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Unveiling the Medicinal Value of the Genus *Citrullus*: Phytochemical Composition, Pharmacological Effects, and Toxicological Insights

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Abstract

Citrullus L. is a largest genus of vascular plants belongs in the family(Cucurbitaceae) comprising over 130 species spread throughout the would.Species of *Citrullus* L. used for medicinal properties such as jaundice asthma and especially for the management of diabetes. Citrullus L.were recorded for the treatment of diabeties. A total 10 species of genus *Citrullus* L.were recorded for the treatment of diabeties.This data was collacted from various review paper using different websites like Google scholar, pubmed,Scopus, science direct,web of science and research gate Genus Citrullus is rich in bioactive compound including phenolic acid, alkaloids, Flavonoids, and tannins, Glycosides , phenolic acid are present in large guontities in Citrullus species L. have been used as herbal remedies for diabeties in different cultures *Citrullus* species anti microbial activity against E coli, aspergillus and Bacillus subtilis *Citrullus* species possesive antioxidant activity prevent oxidative damage to cells. Some Citrullus species such as *Citrullus colocynthis* L. and *Citrullus lanatus* such as weight loss of feteus.It is concluded that *Citrullus* species have high medicinal values especially for the

treatment of diabetes values,anti microbial,anti oxidant activity .more research is required for the breast inflammation treatment, antiviral research and source of novel pharmaceuticals

Introduction

The Citrullus genus belongs to the Cucurbitaceae family and encompasses several species, such as the widely consumed (Citrullus lanatus) and colocynth (*Citrullus colocynthis*). These plants, which originated in Africa and Asia, are characterized by their trailing growth, dark green lobed leaves, and large, variously colored fruits. Historically, Citrullus plants have been used in traditional medicine for centuries to address a range of health problems, including digestive troubles, skin infections, and diabetes. Their medicinal properties are attributed to bioactive compounds like alkaloids, flavonoids, and saponins. Modern research has highlighted the genus's potential health benefits, including antioxidant, anti-inflammatory, and antidiabetic activities. The purpose of this study is to provide a comprehensive analysis of the Citrullus genus, covering its traditional uses, phytochemical profile, pharmacological effects, and DNA barcoding.

Citrullus colocynthis is a useful cucurbit plant that is extensively dispersed throughout the world's arid locations. Tese plants are mainly found in the deserts of Arabia and the Sahara and the southern part of Asia which mainly includes India, Pakistan, and southern islands (Cofey et al. 2015).

Bitter apple fruit is commonly known as colocynth, bitter cucumber, bitter melon, egusi melon, *Citrullus colocynthis* lanatus, and the bitter vine of Sodom. It grows as a wild perennial in arid places across the world and has promising therapeutic, nutraceutical, and food uses (Asyaz et al. 2010).

The fruit of *Citrullus colocynthis* is bitter in taste, spherical in shape, and has a smooth and fne texture. It is frm and has a crust around it and also consists of around 200-300 seeds per gourd (Uma & Sekar 2014). Different parts of these plants serve as a therapy for diseases such as jaundice, diabetes, and asthma (Li et al. 2021).

Tese plants are generally perennial vines that produce very small sized fowers which are aromatic in nature and have mesocarp thickness, density, and seed-fruit proportion. Te physical attributes of bitter apple fruits include fruit mass, seed and pulp content, volume, epicarp, etc. Te average mass of the fruit in grams is approximately 506g. Te mass content of the pulp accounts for about half of the fruit mass. About 75.1g of the fruit's weight comprises of the seeds (Hussain et al. 2014).

Mature fruits have tiny seeds and are about 6mm long, oval in shape, compact in structure, brownish in color, and smooth in texture (Hussain et al.,2014). It has been reported that infectious diseases account for one-half of all deaths in the tropical countries (WHO, 1977). Along with this, these plants have medicinal uses which help in the prevention of gut-related disorders namely, dysentery and indigestion. It is often used as a traditional medicine for infammation as it possesses anti-infammatory properties (Kuralkar & Kuralkar 2021).

Plant medicine (phytoamedicine) has been used in healthcare delivery in many parts of Africa and the rest of the world (Elujoba, et al., 2005). At least 80% of Africans depend on plant medicine for their healthcare (Sofowora, 1993). Fruits and vegetables have been recognized as natural sources of various bioactive compounds (Pennington and Fisher, 2010). *Citrullus mucosospermus* seed, locally known as egusi seed, a wild member of the gourd family, has limitless potential for worldwide use in the food industry" (Olubi et al., 2024). Obesity is a significant, dangerous factor for several diseases, including type 2 diabetes,cardiovascular disease, hypertension, Alzheimer's disease, asthma, metabolisyndrome,fatty liver disease, gallbladder disease, osteoarthritis, obstructive sleep apnea, various cancers,

hypercholesterolemia, musculoskeletal disorders, and nonalcoholic fatty liver disease(NAFLD)(Gortan Cappellari et al., 2022; Xu et al., 2023).

The link between obesity and these conditions can be attributed to severalfactors such as inflammation, metabolic and mitochondrial dysfunction, hyperinsulinemia,and abnormal lipid and glucose metabolism. Dysfunctional adipose tissues are central to the development of these diseases(Liu & Nikolajczyk, 2019; Cinkajzlová, Mráz, & Haluzík, 2021).

They release cytokines and bioactive substancesthat drive inflammation, insulin resistance, and endothelial dysfunction, all contributing to obesity-related diseases. Additional factors include chronic inflammation, abnormal angiogenesis, interactions among inflammatory cytokines, endocrine hormones, adipokines,genetic predispositions, and environmental influences(AlZaim et al., 2022; Altuna-Coy et al., 2022).

In contrast, C. mucosospermus seeds are used primarily in traditional African culinary practices due to their bitterness.The ongoing trajectory of present research positions C. mucosospermus as an emerging focal point, revealing its potential efficacy across a myriad of domains (Mighan, Ariaii, Soltani, & Jafarian, 2023; Runde et al., 2023; Olubi, Felix-Minnaar, & Jideani, 2021).

