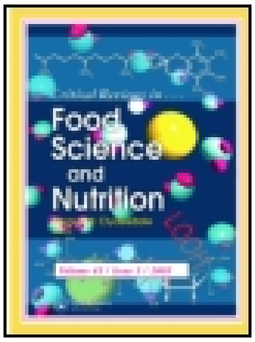

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REVIEW

Nutritional, phytochemical and diverse health-promoting qualities of *Cleome gynandra*

Mack Moyo[a] and Adeyemi O. Aremu[b,c]

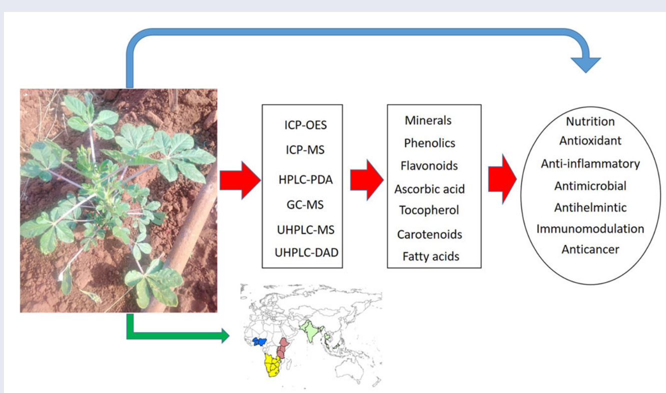
[a]Department of Horticulture, Faculty of Applied Sciences, Durban University of Technology, Durban, South Africa; [b]Indigenous Knowledge Systems Centre, Faculty of Natural and Agricultural Sciences, North-West University, Mmabatho, South Africa; [c]Food Security and Safety Niche Area, Faculty of Natural and Agricultural Sciences, North-West University, Mmabatho, South Africa

ABSTRACT

Cleome gynandra (Syn. *Gynandropsis gynandra*) is fast emerging as one of the most widely consumed leafy vegetables due to its nutrition and health-promoting properties. In addition to its high nutritional content, the plant has a rich pool of diverse antioxidant phytochemicals. The current review provides a critical appraisal on the increasing nutritional significance of *Cleome gynandra* due to its rich pool of natural bioactive compounds and beneficial health-promoting qualities. The rich nutritional content especially the high levels of macro- and micronutrients is an indication of its potential to mitigate malnutrition and the increasing incidence of diet-related obesity and non-communicable diseases. The presence of health-promoting natural compounds, notably polyphenols, glucosinates and terpernoids has been confirmed in *Cleome gynandra* using different analytical methods. *Cleome gynandra* possesses high levels of α-tocopherol, β-tocopherol and γ-tocopherol, ascorbic acid, α-carotene, β-carotene, lutein, violaxanthin, and β-cryptoxanthin. These nutritional compounds could be useful in food applications as supplements, colorants and extending shelf-life of food products. *Cleome gynandra* extracts have demonstrated promising effects in several biological assays using in vitro and in vivo systems. Clearly, diversified diets that include a regular intake of dark green leafy vegetables including *Cleome gynandra*, holds great promise in ensuring food and nutrition security.

KEYWORDS
Antioxidant; ascorbic acid; carotenoids; mineral content; phenolic acids; tocopherols

GRAPHICAL ABSTRACT



Introduction

Cleome gynandra L. (Syn. *Gynandropsis gynandra* (L.) Briq.; *Cleome pentaphylla* L.; *Cleome pentaphylla* DC.; Common names: Spider plant, African cabbage, African spider flower or cat's whiskers; Family: Cleomaceae) is native to sub-Saharan Africa and Asia. *Cleome gynandra* (Figure 1) is widespread throughout the tropics and subtropics where it is cultivated most often in dry areas, and plays a crucial role in food and nutrition security of local communities (Omondi et al. 2017; Wu et al. 2018). As depicted in Figure 2, spider plant is consumed as a vegetable in southern Africa, West Africa, East Africa and South Asia (Bala et al. 2010; Teklehaymanot and Giday 2010; Cernansky 2015; Neamsuvan and Ruangrit 2017; Kwarteng et al. 2018). Indeed, *Cleome gynandra* is fast emerging as one of the most widely consumed vegetable in sub-Saharan Africa and South Asia, regions with a combined population of more than 2 billion people. Beyond these geographic regions, Al-Asmari et al. (2017) reported the use of *Cleome gynandra* to treat scorpion stings in Saudi Arabia. In addition, *Cleome gynandra* is a major component of the indigenous vegetables economy in sub-Saharan African, which generates about 5 billion USD annually (Weinberger and Pichop 2009).

CONTACT Mack Moyo mackm@dut.ac.za Department of Horticulture, Faculty of Applied Sciences, Durban University of Technology, Durban, South Africa

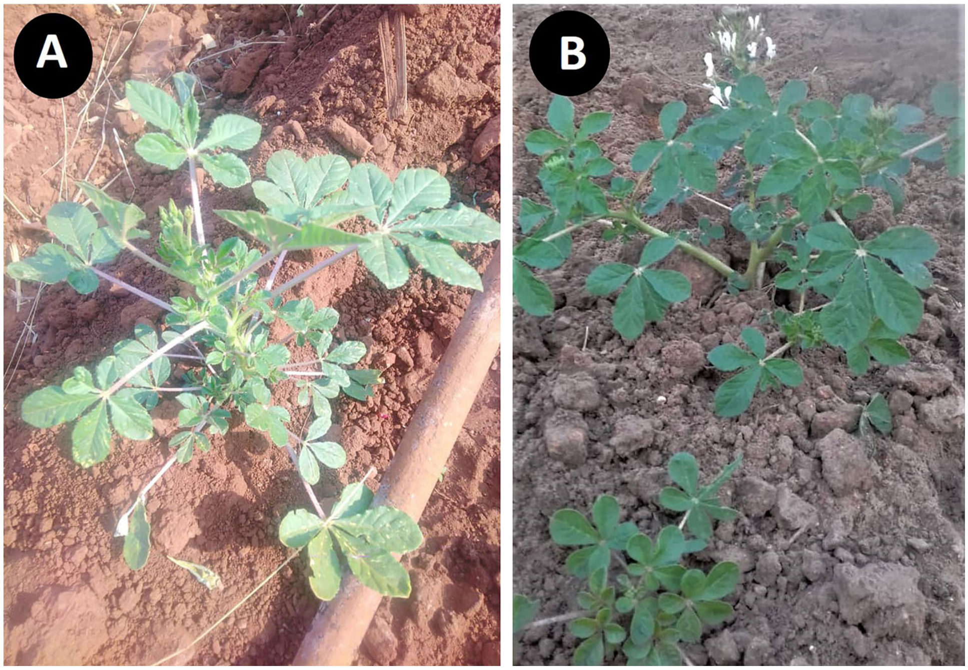


Figure 1. (a) A mature non-flowering *Cleome gynandra* plant. (b) Flowering *Cleome gynandra* plant.

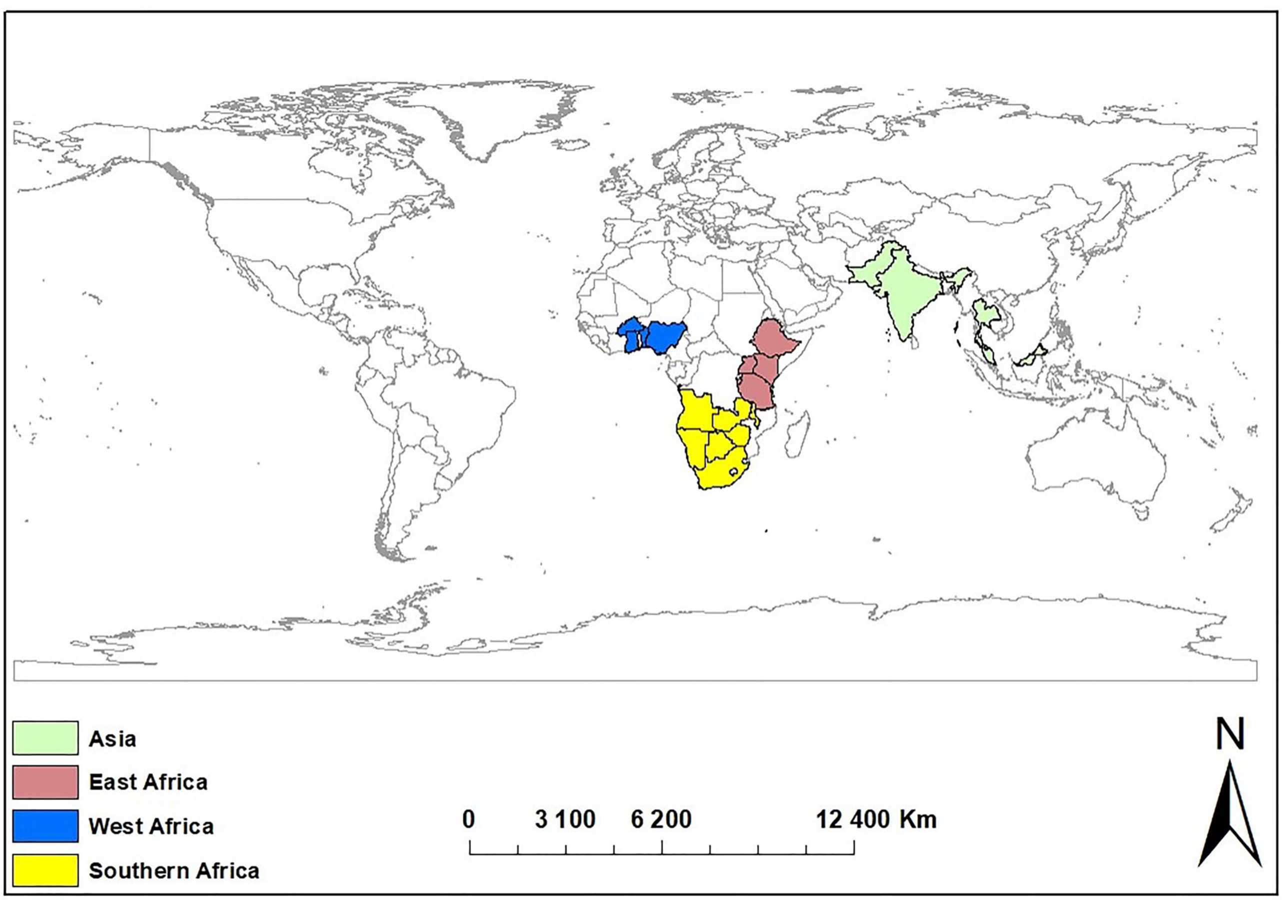


Figure 2. Geographic regions in Southern Africa, East Africa, West Africa and South Asia where there are reports on the uses of *Cleome gynandra*. The specific countries in each region are Angola, Botswana, Malawi, Namibia, South Africa, Zambia, Zimbabwe (Southern Africa); Burundi, Ethiopia, Kenya, Uganda, Tanzania (East Africa); Benin, Burkina Faso, Ghana, Nigeria (West Africa); India, Malaysia, Pakistan, and Thailand (South Asia).

