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Nutritional, phytochemical compositions and natural therapeutic values of citron watermelon (*Citrullus lanatus* var. *citroides*): A Review

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Abstract

Citron watermelon (*Citrullus lanatus* var. *citroides*) is a multi-purpose cucurbit crop serving the food, feed and the pharmaceutical sectors. The fresh and dried young leaves, fruit and seed are sources of vital human nutrients, and unique phytochemical compounds with pharmacological and therapeutic values. Citron watermelon is indigenous to Africa but commercial products are not widely developed and the crop is largely neglected and underutilized in the region. This is attributed to lack of dedicated research and development efforts and well-defined value chains for citron watermelon genetic resources. The objective of this review was to document the nutritional and phytochemical compositions, pharmacological and therapeutic values of citron watermelon to aid future production, utilization, genetic conservation, research and product development. The review serves as a foundation information on the unique values of citron watermelon to guide future research and development. It recommends collaborative and detailed biochemical analysis efforts for product discovery and optimal use of health-promoting bioactive compounds using the diverse genetic resources available in Africa and elsewhere. This will enhance the commercial value and benefit sharing from citron watermelon in the horticulture, food and pharmaceutical industry.

Keywords: Carotenoids, citron watermelon, cucurbitacins, ethnomedicine, flavonoids, macro – and micro-nutrients, organic acids, phenolics, sugars

1. Introduction

Citron watermelon (*Citrullus lanatus* var. *citroides*, 2n=2x=22) belonging to the family *Cucurbitaceae* is a multi-purpose crop serving the food, feed and the pharmaceutical sectors. It supports millions of households in Africa serving as an important source of food prepared from fresh and dried young leaves, fruit and seed (Magwede et al. 2019; Ngwepe et al. 2019). Citron watermelon is a hardy crop (Akashi et al. 2001; Yoshimura et al. 2008; Mo et al. 2015) and thrives under minimum production inputs in arid to semi-arid environments characterized by intense drought and heat stress. It is a suitable companion crop under multiple cropping systems, tolerant to several pests and diseases and succesfully cultivated with limited use of synthetic crop protection chemicals. It has considerable tolerance to the root-knot nematodes (*Meloidogyne* spp.), powdery mildew (*Podosphaera xanthii*), bacterial fruit blotch (*Acidovorax citrulli*), gummy stem blight [*Didymella bryoniae* (Auersw.) Rehm], Zucchini yellow mosaic virus, papaya ringspot virus and *Anthracnose* (Gusmini et al. 2005; Tetteh et al. 2010; Ma and Wehner, 2015; Thies et al. 2015a,b,c, 2016; Daley and Wehner, 2020). These attributes make citron watermelon a crop of choice for cultivation under low-input and smallholder farming systems in sub-Saharan Africa (SSA). Its resistance to biotic and abiotic stresses makes it a preferred rootstock for sweet dessert watermelon (*C. lanatus* var. *lanatus*) (Cohen et al. 2014; Thies et al. 2015a; Nawaz et al. 2018; Pal et al. 2020; Yavuz et al. 2020; García-Mendívil and Sorribas, 2021).

Reports indicated that citron watermelon has unique nutritional and phytochemical compositions with natural pharmacological and therapeutic values. The seeds are rich in oil, protein and unsaturated fatty acids (i.e., linoleic, oleic, palmitic and stearic) (Singh et al. 2010; Jarret and Levy, 2012). The non-sweet fruit has low total soluble solids (TSS) and natural sugars (i.e., fructose, sucrose and glucose) and high organic acids and carotenoids content especially β-carotene (Yoo et al. 2012; Ren et al. 2014; Jawad et al. 2020). The leaves and fruit contain phytochemical compounds including cucurbitacins and their gycosides derivatives with medicinal values (Afifi et al. 1999; Abdelwahab et al. 2011; Davidovich-Rikanati et al. 2015; Alsayari et al. 2018). In Sudan, the crop is used for treating various ailments such as swellings, gout, rheumatism, and gastrointestinal disorders (Abdelwahab et al. 2011). In South Africa, the leaves and fruit of citron watermelon are used by traditional healers for treating hypertension (Semenya and Potgieter, 2015). Roasted seeds are consumed to stimulate appetite (Semenya and Potgieter, 2014) and alleviate constipation. There has been renewed and growing interest regarding the use of natural plant-derived food and non-food products as an alternative to artificial drugs for treatment and management of human ailments. There is scant information on ethnomedicinal uses of citron watermelon when compared with other cucurbit species. The therapeutic values of citron watermelon are largely unknown and poorly documented. Further, commercial products are yet to be developed in Africa to produce value added dietary foods and non-food products.

In SSA, citron watermelon is largely neglected and underutilized and has not been fully recognized and developed as a functional food crop. The lack of dedicated research and development and well-defined value chains for the crop are attributed to its poor utilization, consumption, value-adding and commercialization in SSA. Therefore, concerted research is required to determine the nutritional, phytochemical and medicinal profiles of diverse citron watermelon genetic resources. This will facilitate efficient utilisation and conservation of citron watermelon germplasm, and development of value-added food and non-food products. Therefore, the objective of this review was to document the nutritional and phytochemical compositions, pharmacological and therapeutic values of citron watermelon to aid future production, utilization, genetic conservation, research and product development. The review serves as a foundation information on the unique values of citron watermelon to guide future research and development.

2. Morphological description of citron watermelon

The morphological description of various plant parts of citron watermelon are shown in Fig. 1. Citron watermelon is a trailing cucurbit plant with hairy stems and leaves, forked tendrils and mostly it produces three lobed hairy leaves, though non-lobed leaves rarely occur. Ovate, oblong or linear leaflet lobes occur within the lobed leaf phenotype with finely serrated edges. The crop produces male and female flowers on the same plant (i.e., monoecious). Both male and female flowers are bright yellow in colour and are borne approximately 40–60 days after planting. Male flowers appear first, followed by female flowers that appear approximately after 5-15 days. Citron watermelon is a cross-fertilizer leading to extensive morphological and genetic diversity (Mashilo et al. 2017; Ngwepe et al. 2019). Ovaries and primordial fruits are smooth and glossy during development. The weight of the fruits vary from ~1 kg to 25 kg (Achigan-Dako et al. 2015; Ngwepe et al. unpublished). The fruit shape vary from round, elliptic and broad-elliptic, whereas the fruit size vary from small, medium, large and very large. Fully developed and mature fruit are green, light green or dark green in colour with and without rind stripe patterns. The rind colour vary from light, medium and dark green and the rind stripe pattern are either thin, medium-sized, broad or patchy. The flesh is made up of the mesocarp and endocarp (i.e. the portion of the fruit typically consumed after cooking) and varies from white-green, orange and yellow in colour (Levi et al. 2012; Mashilo et al. 2017; Ngwepe et al. 2019) with medium to hard crisp flesh texture. The number of seeds per fruit vary from 500 to 900 depending on the size of the fruit. The seeds are hard, flat and oval and vary from 9.13 to 15.25 mm in length, and 6.26 to 8.60 mm in width (Achigan-Dako et al. 2015; Ngwepe et al. unpublished). The seed coat colour vary from black, brown, tan, white, cream-white, grey and red-white, with variable pattern and secondary colour mostly being black and brown (Mashilo et al. 2016). The plant has a deep taproot system and approximately eight lateral roots extending more than 2 m long. The drought tolerant nature of this crop is attributed to its well-developed and deep root system (Mo et al. 2016; Guzzon et al. 2017).

3. Traditional uses of citron watermelon

In South Africa, the Bapedi and Venda tribes refer to the crop as “lerotse”, “marotse”, “mutshatsha” or “Motshatsha” (Mashilo et al. 2017; Magwede et al. 2019; Mogale et al. 2019; Ngwepe et al. 2019). Freshly harvested leaves are referred to as “motshatsha” or “Morogo wa motshatsha”, whereas dried leaves are traditionally known as “Kgwaile” in the indigenous South African Sepedi language. Motshatsha, a leaf vegetable dish, is prepared by boiling fresh succulent leaves of citron watermelon (Fig. 2A), ripe tomatoes and salt and consumed with starch staples mostly maize or sorghum porridge. Kgwaile is pre-cooked, sun-dried and preserved leaves of citron watermelon (Fig. 2B) which is used when desired as leafy vegetable as motshatsha. The leaves of citron watermelon are bitter-tasting due to phytochemical compounds (Davidovich-Rikanati et al. 2015; Kim et al. 2018). Boiling and preservation reduce the level of leaf bitterness. The leaves are relatively less-bitter during the vegetative growth stage compared with flowering and fruit set stages. The dry vines serve as fodder for livestock (Laghetti and Hammer, 2007;

Nantoumé et al. 2012, 2013). The fully-developed fruit is used for preparation of various traditional foods (Nantoumé et al. 2013; Mashilo et al. 2017; Ngwepe et al. 2019). For example, “kgodu” is well-known and favoured traditional cuisine by the Bapedi tribe of South Africa. Kgodu is prepared by boiling the crisp yellow or orange flesh to tenderness and adding maize meal to make porridge (Fig. 2D) which can be consumed with roasted citron watermelon seed (Fig. F & G), soup or based on desired consumer preferences. In addition, “mokgapu” is prepared by boiling the flesh, adding white or brown sugar to improve taste and consumed as soup (Fig. 2E). Seeds extracted from the fruit are roasted and salted, and are referred as “dithotse” (Fig. 2F & G) in the local South African Sepedi language and consumed as snack or with kgodu. Brown, red-white and red seeds are preferred for roasting due to their soft -to -medium hard seed coats, easy chewability and being full of flavour. White seeds are soft, whereas black and maroon seeds have hard seed coats, uneasy to chew, and un-suitable for roasting. Raw and roasted seed are processed into fine powder for use as chicken feed (Ngwepe et al. 2019). Fruits are used as animal feed supplement for small – and large-livestock such as cattle, sheep, goats, donkeys and pigs (Fig. 2G). This provides water and vital nutrients especially during dry winter seasons where grazing and water are scarce. Fresh roots of some citron watermelon are extremely bitter (Personal observation). This may be due to the inherent constituents of phytochemicals with possible pharmacological and therapeutic properties. However, there is limited information regarding their medicine use. The roots of *C. lanatus* var. *lanatus* are grounded to powder and used by Bapedi traditional healers for treating tuberculosis (TB) in the Limpopo Province, South Africa (Semenya and Maroyi, 2019). Further, the ripe red fresh of *C. lanatus* var. *lanatus* fruit is mixed with *Aloe* species, boiled and administered orally to treat

TB by South African traditional healers (Semenya and Maroyi, 2019). The unique uses of citron watermelon in South Africa suggests that the edible plant parts may provide vital nutrients and phytochemical compounds with health-promoting benefits and with a potential to develop nutraceutical and pharmaceutical products.

4. Mineral elements composition

Essential mineral elements such as nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), magnesium (Mg), iron (Fe) and zinc (Zn) are vital for optimal human health, growth and development. Citron watermelon edible plant parts such as leaves, fruit and seed could serve as potent sources of essential mineral elements reported in its close relative *C. lanatus* var. *lanatus*. For example, the most abundant macro-nutrients in *C. lanatus* var. *lanatus* leaves is N, K and Ca (Table 1). P, K, Ca and Mg are present in large concentrations in the seed (Table 1). Huang et al. (2016) reported N and K contents of 9.03 and 18.53 mg/g respectively in *C. lanatus* var. *lanatus* fruit flesh, whereas high N, P, K, Ca and Mg concentrations are reported in the root (Table 1). Micro-nutrient deficiency especially Zn and Fe is a serious health concern globally and in Africa (Platel and Srinivasan, 2016). The World Food Programme (WFP, 2018), indicated one-third of Africa's population is affected by micro-nutrient deficiencies. Fe deficiency cause anaemia and mal-functioning of the immune system (Bailey et al. 2015). Zn deficiency is associated with various complications including stunted growth and abnormal brain development, diarrhoea and pneumonia in children (White and Broadley, 2011). In South Africa, 13.8% of children with the age groups of 5 to 12 years were reported to be deficient in Fe, while 27.7% in Zn which were below estimated average requirements (Visser et al. 2019). Tabiri et al. (2016) reported Zn content of 3.71 mg/100g and Fe content of 3.71 mg/100g in the seed of *C. lanatus* var. *lanatus* cv Charleston Gray (Table 1).

Both sweet and non-sweet watermelon are widely grown for their leaves, fruit and edible seeds in SSA. The two varieties exhibit similar morphological features but varied in their genetic make-up (Levi et al. 2013; Nantoumé et al. 2013; Mashilo et al. 2016). Therefore, citron watermelon may also be a rich source of mineral elements though studies on the nutrient profiles are scanty. Detailed nutrient profiles analysis in leaves, fruit and seed of citron watermelon is required for developing functional foods.

Table 1. Reported mineral elements composition in plant parts of sweet dessert watermelon cultivars.

			Macro-nutrients					Micro-nutrients				
Plant part	Growth stage	Cultivar	N	P	K	Ca	Mg	Fe	Mn	Cu	Zn	References
Roots	Vine	Zaojia 8424	35.15	5.09	45.48	9.23	3.74	0.08	0.16	0.005	0.233	Huang et al. (2016)
	Fruit development	Zaojia 8424	35.85	7.08	31.15	6.93	2.95	0.17	0.11	0.011	0.181	Huang et al. (2016)
	Maturity	Zaojia 8424	55.33	5.79	40.52	28.79	6.52	0.07	0.012	0.013	0.118	Huang et al. (2016)
Stem	Vine	Zaojia 8424	57.19	6.51	107.18	11.30	3.98	0.22	0.009	0.005	0.066	Huang et al. (2016)
	Fruit development	Zaojia 8424	39.39	5.23	72.21	15.96	4.83	0.28	0.015	0.005	0.079	Huang et al. (2016)
	Maturity	Zaojia 8424	37.87	3.54	78.39	15.65	5.16	0.39	0.014	0.02	0.059	Huang et al. (2016)
Leaves	Vine	Zaojia 8424	56.36	5.78	78.59	27.61	5.26	0.05	0.027	0.024	0.119	Huang et al. (2016)
	Fruit development	Zaojia 8424	45.29	5.76	61.10	27.01	6.87	0.06	0.049	0.005	0.128	Huang et al. (2016)
	Maturity	Zaojia 8424	45.06	6.71	67.93	61.90	7.55	0.13	0.044	0.003	0.18	Huang et al. (2016)
Leaves	-	Ingrid	34.00	1.20	13.50	26.4	5.00	-	-	-	-	Rouphael et al. (2008)
Fruit-rind	Maturity	Zaojia 8424	15.62	7.81	88.67	3.10	2.72	0.22	0.095	0.005	0.045	Huang et al. (2016)
Fruit-flesh	Maturity	Zaojia 8424	9.03	4.64	18.53	1.87	1.85	0.34	0.057	0.028	0.038	Huang et al. (2016)
Fruit-flesh	Maturity	Ingrid	-	1.60	15.30	1.70	2.20	-	-	-	-	Rouphael et al. (2008)
	Maturity	Ingrid		1.60	18.80	2.10	2.40					Rouphael et al. (2008)
Seed	Maturity	Charleston gray	-	0.17	3.57	0.16	0.15	3.71	0.02	0.38	3.71	Tabiri et al. (2016)
Seed	Maturity	Crimson sweet	-	0.22	3.40	0.11	0.14	2.72	0.04	0.45	0.81	Tabiri et al. (2016)
Seed	Maturity	Black diamond	-	0.18	3.85	0.14	0.17	4.60	0.09	0.58	0.66	Tabiri et al. (2016)
Seed	Maturity	-	-	-	-	100.0	-	7.30	-	-	5.2	Lakshmi and Kaul (2011)

N = Nitrogen, P = Phosphorus, K = Potassium, Ca = Calcium, Mg = Magnesium, Fe = Iron, Mn = Manganese, Cu = Copper, Zn = Zinc. Note Nutrient elements values reported by Rouphael et al. (2008) and Huang et al. (2016) were expressed in mg/g, values reported by Tabiri, et al. (2016) were expressed in mg/100 g values reported by Lakshmi and Kaul (2011) were expressed in g/100g.