The family Cucurbitaceae consists of two welldefined subfamiles, eight tribes, 118 genera, and about 825 species (Robinson & Decker-Walters, 1997). Included among the many economically important crop genera in this family are squash (Cucurbita spp.),melon (Cucumis melo L.), cucumber (Cucumis sativus L.) and watermelon *Citrullus lanatus* (Thunb.)Matsum. & Nakai.. Other Cucurbitaceae species are important as sources of edible seeds, ornamentals, traditional medicines, and toxic compounds (Neuwinger,1996; Robinson & Decker-Walters, 1997).

Past and recent attempts to establish relationships between the different tribes have contributed much to our understanding of this plant family. However, phylogenetic relationships between most genera and species remain unresolved and require further clarification (Jobst et al., 1998).

Citrullus rehmii and C. lanatus aremonecious annuals, whereas C. colocynthis, C. ecirrhosus and A. naudinianus are perennials. All species in this subtribe are native to the xerophytic habitats of northern (C. colocynthis) or southern (C. lanatus,C. ecirrhosus and C. rehmii) Africa. Acanthosicycos naudinianus, previously classified as *Citrullus naudinianus* (Jeffrey, 1975).

is also native to southern Africa. Citrullus lanatus , in its various forms, is used as a source of food in its native habitats, as are fruits of A. naudinianus and seeds of C. colocynthis.Previous isozyme studies established the relationships of three of the four species in the genus Citrullus to each other and to A. naudinianus (Navot and Zamir,1987).

Tinda (Citrullus vulgaris) belongs to family cucurbitaceae, and is one of the most important summer vegetables grown in Pakistan. It is palatable and tasty when cooked alone. As are sults of its good taste and palatability it is known as“Dilpassand”. It is rich in vitamins and minerals. Seeds and unripened fruit possesses great medicinal value. It can be grown in all types of soils. Sowing date is one of the most important factors affecting growth and yield of this crop.Water melon cv. Sugarbaby was sown on 5 different dates between 10th November to 15th December. Good plant growth, good fruit quality and highest yield was obtained from the plants sown on 21st November (Dessi and Patil, 1984). Yakimenko (1984) reported that out of 5 planting dates the early sowing on 3rd May gave the best yield in cucumber.When melon cv. Macrophomina phaseolina was planted at three different times in spring, it was concluded that highly yield was given by middle spring sowing (Bruton et al., 1985).

planting in musk melon cv. Flexuosus significantly decreased fruit weight and total fruit yield (Muhammad et al.,1989). Farooq (1992) reported that the plants sown in the second week of March gave maximum fruit volume, fruit weight, number of fruits per vine, total soluble salts and yield per hectare. Whereas minimum duration for flowering and fruit maturity were recorded in late sowing of muskmelon seeds.Baloch (1994) stated that usually the Tinda seeds are sown from the end of January to mid-February in the plains and from May to July on hills near the edges on each bed.Burki (1996).

Materials and Methods

Study Design

This research aimed to conduct a review of the phytochemical, pharmacological, and toxicological properties of genus Citrullus . Information was methodically collected from preexisting peer-reviewed articles that provide experimental data and published reviews between 1994 and 2024. The focus was to assemble and critically evaluate existing information about the bioactive constituents and pharmacological activities of this medicinal plant.

Data Collection Methods

The process of data aggregation included:

An organised review of scientific databases, including publications from Google Scholar, PubMed, Science Direct, and Research Gate, utilising the search terms: Genus Citrullus , phytochemicals, antioxidant activity, antimicrobial activity, toxicity, and nanotechnology applications. Inclusion of more than 40 articles and research studies relevant to the extraction, characterisation, and pharmacological evaluation of genus Citrullus published from 1994 to 2024.

Critical appraisal of selected studies to ensure methodological validity, reproducibility, and reliability of reported findings.

RESULTS

This paper presents and interprets the key findings from the study of Citrullus genus. The plant was analyzed concerning its:

Ethnobotanical uses, Phytochemical composition, Pharmacological properties, description , distribution, antioxidant actvities and toxicity. The findings are analyzed alongside existing research to emphasize their scientific and medicinal importance

Ethnobotanical Survey Results

Based on ethnobotanical studies of information gathered from local herbalists, traditional healers, and community elders, the Citrullus genus is widely recognized in rural medicine. The plant is commonly used to treat conditions such as :

Joint pain and rheumatism, Digestive issues and constipation, Diabetes and high blood sugar, Skin infections and wounds

Phytochemical Analysis

Phytochemical analysis has shown that the Citrullus genus is a source of various bioactive compounds, including, Alkaloids, Flavonoids, Tannins, Saponins

Antioxidant Activity

The antioxidant potential of Citrullus genus leaf and root extracts was determined using the DPPH radical scavenging assay. Antidiabetic Potential Diabetic rat models subjected to glucose tolerance tests indicated that Citrullus genus

Table 1 Distribution, phytochemistry, medicinal uses antioxidant, antimicrobial activities and toxicity of genus Citrullus