Over the past decade, the global prevalence of undernourishment has fallen from 9.6% in 2010 to 8.9% in 2019, but increased in Africa from 18.9% to 19.1% or 250 million people (FAO et al. 2020). The number of undernourished people in sub-Saharan Africa increased by more than 32 million in the last five years, and the current prevalence of undernourishment in the region is 2.5-fold greater than the world average (8.9%) (FAO et al. 2020). In the next 10 years, the greatest increase in prevalence of undernourishment (+7.4%) is expected to occur in sub-Saharan Africa (FAO et al. 2020). Where food is available, the consumption of low-quality diets result in micronutrient deficiencies which often contribute to the increase in cases of diet-related obesity and non-communicable diseases (Willett et al. 2019). The World Health Organization (WHO)/FAO (2017) recommended a daily per capita intake of at least 400 g of fruits and vegetables for protection against diet-related non-communicable diseases. Under-utilized natural resources such as indigenous leafy vegetables may contribute toward food security and nutritional well-being. Worldwide, an estimated 7000 plants are either semi-cultivated or harvested from the wild for food, but less than 20 plant species provide most of world's food supply. Shifting away from this over-dependence on a limited number of food sources is vital, and indigenous plants can play a significant role, especially in terms of ensuring resilient food production systems and diversification of diets (Willett et al. 2019). However, the lack of attention in the past meant that indigenous plants remained largely oblivious to scientific developments and innovative research; hence, their value and potential is largely under-estimated and they remain grossly under-utilized. Characteristics of indigenous leafy vegetables, which make them attractive, include their ability to grow in inherently low fertility soils, high drought tolerance, faster growth rates, and shorter life-cycles; hence, are harvestable within a short period (Kwarteng et al. 2018). *Cleome gynandra* grows in a wide range of soils from sandy to clay loam, which are deep and well-drained, with a pH of 5.5 to 7.0 (Shilla et al. 2019). Notwithstanding these advantages, indigenous vegetables are often low yielding and less productive when compared to commercial vegetable cultivars. Consumer preference and acceptability is also comparatively lower for indigenous vegetables.

Cernansky (2015) described indigenous leafy vegetables, a largely overlooked food source, as "super vegetables." This narrative signifies the increasing recognition of leafy vegetables such as *Amaranthus* species, *Solanum scabrum* and *Cleome gynandra*, as potential sources of proteins, vitamins and minerals, for example iron and zinc (Omondi et al. 2017). Empirical evidence indicate that leafy vegetables have numerous benefits including high micronutrient content, and agronomic advantages such as low input requirements (Kwarteng et al. 2018). Besides their nutritional value, some indigenous leafy vegetables are also renowned for their therapeutic properties. For example, *Cleome gynandra* possesses dual nutritional and medicinal uses for a variety of conditions, as well as phytochemical compounds with insect repelling properties (Shilla et al. 2019). Notably, some plant-derived foods inhibit or cure age-related, chronic or other related diseases (Sauer and Plauth 2017). The dual nutritional and medicinal role of *Cleome gynandra* has significance in the maintenance of good health and protection against diseases. Based on available literature, *Cleome gynandra* provides nutritional and health benefits due to its bioactive compounds, macro- and micronutrients. This work provides a comprehensive review of the increasing significance of *Cleome gynandra* as a food source and the beneficial health properties of its bioactive compounds.

Botany and germplasm diversity

Although *Cleome gynandra* is native to Africa and Asia, it has become widespread in tropical, sub-tropical, Pacific regions and the New World (Shilla et al. 2019). Cleomaceae is a small family comprising of 25 genera and about 270 species (Patchell, Roalson, and Hall 2014; Bayat et al. 2018). Molecular phylogenetic analyses support the monophyly of Cleomaceae from the closely related Capparaceae and Brassicacae families (Hall 2008). Members of the sister family, Brassicaceae are mainly distributed in cooler temperate regions, whereas Cleomaceae species are found in warm temperate, subtropical and tropical climates as well as desert areas (Bayat et al. 2018). *Cleome* species are erect and branched herbaceous plants, with distinct palmately compound leaves, monosymmetric flowers with a ground plan of four sepals, four petals, six stamens, a bicarpellate gynocieum, and dehiscent fruits (Hall 2008). The floral monosymmetry is an adaptive innovation, which gives rise to widespread speciation and is often linked with specialized pollination syndromes (Bayat et al. 2018). Most Cleomaceae species exhibit gynophores and androphores, stalks that subtend ovaries and stamens, respectively. In *Cleome gynandra*, ovary and staminal stalks form fused structures called androgynophores (Bayat et al. 2018). *Cleome gynandra* is self-pollinated or cross-pollinated by insects such as hawkmoths (Martins and Johnson 2013).

Cleomaceae is one of the 19 families of flowering plants exhibiting C_4 photosynthesis, which represent about 7500 species (Sage 2004). There are three known C_4 plants in the genus *Cleome* with *Cleome gynandra* being the most studied (Brown, Parsley, and Hibberd 2005). The genus is fast emerging as a promising model to investigate the genetic basis of C_4 photosynthesis, floral evolution and comparative genomics (Patchell, Roalson, and Hall 2014). Part of its appeal emanates from its relatively small size, short life-cycle, phylogenetic closeness to Brassicaceae (family of *Arabidopsis thaliana*), self-fertility and high seed production (Brown, Parsley, and Hibberd 2005). The C_4 photosynthetic pathway uses phosphoenolpyruvate carboxylase (PEPC), the primary CO_2-fixing enzyme, to concentrate carbon dioxide near ribulose-1,5-biphosphate carboxylase/oxygenase (RuBsico), thereby enabling efficient assimilation of carbon (Sommer, Bräutigam, and Weber 2012). Reeves et al. (2018) showed significant variation in leaf morphology (size and shape of leaflets, petiole length, presence of trichomes,) and the atriplicoid-type Kranz anatomy traits (vein density, cross sectional area of bundle sheath strands, size of BS cells and stomatal density) between *Cleome gynandra* accessions from Africa and Asia. Despite the observed differences in Kranz anatomy, there was little variation among the accessions with respect to the photosynthetic performance (Reeves et al. 2018).

The variable geographical occurrence of *Cleome gynandra* species in Africa and Asia, has given rise to high germplasm diversity. Plants with wide geographic distribution experience varied biotic and abiotic conditions, which tend to drive the evolution of diverse morphological forms and phytochemical profiles. This immense genetic diversity provides a wide gene pool for plant breeding programs aimed at optimizing desired characteristics such as leaf yield, nutritional content, biotic and abiotic stress tolerance, and consumer taste preferences. Sogbohossou et al. (2019) found significant variability in morphological characteristics from a collection of 76 *Cleome gynandra* accessions from sub-Saharan Africa and Asia. The studied morphological descriptors included both quantitative (e.g. flowering time, leaf area, plant height, stem diameter, leaflet length, leaflet width, petiole length, filament length, pedicel length, pod length, pod width, 1000-seed weight) and qualitative traits (stem color, stem hairiness, branching habit, leaf color, leaf oiliness, petiole color, flower color, leaf margin shape). Overall, West African accessions were characterized by short plants with small leaves compared to Asian accessions with short plants and broad leaves, and tall East-Southern African *Cleome gynandra* (Sogbohossou et al. 2019). In addition, both West African and Asian plants exhibited high tocopherol content whereas East-Southern Africa plants had low levels of tocopherol (Sogbohossou et al. 2019). To date the largest repository of 295 accessions of *Cleome gynandra* germplasm from East Africa, Southern Africa and Asia is available at the World Vegetable Center (http://www.seed.worldveg.org/). Other collections maintained at the National Plant Germplasm System of the USDA (http://www.ars.grin.gov) and country specific gene banks in East and Southern Africa signify the importance of *Cleome gynandra* (Sogbohossou et al. 2018). The observed natural variability provides valuable germplasm for enhancing crop characteristics and nutritional qualities in breeding programs.

Medicinal uses

Cleome gynandra is an important food in many parts of Africa and Asia where it significantly contributes to household food security (Omondi et al. 2017; Wu et al. 2018). Boiled tender leaves, young shoots or flowers are consumed as a tasty relish or side dish (Van den Heever and Venter 2007). Besides its nutritional composition and qualities, the vegetable is widely valued for its diverse medicinal uses against several diseases and conditions (Table 1). Most parts of the plant, namely leaves, roots, flowers and seeds, are used for treating various diseases. Decoction of *Cleome gynandra* leaves is commonly used to treat malaria in several countries, notably Kenya (Jeruto et al. 2008), Benin (Yetein et al. 2013), Zambia (Chinsembu 2016a, 2016b) and Pakistan (Shah and Rahim 2017). Malaria, predominantly caused by the parasitic protists viz. *Plasmodium falciparum* and *Plasmodium vivax*, remains one of the most severe diseases in tropical and sub-tropical regions where approximately 3.4 billion people are at risk of infection (WHO 2019). In 2018, an estimated 93% of the 228 million malaria cases occurred in Africa (WHO 2019). Medicinal food plants including *Cleome gynandra*, can mitigate the impact of malaria in sub-Saharan Africa and parts of Asia where the disease burden is high.