5. Protein, oil and fatty acid contents

Proteins are essential components required in human diets for various biological processes. Seed protein content of 35.9% was reported for *C. lanatus* var. *citroides* which is comparable to *C. lanatus* var. *lanatus* (35%) but higher than *C. colocynthis* (32.4%) and *C. rehmii* (31.8%) (Singh et al. 2010). Further, proportion of seed protein fractions revealed globulins (63.7%) as the major seed protein followed by albumins (18.6%), glutelins (14.0%) and prolamins (3.7%), in that order in *C. lanatus* var. *citroides* (Singh et al. 2010). Globulin content of *C. lanatus* var. *citroides* is comparable to *C. lanatus* var. *lanatus* (65%) and *C. colocynthis* (66.1%) (Singh et al. 2010). This indicates citron watermelon seed are a rich source of protein and protein-fractions. Citron watermelon contain mean seed oil content of 22.6% comparable to *C. lanatus* var. *lanatus* (23.2%) but much lower than 35.6% for *C. colocynthis* (Jarret and Levy, 2012; Prothro et al. 2013). Further, Ziyada and Elhussien (2008) reported oil content of 35% in *C. lanatus* var. *citroides*. Some genotypes of citron watermelon including PI 482302 and PI 482342 recorded high seed oil content of 30.5 and 32.9%, respectively (Jarret and Levy, 2012). The principal fatty acids in seed of *C. lanatus* var. *citroides* is linoleic (63.37%), oleic (16.42%), palmitic (10.60%) and stearic (8.05%) acids in that order (Jarret and Levy, 2012). Meru and McGregor (2014) reported high linoleic acid content of 70.0 and 61.15% in *C. lanatus* var. *lanatus* (cv PI 279261) and *C. colocynthis* (cv PI 560023) comparable to that in *C. lanatus* var. *citroides*. Further, linoleic acid content of *C. lanatus* var. *citroides* is comparable to those several cucurbit species including *C. lanatus* var. *lanatus* (65.15%), *C. colocynthis* (65.17%), *C. ecirrhosus* (62.76%), *C. rehmii* (75.81) and *B. fistulosa* (73.23%) (Jarret and Levy, 2012). This indicated citron watermelon is a valuable source of seed oil, protein-rich seed and fatty acids for use as food and non-food purposes. Further, the high oil content of citron watermelon seed may aid the development of this species as a potential oil crop.

6. Carotenoids content

Yellow and orange-fleshed citron watermelon types are preferred for cooking and for use as livestock feed (Laghetti and Hammer, 2007; Van Wyk et al. 2011; Nantoumé et al., 2013). Orange-fleshed citron watermelon types may contain higher β-carotene contents (Tadmor et al. 2005; Bang et al. 2007; 2010; Davis et al., 2007)**.** Carotenoids are tetraterpenoid pigments which accumulate in the chloroplasts of leaves and chromoplasts of flowers and fruits contributing to the red, orange and yellow colours (Tadmor et al. 2005). Carotenoids, especially lycopene can reduce the risk of various types of human cancers (i.e., breast, colon and prostate) and cardiovascular diseases (McEneny et al. 2013), and various nervous system disorders (Hu et al. 2017; Chen et al. 2019) thus contribute to human nutrition and health (Tang et al. 2009; Grassi et al. 2013; Assar et al. 2016; Mirahmadi et al. 2020). Carotenoid profiles of *C. lanatus* var. *lanatus* cultivars exhibiting red, orange and yellow flesh types are presented in Table 2. Yellow-fleshed watermelon types contain carotenoids such as violaxanthin, neoxanthin and lutein, whereas orange-fleshed types contain mainly β-carotene, prolycopene, phytoene and ξ-carotene but low lycopene content. Red and pink watermelon types contain high lycopene content (Lewinsohn et al. 2005; Tadmor et al. 2005; Perkins-Veazie et al. 2006; Bang et al. 2010; Liu et al. 2012; Branham et al. 2017). For example, Liu et al. (2015) reported trace of lycopene (0.56 µg g^{-1}) in canary yellow-fleshed sweet watermelon. Yoo et al. (2012) and Jin et al. (2019) reported β-carotene content ranging from 1 to 8.5 µg/g and 6.5 to 134 mg/kg in orange-fleshed dessert watermelon types, respectively. *C. lanatus* var. *lanatus* (cv ‘Ju-Bao’) with an orange-yellow flesh had high β-carotene content of 860.50±135.54 µg g^{-1} (Liu et al. 2012). For citron watermelon, Yoo et al. (2012) reported β-carotene and lycopene contents 0.2 and 0.1 µg g^{-1} in yellow-fleshed accession (cv PI 255137). Tlili et al. (2011) reported positive correlations between antioxidant activities (TEAC assay) with lycopene (R^2 = 0.65) and β-carotene (R^2 = 0.40) contents in sweet watermelon, indicating antioxidant potential of carotenoids. Though red-fleshed watermelon types contain more lycopene content, yellow and orange-fleshed may also be a rich source of lycopene (Table 2). There exist extensive differences in carotenoid composition among red, yellow and orange-fleshed watermelon types (Table 2). Variation in carotenoid composition is attributed to differential gene expression in the carotenoid metabolic pathway during fruit development and maturation (Kang et al. 2010; Lv et al. 2015; Dou et al., 2017; Fang et al. 2020). There exists little information that determined carotenoids profiles and composition especially β-carotene in yellow and orange-fleshed citron watermelon types. Low vitamin A intake is attributed to lack of consumption of β-carotene-enriched food crops and poses a serious health risk in developing countries especially in Africa (World Health Organization (WHO), 2018). Health complications including weak immune system and stunted growth in children are associated with insufficient vitamin A intake (WFP, 2018). In South Africa, the diet of children aged between 5 to 12 years were reported to be deficient in vitamin A (Visser et al. 2019). Orange-fleshed citron watermelon types may be a rich source of β-carotene a precursor of vitamin A to boost immune system functioning and overall body health. Orange-fleshed citron watermelon types are currently utilized in SSA for food and in the development various value-added food products such as jam, pickles and traditional recipes (Fig. 2C & D). Biochemical analysis and quantification of β-carotene contents in the available genetically diverse genetic resources of orange-fleshed citron watermelon types available in Africa and elsewhere is required to develop β-carotene-enriched genotypes for dessert, cooking, processing, value-adding and commercialization.

Table 2. Carotenoids composition in sweet dessert watermelon fruit.

		Carotenoids										
Cultivar	Fruits flesh colour	α-Car	AXN	ZXN	NXN	VXN	γ-Car	β-Car	Pro-lyc	LTN	LyC	References
Yellow Doll	Y	-	-	-	-	-	-	-	-	-	14.51	Wehner et al. (2017)
Tendersweet Orange Flesh	Y	-	-	-	-	-	-	-	-	-	20.33	Wehner et al. (2017)
Yellow Crimson	Y	-	-	-	-	-	-	-	-	-	14.86	Wehner et al. (2017)
Allsweet	R	-	-	-	-	-	-	-	-	-	41.77	Wehner et al. (2017)
Sugar Baby	R	-	-	-	-	-	-	-	-	-	53.37	Wehner et al. (2017)
Cream of Saskatchewan	PL	-	0.04	0.09	-	0.28	-	0.03	-	0.248	0.013	Fang et al. (2020)
PI 635597	CY	-	0.05	0.04	-	3.23	-	0.30	-	0.479	0.066	Fang et al. (2020)
PI 192938	O	0.06	0.09	0.54	-	7.60	0.43	16.13	-	0.714	1.523	Fang et al. (2020)
LSW-177	R	0.02	0.04	0.00	-	0.27	0.62	2.61	-	0.589	25.95	Fang et al. (2020)
N-D NIL	O	2.5	-		7.0	-	-	99.2	-	-	47.7	Jin et al. (2019)
NB5410	O	2.6	-		7.9	-	-	89.1	-	-	-	Jin et al. (2019)
Summer Orange	O	2.5	-		7.1	-	-	134.3	-	-	-	Jin et al. (2019)
Summer Orange B	O	2.7	-		5.8	-	-	109.1	-	-	-	Jin et al. (2019)
Golden Honey	O	3.7	-		2.5	-	-	9.2	86.4	-	-	Jin et al. (2019)
Orange Flesh Tendersweet	O	5.7	-		3.8	-	-	5.7	193.7	-	64.5	Jin et al. (2019)
Orangeglo	O	10	-		2.6	-	-	9.4	128.5	-	60.1	Jin et al. (2019)
Tender Gold	O	6.5	-		2.2	-	-	6.5	155.9	-	58.8	Jin et al. (2019)
O-D NIL	CY	2.5	-		7.5	-	-	13.1	-	-	32.3	Jin et al. (2019)
ALDF	CY	2.2	-		9.5	-	-	3.2	-	-	-	Jin et al. (2019)
OTO9491	CY	2.4	-		6.8	-	-	2.2	-	-	-	Jin et al. (2019)
DAH	R	4.7	-		2.4	-	-	47.4	-	-	245.6	Jin et al. (2019)
JB11-3	R	3.8	-		1.9	-	-	60.7	-	-	154.7	Jin et al. (2019)
JB38-1	R	4.7	-		0.9	-	-	13.8	-	-	390.4	Jin et al. (2019)
BIL-53	W	-	-	0.05	-	0.05	ND	0.16	-	ND	ND	Maragal et al. (2019)
BIL-99	Y	-	-	0.13	-	1.13	ND	0.72	-	ND	1.12	Maragal et al. (2019)
Orangeglo	O	-	-	-	-	ND		1.3	4.3	0.1	0.4	Yoo et al. (2012)
Sweet Siberian-1	O	-	-	-	-	0.2		8.5	ND	0.4	0.5	Yoo et al. (2012)
Sweet Siberian-2	O	-	-	-	-	1		3.3	0.2	0.9	0.9	Yoo et al. (2012)

Table 2. (Continued).

		Carotenoids										
Cultivar	Flesh colour	α-Car	AXN	ZXN	NXN	VXN	γ-Car	β-Car	Pro-lyc	LTN	LyC	References
Texas Golden	O	-	-	-	-	0.1	-	1.4	7.4	0.9	0.9	Yoo et al. 2012
Black Diamond Yellow	Y	-	-	-	-	ND	-	0.6	1.4	0.1	0.6	Yoo et al. 2012
Luscious Golden-1	Y	-	-	-	-	ND	-	0.5	0.4	ND	0.3	Yoo et al. 2012
Luscious Golden-2	Y	-	-	-	-	ND	-	1	1.3	0.1	1.5	Yoo et al. 2012
Golden Honey Cream	Y	-	-	-	-	-	-	0.3	1.7	0.1	0.4	Yoo et al. 2012
PI 255137	Y	-	-	-	-	-	-	0.2	0.1	0.1	0.1	Yoo et al. 2012

PL = Pale yellow, CY = canary yellow, O = orange, R = Red, W = White, Y = Yellow, O = Orange, α-Car = α-Carotene, AXN = Avioxanthin, ZXN = Zeaxanthin, NXN = Neolaxanthin, VXN = Violaxanthin, γ-Car = γ-Carotene, β-Car = β –Carotene, Pro-lyc = Prolycopene, LTN = Lutein, LyC = Lycopene. Carotenoid concentrations reported by Yoo et al. 2012; Maragal et al. 2019 and Fang et al. 2020 are expressed in µg g^{-1}, whereas carotenoid concentrations reported by Jin et al. 2019 are expressed in mg g^{-1}. Lycopene content reported by Wehner et al. (2017) are expressed in kg g^{-1}. ND = not detected.

7. Amino acids content

There is scant information on the concentrations of amino acids in edible plant parts of citron watermelon. In sweet watermelon the main amino acids in seed include glutamic acid (20.71 g/100 g protein), arginine (16.89 g/100 g protein), aspartic acid (9.48 g/100 g protein), leucine (7.44 g/100 g protein), alanine (6.25 g/100 g protein), serine (5.91 g/100 g protein), glycine (5.82 g/100 g protein) and phenylalanine (5.18 g/100 g protein) in that order (Lakshmi and Kaul, 2011). Essential amino acids occurring in low concentrations in sweet watermelon seed include methionine (0.33 g/100 g protein), cysteine (0.96 g/100 g protein), tryptophan (1.07 g/100 g protein), isoleucine (1.44 g/100 g protein), lysine (2.18 g/100 g protein), tyrosine (2.85 g/100 g protein), valine (2.91 g/100 g protein) and threonine (3.47 g/100 g protein) (Lakshmi and Kaul, 2011). Amino acids present in sweet dessert watermelon flesh include alanine, arginine, aspartate, asparagine, citrulline, glutamate, glutamine, isoleucine, leucine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine and beta-alanine (Zhong et al. 2019). Of these, arginine and citrulline are the most abundant in watermelon flesh. Citrulline is non-essential amino acids which act as a novel hydroxyl radical scavenger in the human body (Akashi et al. 2001; Rimando and Perkins-Veazie 2005; Liu et al. 2010). Also, citrulline is essential for maintenance of human nitrogen homeostasis (Crenn et al. 2010). Tarazona-Dı´az et al. (2011) reported mean citrulline content of 2.33 mg g^{-1} in the flesh of triploid seedless sweet watermelon cultivars. Rimando and Perkins-Veazie (2005) reported citrulline content varying from 0.5 to 3.6 mg g^{-1} fresh weight in sweet watermelon flesh with an average concentration of 1.8 and 2.4 mg g^{-1} fresh weight for seeded and seedless watermelon types, respectively. Citrulline content ranging from 3.9 to 28.5 and 5.7 to 28.6 mg g^{-1} dry weight were reported in the flesh seeded and seedless watermelon (Rimando and Perkins-Veazie, 2005). Citrulline content of 15.6, 29.4 and 28.2 mg g^{-1} dry weight and 0.8, 1.5 and 1.5 mg g^{-1} fresh weight were reported in the rind of red, yellow and orange-fleshed sweet watermelon types, respectively (Rimando and Perkins-Veazie, 2005). Compared by flesh colours, red fleshed sweet watermelons had slightly less citrulline content (7.4 mg g^{-1} dry weight) compared to yellow (28.5 mg g^{-1} dry weight) and orange fleshed (14.2 mg g^{-1} dry weight) types (Rimando and Perkins-Veazie, 2005). Citrulline concentration varying from 1.26 to 7.21 mg g^{-1} were reported in sweet watermelon (Davis et al. 2011). These reports indicate watermelon is rich source of citrulline, which can be absorbed by the human body to increase plasma arginine levels. Consumption of watermelon fruit increased plasma citrulline ranging from 386–1069 μmol/L) (mean = 593 μmol/L) and arginine plasma ranging from 128–251 μmol/L (mean = 199 μmol/L) in adults (Mandel et al. 2005). Plasma arginine and orthinine concentrations in the human body of adults were increased following intake of citrulline (Osowska et al. 2004; Collins et al. 2007; Jourdan et al. 2015). Ornithine is derived from the catabolism of arginine, proline, glutamine, and glutamate and is also a substrate for the synthesis of these amino acids (Joshi et al. 2019). Various therapeutic benefits are associated with citrulline such as treatment of erectile dysfunctions (Drewes et al. 2003; Shiota et al. 2013), trauma, burn injury, massive small bowel resection, reduces the disturbance of cerebral blood flow, and renal failure (Flynn et al. 2002; Kurauchi et al. 2017). Citrulline ingestion from watermelon fruit (1.17 g of L-citrulline) was shown to reduce muscle soreness and heart rate recovery after exercise (Tarazona-Díaz et al. 2013). Also, watermelon juice enriched with 3.45 g per 500 mL L-citrulline relieved muscle soreness 72 hrs after racing (Martínez-Sánche et al. 2017).