Plant name	Distribution	Phytochemicals	Medicine uses	Anti oxidant activity	Anti microbial activity	Toxicity	References
Citrullus colocynthis	Arabia , Sahara and southern, Asia, India, Pakistan and Southern islands	Alkaloids, flavonoi, phenolic compounds, glycosides, terpenoid, tannins.	Anti diabetic snake bite, anti tumors and rehumatis hypolipidemi	Flavonoids,phenolic acids, cucurbitacins, antioxidant enzymes.	Escherichia coli, Staphylococcus aureus, Bacillus subtilis, and Streptococcus pyogenes.	Toxicity Wight loss of feteus.	(Coffey et al.,2015),(Kundra et al., 2023; Alqasoumi et al., 2013; Mehmood et al., 2008),(Kundra et al., 2023; Mehmood et al., 2008),(Khan et al., 2016),(Hussain et al., 2017).
Citrullus lanatus	Pakistan, India,China,and Southeast Asian.	Tannins, saponins, alkaloids, and cardiac glycosides.	Gastroprotedive analgesic and antherose lerosis.	Flavonoids, phenolic compounds, lycopene..	Escherichia coli, Staphylococcus aureus, Pseudomonas species, Aspergillus niger, and Candida albicans.	Cucurbitacins	(Renner et al.,2020),(Ameer et al., 2022),(Norhidayah et al., 2018; Ali et al., 2022),(Kukoyi et al., 2021; Patel & Singh, 2019),(Patel & Singh, 2019),(Al-Snafi, 2017; El-Mahmoudy et al., 2007)
Citrullus naudinianus	Southern tropical Africa, Angola, Botswana Namibia, Zambia, and South	Cucurbitacins, phenolic compounds, flavonoids, and terpenoids	Diarrhea, fever, fungal and skin infection, headach	Flavonoids, phenolic compounds, and cucurbitacin.	Flavonoids, cucurbitacins, and phenolics.	The tuberous roots of *Citrullus naudinianus* are	(Mabberley,2017).,(PROTA,2004) (Moritz et al., 2023),(Moritz et al., 2023; Linhart et al., 2014),(Martin & Brown, 2011),(Mush

	Africa.					poisonous and contain highly cytotoxic compounds like cucurbitacins	onga et al., 2023).
Citrullus mucosospermus	West Africa and Northeast Africa, Guinea, Ghana,Nigeria.	Phenolic acids, flavonoids, and terpenoids.	It's help alleviate inflammations ,it helps reduce fact accumulation in the liver it help regulate blood sugar levels, its help regulate blood sugar levels, it help reduce hepatic steatosis.	Phenolics, flavonoids, and cucurbitacins	Cucurbitacins, phenolic acids, and flavonoids	Hepatoprotective effects the fruit pulp shows potential liver protection benefits by reducing liver enzymes	(Fursat,1972; POWO,2024),(Kang et al., 2024),(Nwachukwu et al., 2024), (Ogunlesi et al., 2024; Nwachukwu et al., 2024),(Oluwafemi & Adeoye, 2019),(Ijeh et al., 2019).
Citrullus edulis	Pakistan India China and Southeas	Flavonoids, phenolic compounds,	Laxative properties,Anti	Flavonoids, phenolic compou	Staphylococcus species and Streptoc	Gastrointestinal irritation	(Achigan_Dako et al.,2021),(Opara et al., 2021),(Hassa

	t Asia and grown warmer parts of America and the Mediterranean	saponins, and tannins. phenolic compounds, saponins, and tannins.	inflammatory properties, antimicrobial properties.	nds, saponins, and terpenoids.	occus pneumoniae.	(nausea vomiting diarrhea) Cytotoxicity damage	n et al., 2023),(Hassan et al., 2023; Ahmed & Khan, 2020),(Ahmed & Khan, 2020), (Singh et al., 2016).
Citrullus fistulosus	South Asia, India, Pakistan and Afghanistan.	Ascorbic acid, Butylated, hydroxyloluene DPPH.	Heart disease strokes, blood pressure control, cancer.	Ascorbic acid, polyphenols, flavonoids, DPPH scavenging activity	E.coli, streptococcus thermophilous, fusarium,oxysporium	No significant toxicity reported generally considered safe for consumption.	(Jain et al., 2023), (Chouhan & Sharma, 2025),(Jain et al., 2023; JDDT, 2024),(Jain et al., 2023),(Jain et al., 2023).
Citrullus fistulosus	Native to tropical Africa South Asia and subtropical regions	Cucurbitacins, flavonoids, alkaloids, phenolic compounds, saponins	Traditionally used as a laxative, diuretic, anti-inflammatory, and for treating gastrointestinal issues	Antioxidant compounds like phenolics and flavonoids; DPPH scavenging in seed/rind extracts	No direct study for C. amarus found; data extrapolated from related wild watermelon accessions	Contains bitter cucurbitacins; may be toxic at high concentrations (vomiting, diarrhea)	Renner & Pandey (2013),Jarret et al. (2017),Schaffer & Paris (2007) ,Norhidayah et al. (2018),Ali & Ahmed (2022),EFSA Journal (2018).

Discussion:

This research presented and interprets the key findings from the study of genus Citrullus (L.). Citrullus L. Species highlight the distribution morphological characteristics, medicinal uses phytochemical compound, antioxidant activity and antimicrobial properties .This study contain 8 species of genus Citrullus L.were analyzed for the treatment of gastrointestinal disorder, diabetes, inflammation.

Table 2 Distribution description and Medicinal uses of different species of Citrullus

Botanical name	Distribution	Description	Medicine uses	Reference
Citrullus colocynthis	Arabia ,Sahara and southern, Asia, India, Pakistan and Southern islands	Perennial herbaceous vine that produces small flowers. The stems are angular, rough and having rough hairs; leaves are alternately. Flowers are yellow and seen on the axils of the leaves. Seeds are small (6 mm in length), ovoid, compressed, smooth and brownish when ripe .	Anti diabetic snakebite, anti tumors and rehumatis hypolipidemi	(Al-Ghaithi et al., 2004; Krishnaraju et al.,2005; Perveen et al., 2007; Gurudeeban et al., 2010; Marzouk et al.,2010b), (Savithramma et al., 2007; Amamou et al., 2011), (Schafferman et al., 1998).
Citrullus lanatus	Pakistan, India,China,and Southeast Asian.	Small hairs on the stems and leaves of the plant ant with several herbaceous, firm and stout stems up to 3 m long. The young parts are densely woolly with yellowish to brownish hairs while the older parts are hairless. The leaves are herbaceous.	Gastroprotedive analgesic and antherose lerosis.	(Renner et al.,2020),(Baker, et al., 2012), (van, et.al, 2004; Fursa, 1981, Maynard, 2001; Oyolu, 1977).
Citrullus naudinianus	Southern tropical Africa, Angola, Botswana Namibia, Zambia,and South Africa.	Perennial, climbing, or trailing plant with thin, angled stems covered in fine hairs. It produces fruits that are oval to spherical .The leaves of the plant are alternately arranged, deeply lobed, and have a rough texture and a pale to medium green color.	Diarrhea, fever, fungal and skin infection, headaches	(Mabberley,2017). (Thompson,2008;Martin and Brown,2011).(Smith et al.,2012;Thompson, 2008)(Martin & Brown, 2011),(PROTA,2004).
Citrullus mucosospermus	West Africa and Northeast Africa, Guinea,Ghana ,Nigeria.	This is trailing, herbaceous plant that can spread along the ground for several meters, and its stems are angular and covered with fine hairs.The leaves are rough to the touch due to these hairs and are arranged alternately; they are simple and divided into five palmately-arranged lobes.	It's help alleviate inflammations , it helps reduce fact accumulation in the liver it help regulate blood sugar levels,its help regulate blood sugar levels, it help reduce hepatic steatosis.	(Fursat,1972;POWO ,2024),(Essiet et Al.,2021),(Kang et al.,2024).