Leaves and flowers of *Cleome gynandra* have widespread use in treating pain-related conditions such as headache, neuralgia, stomach pain, ear-ache, rheumatoid arthritis, skeletal fractures, colic pain and chest pain (Ajaiyoba 2000; Keding et al. 2007; Sridhar et al. 2014; Ahouansinkpo et al. 2016; Urso et al. 2016). In addition, Al-Asmari et al. (2017) reported the use of *Cleome gynandra* extracts in treating the severe pain and anti-inflammatory reactions caused by scorpion stings. Inflammation is a localized response induced by tissue injury, which protects the body and limits the spread of the injury-causing agent (Mule et al. 2008). The treatment of pain-related ailments suggests that *Cleome gynandra* contains anti-inflammatory phytochemicals, which can alleviate acute and chronic inflammation. Furthermore, several studies have reported the use of boiled leaves and roots in treating fever and respiratory ailments (Keding et al. 2007; Urso et al. 2016; Gumisiriza et al. 2019). Management of influenza, colds and cough proposes the presence of both antiviral and antibacterial phytochemicals in leaves and roots. The use of leaves in treating and managing wounds, abscess, diarrhea and chancroid (Ngezahayo et al. 2015; Ahouansinkpo et al. 2016; Chinsembu 2016b; Neamsuvan and Bunmee 2016) strengthens the hypothesis on the presence of a variety of antimicrobial compounds in *Cleome gynandra*. Based on these medicinal uses, several antimicrobial investigations have been reported.

The use of *Cleome gynandra* in reproductive health is conspicuous in ethnobotanical literature from different geographical regions, namely East Africa, West Africa and India. Roots and/or leaves represent the commonly used plant parts for facilitating childbirth, inducing labor (Tabuti, Lye, and Dhillion 2003; Jeruto et al. 2008; Kamatenesi-Mugisha and Oryem-Origa 2007; Sridhar et al. 2014), treating chancroid (Chinsembu 2016b) and alleviating sexual weakness (Ahouansinkpo et al. 2016). In remote rural areas of Uganda (East Africa), about 80% of pregnant women deliver at home and maternal-related conditions account for 20% of the total disease burden (Kamatenesi-Mugisha and Oryem-Origa 2007). In addition, boiled leaves stimulate milk production in breast feeding mothers (Keding et al. 2007; Dansi et al. 2008). *Cleome gynandra* is widely used in childbirth notably to induce labor, remove the retained placenta and controlling postpartum bleeding (Kamatenesi-Mugisha 2004). Particularly, some studies have reported a reduced carotenoid level in plasma of women prone to preterm deliveries, and a concomitant increase in gestational period upon carotenoid supplementation (Steiner, McClements, and Davidov-Pardo 2018). Management of bleeding-related conditions using *Cleome gynandra* is also evident from several studies (Table 1). Das et al. (1999) reported the use of its seed powder for the treatment of hemorrhages. In addition, iron deficiency anemic, which leads to low hemoglobin and/or red blood cell levels, is the most prevalent anemic disorder arising from insufficient dietary intake (Ku et al. 2017). Treating anemia with *Cleome*

Table 1. Medicinal uses of different plant parts of *Cleome gynandra* in different regions.

Plant parts	Medicinal uses	Preparation	Country	Reference
Leaf	Cough; allergy; hypertension	Boiled	Uganda	Gumisiriza et al. (2019)
Flower	Colic pain			
Root	Induce labor; influenza			
Leaf	Reduce blood pressure	Decoction	South Africa	Mokganya and Tshisikhawe (2019)
Leaf; seed; root	Scorpion sting	NS	Saudi Arabia	Al-Asmari et al. (2017)
Leaf	Malaria	Decoction	Pakistan	Shah and Rahim (2017)
Whole plant	Flatulence	Boiling to drink	Thailand	Neamsuvan and Ruangrit (2017)
Root	Easy delivery; fungal infections on head	Chewing roots	Uganda	Tugume et al. (2016)
Whole plant	Fever	NS	Angola	Urso et al. (2016)
Hypogenous organs	Headache			
Leaf	STI- Chancroid; malaria	Boiled	Zambia	Chinsembu (2016a); Chinsembu (2016b)
Leaf	Abscess	Pulverized leaves mixed with liquid from washing rice or paste	Thailand	Neamsuvan and Bunmee (2016)
Leaf	Abscess, wound, anemia, ear-ache, headache, hernia, jaundice, malaria, sexual weakness	Sauce	Benin	Ahouansinkpo et al. (2016)
Leaf	Diarrhea	Decoction	Burundi	Ngezahayo et al. (2015)
Leaf; seed	Headache; stomach ache	Decoction; infusion	India	Sridhar et al. (2014)
Leaf	Epileptic fits; neuralgia; rheumatism			
Root	Facilitate childbirth			
Leaf	Malaria	Decoction	Benin	Yetein et al. (2013)
Leaf; stem; root	Foods poisonings, rheumatism, sexual asthenia, headache, otitis, stimulant, snake bite	Juice extracted from plant parts	Burkina Faso	Meda et al. (2013)
Leaf	Anemia	NS	Benin	Allabi et al. (2011)
Leaf; flower	Bleeding of gums; headache; epileptic fits; chest pain; constipation; worm infection; stomach ache	NS	Zimbabwe	Chipurura (2010)
Leaf	Rheumatism; scorpion sting; stomach pain; thread-worm infection	Decoction or infusion of boiled leaves	India	Anbazhagi et al. (2009)
Leaf; root	Malaria; stomach congestion; facilitates and removes afterbirth	Decoction	Kenya	Jeruto et al. (2008)
Leaf	Stimulate milk production –breast-feeding	Boiled	Benin	Dansi et al. (2008)
Flower; leaf; root	Induce labor	Chewing	Uganda	Kamatenesi-Mugisha and Oryem-Origa (2007)
Leaf; flower	Ear-ache	Rub leaves, put liquid into ears	Tanzania	Keding et al. (2007)
Leaf	Headache; easy conception; cold; continuous lactation; stomach pain; fever	Boiled; Squeeze leaves and drink juice		
Seeds	Worm infestation	Powdered seeds-sugar mixture	Sri Lanka	Ediriweera (2010)
Flower; Leaf	Migraine, epilepsy	Pounded fresh; infusion	Uganda	Hamil et al. (2003)
Flower	Vomiting	Infusion	Uganda	Tabuti, Lye, and Dhillion (2003)
Root	Antenatal/promote labour; diphtheria	Chewing		
	Septic ears	Sap		
Leaf	Headache; ear-ache	Inhalation of the leaves; leaf juice	Nigeria	Ajaiyeoba (2000)
Seed	Anthelmintic	NS		
Flower; Leaf	Skeletal fractures	NS	India	Das et al. (1999)
Seed	Hemorrhages	Seed powder		
	Skin diseases	Extracted seed oil		

NS – Not specified

gynandra could be attributed to its high iron content in leaves (Ahouansinkpo et al. 2016).

Other noteworthy medicinal uses of *Cleome gynandra* recorded in ethnobotanical surveys include treatment of worm infections (Ajaiyeoba 2000; Ediriweera 2010; Anbazhagi et al. 2009), hypertension (Gumisiriza et al. 2019), epileptic fits (Hamil et al. 2003; Chipurura 2010; Sridhar et al. 2014), stomach congestion (Jeruto et al. 2008), food poisoning (Meda et al. 2013) and management of blood pressure (Mokganya and Tshisikhawe 2019). The use of leaves against worm infections suggests the presence of anthelmintic bioactive compounds. Soil-transmitted helminthiases (STHs) are prevalent in tropical and sub-tropical regions with the greatest rates of infections occurring in sub-Saharan Africa and East Asia (WHO 2015). The prevalence of infection is higher among children (1-14 years) in poor communities (WHO 2015). Dark green leafy vegetables with anthelmintic properties play a vital role in ameliorating health impacts of STHs. The multipurpose use of *Cleome gynandra* in the treatment and management of numerous ailments may explain its widespread consumption across different geographical regions in sub-Saharan Africa and Asia.

Nutritional properties

Several studies have demonstrated that *Cleome gynandra* leaves, young shoots and flowers, predominantly eaten in

Table 2. Nutritional constituents of *Cleome gynandra*.

Analytical technique	Plant part	Chemical constituents	Reference
AAS	Leaf	Calcium, Iron, Zinc	Orech et al. (2007)
EDXRF	Leaf	Calcium, Magnesium, Potassium, Zinc, Iron	Dehayem-Kamadjeu and Okonda (2019)
GC	Leaf	Myristic acid (14 : 0), Myristoleic (14:1), Pentadecylic acid (15:0), Palmitic acid (16 : 0), Palmitoleic acid (16:1n-7), Stearic acid (18 : 0), Vaccenic acid (18:1n-7), Linoleic acid (18 : 2n-6), α-linolenic acid (18:3n-3), Arachidic acid (20 : 0), Behenic acid (22 : 0), Lignoceric acid (24 : 0)	Glew et al. (2009)
GC–MS	Leaf (fresh & sun-dried)	Myristic acid (14 : 0), Palmitic acid (16 : 0), Stearic acid (18 : 0), Arachidic acid (20 : 0), Behenic acid (22 : 0), Lignoceric acid (24 : 0), Palmitoleic acid (16 : 1), Linoleic acid (18 : 2n-6), Linolenic acid (18 : 2n-3), Vitamin B_9 (Folic acid)	van der Walt et al. (2009)
HPLC	Leaf	β-Cryptoxanthin, β-Carotene α-Carotene, γ-Tocopherol α-Tocopherol	Gowele et al. (2019)
HPLC	Leaf, petiole, young stems	Vitamin B2, β-carotene	Schönfeldt and Pretorius (2011)
HPLC	Leaf	Lutein, β-carotene	Akundabweni, Mulokozi, and Maina (2010)
HPLC	Leaf	Alanine, Arginine, Aspartate, Glutamate, Glycine, Histidine, Proline, Isoleusine, Leucine, Lysine, Methionine, Cysteine, Phenylalanine, Tyrosine, Threonine, Valine, Serine	Glew et al. (2009)
HPLC-PDA	Leaf	α-Carotene, β-Carotene, Lutein, violaxanthin, α-Tocopherol, β-Tocopherol, γ-Tocopherol, Ascorbic acid	Sogbohossou et al. (2019)
HPLC-PDA	Leaf	β-carotene; Vitamin C	Moyo et al. (2018)
ICP	Leaf	Phosphorous, Calcium, Copper, Iron, Magnesium, Manganese, Zinc, Sodium	Odhav et al. (2007)
ICP-MS	Leaf	Phosphorous, Magnesium, Potassium, Calcium, Sodium, Manganese, Iron, Copper, Zinc	Moyo et al. (2018)
ICP-OES	Leaf	Iron, Zinc, Calcium, Magnesium, Phosphorous, Phytate	Gowele et al. (2019)
ICP-OES	Leaf	Potassium, Calcium, Magnesium, Phosphorous, Sulfur, Iron, Manganese, Zinc, Copper, Nickel, Molybdenum, Chromium, Cadmium, Lead, Aluminum	Omondi et al. (2017)
ICP-OES	Leaf	Calcium, Potassium, Magnesium, Phosphorous, Sulfur, Boron, Cobolt, Copper, Iron, Manganese, Molybdenum, Sodium, Nickel, Zinc	Jiménez-Aguilar and Grusak (2015)
ICP-OES	(raw/ cooked)	Iron, Zinc, Magnesium, Calcium, Phosphorus	Schönfeldt and Pretorius (2011)
ICP-OES	Leaf	Phosphorous, Magnesium, Potassium, Calcium, Sodium, Manganese, Iron, Copper, Zinc, Molybdenum, Cobolt, Strontium, Chromium, Lead	Glew et al. (2009)
Microplate-adapted colorimetric method	Leaf	Ascorbic acid	Jiménez-Aguilar and Grusak (2015)
UV-Vis detector	Leaf	Ascorbic acid	Gowele et al. (2019)