Citrulline is also a precursor for biosynthesis of arginine which involved in the synthesis of nitric oxide (NO). NO is converted into citrulline from arginine by NO synthase (Curis et al. 2005) and plays essential roles in the coordination of various cardiovascular and immune functions (Osowska et al. 2004; Collins et al. 2007). Further, arginine is an essential amino acid used in protein synthesis (Kawasaki et al., 2000) and maintenance of NO synthesis (Varasteh et al. 2018). Diets supplemented with arginine have been shown to reduce the risk of cardiovascular disease, improve antioxidant capacity, and reduce inflammation (Hong et al. 2018). Zhong et al. (2019) reported arginine content ranging from 2.0 to 2.3 mmol/L, whereas Wehner et al. (2017) reported values ranging from 0.64 to 1.45 mg g^{-1} fresh weight in sweet watermelon. Reports in the literature indicate watermelon is a rich source of citrulline and arginine though concentrations of this amino acids vary among different cultivars (Table 3). The varied concentrations of citrulline and arginine are attributed to differences in expression profiles of putative genes involved in citrulline catabolic pathway (Joshi et al. 2019). Negative and poor correlations were reported between total soluble solids with citrulline (r = - 0.38) and arginine (r = - 0.38) contents (Assefa et al. 2020), which suggested watermelon fruit with high sugar content may have low contents of these amino acids. On the contrary, positive and low associations were reported between total soluble solids and citrulline (Wehner et al. 2017; Hartman et al. 2019). Several other reports indicated positive correlations between citrulline and arginine (Wehner et al. 2017; Joshi et al. 2019; Assefa et al. 2020). In citron watermelon, amino acids contents in edible plant parts (i.e., leaves, fruit and seed) have not been previously determined. Moreover, the contents of citrulline and arginine are not known, limiting the potential value or use of citron watermelon as a natural source of amino acids for treatment of various ailments and for other useful industrial applications.

373 **Table 3**. Citrulline and arginine contents in sweet watermelon fruit.

Cultivar	Flesh colour	Citrulline	Arginine	References
Yellow Doll	Y	3.55 mg g^{-1} FW	0.64 mg g^{-1} FW	Wehner et al. (2017)
Tendersweet Orange Flesh	Y	2.59 mg g^{-1} FW	1.40 mg g^{-1} FW	Wehner et al. (2017)
Yellow Crimson	Y	2.32 mg g^{-1} FW	1.45 mg g^{-1} FW	Wehner et al. (2017)
Allsweet	R	2.82 mg g^{-1} FW	1.15 mg g^{-1} FW	Wehner et al. (2017)
Sugar Baby	R	2.34 mg g^{-1} FW	0.85 mg g^{-1} FW	Wehner et al. (2017)
Yellow Crimson	CY	2.30 mg g^{-1} FW	-	Davis et al. (2011)
Tendersweet Orange Flesh	O	2.35 mg g^{-1} FW	-	Davis et al. (2011)
Cream of Saskatchewan	W	1.00 mg g^{-1} FW	-	Rimando et al. (2005)
Jamboree	R	3.10 mg g^{-1} FW	-	Rimando et al. (2005)
Sangria	R	1.60 mg g^{-1} FW	-	Rimando et al. (2005)
Summer Gold	Y	3.60 mg g^{-1} FW	-	Rimando et al. (2005)
Tender Sweet Orange	O	0.50 mg g^{-1} FW	-	Rimando et al. (2005)
Trix 313	R	0.70 mg g^{-1} FW	-	Rimando et al. (2005)
Orange Sunshine	O	3.00 mg g^{-1} FW	-	Rimando et al. (2005)
Solid Gold	Y	3.50 mg g^{-1} FW	-	Rimando et al. (2005)
IT302244	Y	39.30 mg g^{-1} DW	9.12 mg g^{-1} DW	Assefa et al. (2020)
807364	Y	41.38 mg g^{-1} DW	6.63 mg g^{-1} DW	Assefa et al. (2020)
K192365	R/Y	52.06 mg g^{-1} DW	8.46 mg g^{-1} DW	Assefa et al. (2020)
K192370	R/Y	40.53 mg g^{-1} DW	12.25 mg g^{-1} DW	Assefa et al. (2020)
K192373	Y	32.36 mg g^{-1} DW	13.26 mg g^{-1} DW	Assefa et al. (2020)
K192381	R/Y	28.33 mg g^{-1} DW	10.43 mg g^{-1} DW	Assefa et al. (2020)
K192386	R/Y	38.42 mg g^{-1} DW	10.00 mg g^{-1} DW	Assefa et al. (2020)
K192397	R/Y	33.05 mg g^{-1} DW	11.82 mg g^{-1} DW	Assefa et al. (2020)
K192444	Y	25.04 mg g^{-1} DW	9.24 mg g^{-1} DW	Assefa et al. (2020)
K192469	R/Y	25.41 mg g^{-1} DW	8.89 mg g^{-1} DW	Assefa et al. (2020)
K192471	R/Y	31.14 mg g^{-1} DW	13.81 mg g^{-1} DW	Assefa et al. (2020)
K192504	R/Y	26.91 mg g^{-1} DW	21.25 mg g^{-1} DW	Assefa et al. (2020)
Speedggul	R	22.07 mg g^{-1} DW	8.50 mg g^{-1} DW	Assefa et al. (2020)
Sambokggul	R	25.70 mg g^{-1} DW	8.44 mg g^{-1} DW	Assefa et al. (2020)
Uriggul	R	23.88 mg g^{-1} DW	10.61 mg g^{-1} DW	Assefa et al. (2020)
Newkkokkoma	R/Y	19.50 mg g^{-1} DW	2.54 mg g^{-1} DW	Assefa et al. (2020)
Norangsambokggul	Y	23.85 mg g^{-1} DW	11.46 mg g^{-1} DW	Assefa et al. (2020)

374 Y = Yellow, R = Red, CY = canary yellow, O = orange, W = white, R/Y = Red and yellow, DW = dry weight, FW = fresh weight

8. Organic acids content

The composition and concentration of organic acids improve fruit taste and determines eating and nutritional quality of watermelon fruit. In addition, organic acids play various important roles in the human body. For example, malic acid improves amino acids absorption, whereas citric acid can increase appetite and promote calcium and phosphorus absorption (Gao et al. 2018). Organic acids including malic, quinic, citric, oxalic, and tartaric acids accumulate in watermelon flesh during fruit development and maturation (Liu et al. 2012; Gao et al. 2018). Citric acid and malic acid are the main organic acids in watermelon flesh. Citron watermelon flesh is non-sweet and slightly sour indicating the presence of organic acids (Gao et al. 2018). Jawad et al. (2020) reported high total organic acid content (17.26 mg g^{-1} fresh weight) in a sour citron watermelon genotype PI271769. This genotype has a white-green flesh colour was used to develop a sour and sweet dessert watermelon cultivar "SW" (Gao et al. 2018). This indicated citron watermelon is a potential source of organic acids with health-promoting attributes, however their composition remains to be determined. In *C. lanatus* var. *lanatus*, Gao et al. (2018) reported citric acid content of < 2 mg g^{-1} and malic acid content ranging from 2 to 14 mg g^{-1}. Malic acid concentration ranging from 11.68±2.86 to 24.44±5.55 mg g^{-1} were reported among red, yellow and orange-fleshed *C. lanatus* var. *lanatus* cultivars (Liu et al. 2012). Also, the concentration of citric acid varied from 23.92±1.54 to 64.87±20.17 mg g^{-1} among red, yellow and orange-fleshed *C. lanatus* var. *lanatus* genotypes. Low contents of oxalic acid (0.85±0.92 to 6.63±4.05 mg g^{-1}), tartaric acid (0.47±0.15 to 1.31±0.46 mg g^{-1}) and quinic acid (0.56±0.9 to 3.29±3.06 mg g^{-1}) were reported in *C. lanatus* var. *lanatus* genotypes with varying flesh colours (Liu et al. 2012). Martí et al. (2019) reported malic acid contents ranging from 0.77–3.71 mg g^{-1}

and citric acid contents ranging from 0.08–1.71 mg g^{-1} in sweet watermelon varieties. It is also suggested that citron watermelon genotypes with white, yellow and orange flesh colours have varied concentrations of organic acids. In addition, the slightly sour taste of the yellow and orange fleshed citron watermelon types result in slight sour-tasting food-derived products (Fig. 2C & D). Often, vinegar or synthetic tartaric acid are added during to improve sourness, indicating consumers may prefer citron watermelon types with higher organic acids contents for cooking or dessert. These point the need to develop citron watermelons with higher contents of organic acids, and hence their analysis of in genetically diverse genotypes of citron watermelon with yellow and orange-fleshed types flesh colours is vital to organic acid-enhanced genotypes for production, direct consumption, cooking and processing.

9. Sugar content

Sweetness of watermelon fruit is determined by sugar composition and their ratios mainly glucose, fructose and sucrose (Yativ et al. 2010; Liu et al. 2012). Citron watermelon fruit is non-sweet due low of sugar contents. Relatively low sucrose, fructose and glucose contents of 3.95, 1.57 and 0.35 mg g^{-1} were reported in citron watermelon fruit in that order (Ren et al. 2012). Also, PI271769 a citron watermelon genotype recorded total soluble sugar content of up to 6.83 mg g^{-1} fresh weight in fruits (Jawad et al. 2020). Total soluble solids (TSS) is an indication of sugar content and sweetness. Perkins-Veazie et al. (2006) reported low TSS content of 3.45% for *C. lanatus* var. citroides compared to *C. lanatus*. var. *lanatus* which displayed higher total TSS content of 11.0% in *C. lanatus*. var. *lanatus* fruit. Ngwepe et al. (unpublished data) recorded low TSS content varying from 2.75 to 3.92 °Brix among white, yellow and orange-fleshed citron watermelon accessions. In sweet dessert watermelon, the dominant soluble sugars are sucrose (31.2 mg g^{-1}), fructose (18.75 mg g^{-1}) and glucose (42.7 mg g^{-1}) (Zhu et al., 2017). In addition, Liu et al. (2012) reported fructose content ranging from 118.09±7.69 to 175.29±57.82 mg g^{-1} dry weight, glucose content ranging from 41.43±1.91 to 69.07±15.69 mg g^{-1} dry weight, and sucrose content varying from 10.88±3.48 to 397.26±58.12 mg g^{-1} dry weight in yellow, orange and red-flesh sweet watermelons. Fructose content ranging from 11.13–55.44 mg g^{-1}, glucose ranging from 5.48–37.83 mg g^{-1} and sucrose content ranging from 0.00–69.65 mg g^{-1} were reported in sweet watermelon (Martí et al. 2019). Low sugar and TSS contents citron watermelon types are attractive for consumers requiring minimal sugar intake for personal or dietary preferences (Davis et al. 2007; 2008). Further, the low sugar composition of the fruit is ideal for both cooking and dessert. If required, a sprinkle of sugar can be used for fresh consumption to offer the refreshing, sweet and flavourful watermelon taste (Davis et al. 2007; 2008). Although sugar content of citron watermelon is relatively low, extensive genetic variation for sugar composition and their ratios may exist. Therefore, rigorous sugar profile analysis and quantification in a wide range of genetically and phenotypically diverse citron watermelon genotypes is required. In *C. lanatus* var. *lanatus* germplasm genetic variation for total soluble solids and sugar content were reported (Liu et al. 2012). Brown or white sugar is often added to improve the taste of traditional dishes especially “kgodu” and “mokgapu” in South Africa due to low contents of naturally occurring sugars of yellow and orange-fleshed cooking citron watermelon types. Breeding efforts to develop citron watermelon genotypes with slightly increased sugar profiles is necessary to reduce the use of processed sugar often associated with undesirable health hazards including obesity. Nonetheless, citron watermelon has the potential for cultivation for niche and specialty markets, and for consumers interested in low to moderate carbohydrates and substantial levels of vitamins and phytonutrients (Davis et al. 2007). Furthermore, citron watermelon is useful in crop improvement programmes in the development and commercialization of sweet watermelon genotypes with low sugar profiles for niche and specialty markets (Davis et al. 2007; 2008).