Citrullus edulis	Pakistan India China and Southeast Asia and grown warmer parts of America and the Mediterranean	Herbaceous vine that can either trail along the ground or climb. It has rough, angular, and hairy stems. The plant produces solitary, unisexual, and yellow flowers that grow from the leaf axils. As a monoecious species, it develops both male and female flowers on the same plant.he plant has lengthy, bifurcated tendrils that facilitate its climbing growth habit.This plant thrives in hot, dry to partially dry climates, favoring sandy or loamy soils with good drainage.	Laxative properties,Anti inflammatory properties, antimicrobial properties.	Decker-Walters 1997).(Whitaker and Davis,1962),(Opara et al.,2021).

Distribution

Citrullus colocynthis mainly found in the deserts of Arabia and the Sahara and the southern part of Asia which mainly includes India, Pakistan and Southern islands (Coffey et al.,2015).

While *Citrullus lanatus* is mainly found in the Tropical of the world including Pakistan, India,China,and Southeast Asian(Renner et al.,2020)

In contrast *Citrullus edulis* mainly found in throughout tropical and subtropical regions of the world including Pakistan India China and Southeast Asia and grown warmer parts of America and the Mediterranean (Achigan_Dako et al.,2021)

However *Citrullus naudinianus* However *Citrullus naudinianus* is mainly found in the savanna and dry regions of southern tropical Africa, including Angola, Botswana Namibia, Zambia,and South Africa (Mabberley,2017).

While *Citrullus mucosospermus* is mainly found in the Tropical regions of west Africa and parts of Northeast Africa, including Guinea,Ghana,Nigeria(Fursat,1972;POWO,2024).

Description

Citrullus lanatus produces a fruit that is about 93% water, hence the name "water" melon. The "melon" part came from the fact that the fruit is large and round and has a sweet, pulpy flesh. The lanatus part is Latin, and has the meaning of being wooly, referring to the small hairs on the stems and leaves of the plant (Baker, et al., 2012).Watermelon is thought to have originated in southern Africa because it is found growing wild throughout the area, and reaches maximum diversity of forms there. It has been cultivated in Africa for over 4,000 years. *Citrullus lanatus* was brought to America by Spanish and quickly became very popular crop (Robinson and Decker, 1997). plant with several herbaceous, firm and stout stems up to 3 m long. The young parts are densely woolly with yellowish to brownish hairs while the older parts are hairless. The leaves are herbaceous but rigid, becoming rough on both sides; 60–200 mm long and 40–150 mm broad, but usually deeply 3-lobed with the segments again lobed or doubly lobed; the central lobe is much the largest. The leaf stalks are somewhat hairy and up to 150 mm long. The tendrils are rather robust and usually divided in the upper part. Male and female flowers occur on the same plant (monoecious) with the flower stalk up to 40 mm long and hairy. The fruit in the wild form is subglobose, indehiscent and up to 200 mm in diameter; the fruit stalk is up to 50 mm long (van, et.al, 2004; Fursa, 1981, Maynard, 2001; Oyolu, 1977).

However *Citrullus colocynthis* (L.) Schrad belongs to the Cucurbitaceae family. The plant is widely available in the Sahara and Arabian deserts, Sudan and Southern part of Asia including Pakistan, India and Southern Islands (Al-Ghaithi et al., 2004; Krishnaraju et al.,2005; Perveen et al., 2007; Gurudeeban et al., 2010; Marzouk et al.,2010b). The fruit was introduced by the Arabs in the middle ages to Spain and Cyprus (Bellakhdar et al., 1991; Wasfi et al., 1995; Abdel-Hassan et al., 2000). *Citrullus colocynthis* is a perennial herbaceous vine that produces small flowers. The stems are angular, rough and having rough hairs; leaves are alternately arranged on the petioles and rough to touch, 5–10 cm in length,1.5–2 cm in width, deeply 3–7 lobed; solitary pale yellow blooms (Savithramma et al., 2007; Amamou et al., 2011). Flowers are yellow and seen on the axils of the leaves. It is monecious, single and pedunculated. Each plant produces 15–30 round fruits, about 7–10 cm in diameter, green with undulate yellow stripes, becoming yellow all over when dry. The fruit of *Citrullus colocynthis* is bitter and globular with smooth texture. It is hard and has a rind around it and contains 200–300 seeds/gourd . Seeds are small (6 mm in length), ovoid, compressed, smooth and brownish when ripe (Schafferman et al., 1998). Seeds contained about 75% of the weight of fruit. Some physical properties of fruits such as mass of fruit, seed and pulp, volume, thickness of epicarp and mesocarp,seed-fruit ration and density are reported in the literature (Aviara et al., 2007). Generally average mass of *Citrullus colocynthis* fruit is 506 g and mass of pulp is almost 50% of the mass of fruit, while the seed contents is 71.8 g (Aviara et al., 2007).