AAS, Atomic absorption spectrophotometry, EDXRF, Energy dispersive X-Ray fluorescence; GC-MS, Gas chromatography-Mass spectrometry; HPLC, High performance liquid chromatography; HPLC-PDA, High performance liquid chromatography-photodiode array; ICP-MS, Inductively coupled plasma mass spectrometry; ICP-OES, Inductively Coupled Plasma-Optical Emission Spectrophotometry

stews or sauces, contain high levels of minerals and vitamins (Table 2). It is evident that spider plant has important mineral constituents and dietary vitamins, namely pro-vitamin A carotenoids, vitamin E, and vitamin C (ascorbic acid). Numerous studies have examined occurrence of vitamins in *Cleome gynandra* using qualitative and colorimetric methods, but we focused on quantitative studies that used the best available analytical techniques.

Mineral content

The mineral content of *Cleome gynandra* leaves was quantified using Inductively Coupled Spectrophotometry (Glew et al. 2009; Schönfeldt and Pretorius 2011; Jiménez-Aguilar and Grusak 2015; Omondi et al. 2017; Moyo et al. 2018; Gowele et al. 2019) and Energy Dispersive X-ray Fluorescence (Dehayem-Kamadjeu and Okonda 2019). Overall, the leaves had high concentrations of both macro- and micronutrients. The prominent macronutrients reported in these aforementioned studies are potassium, calcium, magnesium, phosphorous and sulfur; whereas iron, zinc and manganese constitute the main micronutrients. Omondi et al. (2017) observed genotype-dependent variability in mineral content of *Cleome gynandra* leaves. The variation in mineral concentration provides opportunities for breeding improved cultivars with high levels of desired minerals, which are required for normal growth and development of children and the maintenance of good health in adults. Diversification of diets incorporating mineral-rich green leafy vegetables could alleviate the widely recognized impact of phytonutrient deficiencies in sub-Saharan Africa. Besides genotypic factors, variability of mineral concentrations in *Cleome gynandra* was dependent on soil quality. Hutchinson (2011) demonstrated that the application of different fertilizer rates correspondingly altered the mineral content in the leaves. Taken together, mineral content-improved genotypes grown under optimized agronomic conditions can provide high levels of phytonutrients such as calcium, potassium, phosphorous, iron and zinc.

Moyo et al. (2018) reported significantly higher phosphorous, calcium, potassium, iron and zinc concentrations in *Cleome gynandra* leaves when compared to the commercial vegetables, *Beta vulgaris* (Swiss chard) and *Brassica oleracea* (cabbage). Notably, phosphorous content in spider plant leaves was 3.3- and 5.5-fold higher than Swiss chard and cabbage, respectively. Likewise, calcium concentration in spider plant was 2.7- and 10.4-fold higher than Swiss chard and cabbage, respectively (Moyo et al. 2018). The results of the study clearly demonstrated the nutritional superiority of *Cleome gynandra* regarding some of the important minerals in human health, for example calcium, iron and zinc. Therefore, diet diversification incorporating a variety of vegetables can maximize the intake of mineral nutrients. Nonetheless, comprehensive studies that include a higher diversity of spider plant genotypes and commercial vegetables would provide more insights. *Cleome gynandra* and most other green leafy vegetables are consumed in stews; hence, it is vital to assess the impact of boiling on the mineral content of cooked vegetables. Schönfeldt and Pretorius (2011) observed an overall decrease in corresponding mineral content after cooking spider plant leaves for 23 min. The concentration of phosphorous, magnesium and calcium decreased by 25%, 37%, and 32%, respectively, whereas zinc and iron content remained constant (Schönfeldt and Pretorius 2011). Perhaps, some of the minerals were lost in water drained after cooking. The draining of water during cooking may be an uncommon practice at household level, which means the mineral elements may still be available. Notwithstanding the noteworthy results by Schönfeldt and Pretorius (2011), more studies on dynamics of mineral nutrients following cooking are required.

Vitamin content

Indigenous foods play a pivotal role in maintaining health of many people in developing regions of the world. Notably, green leafy vegetables are a major source of pro-vitamin A carotenoids, vitamin C, and vitamin E. For example, about 50% of the vitamin A requirement in rural Tanzania is derived from indigenous leafy vegetables including spider plant (Gowele et al. 2019). Selected studies have confirmed the occurrence of carotenoids (pro-vitamin A), vitamin C and vitamin E in *Cleome gynandra* leaves, petioles and young stems using high performance liquid chromatography–photodiode array (HPLC–PDA) (Table 2). Sogbohossou et al. (2019) observed significant variations in concentration of carotenoids and vitamin E among spider plant accessions from different geographic regions, which is vital for enhancing nutritional value of high yielding genotypes.

Carotenoids

The major carotenoids detected in spider plant include α-carotene, β-carotene, lutein, violaxanthin, and β-cryptoxanthin (Akundabweni, Mulokozi, and Maina 2010; Schönfeldt and Pretorius 2011; Moyo et al. 2018; Gowele et al. 2019; Sogbohossou et al. 2019). Vitamins are potent antioxidants, mostly introduced in fruit and vegetable-rich diets because the human body cannot synthesize them. Major dietary carotenoids are fat-soluble tetraterpenoids, belonging to two major groups, pure hydrocarbons, and xanthophylls, the oxygen-containing carotenoids (Krinsky and Johnson 2005). In spider plant, oxygen-containing xanthophylls include lutein and β-cryptoxanthin, whereas carotenes, notably α-carotene and β-carotene constitute the pure hydrocarbons. The pro-vitamin A carotenoids, α-carotene, β-carotene, and β-cryptoxanthin can be metabolized to vitamin A in the human body (Baiano and Del Nobile 2016). Among the carotenoids, β-carotene exhibits the greatest pro-vitamin A activity (Krinsky and Johnson 2005). Vitamin A plays an important role in immune system function and the prevention of major diseases, including certain cancers (Baiano and Del Nobile 2016). Using an in vivo study, Bala et al. (2010) reported the anticancer activity of *Cleome gynandra* whole plant extracts against Ehrlich ascites carcinoma (EAC) cell line. Other mechanisms of protection by carotenoids, mostly lutein and violaxanthin, include the absorption of blue light that can cause damage to eyes and advance development of cataracts (Krinsky and Johnson 2005). The severity of vision impairment conditions remains greatest among children in Africa and South-East Asia, the main regions contributing a significant proportion of the 250,000 to 500,000 vitamin A-deficient children who become blind every year (WHO 2009). Clearly, nutrition plays a major role in eye health and dietary diversification that includes pro-vitamin A-rich vegetables can reduce occurrence of vision impairment caused by corneal opacity in children and improve the vitamin status in rural communities (Neugart et al. 2017; WHO 2019).

Vitamin E

Vitamin E, a lipid-soluble compound with potent chain-breaking antioxidant activity consists of two main homologous series, tocopherols (α-, β-, γ-, δ-T) and the corresponding tocotrienols, which both contain a chroman ring but different side chain constituents (Gee 2011). Vitamin E forms in spider plant leaves comprise α-tocopherol, β-tocopherol, and γ-tocopherol (Table 2). Sogbohossou et al. (2019) reported a 20-fold variation in which West African and Asian *Cleome gynandra* accessions had higher tocopherol content compared to East and Southern Africa plants. The content of vitamin E in vegetables varies depending on plant species, maturity, environmental conditions, as well as pre- and postharvest factors (Chun et al. 2006). In a comparison of different indigenous leafy vegetables, Gowele et al. (2019) observed low α- and γ-tocopherol concentrations in spider plant of 0.2 μg/g FW and 0.1 μg/g FW, respectively. Likewise, Sogbohossou et al. (2019) reported low γ-tocopherol (0.02–0.4 μg/g FW) but moderate α-tocopherol levels that ranged from 1.8 μg/g to 37.2 μg/g FW depending on geographic origin. The results indicate a notable 186-fold differential in α-tocopherol concentration between the two studies. Even though most plant-derived foods including dark leafy vegetables have low to moderate concentrations of tocopherols, they provide a consistent and significant source of vitamin E in the diet (Chun et al. 2006).

Generally, α- and γ-tocopherols are the principal antioxidant forms of vitamin E in most food sources where they occur (Jiang 2014). Between the two main homologs, α-tocopherol is the most abundant in nature and only form retained and maintained in the human body (Traber and Stevens 2011). Although α-tocopherol has the highest biological activity (Gee 2011), γ-tocopherol exhibits distinctive anti-inflammatory and antioxidant properties, which are superior to those of other vitamin E forms, in treating chronic diseases (Jiang 2014). Several studies have demonstrated the anti-inflammatory (for example, Narendhirakannan, Subramanian, and Kandaswamy 2007a; Mule et al. 2008) and antioxidant (for example, Bala et al. 2012) activities of spider plant extracts using in vivo models (Table 3). Furthermore, medicinal uses of spider plant include treatment of chronic inflammatory diseases such as asthma, scorpion stings and rheumatism (Table 1). Studies at the molecular level have demonstrated that γ-tocopherol scavenges reactive nitrogen species and inhibits cyclooxygenase (COX-1; COX-2) and 5-lipoxygenase (5-LOX), thereby blocking the formation of prostaglandins and leukotriene (Jiang 2014).