10. Volatile compounds

Citron watermelon may be a source of volatile compounds found in its close botanical variety *C. lanatus var. lanatus*; however, the specific profiles of various volatile compounds in the fruit is yet to be identified. During fruit ripening, changes in flesh color of watermelon fruit occurs and aromatic/volatile compounds are enhanced (Fredes et al. 2017; Bianchi et al. 2018; Mendoza-Enano et al. 2019). Volatile compounds including monoterpenes, apo-carotenoids, aldehydes, alcohols, acids, olefins, and furans have been reported in sweet watermelon flesh (Liu et al. 2012). Volatile compounds detected in red, yellow and orange-fleshed *C. lanatus* var. *lanatus* include 2-pentyl-furan, (E)-2-(2-pentenyl) furan, 2-ethyl-1-hexanol; nonanal, (E)-2-nonenal, nonanol, 2-nonen-1-ol; Nol-3, (Z)-3-nonen-1-ol, 2,6-nonadien-1-ol, (E,Z)-3,6-nonadien-1-ol, nonanoic acid, 1,10-undecadiene; (E)-geranyl acetone; limonene, β-ionone (Liu et al. 2012). Beaulieu and Lea (2006) identified 10 volatile compounds in seedless watermelon (*C. lanatus* var. *lanatus*) including hexanal, 6-methyl-5-hepten-2-one, (E)-2-octenal, 4-nonenal, (Z)-6-nonenal, Nonanal, (Z)-3-Nonen-1-ol and (E,Z)-2,6-nonadienal, (Z,Z)-3,6-nonadien-1-ol, (E)-2-nonenal and 1-nonanol. These authors (i.e., Beaulieu and Lea 2006) reported 3-nonen-1-ol/(E,Z)-2,6-nonadienal (16.5-28.2%), (E)-2-nonenal (10.6-22.5%), (Z)-6-nonenal (2.0-11.3%) and Hexanal (37.7%) were the most abundant volatile compounds in sweet watermelon fruit. Additionally, Z)-3-Nonen-1-ol, 2-ethyl-1-hexanol, nonanal, (E,Z)-

3,6-nonadien-1-ol, and nonanol were reported as dominant volatiles accounting for 81-87% in the flesh of sweet watermelon fruit (Liu et al. 2012). In yellow and orange-yellow fleshed sweet watermelon fruit, Z)-3-Nonen-1-ol, 2-ethyl-1-hexanol, nonanal, (E,Z)-3,6-nonadien-1-ol, and nonanol accounted for 75-79% of the total detected volatiles (Liu et al. 2012). Lewinsohn et al. (2006) identified monoterpenes and norisoprenes including farnesyl acetone, geranyl acetone, 6-methyl-5-hepten-2-one, 2,6-dimethylhept-5-1-al, 2,3-epoxygeranial, neral (cis-citral), geranial (trans-citral), dihydro-apo-trans-farnesal, pseudoionone, α-ionone, dihydroactinodiolide, *β*-cyclocitral and *β*-ionone in the fruit of red, yellow and orange-fleshed *C. lanatus* var. *lanatus*. *β*-Ionone, dihydroactinodiolide, and *β*-cyclocitral were the most dominant volatile compounds in sweet watermelon fruit (Lewinsohn et al. 2006). When compared by flesh colour, the concentrations of (Z)-3-nonen-1-ol, nonanol, and total volatiles were higher in red-fleshed *C. lanatus* var. *lanatus* than yellow and orange fleshed types (Liu et al. 2012). Most volatile compounds such as (Z)-6-nonenal, (E,Z)-2,6-nonadienal and (Z)-6-nonen-1-ol are associated with melon, cucumber and squash-like aromas (Fredes et al. 2017). Assessment of volatile compounds in citron watermelon is useful to develop genotypes and value-added products with unique aromatic profiles, odour and flavour.

11. Phytochemical compounds

Citron watermelon synthesize different types of phytochemicals and bioactive metabolites which accumulate in various plant parts. These include flavonoids, cucurbitacin and cucurbitacin glycosides with medicinal values (Abdelwahab et al. 2011; Ogbuji et al. 2012; Davidovich-Rikanati et al. 2015). Reportedly, other cucurbit crops expressed phytochemical compounds such as phenolics, spingolipids, tetranortriterpenoid, and terpenoids which are also pharmacologically and pharmaceutically important bioactive compounds (Gamrath et al. 1988; Marzouk et al. 2010, 2013; Zaini et al. 2011; Attar and Ghane 2018, 2019; Enneb et al. 2020). Various pharmacological activities such as anti-oxidant, anti-hyperglycemic, anti-cancer, analgesic, anti-diabetic, anti-hepatotoxic, anti-inflammatory, anti-helmintics, anti-virus, anti-bacterial, anti-microbial cardioprotective, cytotoxic, and anti-oxidant properties are associated phytochemicals in various cucurbit species (Tannin-Spitz et al. 2007; Mukherjee et al. 2013; Hassan et al. 2017; Abdel-Salam et al. 2019; Torres-Moreno et al. 2019; Bourebaba et al. 2020). Further, bioactive compounds possess therapeutic value for treatment of various diseases including epilepsy, liver disorders, ulcer, cancer, rhinosinusitis diseases, and various skin infections (Uslu et al. 2016; Alsayari et al. 2018). Pharmacological values of various phytochemicals isolated from cucurbit species are presented in Table 4.

513 **Table 4**. Reported phytochemical compounds and pharmacological values of various products isolated from cucurbit species.

Species	Common name	Name of compound extracted	Concentration (IC_{50})	Anti-cancer properties	Pharmacological action	References
Trichosanthes cucumerina	Snake gourd	Cucurbitacin B	48.6 **µ**M	Breast cancer cell: MCF-7	-	Duangmano et al. (2012)
Ecballium elaterium	Squirting cucumber	Cucurbitacin B	68.85 nM	Glioma cell line: U87	Inhibited integrin-mediated cell adhesion, migration and proliferation of glioma tumour cell line U87	Touihri-Barakati et al. (2017)
Ecballium elaterium	Squirting cucumber	Cucurbitacin B	84.6 nM	Glioma cell line: U87	Inhibited integrin-mediated cell adhesion, migration and proliferation of glioma tumour cell line U87	Touihri-Barakati et al. (2017)
Ecballium elaterium	Squirting cucumber	Cucurbitacin B	10nM	Microvascular endothelial cells (HMEC) angiogenesis	Inhibited in vitro human microvascular endothelial cells (HMEC) angiogenesis	Touihri-Barakati et al. (2017)
Ecballium elaterium	Squirting cucumber	Cucurbitacin B	70.1 nM	U87 cells	Inhibited cell proliferation	Touihri-Barakati et al. (2017)
Cucurbita texana	Texas Gourd	Cucurbitacin B	27.67 µM	Liver cell: HepG2	Cytotoxic	Bartalis et al.(2011)
Cucurbita texana	Texas Gourd	Cucurbitacin B	0.8 µM	Human cervical cancer cell line (HeLa)	Cytotoxic	Bartalis et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin B	4.42 µM	HSC-T6 cells	Cytotoxic	Bartalis et al. (2011)
Cayaponia tayuya	Tayuya	23, 24-dihydrocucurbitacin B	98 µM	Colon cancer: HCT116	-	Escandell et al. (2008)
Cayaponia tayuya	Tayuya	23, 24-dihydrocucurbitacin B	4.9 µM	Colon cancer cell: HKe3	-	Escandell et al. (2008)
Cucurbita andreana	Winter squash	Cucurbitacin I	-	Breast cancer cell line: MCF-7	Inhibited cell proliferation	Jayaprakasam et al. (2003)
Cucurbita andreana	Winter squash	Cucurbitacin I	-	Lung cancer line: NCI-H460	Inhibited lung cancer cell growth	Jayaprakasam et al. (2003)
Cucurbita andreana	Winter squash	Cucurbitacin D	-	Lung cancer line: NCI-H460	Inhibited colon cancer cell growth	Jayaprakasam et al. (2003)
Cucurbita andreana	Winter squash	Cucurbitacin E	-	Lung cancer line: NCI-H460	Inhibited colon cancer cell growth	Jayaprakasam et al. (2003)

Table 4. (Continued).

Species	Common name	Name of compound extracted	Concentration (IC_{50})	Anti-cancer properties	Pharmacological action	References
Cucurbita andreana	Winter squash	Cucurbitacin E	-	Lung cancer line: NCI-H460	Inhibited colon cancer cell growth	Jayaprakasam et al. (2003)
Citrullus colocynthis	Bitter apple	Cucurbitacin E	8.29 µM	Drug resistant leukaemia cell line (CCRF-CEM)	Cytotoxic activity towards resistant leukemia cell lines	Saeed et al. (2019)
Citrullus colocynthis	Bitter apple	Cucurbitacin E	13.72 µM	Multi-drug resistant leukaemia cell line (CEM/ADR5000)	Cytotoxic activity towards multi-drug resistant leukemia cell lines	Saeed et al. (2019)
Cucurbita texana	Texas gourd	Cucurbitacin E-glycoside	37.0 µM	Human cervical cancer cell line (HeLa)	Cytotoxic	Bartalis et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin E	0.10 µM	Human cervical cancer cell line (HeLa)	Cytotoxic	Bartalis et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin D	0.70 µM	Human cervical cancer cell line (HeLa)	Cytotoxic	Bartalis et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin B	0.80 µM	HSC-T6 cells	Cytotoxic	Bartalis et al 2011
Cucurbita andreana	Winter squash	Cucurbitacin E	0.10 µM	Lung cancer cell: NCI-H460	Inhibited lung cancer cell growth	Jayaprakasam et al. (2003)
Citrulus lanatus var. citroides	Citron watermelon	Cucurbitacin E	51.91 µM	Liver cancer cells: WRL-68	Inhibited the production of nitric oxide	Abdelwahab et al. (2011)
Cayaponia tayuya	Tayuya	Cucucrbitacin I	0.29 µM	Colon cancer: HCT116	Antitumorigenic activity	Escandell et al. (2008)
Cayaponia tayuya	Tayuya	Cucucrbitacin I	0.09 µM	Colon cancer cell: HKe3	Antitumorigenic activity	Escandell et al. (2008)
Cayaponia tayuya	Tayuya	Cucurbitacin R	39.0 µM	Colon cancer line: HCT116	Exerted potent anti-inflammatory activity	Escandell et al. (2008)
Cayaponia tayuya	Tayuya	Cucurbitacin R	27.0 µM	Colon cancer cell line: HKe3	-	Escandell et al. (2008)
Citrullus colocynthis	Bitter apple	Cucurbitacin glucosides (B + E)	145.0 µM	Breast cancer cell: ER+MCF-7	Reduced proliferation of human cancer cells	Tannin-Spitz et al. (2007)
Momordica charantia	Bitter gourd	Cucurbitane: goyaglycoside I	24.7 µM	Murine hepatic stellate cells: t-HSC/Cl-6	Anti-hepatic fibrosis Activity	Yue et al. (2019)

Table 4. (Continued).

Species	Common name	Name of compound extracted	Concentration (IC_{50})	Anti-cancer properties	Pharmacological action	References
Momordica charantia	Bitter gourd	Cucurbitane: goyaglycoside I	50.6 µM	Liver cells: Hep3B	Anti-hepatoma activity	Yue et al. (2019)
Momordica charantia	Bitter gourd	Cucurbitane: goyaglycoside I	58.10 µM	Liver cells: HepG2	Anti-hepatoma activity	Yue et al. (2019)
Momordica charantia	Bitter gourd	Cucurbitane-type triterpene glycoside	158.3 µM	xanthine oxidase	Inhibitory effect	Lin et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin D	77.30 µM	Liver cells: HepG2	Cytotoxic	Bartalis et al. (2011)
Cucurbita texana	Texas gourd	Cucurbitacin D	0.70 µM	Human cervical cancer cell line (HeLa)	Cytotoxic	Bartalis et al 2011
Cucurbita texana	Texas gourd	Cucurbitacin D	26.0 µM	HSC-T6 cells	Cytotoxic	Bartalis et al. (2011)
Hemsleya amabilis	Xue dan	23,24-dihydrocucurbitacin E	3.87 µM	Human cervical cancer cell line (HeLa)	Cytotoxic against HeLa cell lines	Chen et al. (2014)
Hemsleya amabilis	Xue dan	23,24-dihydrocucurbita-cin F	3.31 µM	Human cervical cancer cell line (HeLa)	Potent cytotoxicity against HeLa cell lines	Chen et al. (2014)
Hemsleya amabilis	Xue dan	23,24-dihydrocucurbitacin B	2.79 µM	Human cervical cancer cell line (HeLa)	Potent cytotoxicity against HeLa cell lines	Chen et al. (2014)
Hemsleya amabilis	Xue dan	7-hydroxy-cucurbitacin F-25-O-acetate	12.30 µM	Cervical epithelial adenocarcinoma (HeLa) human cell lines	Moderate cytotoxic effect against HeLa cell lines	Chen et al. (2014)
Hemsleya amabilis	Xue dan	2β,3α,16α,20(R),24(S),25-hexahydroxy-9-methyl-19-norlanost-5-en-11,22-dione	16.40 µM	Human cervical cancer cell line (HeLa)	Moderate cytotoxic effect against HeLa cell lines	Chen et al. (2014)
Hemsleya amabilis	Xue dan	23,24-dihydro-3-epi-isocucurbitacin B	7.45 µM	Human cervical cancer cell line (HeLa)	Potent cytotoxicity against HeLa cell lines	Chen et al. (2014)

Table 4. (Continued).

Species	Common name	Name of compound extracted	Concentration (IC_{50})	Anti-cancer properties	Pharmacological action	References
Hemsleya amabilis	Xue dan	Hemslecin A	0.39 µM	Human cervical cancer cell line (HeLa)	Cytotoxic against HeLa cell lines	Chen et al. (2014)
Momordica charantia	Bitter gourd	3*β*-hydroxymultiflora-8-en-17-oic acid	268.5 µM	-	Potent ABTS radical cation scavenger	Liu et al. (2010)
Momordica charantia	Bitter gourd	cucurbita-1(10),5,22,24-tetraen-3*α*-ol	352.1 µM	-	Potent ABTS radical cation scavenger	Liu et al. (2010)
Momordica charantia	Bitter gourd	5*β*,19*β*-epoxycucurbita-6,22,24-trien-3*α*-ol	458.9 µM	-	Potent ABTS radical cation scavenger	Liu et al. (2010)
Momordica charantia	Bitter gourd	Karavilosides XIII	>40.0 µM/L	Human cancer cell lines (HL-60, SMMC-7721, A-549,MCF-7, and SW480)	Cytotoxic	Zhao et al. (2014)
Momordica charantia	Bitter gourd	Momordicines VI	>40.0 µM/L	Human cancer cell lines (HL-60, SMMC-7721, A-549,MCF-7, and SW480)	Cytotoxic	Zhao et al. (2014)
Momordica charantia	Bitter gourd	Karaviloside III	16.68 µM	HepG2 liver cancer cell line	Cytotoxic	Yue et al. (2019)
Momordica charantia	Bitter gourd	Karaviloside III	4.12 µM	Hep3B liver cancer cell line	Cytotoxic	Yue et al. (2019)
Gynostemma pentaphyllum	Jiaogulan	Gypensapogenin H	-	Human prostate cancer cells (DU145 and 22RV-1)	Inhibited proliferation, reduced survival, led to G1 cell cycle arrest and induced apoptosis in both cell lines	Zhang et al. (2015)
Gynostemma pentaphyllum	Jiaogulan	Lobatoside O	8.61 µM/L	Colorectal cancer cell line (HCT-116)	Cytotoxic	Cao et al. (2015)
Gynostemma pentaphyllum	Jiaogulan	Lobatoside O	12.56 µM/L	Colorectal cancer cell line (HT-29)	Cytotoxic	Cao et al. (2015)

Table 4. (Continued).