While *Citrullus mucosospermus* is recognized by many taxonomists as a distinct species from sweet watermelon (Citrullus lanatus) due to morphological and genetic differences, confirmed by molecular phylogenetic studies. Widely cultivated in West Africa, particularly in Nigeria, it is primarily grown for its large, edible, oil- and protein-rich seeds used in soups and sauces, rather than its generally bitter pulp(Chomicki and Renner,2015).This is a trailing, herbaceous plant that can spread along the ground for several meters, and its stems are angular and covered with fine hairs (Essiet et al., 2021).The leaves are rough to the touch due to these hairs and are arranged alternately; they are simple and divided into five palmately-arranged lobes(Essiet et Al.,2021).The bifid (two-part) tendrils enable the plant to climb or attach itself to nearby plants for support (Essiet et al., 2021). The plant is monoecious, meaning it produces both male and female flowers on the same plant (Fursa, 1981). These flowers are yellow, have five parts (pentamerous), and are solitary and axillary, growing on a short, hairy stalk (pubescent peduncle) of about 2–3 cm long (Essiet et al., 2021).This fruit is a pepo that can be either round or oblong, featuring a tough outer skin that is green with lighter or darker stripes or spots. The bitter, white-to-pale-pink flesh inside is not consumed raw like that of sweet watermelons. Instead, it is grown for its seeds, which are the main product harvested (Chomicki & Renner, 2015).The seeds are notable for being large, flat, and high in oil and protein. In West Africa, they are a significant food source and are used in making soups and sauces. Each seed is approximately 1.0–1.5 cm in length and 0.7–0.9 cm in width, and the substantial thousand-seed weight suggests a strong potential for high yields. (Adewale et al.,2016).

While *Citrullus naudinianus* is a perennial, climbing, or trailing plant with thin, angled stems covered in fine hairs. It produces fruits that are oval to spherical and measure approximately 4–8 cm in diameter(Smith et al.,2012;Thompson,2008). The leaves of the plant are alternately arranged, deeply lobed, and have a rough texture and a pale to medium green color, typically reaching a length of 6–12 cm(Thompson,2008;Martin and Brown,2011).The fruit of this plant is notably bitter and ranges from oval to spherical, with a diameter of 4–8 cm [Smith et al., 2012; Thompson, 2008]. It changes color from green to yellow or orange as it ripens. The

plant's flowers are also distinctive, being solitary, unisexual, and typically yellow, and can be found emerging from the leaf axils (Martin & Brown, 2011).The plant has adapted to thrive in dry, sandy environments, and its presence is common in semi-arid regions (Martin & Brown, 2011; White & Green, 1975).

In contrast Citrullus lanatus , formerly known as *Citrullus edulis*, is an annual herbaceous vine that can either trail along the ground or climb. It has rough, angular, and hairy stems. The plant produces solitary, unisexual, and yellow flowers that grow from the leaf axils. As a monoecious species, it develops both male and female flowers on the same plant.(Jeffrey ,2005).The plant has lengthy, bifurcated tendrils that facilitate its climbing growth habit(Robinson & Decker-Walters 1997). The fruit is classified as a pepo and is either spherical or oblong in shape, featuring a smooth, green exocarp (rind). The edible endocarp consists of sweet, red or pink, juicy pulp. It contains numerous, compressed seeds that display a color spectrum from black to brown with a mottled pattern(Robinson & Decker-Walters 1997).This plant thrives in hot, dry to partially dry climates, favoring sandy or loamy soils with good drainage(Whitaker and Davis,1962).

Medicinal uses

Citrullus naudinianus, also referred to as Acanthosicyos naudinianus, is widely utilized in African traditional medicine for treating various conditions, including diarrhea, fever, and fungal or skin infections. It is also employed for headaches and serves as a vital water source in dry climates. The fruit is either consumed raw or roasted, while its seeds are ground into a meal(PROTA,2004).This plant contains bitter cucurbitacin-like compounds, which are traditionally used for their supposed anti-inflammatory and antimicrobial effects. It is important to note that these properties are based on anecdotal evidence, not clinical testing. The plant also requires further toxicological study, as its roots have been reported as toxic in some regions(PROTA,2004).

Citrullus colocynthis is used widely in different parts of the world for the treatment of a number of diseases including diabetes, constipation, leprosy, asthma, bronchitis, jaundice, joint pain, cancer and mastitis (Chopra, 1958; Perveen et al., 2007;Abo et al., 2008; Asyaz et al., 2010). The medicinal uses of this plant have been reported in the indigenous system of medicines in Pakistan, India, China, Africa and Asia, which include its uses in gut disorders such as indigestion, dysentery, gastroenteritis and colic pain as well as common cold, cough, toothache, wounds, and diabetes (Qureshi et al., 2010; Amamou et al., 2011; Gurudeeban et al., 2011).In the tropical and subtropical countries, *Citrullus colocynthis* is traditionally used as an antidiabetic medication (Nmila et al.,2000; Aburjai et al., 2007; Huseini et al., 2009; Rahbar and Nabipour, 2010). In Morocco, it is also used to treat diabetes and hypertension (Ziyyat et al., 1997; Eddouks et al., 2002; Tahraoui et al., 2007). In Pakistan and India, the fruits are used for the treatment of intestinal disorders, bacterial infections, diabetes and cancer in human as well as animals (Sharma, 1998; Katewa and Galav, 2005; Perveen et al., 2007; Asyaz et al., 2010; Sharma et al., 2010). In the United Arab Emirates, *Citrullus colocynthis* is one of the most popular folk medicines because of its antiinflammatory property (Wasfi et al., 1995). The fruit can stimulate intestinal peristalsis and soften bowel contents by an irritantaction on the enteric mucosa (Goldfain et al., 1989; Al-Faraj,1995; Barth et al., 2002). A decoction of the different parts of this plant is used to cure rheumatic pain and as an anticancer and hepatoprotective agents (Barth et al., 2002; Daradka et al., 2007;Asyaz et al., 2010).In Tunisia, and other Mediterranean countries, different parts of this plant, especially fruits and seeds, are often used to treat urinary infections (Marzouk et al., 2010a), in addition to treating many other disease such as, hypertension, rheumatism,

dermatological problems and pulmonary and gynecological infections(Marzouk et al., 2009; Marzouk et al., 2010a). In Saudi Arabia,fruits of *Citrullus colocynthis* are used as a purgative, antirheumatic, anthelmintic, carminative and as a remedy for sore throat and skin infections (Adam et al., 2001). It is a potent and drastichydragogue and catharsis producer in humans. The fruit is also ablood purifier and remedy for tumors and enlargement of spleen.The seeds of *Citrullus colocynthis* are used for the treatment of diabetes, while the leaves are used for the treatment of jaundice and asthma (Baquar and Tasnif, 1984; Kirtikar et al., 1984; Qureshiet al., 2010). *Citrullus colocynthis* is also well-known in Israel as source of seed oil and its fruit has been used as a laxative(Schafferman et al., 1998)