In many food sources, vitamin E coexists with lipids and its consumption is often associated with intake of certain fatty acids occurring in the diet (Jiang 2014). The fatty acid profile of wild-harvested spider plant consisted of six saturated fatty acids, one monounsaturated fatty acid and two polyunsaturated fatty acids, namely linoleic acid and linolenic acid (van der Walt et al. 2009). Not surprisingly, γ-tocopherol endowed foods often contain high content of polyunsaturated fatty acids, whereas α-tocopherol rich plant oils exhibit high levels of monounsaturated fatty acids (Kamal-Eldin and Andersson 1997). Based on the study by van der Walt et al. (2009), it is compelling to suggest that spider plant and other dark green leafy vegetables could provide notable levels of essential polyunsaturated fatty acids, namely omega-3 (n-3) fatty acids and omega-6 (n-6) fatty acids. However, there is a conspicuous paucity of empirical data on spider plant on the interrelationship between tocopherols and fatty acids.

Vitamin C

Vitamin C, a water-soluble antioxidant, occurs in spider plant leaves as quantified using HPLC-PDA (Table 2). Unlike some mammals, birds and reptiles that can synthesize vitamin C, humans lack L-gulonolactone oxidase, the terminal enzyme in the ascorbic acid biosynthetic pathway (FAO/WHO 2004). Moyo et al. (2018) compared vitamin C content in spider plant, Swiss chard and cabbage, and noted a 3.2- and 4.7-fold higher concentration of vitamin C in spider plant compared to its counterparts, respectively. Jiménez-Aguilar and Grusak (2015) found high ascorbic acid levels in spider plant accessions collected in Zambia, but without significant variation among them. On the other hand, Sogbohossou et al. (2019) established a nine-fold geographic-independent variability in ascorbic acid content of spider plant, which ranged from 173.7 to 1556.8 μg/g FW. Likewise, a genotype from Tanzania yielded an ascorbate concentration of 1544 μg/g FW, which was significantly higher than 12 other indigenous leafy vegetables (Gowele et al. 2019). Clearly, spider plant and other green leafy vegetables can significantly contribute to the vitamin C recommended dietary allowance (RDA) of 90 mg/day and 75 mg/day for adult men and women, respectively (Institute of Medicine, Food and Nutrition Board 2000).

According to FAO/WHO (2004), leafy vegetables represent a more stable source of vitamin C, given their extended supply over longer periods of the year compared to fruits. The nutritional significance of vitamin C resides in its chain-breaking scavenger capacity against reactive oxygen species (ROS) and reactive nitrogen species (RNS), which would otherwise attack low-density lipoproteins (Baiano and Del Nobile 2016). It is most probable that vitamin C substantially contributes to the observed antioxidant and vasodilatory activities of spider plant extracts (Table 3). Vitamin C functions as a cofactor for enzymes involved in collagen synthesis as well as hormone and amino acid biosynthesis (Institute of Medicine, Food and Nutrition Board 2000; Traber and Stevens 2011). Ascorbic acid deficiency in the body leads to defective and impaired collagen synthesis, which causes the physical symptoms of scurvy, notably fatigue and muscle weakness. Further to its role in maintaining normal metabolic body functions, ascorbic acid enhances non-haem iron absorption in the human gut (Traber and Stevens 2011). Increased plasma vitamin C levels are associated with decreased risk of coronary heart and cardiovascular diseases (Institute of Medicine, Food and Nutrition Board 2000). Perhaps, dietary intake of vitamin C from dark green leafy vegetables remains the best option for most rural communities in low and medium income countries.

Phytochemistry

The therapeutic importance of the various compounds found in plants has progressively received interest globally (Jiang, Doseff, and Grotewold 2016). *Cleome* species are well-known for their diverse chemical groups especially the terpenes and phenols (Singh, Mishra, and Mishra 2018). As shown in Table 4, different analytical techniques have been used to determine the phytochemicals in different parts of *Cleome gynandra*. The majority of the phytochemical evaluations have focused on leaves. Based on UHPLC-MS/MS analysis, phenolic acids including the hydroxycinnamic and hydroxybenzoic acids at varying concentrations were quantified in spider plant leaves (Moyo et al. 2018). Likewise, the concentrations of glucosinolates and flavonoids in leaves and flowers of 30 *Cleome gynandra* accessions were determined using UHPLC-DAD (Omondi et al. 2017). The therapeutic effects of some of these aforementioned compounds especially the phenolic acids as antioxidant, antimicrobial and anti-inflammatory agents are well-established (Jiang, Doseff, and Grotewold 2016; Van Vuuren and Holl 2017; Altemimi et al. 2017). Particularly, ferulic acid exhibits a wide range of biological activities including antioxidant, anti-inflammatory, antimicrobial, anti-allergic, hepatoprotective, anti-carcinogenic, antithrombotic, antiviral and vasodilatory actions (Kumar and Pruthi 2014). Varying concentrations of flavonoids have been quantified in the leaves, stem and flower of *Cleome gynandra* (Kasem and Fatahy 2016; Neugart et al. 2017). Jiang, Doseff, and Grotewold (2016) have underlined evidence of the therapeutic value of these different types of flavonoids.

Table 3. Biological activities of *Cleome gynandra*.

Biological activity	Method/Assay	Key results	References
Anticancer	In vivo study - Swiss albino mice against Ehrlich Ascites Carcinoma (EAC) cell line at the doses of 200 and 400 mg/kg of methanol crude whole-plant extract Positive Control — 5-fluorouracil (20 mg/kg i.p)	Significant decrease ($p < 0.01$) in tumor volume, viable cell count, tumor weight. Dose dependent anticancer activity	Bala et al. (2010)
Anti-inflammatory	In vivo study - writhing test (abdominal constriction test) in adult Wister rats with aqueous stem extracts Positive Control -Aceclofenac sodium 10 mg/kg, i.p	Stem extract (100 mg/kg, i.p.) significant reduction ($P < 0.01$) of rat paw edema	Mule et al. (2008)
Anti-inflammatory	In vivo study -adjuvant induced arthritic Wister male albino rats administered with leaf extract —150 mg/kg body weight/rat Positive Control -Indornethacin (10 mg/kg body weight)	Extract decreased carrageenan paw edema and cotton pellet granuloma; reduced lipid peroxide levels	Narendhirakannan, Subramanian, and Kandaswamy (2007b)
Anti-inflammatory	In vivo study -adjuvant induced arthritic Wister male albino rats administered with leaf extract —150 mg/kg body weight/rat/day for 30 days Positive Control - *p*-Nitrophenol; N-Acetyl neuraminic acid	Lysosomal enzymes, protein-bound carbohydrates and plasma TNF-α in arthritic rats restored reduced to normal levels	Narendhirakannan, Subramanian, and Kandaswamy (2007a)
Anti- inflammatory	In vivo study -adjuvant induced arthritic Wister male albino rats administered with leaf extract —150 mg/kg body weight/rat/day for 30 days Positive Control — 1,1,3,3-Tetramethoxypropane	Reduced paw edema volume; Increased level of lipid peroxides, catalase, glutathione peroxidase; Reduced level of reduced glutathione, superoxide dismutase	Narendhirakannan, Subramanian, and Kandaswamy (2005b)
Anti-inflammatory	In vivo study -adjuvant induced arthritic Wister male albino rats administered with leaf extract-150 mg/kg body weight/rat/day for 30 days Controls –Normal rats; adjuvant-induced arthritic rats	Extracts restored Hb, RBC count, and PCV to near normal levels. Increased levels of WBC, platelets, and ESR significantly ($p < .05$) suppressed by *Cleome gynandra* extract	Narendhirakannan, Subramanian, and Kandaswamy (2005a)
Antinociceptive	In vivo study- hot plate test in mice using six (6) solvent extracts of the leaves at 100 mg/kg i.p. Positive control -Pentazocine (10 mg/kg i.p.)	Ethanol and water extracts significantly increased the reaction time and compared favorable to the positive control	Ghogare et al. (2009)
	In vivo study- acetic acid-induced (0.6% solution of 10 mL/kg acetic acid) writhing test in mice of the six leaf extrcats at 100 mg/kg i.p. Positive control –Paracetamol (50 mg/kg i.p.)	Ethanol, ethyl acetate and water extracts produced significant inhibition of writhing reaction induced by acetic acid which was comparable to the positive control. Percentage inhibition of writhing by this extracts was water > ethanol > ethyl acetate extracts	
Antioxidant	In vitro study –antiradical activity (DPPH) of varying (20, 50, 70 and 100) % of ethanolic extracts Positive controls –Curcumin (500 μg/mL); Quercetin (350 μg/mL)	Most noteworthy antioxidant activity was exhibited by 20% ethanolic extract-$IC_{50} = 40.36$ µg/mL	Chandradevan et al. (2020)
Antioxidant	In vitro study – ORAC of methanolic leaf extracts Positive control -Ascorbic acid (14 µg/mL); Trolox	Higher antioxidant activity of *Cleome gynandra* than Beta vulgaris and Brassica oleraceae	Moyo et al. (2018)
Antioxidant	In vitro study –antiradical activity (DPPH); β-carotene-linoleic acid assay of methanolic and water extracts Positive control -Ascorbic acid (14 µg/mL); Butylated hydroxytoluene (250 µg/mL)	Higher radical scavenging activities of aqueous methanolic (EC_{50}=106 μg/mL) extracts compared to water (EC_{50}=160 μg/mL) extracts	Moyo et al. (2013)
Antioxidant	In vivo study using peritoneal macrophages and peripheral blood lymphocytes N-acetyl cysteine (NAC at 150 mg/kg i.p)	*Cleome gynandra* flavonoid fractions scavenged the superoxide anion (O_2□, produced by carbon tetrachloride, CCl_4) in chronic inflammatory cells	Bala et al. (2012)
Antioxidant	In vitro study –antiradical activity of methanolic extracts Positive control –Ascorbic acid (5%)	Extracts exhibited time dependent decrease in radical scavenging of DPPH and β-carotene; increase in reducing power ($FeCl_3$) and inhibition of lipid peroxidation	Muchuweti et al. (2007)
Antimicrobial (fungi)	In vitro study - MIC and MFC of ethanol and water extracts (aerial plant parts) against three (3) clinical fungal isolates (M.c, T.m and T.r) Positive control – Chloramphenicol (0.5 mg/mL)	Notable antifungal activity by both extracts, which varied with type of organism. For ethanol extracts: T.r = 0.03-0.06 mg/mL M.c and T.m = 0.25-0.5 mg/mL For water extract: T.r = 0.13-0.25 mg/mL M.c and T.m = 0.25-0.5 mg/mL Generally, *T.r* was more sensitive than *M.cs* and than *T.m.*	Imanirampa and Alele (2016)

(*continued*)

Table 3. Continued.