Species	Common name	Name of compound extracted	Concentration (IC_{50})	Anti-cancer properties	Pharmacological action	References
Gynostemma pentaphyllum	Jiaogulan	Lobatoside O	18.72 µM/L	Lung cancer cell (A549)	Cytotoxic	Cao et al. (2015)
Gynostemma pentaphyllum	Jiaogulan	Lobatoside O	7.58 µM/L	Breast cancer cell line (MCF-7)	Cytotoxic	Cao et al. (2015)
Ibervillea sonorae	Wareke	Kinoin A	-	Human cervical cancer cell line (HeLa)	Antiproliferative activity	Torres Moreno et al. (2020a)
Ibervillea sonorae	Wareke	Cucurbitacin IIb/23,24-dihydrocucurbitacin F	7.3 µM	Human cervical cancer cell line (HeLa)	Antiproliferative activity against HeLa cell lines by inducing cell death by apoptosis	Torres Moreno et al. (2020b)
Ibervillea sonorae	Wareke	Cucurbitacin IIb/23,24-dihydrocucurbitacin F	7.8 µM	Lung cancer cell (A549)	Antiproliferative activity against A549 cell lines by inducing cell death by apoptosis	Torres Moreno et al. (2020b)

µM = micro mole, nM=nano mole, IC_{50} = half maximal inhibitory concentration value

11.1. Cucurbitacins

Cucurbitacins are reported as major phytochemical compounds in cucurbits including citron watermelon and possess a wide range of pharmacological properties (Tannin-Spitz et al. 2007; Davidovich-Rikanati et al. 2015; Kim et al. 2018). Cucurbitacins biosynthesis occurs via the cyclization of 2, 3-oxidosqualene to cucurbitadienol (Shibuya et al. 2004). Cucurbitadienol metabolizes through several steps into various cucurbitacins (Zhou et al. 2016; Cardenas et al. 2019). *C. lanatus* var. citroides biosynthesize several types of cucurbitacin such as cucurbitacin B, D, E and I in leaves, fruit, seed and roots (Abdelwahab et al. 2011; Davidovich-Rikanati et al. 2015). In addition, various cucurbitacins glycosides such as cucurbitacin B, D, E and I-glycoside are also biosynthesized by *C. lanatus* var. *citroides* (Davidovich-Rikanati et al. 2015). The pharmacological and therapeutic values of cucurbitacins, cucurbitacin-gycosides and cucurbitacin-type triterpenoids investigated in various cucurbit species are discussed below.

11.1.1. Cucurbitacin B

The pharmacological values of Cucurbitacin B (Cuc B) from citron watermelon has not been established when compared to other cucurbit crops. CuC B extracted from leaves of *Ecballium elaterium* exhibited anti-integrin activity and proliferation of U87 cells at half maximal inhibitory concentration (IC_{50}) value of 70.1 nM. In addition, Cuc B exhibited cytotoxic effect against various human cancer including ovarian and breast cancer (Duangmano et al. 2012; El-Senduny et al. 2016; Touihri-Barakati et al. 2017; Alsayari et al. 2018). Cuc B content of 0.4 µM extracted from *Cucurbita andreana* fruit inhibited colon cancer cell lines (HCT-116) by 81.5% and breast cancer cells (MCF-7) by 87%, whereas 0.1 µM inhibited lung cancer cells

(NCI-H460) by 96% compared to Adriamycin (doxorubicin) with cytotoxic effect of 64, 47 and 45% inhibition against colon, breast and lung cancer lines, respectively (Jayaprakasam et al. 2003). This indicated the potency of Cuc B for use as effective cancer treatment in humans. Cuc B inhibited growth activity and exhibited synergistic effect against various strains of *Staphylococcus aureus* at minimum inhibitory concentration (MIC) values ranging from 0.12 to 0.44 μg/mL and fractional inhibitory concentration (ΣFIC) ranging from 0.29 to 0.43 (Hassan et al. 2017). *S. aureus* is a Gram-positive bacterium that cause serious infections in humans (Hassan et al. 2017). Cuc B also showed anti-viral activity against Herpes simplex virus (HSV) at IC_{50} values of 0.94 and 1.74 μM, and 50% cytotoxic concentration (CC_{50}) of 120 μM (Hassan et al. 2017). HSV is the primary cause oral or facial infections in humans (Hassan et al. 2015). Therefore, Cuc B extracts from cucurbit crops including citron watermelon may act as a natural anti-microbial, anti-viral and anti-cancer phytochemical compound for treatment of various bacterial and viral diseases, and various types of cancers in humans.

11.1.2. Cucurbitacin D

The pharmacological properties of Cucurbitacin D (Cuc D) in citron watermelon is yet to be established like other cucurbit crops. For example, CuC D extracted from *E. elaterium* and *C. andreana* were reported to possess antioxidant, anti-inflammatory and anti-cancer properties (Jayaprakasam et al. 2003; Mansour et al. 2007). Cuc D isolated from *Trichosanthes kirilowii* (Cucucrbitaceae) induced apoptosis of human hepatocellular carcinoma cells and human T cell leukemia cells in vitro (Takahashi et al. 2009; Ding et al, 2011). Further, inhibition of breast cancer, human endometrial and ovarian cancer cells by Cuc D has been reported (Ishii et al. 2013; Ku et al. 2015). Jayaprakasam et al. (2003) reported Cuc D fruit extracts isolated from

C. andreana showed inhibitory effects of 80.4 and 78% at 0.4 μM on colon and breast cancer cells. Further, Cuc D inhibited cyclooxygenase-2 (COX-2) enzyme associated with anti-inflammation by 29% though lower compared to anti-inflammatory drugs such as Ibuprofen (59%), naproxen (95%) and Vioxx (71%) at lower concentrations of <3 μg/ml (Jayaprakasam et al. 2003). Overall, Cuc D which naturally occurs in cucurbit crops including citron watermelon could be valuable for development of anti-tumor, anti-cancer and anti-inflammatory drugs.

11.1.3. Cucurbitacin E

Anti-inflammatory activity of CuC E isolated from citron watermelon has been reported (Abdelwahab et al. 2011). The IC_{50} value of CuC E isolated from citron watermelon on human normal hepatic cells (WRL-68) was 51.91±5.22 μg/ml compared to an IC_{50} of 0.10±0.05 μg/ml for Paclitaxel (positive cytotoxic control) (Abdelwahab et al. 2011). Also, Cuc E extracted from citron watermelon COX-1 and COX-2 enzymes and production of nitric oxide (NO) which are linked to inflammation and various types of cancers (Abdelwahab et al. 2011). Cytotoxic effects of CuC E isolated from the fruit of *C. colocynthis* against leukemia cell lines, breast cancer, colon cancer cells, lung cancer, renal cancer, ovarian cancer and prostate cancer cell lines was recently reported (Saeed et al. 2019). On the contrary, CuC E extracted from *C. lanatus* var. *citroides* was reported non-effective radical oxygen scavenger based oxygen radical absorbance capacity (ORAC) and ferric reducing-antioxidant power (FRAP) assays (Abdelwahab et al. 2011). The FRAP value for CuC E was 38± 2.61 μmol/l lower than a comparative control with values of 350±9.5 (Ascorbic acid) and 251±5.7 (Quercetin), respectively. For ORAC assay, CuC E concentration of 40.25±1.56 μM of Trolox was also lower compared to 160.32±2.75 μM of Trolox for quercetin (comparative control) (Abdelwahab et al. 2011).

Nevertheless, CuC E possess pharmacological value and can prove an effective treatment for inflammation-mediated diseases and various types of cancers. Medicinal and drug formulation of CuC E or utilization as plant-based medicine in cucurbit crops such as *C. lanatus* var. *citroides* is recommended (Abdelwahab et al. 2011).

11.1.4. Cucurbitacin I

Cucurbitacin I (CuC I) accumulates in leaves and fruit of citron watermelon (Davidovich-Rikanati et al. 2015) though the pharmacological value of this compound has not been specifically determined in this crop. CuC I extracted from wild *L. siceraria* fruit inhibited human cancer (MCF-7) and colon cancer (HT-29) cells (Atter and Ghane 2019). The highest concentration which caused 50% inhibition/toxicity of cell growth (GI_{50}) against cancer cell line MCF-7 was $GI_{50} < 10$ µg/mL, 133.42 µg/mL for concentration causing total inhibition of cell growth (TGI) and concentration of 301.21 µg/mL causing 50% cell kill rate (LC_{50}) (Atter and Ghane 2019). This was comparable to Adriamycin (control drug) with GI_{50} of < 10 µg/mL, TGI of 104.27 µg/mL and LC_{50} of 385.17 µg/mL (Atter and Ghane 2019). In addition, cucurbitacin I at LC_{50} of 664.02 µg/mL inhibited growth of HT-29 cell line compared LC_{50} of 63.20 µg/mL using adriamycin (Atter and Ghane 2019). CuC I decreased cell viability and cell proliferation of human colon cancer cells (SW480), indicating its potency to treat or cure colon cancer (Kim et al. 2014). CuC I isolated from *C. andreana* fruit displayed inhibitory effects of 65 and 12% against colon (HCT-116) and breast (MCF-7) cancer cells at concentration of 0.4 µM (Jayaprakasam et al. 2003). Also, CuC I inhibited COX-2 enzyme by 27% at 100 µg/ml (Jayaprakasam et al. 2003). Therefore, CuC I is potential therapeutic compound for treatment of inflammation and cancer.

11.1.5. Cucurbitacin glycosides

Cucurbitacin B, D, E and I glycosides reportedly accumulate in *C. lanatus* var. *citroides* (Davidovich-Rikanati et al. 2015). Despite the presence of cucurbitacin-glycosides, the concentrations of these medicinal compounds in edible and non-edible plant parts of citron watermelon have not been previously quantified. Various other types of cucurbitacin-glycosides including 2-*O*-β-D-glucopyranosyl-cucurbitacin E, 2-O-β-D-glucopyranosyl-Cucurbitacin I, 2-O-β-D-glucopyranosyl-Cucurbitacin L, and 2-*O*-β-D-glucopyranosyl-(22–27)-hexanorcucurbitacin I have been identified in fruit and seed of *C. colocynthis* (Hatam et al. 1989) but previously not isolated in citron watermelon. *In vitro* ABTS radical scavenging capacity revealed cucurbitacin glycosides (i.e., cucurbitacin B + E glucosides) extracted from *C. colocynthis* at IC_{50} values of 0.38, and 11 mM were efficient ROS scavenger (Tannin-Spitz et al., 2007). These suggested cucurbitacin glycosides from citron watermelon may exhibit antioxidant properties by directly inhibiting scavenging ROS though these properties are yet to be determined.

11.1.6. Triterpenes

Since citron watermelon accumulated various types of cucurbitacins, it may be speculated that the crop may also contain cucurbitacin-type triterpenoids with valuable medicinal properties. In *Ibervillea sonorae* (*Cucurbitaceae*), cucurbitacin-type triterpenes namely kinoin A and kinoin B diglucoside were identified from the root (Torres-Moreno et al. 2015). Kinoin B diglucoside displayed antiproliferative activity by inhibiting growth of HeLa (human cervical carcinoma), M12A^{K}.C3F6, A549 (human lung carcinoma) and RAW 264.7 (macrophages transformed by Abelson leukemia virus) cancer cell lines at IC_{50} concentration of 18.0, 31.4, 40.2, and 61.5 μM, in that order (Torres-Moreno et al. 2015). Further, kinoin A cause HeLa cell death by apoptosis (Torres-Moreno et al. 2015). Cucurbitane-type triterpene 20, 21, 22, 23, 24, 25, 26, 27-octanorcucurbita-5-ene-3, 11, 16-trione also referred to as kinoin D isolated from the roots *I. sonorae* exhibited anti-inflammatory activity in mice (Jardón-Delgado et al. 2014). Cucurbitane-type triterpenoids including karavilagenin F, karavilosides III, XII and XIII, momordicines VI, VII, and VIII, 5*β*,19-epoxy-25-methoxycucurbita-6,23-diene-3*β*,19-diol, 5*β*,19-epoxycucurbita-6, 23-diene-3*β*,19,25-triol, kuguacin R, and (19*R*,23*E*)-5*β*,19-epoxy-19-methoxycucurbita-6,23,25-trien-3*β*-ol have also been identified and isolated in stems, leaves and fruit of bitter gourd (*M. charantia*) (Lin et al. 2011; Liu et al. 2011; Zhao et al. 2014). Of these, karaviloside III exhibited inhibitory activity against t-HSC/Cl-6 cells and cytotoxic activity against Hep3B and HepG2 liver cancer cell lines with IC_{50} values of 3.74 ± 0.13, 16.68 ± 2.07 and 4.12 ± 0.36 *μ*M, respectively (Yue et al. 2019). Cucurbitane triterpenoids 7β-hydroxycucurbitacin F-25-O-acetate and 2β,3β,20(S),26,27-pentahydroxy-16α,23(S)-epoxycucurbita-5,24-dien-11-one were isolated from the rhizomes of *Hemsleya amabilis* Diels (Cucurbitaceae). Hemslecin A, which is the main triterpenoid of *H. amabilis* exhibited cytotoxicity against HeLa human cancer cell lines at IC_{50} concentration of 0.389 μM (Chen et al. 2014). Also, Kuguacin J, a triterpenoid extracted from *M. charantia* leaf possess inhibitory growth arrest and apoptosis against prostate cancer cells (LNCaP) (Pitchakarn et al. 2011). This indicated cucurbitacin-type triterpenoids compounds possess various pharmacological activities. Isolation, characterization and pharmacological properties of cucurbitacin-type triterpenoids in citron watermelon are yet to be determined.

Conclusions, and perspective and outlook for future research

Citron watermelon serve as a food and nutrition security crop in many parts of sub-Saharan Africa. However, the utilization and consumption of the crop is very low in the region partly attributed to lack of knowledge on its nutritional and phytochemical composition. Comprehensive nutrient analysis including minerals, amino acids, organic acids, sugars and carotenoids contents of the crop is required to promote and improve the utilization of citron watermelon as a functional food crop for improving nutrition and dietary needs of the population especially in Africa. The ethnomedicinal uses of citron watermelon are scarcely reported and its use as a medicinal plants remains largely unknown and unexplored. Several phytochemical bioactive compounds including cucurbitacins and cucurbitacin-glycosides have been reported to accumulate in citron watermelon though limited studies are available that isolated, identified and quantified specific phytochemical compounds in this crop. Therefore, there is need for further studies to characterize and quantify the concentrations of various phytochemical compounds present in citron watermelon. Further, *in vitro* and *in vivo* pharmacological and therapeutic studies of phytochemical compounds occurring in citron watermelon are required for effective use of this crop as a medicinal plant. Overall, the present study recommends concreted and detailed biochemical analysis efforts to aid the discovery of health-promoting bioactive compounds using the diverse genetic resources of citron watermelon. This will enhance the commercial value and benefit sharing from citron watermelon in the horticulture, food and pharmaceutical industry. Citron watermelon is a vital source of novel genes for breeding in sweet dessert watermelon to enhance biotic and abiotic stress tolerance and fruit quality. The use of citron watermelon genetic resources to design sweet watermelon genotypes with various attributes including biotic and abiotic stress tolerance, and desired horticultural and agronomic attributes for diverse markets and consumers is required in sub-Saharan Africa. Also, the crop is a valuable rootstock for production of sweet watermelon to improve biotic and abiotic stress resistance, fruit quality and overall productivity. Therefore, it is recommended to use the diverse citron watermelon germplasm available in sub-Saharan Africa for their rootstock potential and for breeding of desired cultivars based on farmer and consumer-preferred attributes, and market opportunities.

Conflict of interest

The authors declare that they have no conflict of interest.

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References

Abdelwahab, S.I., Hassan, L.E., Sirat, H.M., Yagi, S.M., Koko, W.S., Mohan, S., Taha, M.M., Ahmad, S., Chuen, C.S., Narrima, P., Rais, M.M., Hadi, A.H., 2011. Anti-inflammatory activities of cucurbitacin E isolated from *Citrullus lanatus* var. *citroides*: role of reactive nitrogen species and cyclooxygenase enzyme inhibition. Fitoterapia 82:1190–1197.