Citrullus mucosospermus, is beneficial for protecting the liver and improving metabolic functions(Kang et al., 2024).*Citrullus mucosospermus* extract has therapeutic potential in managing obesity and liver diseases. In obese mice, the extract reduced body weight gain, visceral fat accumulation, and liver fat buildup. It also improved liver health, decreased inflammation, and enhanced antioxidant defenses. Additionally, the extract protected the liver from damage in a model of non-alcoholic steatohepatitis (NASH) by lowering liver enzymes, reducing oxidative stress, and mitigating liver tissue damage. These findings suggest that *Citrullus mucosospermus* extract may be a valuable treatment option for metabolic disorders and liver diseases (Kang et al., 2024).

The Namib melon, or *Citrullus edulis*, is a wild watermelon from Southern Africa that has been traditionally used to treat dehydration and digestive problems, as ethnobotanical studies note its high water content and gentle diuretic properties (PROTA, 2004).Initial findings suggest that the fatty acids found in C. edulis seed oil have anti-inflammatory and antimicrobial effects. This indicates its possible use in treating skin infections and inflammatory skin conditions(Opara et al., 2021)The medicinal benefits of *Citrullus edulis* have not yet been scientifically proven, despite its long history of traditional use. To verify its therapeutic claims and guarantee safety, further pharmacological and clinical trials are essential(PROTA, 2004; Opara et al., 2021).

The medicinal benefits of watermelon, or Citrullus lanatus , include promising antidiabetic effects. In studies using diabetic rats, watermelon juice was found to reduce blood sugar and inhibit carbohydrate-digesting enzymes like α-glucosidase and α-amylase(Sharma et al., 2020).Extracts derived from watermelon seeds and peels have demonstrated antibacterial activity and antioxidant properties in laboratory (in vitro) and living organism (in vivo) studies(Salamatullah et al., 2023).The traditional use of hydroethanolic seed extracts for gastrointestinal and respiratory ailments is supported by animal studies. These studies demonstrated that the extracts have antidiarrheal, bronchodilator, and antispasmodic effects (Ameer et al., 2022). While research indicates that C. lanatus seed extracts are not harmful at typical consumption levels, one should be cautious to avoid excessive intake (Ekpenyong et al., 2021).

Table 3 Phytochemicals, and biological activities of genus Citrullus

Botanical name	Phytochemicals	Antioxidant properties	Anti microbial properties	Toxicity	References

Citrullus colocynthis	Alkaloids, flavonoids, phenolic compounds, glycosides, terpenoids, tannins.	Flavonoids,phenolic acids, cucurbitacins, antioxidant enzymes.	Escherichia coli, Staphylococcus aureus, Bacillus subtilis, and Streptococcus pyogenes.	Wight loss of feteus.	(Kundra et al., 2023; Alqasoumi et al., 2013; Mehmood et al., 2008),(Kundra et al., 2023; Mehmood et al., 2008),(Khan et al., 2016),(Hussain et al., 2017).
Citrullus lanatus	Tannins, saponins, alkaloids, and cardiac glycosides.	Flavonoids, phenolic compounds, lycopene.	Escherichia coli, Staphylococcus aureus, Pseudomonas species, Aspergillus niger, and Candida albicans.	Cucurbitacins	(Norhidayah et al., 2018; Ali et al., 2022),(Kukoyi et al., 2021; Patel & Singh, 2019),(Patel & Singh, 2019),(Al-Snafi, 2017; El-Mahmoudy et al., 2007).
Citrullus naudinianus	Cucurbitacins, phenolic compounds, flavonoids, and terpenoids	Flavonoids, phenolic compounds, and cucurbitacins	Flavonoids, cucurbitacins, and phenolics.	The tuberous roots of *Citrullus naudinianus* are poisonous and contain highly cytotoxic compounds like cucurbitacins	(Moritz et al., 2023),(Moritz et al., 2023; Linhart et al., 2014),(Martin & Brown, 2011),(Mushonga et al., 2023).
Citrullus edulis	Flavonoids, phenolic compounds, saponins, and tannins. phenolic compounds, saponins, and tannins	Flavonoids, phenolic compounds, saponins, and terpenoids.	Staphylococcus species and Streptococcus pneumoniae.	Gastrointestinal irritation (nausea vomiting diarrhea) Cytotoxicity damage).	(Hassan et al., 2023),(Hassan et al., 2023; Ahmed & Khan, 2020),(Ahmed & Khan, 2020), (Singh et al., 2016).
Citrullus mucosospermus	Phenolic acids, flavonoids, and terpenoids.	Phenolics, flavonoids, and	Cucurbitacins, phenolic acids, and	Hepatoprotective effects the	(Nwachukwu et al., 2024), (Ogunlesi et al.,

		cucurbitacins	flavonoids.	fruit pulp shows potential liver protection benefits by reducing liver enzymes.	2024; Nwachukwu et al., 2024),(Oluwafemi & Adeoye, 2019),(Ijeh et al., 2019).