Biological activity	Method/Assay	Key results	References
Antimicrobial (bacteria and fungi)	In vitro study –MIC and MBC of methanolic leaf extracts against 4 MTCC bacterial (B.s, S.a, E.c and P.a) and 4 MTCC fungal (A.f, A.n, C.a and F.a) strains Positive controls - Streptomycin (10 μg/disk); Nystatin (10 μg/disk)	*S.a* (MTCC 3160; MIC- 0.039 mg/mL, MBC- 0.039 mg/mL); *B.s* (MTCC 441; MIC- 0.078 mg/mL, MBC- 0.078 mg/mL); *C.a* (MTCC 183; MIC- 0.039 mg/mL, MFC- 0.078 mg/mL); *A.n* (MTCC 2723; MIC- 0.078 mg/mL, MFC-0.156 mg/mL)	Sridhar et al. (2014)
Antimicrobial (bacteria and fungi)	In vitro study - disk diffusion method of isolated compounds from stems (100 mg/mL) against 2 bacterial (S.a and E.c) ATCC and 2 fungal (C.a and C.g) MTCC strains Positive controls - Trimethoprim; Miconazole (100 µg/mL)	*S.a* (IZ = 29 mm); *E.c* (IZ = 33 mm); *C.a* (IZ = 36 mm); *C.g* (IZ = 29 mm)	Ranjitha et al. (2014)
Antimicrobial (bacteria and fungi)	In vitro study –disk diffusion method of leaf and stem methanolic extracts against 8 microbial strains (E.c, P.a, C.a, S.a ATCC29213, S.a NCRL, S.e, S.f, B.s-NCRL)) Positive controls - Amphotericin B (25 µg/mL); streptomycin (10 mg/mL) mm	*Cleome gynandra* extracts were only potent against *S.a* (ATCC29213) and *B.s* (IZ = 25 mm Ø) while C.a was poorly susceptible to the extract. Sa (NCRL) and S.e (NCRL) were moderately susceptible to the extracts	Hamil et al. (2003)
Antimicrobial	In vitro study –disk diffusion leaf and stem hexane and methanol extracts (200 mg/mL) against 6 bacterial (B.c, B.s, S.a, P.a, E.c and S.f) and 5 fungal (C.a, P.sp, F.o, A.f and A.n) clinical strains Positive control - Ampicillin (2.5 ug/mL) IZ = 10-25 mm; Tioconazole (1 mg/mL) IZ = 10—25 mm	Degree of susceptibility to extracts: *B.s* > *S.f* > *B.c* > *E.c* > *S.a* > *P.a* For fungal strains, C.a (IZ = 10-17 mm); P.sp (IZ = 12-18 mm); F.o (IZ =10-13.5 mm); A. flavus (IZ = 10-14 mm); A.n (IZ = 10-13 mm)	Ajaiyeoba (2000)
Antimicrobial (bacteria)	In vitro study - disk diffusion method of aqueous leaf extracts against 10 bacterial (A.v, A.h, E.c, K.a, P.a, V.d, V.p, B.c, S.p, C.s) strains Negative control Disks with no residues	After 24 h, A.v (IZ = 10 mm Ø); B.c (IZ= 13); S.p (IZ= 15); P.a (IZ = 10) After 48 h, A.v (IZ = 12 mm Ø); B.c (IZ= 15); S.p (IZ= 17); P.a (IZ = 10)	Samy, Ignacimuthu, and Raja (1999)
Anthelmintic	In vitro study – stem and leaf extracts (10, 20, 50, 80 and 100 mg/mL in distilled water) Positive control - Piperazine citrate (10 mg/mL)	Degree of susceptibility to extracts: *P.p* > *F.g* > *T.s*	Ajaiyeoba, Onocha, and Olarenwaju (2001)
Immunomodulation	In vivo study - phagocytic activity, cell mediated and humoral immune in Wister albino rats Control – 5 % dextrose normal saline	Immunosuppression activity in *C. gynandra* ethanolic extracts	Kori, Gaur, and Dixit (2009)
Immunomodulation	In vivo study - phagocytic activity, cell mediated and humoral immune in Wister albino rats Positive control – Septilin (500 mg/kg, p.o.)	Dose dependent immunosuppression	Gaur et al. (2009)
Vasodilatory	In vitro study -thoracic aortic rings (3 mm) from Wistar Kyoto (WKY) rats Positive control –Acetylcholine; Histamine ($10□^{1}_{10}$ to $10□_{10}$ M)	Dose-dependent vasodilatory effect in endothelium-intact aortic rings	Runnie et al. (2004)

A.h, *Aeromonas hydrophilla*; A.v, *Alkaligens viscolactis*; A.n, *Aspergillus niger*; A.f, *Aspergillus flavus*; ATCC, American Type Culture Collection; B.c, *Bacillus cereus*; B.s, *Bacillus subtilis*; C.a, *Candida albicans*; C.g, *Candida glabrata*; C.s, *Cytophage* species; ESR, erythrocyte sedimentation rate; E.c, *Escherichia coli*; F.a, *Fusarium axisporum*; F.o, *Fusiparum oxyposirum*; F.g, *Fasciola gigantica*; Hb, Hemoglobin; i.p., intra-peritoneal; IZ, inhibition zone; K.a, *Klebsiella aerogenas*; M.c, *Microsporum canis*; MIC, minimum inhibitory concentration; MFC, minimum fungicidal concentration; MTCC, Microbial Type Culture Collection and Gene Bank; NAC, N-acetyl cysteine; NCRL, Natural Chemotherapeutics Research Laboratory; PCV, Packed cell volume; P.s, *Penicillum* sp.; P.p, *Pheritimia pasthuma*; P.a, *Pseudomonas aeruginosa*; RBC, Red blood cell; S.a, *Staphylococcus aureus*; S.e.; *Staphylococcus epidermidis*, S.f, *Streptococcus faecalis*; S.p, *Streptococcus pyogens*; V.d, *Vibrio damsela*; V.p, *Vibrio parahaemolytica*, T.r, *Trichophyton rubrum*; T.m, *Trichophyton mentagrophytes*; T.s, *Tenia solium*; WBC, White blood cells

The use of GC-MS revealed the presence of approximately 28 compounds in the aerial part of *Cleome gynandra* (Lwande et al. 1999). In terms of quantity, the major compounds were carvacrol (29%), trans-phytol (24%) and Linalool (13%). The potential of the identified compounds as livestock tick repellent was demonstrated against *Rhipicephalus appendiculatus*. At the highest concentration (0.1 μL) tested, the majority of the compounds had more than 50% inhibitory activity against the test organism. At 0.1 μL, the inhibitory activity (%) for some of the compounds (for e.g. carvacrol, linolool, nerolidol and *m*-cymene) were comparable to the effect exhibited by the positive control (*N,N*-diethyl-toluamid, DEET) (Lwande et al. 1999). However, it remains imperative to explore the bioactive principles of phytochemicals or their derivatives to diversify the base of effective acaricides in the field of human and veterinary medicine. Thus, spider plant has the potential to contribute to this on-going drive based on the promising anti-tick effects.

The isolation and structural elucidation of the active compound(s) remain essential to obtain new leads in drug discovery. This is often achieved using data from a wide range of spectroscopic techniques such as UV-visible, Infrared (IR), Nuclear Magnetic Resonance (NMR) and mass spectroscopy (Altemimi et al. 2017). Cleogynol [(20S,24S)-epoxydammarane triterpenoid], a novel compound, was isolated from the whole plant extract of *Cleome gynandra* using spectral and chemical methods (Das et al. 1999). Jain and Gupta (1985) isolated and identified three polyphenols from seeds using a combination of analytical methods. Different researchers (Kjaer and Thomsen 1963; Kjaer, Conti, and Larsen 1953; Songsak and Lockwood 2002) have established evidence of the presence of

Table 4. Phytochemical characterization of *Cleome gynandra* plant parts.

Analytical technique	Plant part	Chemical constituents	Reference
Column chromatography	Seed	5,7-Dihydroxychromone, 5-Hydroxy-3,7,4′-trimethoxyflavone, Luteolin	Jain and Gupta (1985)
GC	Aerial parts	Carvacrol, *trans*-Phytol, Linalool, *trans*-2-Methylcyclopentanol,	Lwande et al. (1999)
GC-FID, EI-MS, CI-MS	Seed	Methyl isothiocyanate (Glucocapparin)	Songsak and Lockwood (2002)
GC-MS	Aerial parts	*β*-caryophyllene, *m*-Cymene, Nonanal, 1-*α*-Terpineol, *β*-cyclocitral, nerol, trans-Geraniol, Carvacrol, *β*-Ionone, *trans*-Geranyl-acetone, Nerolidol, methyl isothiocyanate, cis-3-Hexen-1-ol, *β*-Ocimene, *trans*-2-Hex en-1-ol, heptan-2-one, anisole, benzaldehyde, 2,4,5-Trimethyl-thiazole, Phenyl-acetaldehyde, *d*-Limonene, Phenyl acetonitrile, Methyl salicylate, *α*-Ionone, Tridecanal, Cedrene	Lwande et al. (1999)
GC–MS	Leaf	Methyl-isothiocyanate, Propyl- isothiocyanate, Butyl-isothiocyanate, (E)-2-Hexenal, Hexanal, (Z)-3-Hexenal, (E)-2-Pentenal, 2,4-Hexadienal, 2,4-Heptadienal, (E)-2-Heptenal, 2-Octenal, Decanal, Propanal, *β*-Ionone, *β*-Cyclocitral, *α*-Humulene, Linalool, *α*-Pinene, (E)-*β*-Ocimene, *α*-Terpineole, (Z)-3-Hexenol, (Z)-2-Pentenol, (E)-2-Hexenol, 1-Hexanol, Cyclopentanol, (Z)-3-Hexenyl acetate, Decyl acetate, Hexyl acetate, 2,3-Pentanedione, 3,5-Octadien-2-one	Nyalala, Petersen, and Grout (2013)
HPLC	Stem, Leaf, Flower	Quercetin 7-rhamnoside, Quercetin 3-rutinoside, Quercetin 7-rutinoside, Quercetin 3,7-dirhamnoside, Quercetin-3-glucoside, Quercetin 7-rhamnoside, Kaempferol-3-o-glucoside, Kaempferol 7-rhamnoside, Kaempferol 3-rutinoside, Kaempferol 3-glucoside-7-rhamnoside	Kasem and Fatahy (2016)
HPLC-DAD-ESI-MS	Leaf	Caffeoylglucaric, Coumaroylglucaric, Feruloylglucaric, Quercetin-3-diglucoside, Quercetin-3-rutinoside-7-glucoside, Aglycone-3-rutinoside, Quercetin-3-rutinoside, Kaempferol-3-diglucoside, Isorhamnetin-3-diglucoside, Quercetin-3-neohesperidoside, Kaempferol-3-rutinoside, Isorhamnetin-3-rutinoside, Isorhamnetin-3-glucoside	Neugart et al. (2017)
HPLC-DAD-ESI-MS	Leaf, Flower	Quercetin-3-diglucoside, Quercetin-3-rutinoside, Isorhamnetin-3-diglucoside, sorhamnetin-3-rutinoside, Kaempferol-3-diglucoside, Kaempferol-3-rutinoside	
HPLC-PDA	Leaf	*β*-carotene; Vitamin C	Moyo et al. (2018)
NMR	Stem	*β* –Amyrin, *β*-Amyrin-3-O- *β*-Glucopyranoside, Sitosterol, Stigmasterol	Ranjitha et al. (2014)
NMR	Whole part (excl. seeds)	Cleogynol – [(20S,24S)-epoxydammarane triterpenoid]	Das et al. (1999)
Paper chromatography	Seed	Methyl isothiocyanate (Glucocapparin)	Kjaer and Thomsen (1963); Kjaer et al. (1953)
UHPLC-DAD	Leaf, Stem, Flower, Silique	3-Hydroxypropyl glucosinolate, 3-Indolylmethyl glucosinolate, 4-Hydroxy-3-indolylmethyl glucosinolate	Omondi et al. (2017)
UHPLC-MS	Leaf	Protocatechuic acid, *p*-Hydroxybenzoic acid, Salicylic acid, Caffeic acid, *p*-Coumaric acid, Sinapic acid, Ferulic acid	Moyo et al. (2018)