Abdel-Salam, I.M., Abou-Bakr, A.A., Ashour, M., 2019. Cytotoxic effect of aqueous ethanolic extract of *Luffa cylindrica* leaves on cancer stem cells CD44+/24- in breast cancer patients with various molecular sub-types using tissue samples in vitro. Journal of Ethnopharmacology 238, 111877.

Afifi, M.S., Ross, S.A., Elsohly, M.A., Nseem, Z.E., Haluweish, F.T., 1999. Cucurbitacin of *Cucumis propheturum*. Journal of Chemical Ecology 25, 847-859.

Akashi, K., Miyake, C., Yokota, A., 2001. Citrulline, a novel compatible solute in drought-tolerant wild watermelon leaves, is an efficient hydroxyl radical scavenger. FEBS Letters 508, 438-442.

Alsayari, A., Kopel, L., Ahmed, M.S., Soliman, H.S.M., Annadurai, S., Halaweish, F.T., 2018. Isolation of anticancer constituents from *Cucumis prophetarum* var. *prophetarum* through bioassay-guided fraction. BMC Complementary and Alternative Medicine 18, 274-286.

Assefa, A.D., Hur, O.S., Ro, N.Y., Lee, J.E., Hwang, A.J., Kim, B.S., Rhee, J.H., Yi, J.Y., Kim, J.H., Lee, H.S., Sung, J.S., Kim, M.K., Noh, J.J., 2020. Fruit morphology, citrulline, and arginine levels in diverse watermelon (*Citrullus lanatus*) germplasm collections. Plants 9*,* 1054.

Attar, U.A., Ghane, S.G., 2018. Optimized extraction of anti-cancer compound – cucurbitacin I and LC–MS identification of major metabolites from wild Bottle gourd (*Lagenaria siceraria* (Molina) Standl.). South African Journal of Botany 119, 181-187.

Attar, U.A., Ghane, S.G., 2019. In vitro antioxidant, antidiabetic, antiacetylcholine esterase, anticancer activities and RP-HPLC analysis of phenolics from the wild bottle gourd (*Lagenaria siceraia* Molina). South African Journal of Botany 125, 360-370.

Assar, E.A., Vidalle, M.C., Chopra, M. et al., 2016. Lycopene acts through inhibition of IκB kinase to suppress NF-κB signaling in human prostate and breast cancer cells. Tumor Biology 37, 9375–9385.

Ayyad, S.N., Abdel-Lateff, A., Alarif, W.M., Patacchioli, F.R., Badria, F.A., Ezmirly, S.T., 2012. In vitro and in vivo study of cucurbitacins-type triterpene glucoside from *Citrullus colocynthis* growing in Saudi Arabia against hepatocellular carcinoma. Environmental Toxicology and Pharmacology 33, 245-251.

Bailey, R.L., West, J.K.P., Black, R.E., 2015. The epidemiology of global micronutrient deficiencies Annals of Nutrition and Metabolism 66, 22-33.

Bang, H., Davis, A., Kim, S., Leskovar, D.I., King, S.R., 2010. Flesh color inheritance and gene interactions among canary yellow, pale yellow, and red watermelon. Journal of the American Society for Horticultural Science 135, 362–368.

Bartalis, J., Halaweish, FT., 2011. In vitro and QSAR studies of cucurbitacins on HepG2 and HSC-T6 liver cell lines. Bioorganic and Medicinal Chemistry 19, 2757-2766.

Beaulieu, J.C., Lea, J.M., 2006. Characterization and semiquantitative analysis of volatiles in seedless watermelon varieties using solid-phase microextraction. Journal of Agriculture and Food Chemistry 54, 7789-7793.

Bianchi, G., Rizzolo, A., Grassi, M., Provenzi, L., Lo Scalzo, R., 2018. External maturity indicators, carotenoid and sugar compositions and volatile patterns in 'Cuoredolce®' and 'Rugby' mini-watermelon (*Citrullus lanatus* (Thunb) Matsumura & Nakai) varieties in relation of ripening degree at harvest. Postharvest Biology and Technology 136, 1-11.

Blaskovich, M.A., Sun, J., Cantor, A., Turkson, J., Jove, R., Sebti, S.M., 2003. Discovery of JSI-124 (Cucurbitacin I) a selective janus kinase/signal transducer and activator of transcritption 3 signaling pathway inhibitor with potent antitumor activity against human and murine cancer cells in mice. Cancer Research 63, 1270-1279.

Branham, S., Vexler, L., Meir, A., Tzuri, G., Frieman, Z., Levi, A., Gur, A., 2017. Genetic mapping of a major codominant QTL associated with β-carotene accumulation in watermelon. Molecular Breeding 37, 146.

Cao, J., Li, W., Tang, Y., Zhang, X., Li, W., Zhao, Y., 2015. Three new triterpene saponins from Actinostemma lobatum MAXIM and their cytotoxicity in vitro, Phytochemistry Letters 11, 301-305.

Chen, X.B., Chen, G.Y., Liu, J.H., Lei, M., Meng, Y.H., Guo, D.A., Liu, X., Hu, L.H., 2014. Cytotoxic cucurbitane triterpenoids isolated from the rhizomes of *Hemsleya amabilis*. Fitoterapia 94, 88-93.

Chen, D., Huang, C., Chen, Z., 2019. A review for the pharmacological effect of lycopene in central nervous system disorders. Biomedicine and Pharmacotherapy 111, 791-801.

Cohen, R., Tyutyunik, J., Fallik, E., Oka, Y., Tadmor, Y., Edelstein, M., 2014. Phytopathological evaluation of exotic watermelon germplasm as a basis for rootstock breeding. Scientia Horticulturae 165, 203-210.

Collins, J.K., Wu, G., Perkins-Veazie, P., Spears, K., Claypool, P.L., Baker, R.A., Clevidence, B.A., 2007. Watermelon consumption increases plasma arginine concentrations in adults. Nutrition 23, 261-266.

Crenn, P., Cynober, L., 2010. Effect of intestinal resections on arginine metabolism: practical implications for nutrition support. Current Opinion in Clinical, Nutrition and Metabolism Care 13, 65-69.

Curis E., Nicolis I., Moinard C., Osowska S., Zerrouk N., Bénazeth S., Cynober L., 2005. Almost all about citrulline in mammals. Amino Acids 29, 177.

Daley, J., Wehner, T.C., 2020. Screening for bacterial fruit blotch resistance in watermelon fruit. Crop Science. doi:10.1002/csc2.20329.

Davidovich-Rikanati, R., Shalev, L., Baranes, N., Meir, A., Itkin, M., Cohen, S., Zimbler, K., Portnoy, V., Ebizuka, Y., Shibuya, M., Burger, Y., Katzir, N., Schaffer, A.A., Lewinsohn, E., Tadmor, Y., 2015. Recombinant yeast as a functional tool for understanding bitterness and cucurbitacin biosynthesis in watermelon (*Citrullus* spp). Yeast 32, 103-114.

Davis, A. R., King, S.R., 2007. MSW-28, a full-flavor crisp watermelon line with high lycopene and medium Brix. HortScience 42, 1715-1716.

Davis, A.R., Perkins-Veazie, P., Collins, J., Levi, A., 2008. LSW-177 and LSW-194: Red-fleshed watermelon lines with low-total soluble solids. HortScience 43, 538-539.

Davis, A.R., Webber, C.L., Fish, W.W., Wehner, T.C., King, S., Perkins-Veazie, P., 2011. L-Citrulline levels in watermelon cultigens tested in two environments. HortScience 46, 1572-1575.

Ding, N., Yamashita, U., Matsuoka, H., et al., 2011. Apoptosis induction through proteasome inhibitory activity of cucurbitacin D in human T-cell leukemia. Cancer 117, 2735–2746.

Dou, J., Yuan, P., Zhao, S., He, N., Zhu, H., Gao, L., Ji, W., Lu, X., Liu, W., 2017. Effect of ploidy level on expression of lycopene biosynthesis genes and accumulation of phytohormones during watermelon (*Citrullus lanatus*) fruit development and ripening. Journal of Integrative Agriculture 16, 1956-1967.

Drewes, S.E., George, J., Khan, F., 2003. Recent findings on natural products with erectile-dysfunction activity. Phytochemistry 62, 1019-1025.

Duangmano, S., Sae-Lim, P., Suksamrarn, A., Domann, F.E., Patmasiriwat, P., 2012. Cucurbitacin B inhibits human breast cancer cell proliferation through disruption of microtubule polymerization and nucleophosmin/B23 translocation. BMC Complementary and Alternative Medicine 12, 85.

Enneb, S., Drine, S., Bagues, M., Triki, T., Boussora, F., Guasmi, F., Nagaz, K., Ferchichi, A., 2020. Phytochemical profiles and nutritional composition of squash (*Cucurbita moschata* D.) from Tunisia. South African Journal of Botany 130, 165-171.

El-Senduny, F.F., Badria, F.A., EL-Waseef, A.M. et al., 2016. Approach for chemosensitization of cisplatin-resistant ovarian cancer by cucurbitacin B. Tumor Biology 37, 685–698.

Escandell, J.M., Kaler, P., Recio, M.C., Sasazuki, T., Shirasawa, S., Augenlicht, L., Ríos, J.L., Klampfer, L., 2008. Activated kRas protects colon cancer cells from cucurbitacin-induced apoptosis: the role of p53 and p21. Biochemical Pharmacology 76, 198-207.

Fang, X., Liu, S., Gao, P., Liu, H., Wang, X., Luan, F., Zhang, Q., Dai, Z., 2020. Expression of ClPAP and ClPSY1 in watermelon correlates with chromoplast differentiation, carotenoid accumulation, and flesh color formation. Scientia Horticulturae 270,109437.

Fredes, A., Roselló, S., Beltrán, J., Cebolla-Cornejo, J., Pérez-de-Castro, A., Gisbert, C., et al., 2017. Fruit quality assessment of watermelons grafted onto citron melon rootstock. Journal of the Science of Food and Agriculture 97, 1646–1655.

Gao, L., Zhao, S., Lu, X., He, N., Liu, W., 2018. ‘SW’, a new watermelon cultivar with a sweet and sour flavour. HortScience 53, 895-896.

Gamlath, C.B., Gunatilaka, A.A.L, Alvi, K.A., Rahman, A., Balasubramaniam, S., 1988. Cucurbitacins of *Colocynthis vulgaris*. Phytochemistry 27, 3225-3229.

Grassi, S., Piro, G., Lee, J.M., Zheng, Y., Fei, Z.J., Dalessandro, G., 2013. Comparative genomics reveals candidate carotenoid pathway regulators of ripening watermelon fruit. BMC Genomics 14, 781.

Gusmini, G., Song, G., Wehner, T.C., 2005. New sources of resistance to Gummy stem blight in watermelon. Crop Science 45, 582-588.

Guzzon, F., Müller, J.V., do Nascimento Araujo, M., Cauzzi, P., Orsenigo, S., Mondoni, A., Abeli, T., 2017. Drought avoidance adaptive traits in seed germination and seedling growth of *Citrullus amarus* landraces. South African Journal of Botany 113, 382-388.

Hartman, J. L., Perkins-Veazie, P., Wehner, T.C., 2019. Citrulline and arginine are moderately heritable in two red-fleshed watermelon populations. HortScience 54, 200-205.

Hassan, S.T.S., Masarčíková, R., Berchová, K., 2015. Bioactive natural products with anti-herpes simplex virus properties. The Journal of Pharmacy and Pharmacology 67, 1325-1336.

Hassan, S.T.S., Berchová-Bímová, K., Petráš, J., Hassan, K.T.S., 2017. Cucurbitacin B interacts synergistically with antibiotics against *Staphylococcus aureus* clinical isolates and exhibits antiviral activity against HSV-1. South African Journal of Botany 108, 90-94.

Hatam, N.A.R., Whiting, D.A., Yousif, N.J., 1989. Cucurbitacin glycosides from *Citrullus colocynthis*. Phytochemistry 28, 1268-1271.

Hu, W., Wang, H., Liu, Z., Liu, Y., Wang, R., Luo, X., Huang, Y., 2017. Neuroprotective effects of lycopene in spinal cord injury in rats via antioxidative and anti-apoptotic pathway. Neuroscience Letters 642,107-112.

García-Mendívil, H.A., Sorribas, F.J., 2021. Effect of *Citrullus amarus* accessions on the population dynamics of *Meloidogyne incognita* and *M. javanica* and watermelon yield. Scientia Horticulturae 275, 2021.

Hong, M.Y., Beidler, J., Hooshmand, S., Figueroa, A., Kern, M., 2018. Watermelon and l-arginine consumption improve serum lipid profile and reduce inflammation and oxidative stress by altering gene expression in rats fed an atherogenic diet. Nutrition Research 58, 46-54.

Huang, Y., Zhao, L., Kong, Q., Fei, C., Mengliang, N., Xie, J., Bie, Z., 2016. Comprehensive mineral nutrition analysis of watermelon grafted onto two different rootstocks. Horticultural Plant Journal 2, 105-113.

Hussain, A.I., Rathore, H.A., Sattar, M.Z.A., Chatha, S.A.S., Ahmad, F., Ahmad, A., Johns, E.J., 2013. Phenolicprofile and antioxidant activity of various extracts from *Citrullus colocynthis* (L.) from the Pakistani flora. Industrial Crops and Products 45, 416–422.

Hussain, A.I., Rathore, H.A., Sattar, M.Z.A., Chatha, S.A.S., Sarker, S.D., Gilani, A.H., 2014. *Citrullus colocynthis* (L.) Schrad (bitter apple fruit): A review of its phytochemistry, pharmacology, traditional uses and nutritional potential. Journal of Ethnopharmacology 155, 54-66.

Ishii, T., Kira, N., Yoshida, T. et al., 2013. Cucurbitacin D induces growth inhibition, cell cycle arrest, and apoptosis in human endometrial and ovarian cancer cells. Tumor Biology 34, 285–291.

Jardón-Delgado, A., Magos-Guerrero, G.A., Martínez-Vázquez, M., 2014. Isolation of a new anti-inflammatory 20, 21, 22, 23, 24, 25, 26, 27-octanorcucurbitacin-type triterpene from *Ibervillea sonorae*. Natural Products Communication 9, 15-16.

Jawad, U.M., Gao, L., Gebremeskel, H., Safdar, L.B., Yuan, P., Zhao, S., Xuqiang, L., Nan, H., Hongju, Z., Liu, W., 2020. Expression pattern of sugars and organic acids regulatory genes during watermelon fruit development. Scientia Horticulturae 265,109102.

Jayaprakasam, B., Seeram, N.P., 2003. Nair MG, Anticancer and antiinflammatory activities of cucurbitacins from *Cucurbita andreana*. Cancer Letters 189, 11-16.

Joshi, V., Joshi, M., Silwal, D., Noonan, K., Rodriguez, S., Penalosa, A., 2019. Systematized biosynthesis and catabolism regulate citrulline accumulation in watermelon. Phytochemistry 162, 129-140.

Jourdan, M., Nair, K.S., Carter, R.E., Schimke, J., Ford, G.C., Marc, J., Aussel, C., Cynober, L., 2015. Citrulline stimulates muscle protein synthesis in the postabsorptive state in healthy people fed a low-protein diet – A pilot study. Clinical Nutrition 34, 449-456.