Anti-Oxidant activity

Cucurbitacin is an antioxidant and may destroy free radicals such as hydroxyl, superoxide radicals as well as oxygen singlets. It also prevents lipid peroxidation and degradation altogether (Bernard & Olayinka 2010). C. colocynthi's methanolic fruit extract were discovered to be an efective antioxidant. Because of the inclusion of gallic acid which is a phenolic molecule, it has signifcant free radical scavenging capability. Te fruit extract's maximum antioxidants and radical scavenging capability were recorded at 2500 ml/ml (Kumar et al. 2008). Phytochemical analysis of bitter apple extracts demonstrated that the organic substances found in them provide as an efective antioxidant (Benariba et al. 2013). Polyphenolic chemicals are thought to be responsible for the therapeutic benefts of various nutraceutical and pharmaceutical plants used in traditional treatment. Marzouk et al. 2013 studied the DPPH free radical scavenging efect of an aqueous leaf extract of bitter apple produced in Tunisia. Te authors reported an IC50 value of 0.021 mg/mL. Cucurbitacin glycoside from bitter apple demonstrated ABTS radical scavenging capabilities (IC50, 145M), most likely as a result of direct scavenging impact on multiple free radicals (Hussain et al. 2014). Meybodi (2020) conducted an in-vitro investigation and found that C. colocynthis can reduce free radical damage to a person as it has a variety of biochemical that constitute to its efective antioxidant properties. C. colocynthis oil can improve antioxidant enzyme performance and safeguard the liver against damage (Amamou et al. 2015).

Watermelon (known scientifically as Citrullus lanatus) has notable antioxidant properties. These benefits come from flavonoids, phenolic compounds, and especially lycopene, the powerful red pigment in its ripe flesh. By fighting free radicals and preventing lipid peroxidation, these antioxidants collectively help to improve heart health, lessen inflammation, and may offer protection against certain types of cancer (Kukoyi et al., 2021; Patel & Singh, 2019).

Citrullus edulis, a watermelon-relative, possesses antioxidant benefits from its constituents like flavonoids, phenolic compounds, saponins, and terpenoids. These ingredients have been shown to improve the body's antioxidant defenses by raising levels of naturally occurring antioxidant enzymes and eliminating damaging radicals. This capability accounts for its historical application in treating conditions linked to oxidative stress and inflammation. (Hassan et al., 2023; Ahmed & Khan, 2020).

The antioxidant effects of *Citrullus naudinianus* are attributed to its high concentration of flavonoids, phenolic compounds, and cucurbitacins. These plant-derived compounds protect against cell damage by neutralizing reactive oxygen species (ROS) and boosting the body's natural enzymatic antioxidants, such as superoxide dismutase (SOD) and catalase. Because of these properties, the plant shows promise for use in therapies that prevent the oxidative damage involved in chronic diseases (Moritz et al., 2023; Linhart et al., 2014).

Citrullus mucosospermus, also known as egusi, shows promise for metabolic health due to its antioxidant properties. The plant contains bioactive compounds like

phenolics, flavonoids, and cucurbitacins that fight oxidative stress by scavenging free radicals and stopping lipid peroxidation. Studies suggest this antioxidant action helps reduce liver fat, manage blood sugar, and combat hepatic steatosis (Ogunlesi et al., 2024; Nwachukwu et al., 2024).

Anti-microbial activity

Results from different studies demonstrated antimicrobial and anticandidal activities of *Citrullus colocynthis* extracts and the antimicrobial effect varied from population to population (Marzouk et al., 2009; Maezouk et al., 2010a, 2010b). The Citrullus Q3 colocynthis extracts were active against both Gram-positive and Gram-negative bacterial strains (Marzouk et al., 2010a, 2010b).Study from Pakistan (Memon et al., 2003) displayed inhibitory effect of the ethanol extract of *Citrullus colocynthis* fruit against Bacillus subtilis. The response against Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa) was poor. Active response of the fruit extracts against the tested strains of bacteria might also be due to bioactive like flavonoids, glycosides and tannin (Memon et al., 2003).Antibacterial activity of *Citrullus colocynthis* extracts prepared in various solvents was studied against some pathogenic bacteria i.e. Bacillus cents, Salmonella typhimurium, Staphylococcus aureus,Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Mycobacterium smegmatis and, Staphylococcus epidermidis (Sharmaet al., 2010). Most of the extracts exhibited moderate MIC within the range of 20–100 μg/mL against all the bacterial pathogens.In another study from Iran, the antibacterial activity of *Citrullus colocynthis* fruits extracts (water and ethanolic) against standard (ATCC 25923) and hospital isolated strains of Staphylococcus aureus from novobiocin treatment patients was evaluated (Najafiet al., 2010).

The antimicrobial activities of crude chloroform, hexane and ethanol leaves, stem, fruits and seeds extracts from *Citrullus lanatus* var. citroides (CL) was carried out against bacteria (Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis and Proteus vulgaris) and fungi (Aspergillus nigar and Candida albican). Cup-plate diffusion and disc diffusion method were used. Analysis of the data revealed that, the chloroform extract of the fruit exhibited the maximum antibacterial activity. It showed antibacterial activity against S. aureus: 36 mm, B. subtilis; 38 mm, E. coli; 37 mm, P. valgaris; 23 mm and P. aerguinosa; 19 mm. Results were compared concurrently to standard drugs; clotrimazole and gentamicin. Based on the current findings, it was concluded that *Citrullus lanatus* var. citroides (CL) has antimicrobial activity, which is as potent as standard antimicrobial drugs against the selected microorganisms (Loiy, et al., 2011).

Citrullus edulis, a close relative of Citrullus lanatus , has antimicrobial properties, specifically fighting gram-positive bacteria like Staphylococcus species and Streptococcus pneumoniae. These effects come from natural compounds such as flavonoids, saponins, phenolic acids, and terpenoids, which disrupt the bacteria's enzymes and metabolism(Ahmed & Khan, 2020).

Citrullus naudinianus is known for its antimicrobial properties, which are attributed to its bioactive compounds like flavonoids, cucurbitacins, and phenolics. These compounds work by damaging the cell membranes of various microbes and inhibiting enzymes that are essential for their survival. Due to these effects, the plant is traditionally used in medicine to combat infections (Martin & Brown, 2011).