CI-MS, chemical ionization-mass spectra; EI-MS, electron impact-mass spectra; GC, Gas-liquid chromatography; GLC, gas liquid chromatography; GC-FID, Gas chromatography with Flame-Ionization Detector; GC-MS, Gas Chromatography-Mass Spectrometry; HPLC-PDA, High performance liquid chromatography with a photodiode array detector; HPLC-DAD-ESI-MS, high-performance liquid chromatography with electrospray ionization and mass spectrometry; ICP-MS, Inductively coupled plasma mass spectrometry; NMR, nuclear magnetic resonance; UHPLC-MS, Ultra-high performance liquid chromatography coupled to a mass spectrometer

glucocapparin in *Cleome gynandra* seeds. Furthermore, four well-characterized compounds (*β*-amyrin, *β*-amyrin-3-O-*β*-Glucopyranoside, sitosterol, stigmasterol) were isolated from the stem of spider plant by Ranjitha et al. (2014). The potential antimicrobial ability of these four compounds were demonstrated against four microbes (Gram-positive and Gram-negative bacteria as well as fungi strains). However, the reported antimicrobial activity may be of little clinical significance given the applied method (agar-diffusion) which is associated with some inherent limitations (Van Vuuren and Holl 2017).

Pharmacological properties

Some *Cleome* species are generally well-prized for their diverse pharmacological effects such as wound-healing, pain and inflammation relieving activities (Singh, Mishra, and Mishra 2018). As further highlighted by the authors, *Cleome viscosa* extracts demonstrated promising therapeutic potential based on the different biological assays including antinociceptive, anti-diarrheal and antimicrobial activities. These promising effects strongly suggest the need to explore other *Cleome* species in an attempt to evaluate and establish their biological activities. As summarized in Table 3, the pharmacological effects of *Cleome gynandra* has been investigated in eight different categories using in vitro and in vivo systems. Even though a wide range of *Cleome gynandra* plant parts has been tested, the leaves remain the most preferred in the different biological assays.

Antimicrobial activity

All the existing studies have evaluated the antimicrobial potential of different solvent extracts of *Cleome gynandra* based on in vitro systems (Table 3). Extracts were evaluated using both the zone of inhibition and micro-dilution assays. Even though the zone of inhibition assay is one of the common methods to rapidly screen for antimicrobial activity, its inherent limitations often justify the need for complementary testing (Heinrich et al. 2020). Researchers have reported the antimicrobial effect of *Cleome gynandra* against a variety of microbial strains, which were often, tested using micro-dilution assay, a system that is largely well-accepted as efficient antimicrobial assay (Van Vuuren and Holl 2017).

In terms of antibacterial activity, *Cleome gynandra* extracts have been screened against more than 10 Gram-positive and Gram-negative bacteria. Hexane and methanol spider plant extracts (200 mg/mL) demonstrated varying magnitudes of zone of inhibition against the panel of six bacterial strains (Ajaiyeola 2000). *Bacillus subtilis* and *Streptococcus faecalis* were relatively the most susceptible bacteria when compared to resistant strains such as *Pseudomonas aeruginosa* and *Escherichia coli*. Both the plant part and extraction solvent had remarkable effects on the antibacterial activity. In the study by Sridhar et al. (2014), methanolic leaf extracts had an MIC of 39 μg/mL against *Staphylococcus aureus*. As observed by Hamil et al. (2003), the effect of bacterial strain strongly influence the antibacterial activity of *Cleome gynandra*. The authors demonstrated that ATCC strain of *Staphylococcus aureus* was susceptible while the clinical isolate strain (NCRL) was resistant to methanolic extracts of *Cleome gynandra*. Despite the wide range of bacterial strains tested, limited to lack of antibacterial activity was exhibited by water extract of *Cleome gynandra* (Samy, Ignacimuthu, and Raja 1999). Although water is the most common solvent available and utilized for preparing medicinal plant remedies, it is generally known that water does not extract antimicrobial compounds (which are often intermediate or non-polar in nature) from many plants (Eloff 2019). Approximately 60% of the bacterial strains were resistant to the extract regardless of the concentration (30 and 40 mg) tested and duration of incubation (24 and 48 h). The antibacterial activity of the four compounds isolated from *Cleome gynandra* were generally moderate with IZ ranging from 21-29 mm for *Staphylococcus aureus* and 24-33 mm for *Escherichia coli* at 100 mg/mL (Ranjitha et al. 2014).

Antifungal potential of *Cleome gynandra* extracts have been tested against at least 7 fungal strains from several genera namely *Candida*, *Aspergillus* and *Trichophyton*, using both zone of inhibition and micro-dilution assays. In the study by Hamil et al. (2003), *Candida albicans* was not susceptible to *Cleome gynandra* methanol extract. In an attempt to establish the use of spider plant in folk medicine, Imanirampa and Alele (2016) explored its antifungal activity against ringworm of the scalp and hair shafts (*Tinea capitis*), a superficial fungal (dermatophytes or mycoses) infection. Varying degree of sensitivity was demonstrated by the three fungal strains with *Trichophyton rubrum* the most susceptible fungus in response to *Cleome gynandra* water and ethanol extracts (Table 3). Apart from the crude extract, four compounds isolated from *the plant* demonstrated moderate antifungal activity especially against *Candida albicans* with IZ ranging from 19 to 36 mm when tested at 100 mg/mL (Ranjitha et al. 2014). Sitosterol, a well-known phytosterol had the highest IZ among the four isolated compounds.

Anthelmintic activity

The importance of mitigating helminth infection on the health of humans and livestock cannot be over-emphasized. In folk medicine, the use of plants as a remedy against diverse group of parasites in humans and livestock are well-known among different ethnic groups (Aremu, Finnie, and Van Staden 2012). Likewise, the use of *Cleome gynandra* for treating parasitic infections has been documented (Table 1). Ajaiyeoba, Onocha, and Olarenwaju (2001) investigated the anthelmintic potential of stem and leaf extracts of *Cleome gynandra* against three parasites (liverfluke and tapeworm) namely *Fasciola gigantica*, *Pheritimia pasthuma* and *Tenia solium*. Anthelmintic efficacy of the methanolic extracts at varying concentrations were evaluated in terms of the duration (min) taken for the paralysis and death of the tested parasites. Generally, the leaf extracts had higher anthelmintic activity when compared to the stem extracts at similar concentrations (Table 3). The ability of the extracts to paralyze and kill the parasites albeit at higher concentration when compared to piperazine (positive control) support the utilization of the plant in folk medicine (Ajaiyeoba, Onocha, and Olarenwaju 2001). Given the limitations associated with in vitro-based systems, further research using in vivo test models will be essential to generate evidence to justify the use of spider plant in tradition medicine as an anthelmintic.

Antioxidant activity

The majority of the studies evaluating the antioxidant property of *Cleome gynandra* were conducted using chemical tests particularly DPPH assay (Table 3). Chandradevan et al. (2020) indicated the significant influence of extracting solvents on the antioxidant activity of *Cleome gynandra* as 20% ethanol had the most noteworthy DPPH scavenging activity ($EC_{50} \approx 40\,\mu$g/mL). Similarly, 50% methanolic leaf extract had a significantly better radical scavenging activity than the corresponding water extract (Moyo et al. 2013). Antioxidant potential of *Cleome gynandra* has been demonstrated using other in vitro systems such as ORAC and beta-carotene assays (Moyo et al. 2013; 2018; Muchuweti et al. 2007). Despite the relatively noteworthy antioxidant capacity exhibited by *Cleome gynandra* extracts (Table 3), the pharmacological relevance based on these aforementioned chemical tests are low from a clinical perspective (Heinrich et al. 2020). In vivo antioxidant effect of flavonoid fractions from spider plant (25 and 50 mg/kg) on macrophages and lymphocytes significantly scavenged the superoxide anion in chronic inflammatory cells (Bala et al. 2012). The observed antioxidant response was comparable to the positive control (N-acetyl cysteine, NAC). Thus, the antioxidant activity of *Cleome gynandra* may be attributed to the active principles, which are flavonoid-based.

