (Abdulridha *et al*., 2020; Mandour *et al*.,2023).

6.3 Anti-inflammatory

The anti-inflammatory potential of *C. colocynthis* and *C. lanatus* is attributed to their rich content of cucurbitacins and terpenoids. These compounds inhibit pro-inflammatory mediator NF-κB signalling pathway, thereby reducing inflammation (Mandour *et al*., 2023), noted for alleviating symptoms of rheumatoid arthritis and inflammatory bowel diseases (Raziani *et al*., 2023).These actions might help lower inflammatory responses in macrophages and improve cardiovascular health due to the presence of bioactive compounds like cucurbitacins and glycosides, which have been shown to reduce edema and inflammatory cell infiltration in animal models. The extracts from *C. mucosospermus* show anti-inflammatory effects against non-alcoholic fatty liver disease (NAFLD) due to the presence of cucurbitacin E and its glucosides (Park *et al*., 2024).

6.4 Antifertility

The antifertility effects of *C. colocynthis* are well-documented, with bioactive constituents affecting spermatogenesis and hormone regulation. Chaturvedi *et al*. (2003) found that when male rats were given a 50% ethanol extract of *C. colocynthis* fruit orally, the cauda epididymal sperm motility and density considerably decreased, as did fertility rates, the number of pups produced, and the levels of testosterone in the blood. In addition, the medication caused degenerative alterations in the seminiferous epithelium, including the halt of spermatogenesis at the secondary spermatocyte stage, increased testicular cholesterol, and decreased weights of the reproductive organs. Crucially, normal reproductive parameters were restored following a period of recuperation without therapy, indicating that these antifertility effects were reversible.

6.5 Antigout

C. colocynthis has shown great promise in antigout treatments. According to recent research biosynthesized silver nanoparticles from ethanolic extract of colocynth fruit have potent antigout properties *in vitro*, particularly through the inhibition of xanthine oxidase a key enzyme in uric acid production linked to gout, a crucial target in the treatment of gout because it lowers the formation of uric acid (Karunakaran and Hari, 2022). In addition to lowering inflammation and uric acid levels, they help stabilize cell membranes and prevent protein denaturation, all of which are important for managing gout. Rich in flavonoids and other bioactive substances, the plant has antioxidant properties that help reduce inflammation and oxidative stress linked to gout.

6.6 Immunomodulatory

Du Preez *et al*. (2020) investigated the immunomodulatory effects of *C. naudinianus,* where the results showed dose-dependent inhibition of T-lymphocyte proliferation without causing apoptosis. This immunomodulatory effect was mediated by suppressing activation markersand reducing cytokine production (IL-2, IFN-γ), making it effective in boosting overall immunity. Furthermore, in phagocytosis tests, both ethanolic and aqueous extracts of *C. colocynthis* demonstrated a moderate level of immunological activation, suggesting the ability to improve particular immune functions at particular dosages (Stein *et al*., 2024). In skin inflammation models, colocynth extracts downregulated the expression of inflammatory genes and elevated anti-inflammatory mediators, further demonstrating its immunomodulatory and anti-inflammatory activities.

6.7 Antioxidant property

Citrullus spp. is a rich source of antioxidants, including lycopene, flavonoids, and ascorbic acid. These antioxidants scavenge free radicals, reducing oxidative stress and preventing cellular damage (Gill *et al*., 2011). *C. colocynthis* extracts, both methanolic and aqueous, have shown strong free radical scavenging activity, these extracts can prevent oxidative damage to biomolecules like proteins, lipids, and DNA by neutralizing a variety of reactive oxygen species, such as hydroxyl radicals and peroxyl free radicals (Terki *et al*., 2023). Studies have also shown that endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) can reduce oxidative stress in animal models. The consumption of *C. lanatus* has been particularly associated with enhanced antioxidant status in clinical trials (Singh *et al*., 2011).

7. Industrial applications

Citrullus spp. are increasingly recognized for their industrial applications, with *C. colocynthis* agricultural waste being used to create advanced nanocomposites for superior insulation and biomedical purposes due to its excellent insulating and dielectric properties (Kamel *et al*., 2024). Additionally, colocynth fruit extract has been utilized in the green synthesis of silver nanoparticles, making it suitable for photovoltaic, nanoelectronic, and optoelectronic applications (Barzinjy *et al*., 2022). The seeds of colocynth, containing around 47% oil, serve as a promising source for biodiesel production, providing a sustainable energy option for regions with limited agricultural resources (Ahmed *et al*., 2020a).

Colocynth seeds are abundant in oil, which is extracted and utilized in the production of soap and other products. Following oil extraction, the leftover oil meal from *C. colocynthis* seeds is investigated as a component for animal feed. It can assist lower feed costs and provide a protein supplement in areas without native sources by partially replacing conventional protein sources in cattle, sheep, and goats (Mathur *et al*., 1989). In India, rumen methane emissions were reduced when cattle were fed 1% colocynth fruit (Hundal *et al*., 2020). The oil's high oleic and linoleic acid content also exhibits strong insecticidal properties, highlighting its potential for eco-friendly biopesticide development (Ahmed *et al*., 2020b). The plant's resilience and minimal cultivation needs further support its industrial potential in harsh climates.

Colocynth seeds have demonstrated strong potential as green corrosion inhibitors, achieving up to 94.3% efficiency in protecting mild steel from acid-induced corrosion (Doumane *et al*., 2024). Additionally, water melon byproducts, including rinds and seeds, are rich in vitamins, minerals, and functional compounds, making them valuable for nutraceuticals, food additives, and dietary supplements (Sorokina *et al*., 2021). Water melon flesh and rind are processed into juices, jams, and pickles. Water melon's squalene is one of the compounds utilized in pharmaceutical and cosmetic formulations because of its positive effects on skin and health. These applications underscore the industrial importance of *Citrullus* spp. as sources of bioactive compounds and sustainable solutions in food, energy, and health sectors.

8. Future trends and research needs

Citrullus, a potent phytochemical and pharmaceutical, holds immense potential for therapeutic benefits. However, further research is needed to fully unlock its pharmacological potential. This includes standardizing extracts, conducting clinical trials, and leveraging nanotechnology for drug delivery. Pharmacokinetic studies, molecular characterization, and genetic resources from wild species can help identify genes causing disease resistance and nutritional value. Additionally, personalized medical strategies and sustainable farming practices are crucial for long-term success.

9. Conclusion

The *Citrullus* spp. has numerous medicinal properties, with *C. colocynthis* being particularly promising for treating diabetes, cancer, and dermatitis. Its extracts have shown antidiabetic effects and anticancer properties through various pathways. *C. lanatus* also holds potential due to its antioxidant, laxative, hepatoprotective activity, and purgative properties. Both species highlight the potential of *Citrullus* spp. for developing novel treatments across various health conditions. Clinical trial data is scarce for other *Citrullus* species, but comprehensive *in vitro* and *in vivo* studies, rigorous clinical trials, and meticulous isolation and characterization of bioactive constituents could lead to innovative treatments for various diseases and health conditions.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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