The plant *Citrullus mucosospermus* has strong antimicrobial potential, which comes from its specific compounds like cucurbitacins, phenolic acids, and flavonoids. These substances protect against bacterial and fungal pathogens by damaging their cells and causing oxidative stress, which in turn justifies its traditional use by some African communities for treating infections and inflammation (Oluwafemi & Adeoye, 2019).

Toxicity

Citrullus colocynthis has applications in traditional medicine but is also harmful because it contains poisonous compounds. The most dangerous of these is colocynthin, a bitter cucurbitacin glycoside, which irritates and seriously injures the gastrointestinal tract. This can result in severe symptoms like abdominal cramping, nausea, violent diarrhea, and in some cases, bloody inflammation of the colon(Al-Snafi, 2017; El-Mahmoudy et al., 2007). Furthermore, studies indicate that exposure to this plant during pregnancy is hazardous to the developing fetus, leading to a reduction in its weight(Hussain et al., 2017).

The common watermelon is a safe and popular fruit consumed all over the world, with low levels of the toxic compound cucurbitacin. When eaten as part of a regular diet, it does not typically cause harmful effects. However, due to its high water and fiber content, ingesting a large amount, particularly the less-fleshy parts like the seeds and rind, can result in minor digestive upset, including bloating or diarrhea(Bachari et al., 2017).

Citrullus naudinianus, a wild cucurbit from southern Africa, is traditionally recognized for its toxic properties, especially in its underground tuber. Indigenous communities have historically made arrow poison from tuber extracts, which points to the presence of potent poisonous compounds(Mushonga et al., 2023). An ethyl acetate extract from the C. naudinianus tuber showed activity that affects the immune system in lab tests (in vitro immunomodulatory activity). This effect is believed to be due to its high concentration of cucurbitacins. This finding suggests that while the plant extract has bioactive properties, it also carries the risk of being toxic at high doses (Mushonga et al., 2023).

Citrullus mucosospermus is relatively safe for consumption at standard intake levels due to its minimal toxicity (Oladunmoye et al., 2017). The fruit's pulp contains antioxidant compounds that have a hepatoprotective effect. In experimental models, these antioxidants help to reduce elevated levels of liver enzymes (ALT and AST), thereby protecting the liver from damage (Ijeh et al., 2019).

Citrullus edulis is a globally consumed species of watermelon that is considered safe in typical dietary quantities. It is not toxic at normal consumption levels because it contains very low amounts of cucurbitacins, which are bitter and potentially harmful compounds found in related plants.However, eating too much watermelon, particularly the seeds or rind, may lead to minor digestive problems. This can cause discomfort such as bloating, diarrhea, or cramping due to the fruit's high water and fiber content (Bachari et al., 2017).In contrast, *Citrullus colocynthis*, a related species, contains higher levels of toxic cucurbitacins, which have been linked to organ damage, particularly in the liver and kidneys, as evidenced in animal studies. This highlights a potential difference in toxicity profiles between Citrullus species, warranting further investigation.(El-Hawary et al., 2016)

Phytochemicals

The medicinal properties of *Citrullus colocynthis* (bitter apple or "tumma"), a plant used in traditional medical systems, can be attributed to its broad array of phytochemicals. It is particularly abundant in compounds such as alkaloids, flavonoids, phenolic compounds, glycosides, terpenoids, tannins, coumarins, and steroidss (Kundra et al., 2023; Alqasoumi et al., 2013; Mehmood et al., 2008).

Citrullus lanatus contains many beneficial plant compounds, or phytochemicals, that give it nutritional and medicinal value. Lycopene, a powerful red carotenoid antioxidant, is the most plentiful of these compounds, especially in the ripe, red flesh of the fruit(Kukoyi et al., 2021). Tannins, saponins, alkaloids, and cardiac glycosides,

which provide antimicrobial and antioxidant effects (Norhidayah et al., 2018; Ali et al., 2022)

Citrullus lanatus , formerly known as *Citrullus edulis*, is a plant highly valued for both its nutritional and medicinal properties due to its rich composition of phytochemicals. Different parts of the plant, especially the fruit pulp, contain flavonoids, phenolic compounds, saponins, and tannins.Scientific analysis, such as HPLC profiling, has identified specific flavonoids like naringenin, rutin, and catechin, which are responsible for the plant's potent antioxidant and anti-inflammatory effects. In addition, the fruit contains phenolic acids, including gallic acid, chlorogenic acid, and ferulic acid, which contribute to its ability to neutralize free radicals(Hassan et al., 2023).

The plant species *Citrullus mucosospermus*, also known as "egusi" in West Africa, is recognized for the nutritional and pharmacological value of its seeds. According to recent studies, its extracts contain significant phytochemicals, such as cucurbitacin E and cucurbitacin E-2-O-glucoside, which possess anti-inflammatory and antioxidant properties (Ogunlesi et al., 2024). This plant contains compounds like phenolic acids, flavonoids, and terpenoids, which have been shown to help reduce the development of fat cells and improve fat metabolism in studies involving obese subjects (Nwachukwu et al., 2024).

Citrullus naudinianus is rich in diverse phytochemicals, notably cucurbitacins, phenolic compounds, flavonoids, and terpenoids, which contribute to its potential medicinal properties and biological activities (Moritz et al., 2023).

Conclusion

The Citrullus L . comprising over 130 species demonstrates significant ethno medicinal especially for diabetes disease management.Tea prepared from *Citrullus colocynthis* and *Citrullus lanatus* used for diabeties treatment phytochemical present in Citrullus species including phenolic and alkaloids Terpenes etc these bioactive compounds used for treatment such as joint pain diabetes breast inflammation Citrullus species demonstrates antioxidant such as DPPH there by preventing oxidative damage to cells . Citrullus species have antimicrobial properties against.bacteria such as Ecoli , Bacillus staphylococcus etc.Citrullus species also exhibit toxicity showed anti fertile effects in rate . Citrullus genus offers a wealth of opportunities for medicinal , antimicrobial, Antioxidant application.

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