Anti-inflammatory activity

Pain and inflammation remain a common symptom often associated with many human disorders and diseases, which are frequently mitigated using natural resources especially plants. In folk medicine, several uses of *Cleome gynandra* are related to pain and inflammation (Table 1). The anti-inflammatory activity has been demonstrated using different in vivo studies (Table 3). Given the complexity in inflammation, the evidence of anti-inflammatory activity is measured using different responses. Narendhirakannan, Subramanian, and Kandaswamy (2007a) demonstrated the anti-inflammatory activity of spider plant leaf extracts (150 mg/kg body weight) in its ability to restore to normal level, the lysosomal enzymes, protein-bound carbohydrates and plasma TNF-α in arthritic rats. In carageenin-induced raw paw edema methods, the stem extract (100 mg/kg, i.p.) caused a significant reduction ($p < 0.01$) of rat paw edema at all assessment times. The highest inhibition of 47% observed for the extract, compared favorably with 52% exhibited by the positive control (10 mg/kg, i.p) after 2 h (Mule et al. 2008). However, the significant difference in the concentration (100 vs 10 mg/kg, i.p) between the extract and positive control must be taken into consideration in the interpretation and clinical significance of these findings.

Antinociceptive activity

In an attempt to establish the anecdotal evidence for pain alleviation, Ghogare et al. (2009) explored the antinociceptive activity of six solvent extracts of *Cleome gynandra* leaves using two in vivo systems. The study included male Swiss albino mice as the test organisms for the hot plate and acetic acid-induced writhing tests. In hot plate test, the effects of ethanol and water extracts were comparable to the positive control (pentazocine, 10 mg/kg) in terms of the significant increase in reaction time. However, both extracts did not display any significanct increase in the presence of naloxone (1 mg/kg), an opioid antagonist. In response to the acetic acid-induced writhing test, water, ethanol and ethyl acetate extracts significantly reduced the writhing induced in the test mice. Previous studies have also indicated the potential effectiveness of *Cleome* species as antinociceptive agents (Singh, Mishra, and Mishra 2018).

Anticancer activity and toxicity

Bala et al. (2010) evaluated the anticancer activity of *Cleome gynandra* against Ehrlich's Ascites Carcinoma (EAC) in Swiss albino mice. The methanolic extract exhibited significant decrease ($p < 0.01$) in tumor volume, viable cell count, tumor weight and elevated the life span of EAC tumor bearing mice. In addition, haematological profile including the red blood cell, hemoglobin, white blood cell and lymphocyte counts reverted to normal level following treatment with *Cleome gynandra* extracts.

Based on preliminary findings (Gaur et al. 2009), spider plant can be considered safe at varying concentrations (50, 100, and 200 mg/kg, p.o). However, Glew et al. (2009) and Omondi et al. (2017) have reported detectable levels of potentially toxic cadmium, lead, aluminum and strontium in spider plant leaves. More studies are needed to ascertain the source of these elements, some of which could be accredited to external surface contamination. Furthermore, research to evaluate possible heavy metal hyper-accumulator activity by spider plant is vital to ascertain its safety.

Immunomodulation and vasodilatory effects

Generally, immunomodulation consists of all therapeutic interventions geared at modifying the human immune response. The ability to augment the immune response is desirable to prevent infection in states of immunodeficiency, to fight established infections and to mitigate many diseases including cancer. In traditional medicine, many plants including *Cleome gynandra* are used as tonics and associated health supplements to boost the immune systems. Ethanolic extract (50, 100, and 200 mg/kg body weight, orally) of spider plant aerial parts significantly stimulated the immune system in dose-dependent manner while the water extract (125, 250, and 500 mg/kg body weight, orally) had weak immunosuppressive effect (Kori, Gaur, and Dixit 2009). In another study (Gaur, Kori, and Nema 2009), varying concentrations (50, 100, and 200 mg/kg, p.o) of an ethanolic extract given daily for 14 days to Wister albino rats exhibited significant immunosuppression effects in dose-dependent manner relative to the control group.

Runnie et al. (2004) demonstrated evidence of the vasodilatory action of *Cleome gynandra* extract. The ability to relax the vascular systems is relevant to the reduction of the risk of cardiovascular diseases. This effect can also be linked to the use of spider plant for promoting general well-being in folk medicine. In recently times, plants that confer such protective effects on the vascular systems are potential functional food ingredients or supplements widely desired by a large portion of the populations for diverse health benefits.

The promising outlook for *Cleome gynandra*

Clearly, *Cleome gynandra* is an important dark green leafy vegetable in sub-Saharan Africa and South East Asia. Notwithstanding its highly acclaimed nutritional qualities, communities across these geographical regions use the plant as a medicinal remedy for numerous disease conditions. Hence, it is apparent that spider plant could exert profound health beneficial effects on its consumers. The dual nutritional and therapeutic property is common for foods that are sources of both nutrients and bioactive compounds (Khorasani, Danaei, and Mozafari 2018). Evidence from phytochemical studies using advanced biomolecular methods such as ultra-performance liquid chromatography, mass spectrometry and nuclear magnetic resonance spectroscopy indicates that spider plant contains different classes of bioactive compounds, notably vitamins, carotenoids, polyphenols and fatty acids, which could be responsible for its biological activity. Sauer and Plauth (2017) observed that plant-based foods could retard progression of age-related and chronic diseases such as cancer due to the presence of health-promoting natural compounds, notably polyphenols, glucosinates and terpernoids. Coupled with scientific validation of its nutritional, phytochemical and pharmacological properties, spider plant provides a compelling case for its commercialization in the reported regions (Figure 2) and beyond.

The extensive germplasm diversity of spider plant provides a valuable gene pool, for breeding improved cultivars with better nutritional quality with respect to specific minerals, vitamin C, vitamin E, and carotenoids content. Already, studies have documented significant genotype-dependent variation in vitamins (α-tocopherol, β-tocopherol, γ-tocopherol, and ascorbic acid) and carotenoid (α-carotene, β-carotene, lutein and violaxanthin) content of *Cleome gynandra* accessions from different geographical regions (Sogbohossou et al. 2019). This variation is exploitable using a combination of conventional plant breeding and advanced molecular tools to produce cultivars exhibiting superior nutritional qualities. Research efforts aimed at elucidating molecular and physiological mechanisms of C_4 photosynthesis using *Cleome gynandra* as a model are likely to provide insightful clues on the control and regulation of photosynthesis, a process with a direct influence on crop productivity. Taken together, genetic optimization of plant productivity traits and its nutritional constituents is critical for producing high yielding cultivars with high tocopherol, carotenoid, ascorbic acid content, and other bioactive secondary metabolites. More studies on causes and magnitude of bitterness in different accessions of spider plant is a priority research area. Depending on consumer taste preferences, it may be vital to exploit the high geographical diversity of *Cleome gynandra* to breed for desired levels of bitterness.

Future directions and prospects

Given its nutritional and phytochemical composition, the spider plant can become a source of bioactive compounds such as tocopherols, carotenoids, ascorbic acids, flavonoids and phenolic acids. Unleashing the full potential of these health-promoting bioactive compounds could involve application of colloidal encapsulation technology, which preserves the food chemical structure. Furthermore, encapsulation increases absorption and bioavailability of the food bioactive constituents and facilitates their controlled release thereby mitigating nutritional losses (Khorasani, Danaei, and Mozafari 2018). Some of the most promising delivery vehicles include lipid-based carrier systems, which are suitable for a range of molecules. These novel lipid-based vesicles, for example liposomes and proteoliposomes, are composed of lipids, phospholipids and other biomolecules such as carbohydrates, proteins, and cholesterol, natural molecules found in the human body (Khorasani, Danaei, and Mozafari 2018). On the other hand, nanoliposomes are nanoscale versions of liposomes with the stealth capability to evade sensory perception, thereby facilitating food fortification with otherwise undesirable flavored molecules (Khorasani, Danaei, and Mozafari 2018; Tan et al. 2016). Another distinct advantage of lipid-carrier vesicles, namely liposomes and nanoliposomes, is the capacity to deliver molecules that differ in solubility characteristics, simultaneously. Liposomes and nanoliposomes can deliver lipophilic, hydrophilic, and amphiphilic molecules, concurrently. Thus, plant-derived antioxidants from *Cleome gynandra* would significantly benefit from bi-functional nano-delivery antioxidant formulations containing combinations of α-tocopherol, a lipophilic molecule and ascorbic acid, which is water-soluble. Carotenoids such as lutein, an oxidation-prone molecule with low chemical stability and limited water solubility, is also amenable to liposomal and nanoliposomal carrier systems (Steiner, McClements, and Davidov-Pardo 2018). Major sources of lutein, a carotenoid known to retard development of age-related macular degeneration and cataract development, include marigold flowers and dark leafy green vegetables. Spider plant has nutritional therapeutic qualities, hence, its use in folk medicine in sub-Saharan Africa and South East Asia, where incidences of blindness remain significantly high. The dietary intake of lutein, which can reduce the risk of blindness due to age-related macular degeneration (Tan et al. 2008), is achievable using lipid-based encapsulation systems. Furthermore, as the demand for natural ingredients in food manufacturing intensifies, lutein obtained from leafy green sources like spider plant can replace synthetic colorants and inadvertently impart its antioxidant properties (Steiner, McClements, and Davidov-Pardo 2018). Going forward, spider plant and other dark-green leafy vegetables will become natural choices for extraction of tocopherols, ascorbic acid, carotenoids and other bioactive antioxidant compounds for food applications as nutritional supplements, colorants, and extending shelf life of food products.

Diversification of diets that includes indigenous dark green leafy vegetables holds great promise in ensuring food and nutrition security especially in the developing world. A distinct advantage of *Cleome gynandra* is its sustained long-term use in folk medicine as a remedy against a variety of disease conditions, across different geographic regions in Africa and Asia. *Cleome gynandra* contains significantly high levels of macro- and micronutrients, tocopherols, ascorbic acid, carotenoids, flavonoids, and phenolic acids, which are responsible for the notable nutritional, antioxidant, anti-inflammatory, antimicrobial, anthelmintic, and immunomodulatory activities as demonstrated in both in vitro and in vivo studies. The wide genetic diversity of *Cleome gynandra* across different geographic regions provides boundless opportunities for breeding cultivars with superior nutritional attributes. In the future, spider plant and related dark green leafy vegetables could provide a source of vitamins, carotenoids and other antioxidant compounds for food fortification and nutritional supplements. Moreover, the possibility of using nanoencapsulation technology, which offers the capability of efficient targeted and controlled release of bioactive compounds, can unlock the nutritional qualities and health benefits of *Cleome gynandra*.

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Declaration of competing interest

There is no conflict of interest.

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