Kim, H.J., Park, J.H.Y., Kim, J.K., 2014. Cucurbitacin-I, a natural cell-permeable triterpenoid isolated from Cucurbitaceae, exerts potent anticancer effect in colon cancer. Chemico-Biological Interactions 219, 1-8.

Kim, J.K., Kim, J., 2015. Antiangiogenic effects of cucurbitacin-I. Archives of Pharmacal Research 38, 290–298.

Kim, Y.C., Choi, D., Zhang, C., Liu, H.F., Lee, S., 2018. Profiling cucurbitacin from diverse watermelons (*Citrullus* spp). Horticulture, Environment and Biotechnology 59, 557-566.

Ku, J.M., Kim, S.R., Hong, S.H. et al., 2015. Cucurbitacin D induces cell cycle arrest and apoptosis by inhibiting STAT3 and NF-κB signaling in doxorubicin-resistant human breast carcinoma (MCF7/ADR) cells. Molecular and Cellular Biochemistry 409, 33–43.

Ku, J.M., Hong, S.H., Kim, H.I., Lim, Y.S., Lee, S.J., Kim, M., Seo, H.S., Shin, Y.C., Ko, S.G., 2017. Cucurbitacin D exhibits its anti-cancer effect in human breast cancer cells by inhibiting stats and ATk signaling. European Journal of Inflammation 16, 1-9.

Kurauchi, Y., Mokudai, K., Morita, M., Kamimura, A., Mori, A., Sakamoto, K., Nakahara, T., Ishii, K., 2017. L-Citrulline improves cerebral blood flow in migraine model rats. Journal of Functional Foods 38, 540-544.

Lakshmi, A.J., Kaul, P., 2011. Nutritional potential, bioaccessibility of minerals and functionality of watermelon (Citrullus vulgaris) seeds. LWT - Food Science and Technology 44, 1821-1826.

Levi, A., Thies, J.A., Wechter, W.P. et al., 2013. High frequency oligonucleotides: targeting active gene (HFO-TAG) markers revealed wide genetic diversity among *Citrullus* spp. accessions useful for enhancing disease or pest resistance in watermelon cultivars. Genetic Resources and Crop Evolution 60, 427–440.

Lewinsohn, E., Sitrit, Y., Bar, E., Azulay, Y., Meir, A., Zamir, D., Tadmor, Y., 2005. Carotenoid pigmentation affects the volatile composition of tomato and watermelon fruits, as revealed by comparative genetic analyses. Journal of Agriculture and Food Chemistry 53, 3142-3148.

Lv, P., Li, N., Liu, H., Gu, H.H., Zhao, W.E., 2015. Changes in carotenoid profiles and in the expression pattern of the genes in carotenoid metabolisms during fruit development and ripening in four watermelon cultivars. Food Chemistry 174, 52–59.

Lin, K.W., Yang, S.C., Lin, C.N., 2011. Antioxidant constituents from the stems and fruits of *Momordica charantia*. Food Chemistry 127, 609-614.

Liu, C.H., Yen, M.H., Tsang, S.F., Gan K.H., Hsu, H.Y., Lin, C.N., 2010. Antioxidant triterpenoids from the stems of *Momordica charantia*. Food Chemistry 118, 751-756.

Liu, C., Zhang, H., Dai, Z., Liu, X., Liu, Y., Deng, X., Xu, J., 2012. Volatile chemical and carotenoid profiles in watermelons [*Citrullus vulgaris* (Thunb.) Schrad

(Cucurbitaceae)] with different flesh colors. Food Science and Biotechnology 21, 531-541.

Liu, S., Gao, P., Wang, X., Davis, A., Baloch, A.M., Luan, F., 2015. Mapping of quantitative trait loci for lycopene content and fruit traits in *Citrullus lanatus*. Euphytica 202, 411–426.

Luo, F., Li, Q., Yu, L., Wang, C., Qi, H., 2020. High concentrations of CPPU promotes cucurbitacin B accumulation in melon (*Cucumis melo* var. makuwa Makino) fruit by inducing transcription factor CmBt. Plant Physiology and Biochemistry 154, 770-781.

Ma, S., and Wehner, T.C., 2015. Flowering stage resistance to bacterial blotch in the watermelon germplasm collection. Crop Science 55, 727-736.

Ma, G., Luo, W., Lu, J., Ma, D.L., Leung, C.H., Wang, Y., Chen. X., 2016. Cucurbitacin E induces caspase-dependent apoptosis and protective autophagy mediated by ROS in lung cancer cells. Chemico-Biological Interactions 253, 1-9.

Magwede, K., van Wyk B.E., van Wyk, A.E., 2019. An inventory of Vhaveṋḓa useful plants. South African Journal of Botany 122, 57-89.

Mandel, H., Levy, N., Izkovitch, S. et al., 2005. Elevated plasma citrulline and arginine due to consumption of *Citrullus vulgaris* (watermelon). Journal of Inherited Metabolic Disease 28, 467–472.

Martínez-Sánchez, A., Ramos-Campo, D.J., Fernández-Lobato, B., Rubio-Arias, J.A., Alacid, F., Aguayo, E., 2017. Biochemical, physiological, and performance response of a functional watermelon juice enriched in L-citrulline during a half-marathon race. Food and Nutrition Research, 61:1.

Marzouk, B., Marzouk, Z., Décor, R., Mhadhebi, L., Fenina, N., Aouni, M., 2010. Antibacterial and antifungal activities of several populations of Tunisian *Citrullus colocynthis* Schrad. immature fruits and seeds. Journal de Mycologie Médicale 20, 179-184.

Marzouk, B., Mahjoub, M.A., Bouraoui, A. et al., 2013. Anti-inflammatory and analgesic activities of a new cucurbitacin isolated from *Citrullus colocynthis* seeds. Medicinal Chemistry Research 22, 3984–3990.

Mashilo, J., Shimelis, H., Odindo, A., Amelework, B., 2016. Simple sequence repeat markers reveal genetic diversity within and among landrace collections of citron and dessert watermelon from South Africa. Journal of the American Society for Horticultural Science 141, 598-608.

Mashilo, J., Shimelis, H., Odindo, A.O., Amelework, B., 2017. Genetic diversity and differentiation in citron watermelon [*Citrullus lanatus* var. *citroides*] landraces assessed by simple sequence repeat markers. Scientia Horticulturae, 214, 99-106.

Mashilo, J., Odindo, A.O., Shimelis, H.A., Musege, P., Tesfay, S.Z., Magwaza, L.S., 2018. Phothosyntheic response of bottle gourd [*Lagenaria sicerana* (Molina) Standl.] to drought stress: Relationship between cucurbitacins accumulation and drought tolerance. Scientia Horticulturae 231, 133-143.

McEneny, J., Wade, L., Young, I.S., Masson, L., Duthie, G., McGinty, A., McMaster, C., Thies, F., 2013. Lycopene intervention reduces inflammation and improves HDL functionality in moderately overweight middle-aged individuals. The Journal of Nutritional Biochemistry 24, 163-168.

Mendoza-Enano, M.L., Stanley, R., Frank, D., 2019. Linking consumer sensory acceptability to volatile composition for improved shelf-life: A case study of fresh-cut watermelon (*Citrullus lanatus*). Postharvest Biology and Technology 154, 137-147.

Meru, G., McGregor, C., 2014. Quantitative trait loci and candidate genes associated with fatty acid content of watermelon seed. Journal of the American Society for Horticultural Science 139, 433-441.

Mirahmadi, M., Azimi-Hashemi, S., Saburi, E., Kamali, H., Pishbin, M., Hadizadeh, F., 2020. Potential inhibitory effect of lycopene on prostate cancer. Biomedicine and Pharmacotherapy 129, 110459.

Mo, Y., Yang, R., Liu, L., Gu, X., Yang, Y., Wang, Y., Zhang, X., Li, H., 2015. Growth, photosynthesis and adaptive responses of wild and domesticated watermelon genotypes to drought stress and subsequent rewatering. Plant Growth Regulation 79, 229-241.

Mogale, M.M.P., Raimondo, D.C., Van Wyk, B.E., 2019. The ethnobotany of Central Sekhukhuneland, South Africa. South African Journal of Botany 122, 90-119.

Mokganya, M.G., Tshisikhawe, M.P., 2019. Medicinal uses of selected wild edible vegetables consumed by Vhavenda of the Vhembe District Municipality, South Africa. South African Journal of Botany 122, 184-188.

Mukherjee, P.K., Nema, N.K., Maity, N., Sarkar, B.K., 2013. Phytochemical and therapeutic potential of cucumber. Fitoterapia 84, 227-236.

Nawaz, M.A., Han, X., Chen, C., Zheng, Z., Shireen, F., Bie, Z., Huang, Y., 2018. Nitrogen use efficiency of watermelon grafted onto 10 wild watermelon rootstocks under low nitrogen conditions. Agronomy 8*,* 259.

Ngwepe, R.M., J. Mashilo and H. Shimelis., 2019. Progress in genetic improvement of citron watermelon (Citrullus lanatus var. citroides): a review. Genet Resour Crop Evol 66: 735-758.

Ogbuji, K., McCutcheon, G. S., Simmons, A. M., Snook, M. E., Harrison, H. F., & Levi, A., (2012). Partial leaf chemical profiles of a desert watermelon species (*Citrullus colocynthis*) and heirloom watermelon cultivars (*Citrullus lanatus* var. lanatus). HortScience 47, 580-584.

Osowska, S., Moinard, C., Neveux, N., Loï, C., Cynober, L., 2004. Citrulline increases arginine pools and restores nitrogen balance after massive intestinal resection. Gut 53, 1781-1786.

Pal, S., Rao, S.E., Hebbar, S.S., Sriram, S., Pitchaimuthu, M., Rao, K.V., 2020. Assessment of *Fusarium* wilt resistant *Citrullus* sp. rootstocks for yield and quality traits of grafted watermelon. Scientia Horticulturae 272, 109497.

Perkins-Veazie, P., Collins, J.K., Davis, A.R., Roberts, W., 2006. Carotenoid content of 50 watermelon cultivars. Journal of Agricultural and Food Chemistry 54, 2593-2597.

Platel, K., Krinivasan, S., 2016. Bioavailability of micronutrients from plant foods: an update Critical Reviews in Food Science and Nutrition 56, 1608-1619.

Pitchakarn, P., Suzuki, S., Ogawa, K., Pompimon, W., Takahashi, S., Asamoto, M., Limtrakul, P., Shirai, T., 2011. Induction of G1 arrest and apoptosis in androgen-dependent human prostate cancer by Kuguacin J, a triterpenoid from *Momordica charantia* leaf. Cancer Letters 306, 142-150.

Prothro, J., Sandlin, K., Gill, R., Bachlava, E., White, V., Knapp, S. J., McGregor, C., 2012. Mapping of the egusi seed trait locus (eg) and quantitative trait loci associated with seed oil percentage in watermelon. Journal of the American Society for Horticultural Science 137, 311-315.

Martí, R., Sánchez, G., Valcárcel, M., Roselló, S., Cebolla-Cornejo, J., 2019. High throughput FT-MIR indirect analysis of sugars and acids in watermelon. Food Chemistry 300, 125227.

Ren, Y., McGregor, C., Zhang, Y., Gong, G., Zhang, H., Guo, S., Sun, H., Cai, W., Zhang, J., Xu, Y., 2014. An integrated genetic map based on four mapping populations and quantitative trait loci associated with economically important traits in watermelon (*Citrullus lanatus*). BMC Plant Biology 14:33.

Rimando, A.M. Perkins-Veazie, P. 2005. Determination of citrulline in watermelon rind. Journal of Chromatography 1078, 196–200.

Rouphael, Y., Cardarelli, M., Colla, G., Rea, E., 2008. Yield, mineral composition, water relations, and water use efficiency of grafted mini-watermelon plants under deficit irrigation. HortScience 43, 730-736.

Saeed, M.E.M., Boulos, J.C., Elhaboub, G., Rigano, D., Saab, A., Loizzo, M.R., Hassan, L.E.A., Sugimoto, Y., Piacente, S., Tundis, R., Yagi, S., Khalid, H., Efferth, T., 2019. Cytotoxicity of cucurbitacin E from *Citrullus colocynthis* against multidrug-resistant cancer cells. Phytomedicine 62, 152945.

Semenya, S.S., Maroyi, A., 2019. Ethnobotanical survey of plants used by Bapedi traditional healers to treat tuberculosis and its opportunistic infections in the

Limpopo Province, South Africa. South African Journal of Botany 122, 401-421.

Shiota, A., Hotta, Y., Kataoka, T., Morita, M., Maeda, Y., Kimura, K., 2013. Oral L-citrulline supplementation improves erectile function in rats with acute arteriogenic erectile dysfunction. The Journal of Sexual Medicine 10, 2423-2429.

Singh, N.P., Matta, N.K., 2010. Levels of seed proteins in *Citrullus* and *Praecitrullus* accessions. Plant Systematics and Evolution 290, 47–56.

Tabiri, B., Agbenorhevi, J.K., Wireko-Manu, F.D., Ompouma, E.I., 2016. Watermelon seeds as food: nutrient composition, phytochemicals and antioxidant activity. International Journal of Nutrition and Food Sciences 5, 139 144

Takahashi, N., Yoshida, Y., Sugiura, T., et al., 2009. Cucurbitacin D isolated from *Trichosanthes kirilowii* induces apoptosis in human hepatocellular carcinoma cells in vitro. International Immunopharmacology 9, 508–513.

Tang, F.Y., Cho, H.J., Pai, M.H., Chen, Y.H., 2009. Concomitant supplementation of lycopene and eicosapentaenoic acid inhibits the proliferation of human colon cancer cells. The Journal of Nutritional Biochemistry 20, 426-434.

Tannin-Spitz, T., Bergman, M., Grossman, S., 2007. Cucurbitacin glycosides: antioxidant and free-radical scavenging activities. Biochemical and Biophysical Research Communications 364,181–186.

Tarazona-Dı´az, M.P., Viegas, J., Moldao-Martinsc, M., Aguayoa, E., 2011. Bioactive compounds from flesh and by-product of fresh-cut watermelon cultivars. Journal of the Science of Food and Agriculture 91, 805–812.

Tarazona-Díaz, M.P., Alacid, F., Carrasco, M., Martínez, I., Aguayo, E., 2013. Watermelon juice: Potential functional drink for sore muscle relief in athletes. Journal of Agricultural and Food Chemistry 61, 7522-7528.

Thies, J.A., Levi, A., Ariss, J.J., Hassell, R.L., 2015a. RKVL-318, a root-knot nematode-resistant watermelon line as rootstock for grafted watermelon. HortScience 50, 141-142.

Thies, J.A., Buckner, S., Horry, M., Hassell, R., Levi, A., 2015b. Influence of *Citrullus lanatus var. citroides* rootstocks and their F_1 hybrids on yield and response to root-knot nematode, *Meloidogyne incognita*, in grafted watermelon. HortScience 50, 9-12.

Thies, J.A., Ariss, J.J., Hassell, R.L., Buckner, S., Levi, A., 2015c. Accessions of *Citrullus lanatus var. citroides* are valuable rootstocks for grafted watermelon in fields infested with root-knot nematodes. HortScience 50, 4-8.

Thies, J.A., Ariss, J.J., Kousik, C.S., Hassell, R.L., Levi, A., 2016. Resistance to Southern root-knot nematode (*Meloidogyne incognita*) in wild watermelon (*Citrullus lanatus var. citroides*). Journal of Nematology 48, 14–19.

Tlili, I., Hdider, C., Lenucci, M.S., Ilahy, R., Jebari, H., Dalessandro, G., 2011. Bioactive compounds and antioxidant activities during fruit ripening of watermelon cultivars. Journal of Food Composition and Analysis 24, 923-928.

Touihri-Barakati, I., Kallech-Ziri, O., Ayadi, W., Kovacic, H., Hanchi, B., Hosni, K., Luis, J., 2017. Cucurbitacin B purified from *Ecballium elaterium* (L.) A. Rich from Tunisia inhibits α5β1 integrin-mediated adhesion, migration, proliferation of human glioblastoma cell line and angiogenesis. European Journal of Pharmacology 797, 153-161.

Torres-Moreno, H., Velázquez, C.A., Garibay-Escobar, A., Curini, M., Marcotullio, M.C., Robles-Zepeda, R.E., 2015. Antiproliferative and apoptosis induction of cucurbitacin-type triterpenes from *Ibervillea sonorae*. Industrial Crops and Products 77, 895-900.

Torres-Moreno, H., López-Romero, J.C., Vázquez-Solorio, J.Y., Velázquez-Contreras, C.A., Garibay-Escobar, A., Díaz-López, R., Robles-Zepeda, R.E., 2019. Antioxidant, anti-inflammatory and antiproliferative properties of *Ibervillea sonorae*. South African Journal of Botany. Volume 125, 207-213.

Torres-Moreno, H., Lanni, F., Zepeda, R.E.R., López-Romero, J.C., Vidal-Gutiérrez, M., Durán, M.D.J., Galarini, R., Camaioni. E., Sardella, R., Marcotullio, M,C., 2020a. Quantitative analysis of cucurbitane-type triterpenes in *Ibervillea sonorae* extracts: Relationship study with their antiproliferative activity. Steroids161, 108676.

Torres-Moreno, H., Marcotullio, M.C., Velázquez, C., Lanni, F., Garibay-Escobar, A., Robles-Zepeda, R.E., 2020b. Cucurbitacin IIb, a steroidal triterpene from *Ibervillea sonorae* induces antiproliferative and apoptotic effects on cervical and lung cancer cells. Steroids 157, 108597.

Varasteh, S., Braber, S., Kraneveld, A.D., Garssen, J., Fink-Gremmels, J., 2018. L-Arginine supplementation prevents intestinal epithelial barrier breakdown under heat stress conditions by promoting nitric oxide synthesis. Nutrition Research 57, 45-55.

Visser, M., Van Zyl, T., Hanekom, S.M., Baumgartner, J., van der Hoeven, M., Taljaard-Krugell, C., Smuts, C.M., Faber, M., 2019. Nutrient patterns and their relation to anemia and iron status in 5- to 12-y-old children in South Africa. Nutrition 62, 194-200.

Uslu, C., Karasen, R.M, Sahin, F., Taysi, S., Akcay, F., 2006. Effect of aqueous extracts of *Ecballium elaterium* rich, in the rabbit model of rhinosinusitis. International Journal of Pediatric Otorhinolaryngology 70, 515-518.

Van Wyk, B.E., 2011. The potential of South African plants in the development of new food and beverage products. South African Journal of Botany 77, 857-868.

Wang, C., Qiao, A., Fang, X., Sun, L., Gao, P., Davis, A.R., Liu, S., Luan, F., 2019. Fine mapping of lycopene content and flesh color related gene and development of molecular marker–assisted selection for flesh color in watermelon (*Citrullus lanatus*). Frontiers in Plant Science 10, 1240.

Wehner, T.C., Naegele, R.P., Perkins-Veazie, P., 2017. Heritability and genetic variance components associated with citrulline, arginine, and lycopene content in diverse watermelon cultigens. HortScience 52, 936-940.

White P.J., Broadley M.R., 2011. Physiological limits to zinc biofortfication of edible crops Frontiers in Plant Science 2, 80.

World Food Programme (WFP), 2018. Scaling up Rice Fortification in West Africa Sight and Life, Basel, Switzerland. World Health Organization (WHO)

Guideline: Fortification of Rice with Vitamins and Minerals as a Public Health Strategy World Health Organization, Geneva (2018) Licence: CC BY-NC-SA 3.0 IGO.

Yativ, M., Harary, I., Wolf, S., 2010. Sucrose accumulation in watermelon fruits: Genetic variation and biochemical analysis. Journal of Plant Physiology 167, 589-596.

Yavuz, D., Seymen, M., Süheri, S., Yavuz, N., Türkmen, Ö., Kurtar, E.S., 2020. How do rootstocks of citron watermelon (*Citrullus lanatus* var. citroides) affect the yield and quality of watermelon under deficit irrigation? Agricultural Water Management 241, 106351.

Yue, J., Sun, Y., Xu, J., Cao, J., Chen, G., Zhang, H., Zhang, X., Zhao, Y., 2019. Cucurbitane triterpenoids from the fruit of *Momordica charantia* L. and their anti-hepatic fibrosis and anti-hepatoma activities. Phytochemistry 157, 21-27.

Zhang, T., Li, J., Dong, Y. et al., 2012. Cucurbitacin E inhibits breast tumor metastasis by suppressing cell migration and invasion. Breast Cancer Research Treatment 135, 445–458.

Zhang, X., Zhao, C., Tang, W., Wu, X., Zhao, Y., 2015. Gypensapogenin H, a novel dammarane-type triterpene induces cell cycle arrest and apoptosis on prostate cancer cells. Steroids 104, 276-283.

Zhao, G.T., Liu, J.Q, Deng, Y.Y., Li, H.Z., Chen, J.C., Zhang, Z.R., LZ, Qiu, M.H., 2014. Cucurbitane-type triterpenoids from the stems and leaves of *Momordica charantia*. Fitoterapia 95, 75-82.

Ziyada, A.K., Elhussien, S.A., 2008. Physical and chemical characteristics of *Citrullus lanatus* var. colocynthoide seed oil. Journal of Physical Therapy Science 19, 69–75.

Zhong, Y., Shi, J., Zheng, Z., Nawaz, M.A., Chen, C., Cheng, F., Kong, Q., Bie, Z., Huang, Y., 2019. NMR-based fruit metabonomic analysis of watermelon grafted onto different rootstocks under two potassium levels. Scientia Horticulturae 258, 108793.

Yoon, J.Y., Chung, I.M., Thiruvengadam, M., 2015. Evaluation of phenolic compounds, antioxidant and antimicrobial activities from transgenic hairy root cultures of gherkin (*Cucumis anguria* L.). South African Journal of Botany 100, 80-86.

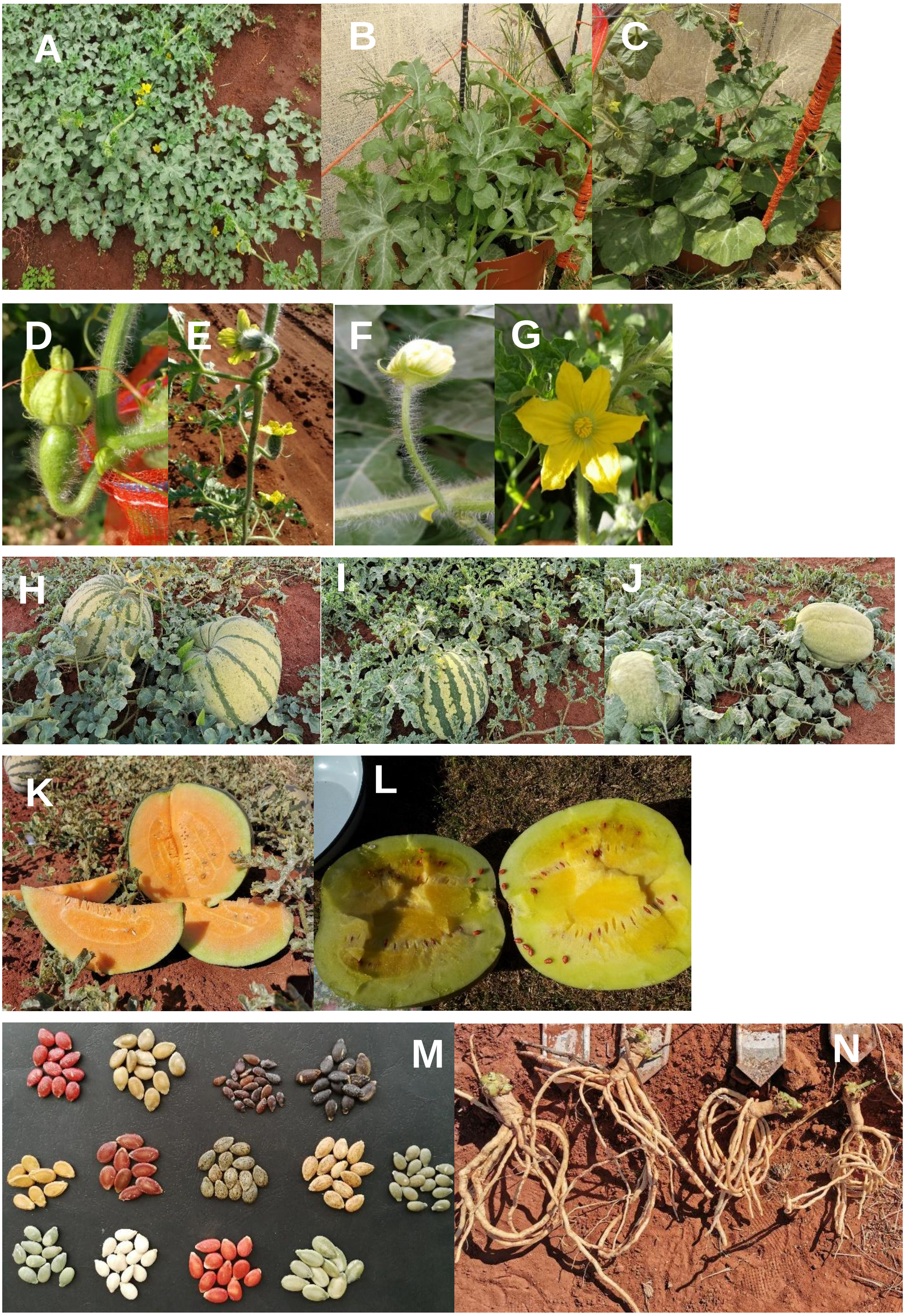

Fig. 1. Morphological description of citron watermelon. A = Leaves and flowers, B = lobed leaf shape, C = non-lobed leaf shape, D = closed female flower, E = open female

flower, F = closed male flower, G = open male flower, H to J = fruit with different shapes and rind stripe patterns and colours, K = orange-flesh, L = yellow flesh, M = seed coat colours, N = tap and lateral roots.

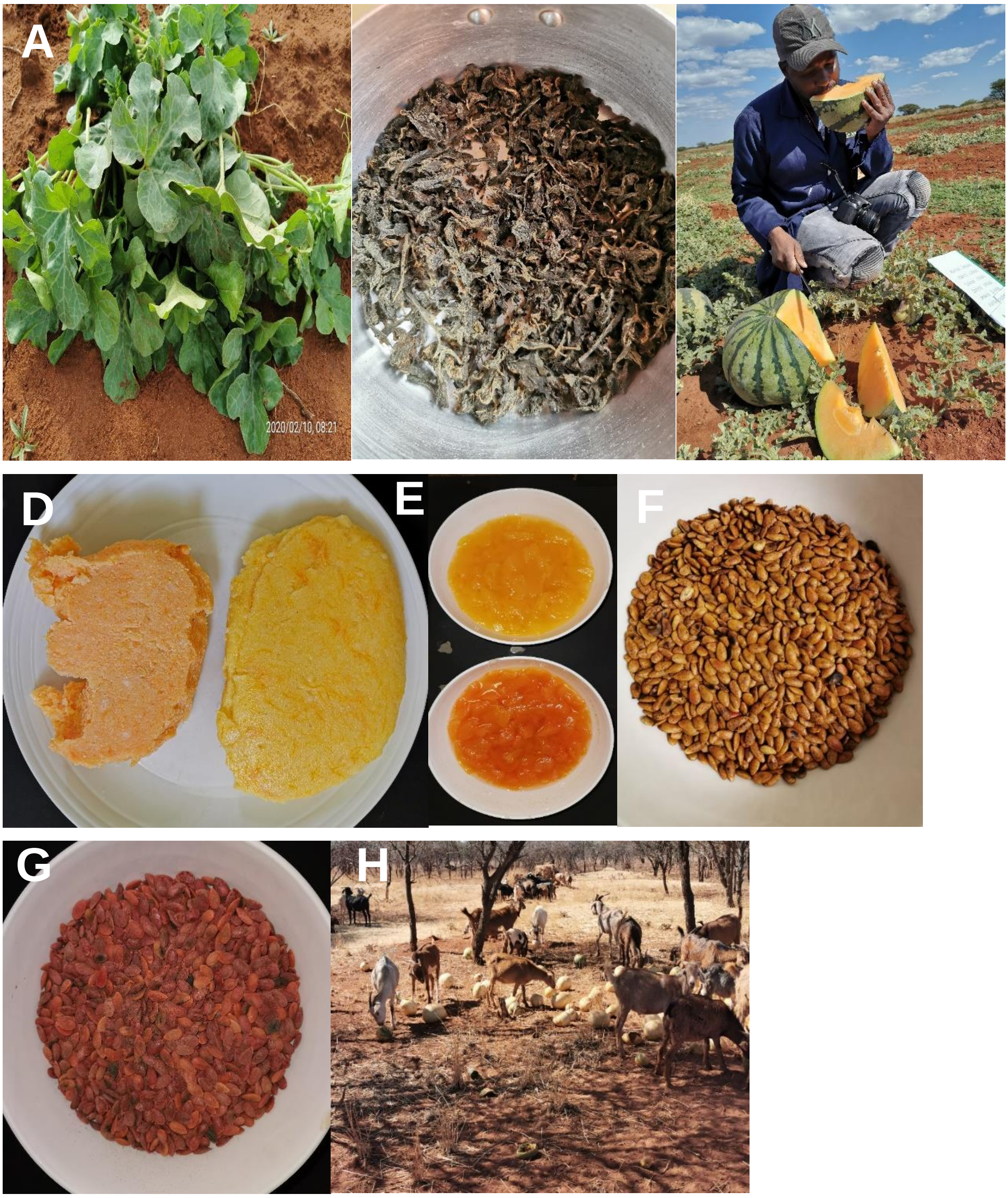

Fig. 2. Food products derived from citron watermelon. A = freshly harvested leaves used as leafy vegetable, B = pre-cooked and dried leaves, C = orange-fleshed fruit used for cooking or consumed as dessert, D = porridge referred as "Kgodu" prepared from yellow- and orange-fleshed fruit, E = Traditional dish referred to as "Mokgapu" prepared by boiling yellow and orange flesh and adding sugar for taste, F & G = roasted brown and red seed, H = fruits used as animal feed.