Journal of Ethnopharmacology 303 (2023) 115988

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Ethnopharmacology and biological activities of the Aizoaceae

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ARTICLE INFO

Keywords:
Aizoaceae
Mesembryanthemum
Succulent
Antimicrobial
Antioxidant
Cosmetics

ABSTRACT

Ethnopharmacological relevance: The Aizoaceae is one of the largest succulent plant families. Most members of the family are ornamental and form part of specialist succulent collections. The exceptional diversity of the Aizoaceae is not only limited to its growth forms, habitat, and chemistry, but is also reflected in its many traditional uses. Selected species are well known for their use in traditional medicines, with recent scientific studies validating their biological activity.
Aim of the study: Herein, this review aimed to articulate foundational and current global research endeavors related to the traditional uses and pharmacological activities of the Aizoaceae.
Materials and methods: Research articles and search terms related to the ethnopharmacology and bioactivities of the Aizoaceae between 1940 and 2022 were evaluated using electronic databases such as Google Scholar, PubMed, ScienceDirect, Scopus, JSTOR, and Web of Science.
Results: Popular Aizoaceae genera including *Mesembryanthemum, Trianthema,* and *Tetragonia* are noted for their cultural value and are key components in herbal medicines for the treatment of a myriad of disorders. Isolated bioactive compounds isolated from selected species demonstrated varied antimicrobial, antioxidant, and neuroprotective functions in basic pharmacological studies. However, most studies lacked reliable correlation to *in vivo* activity and did not adequately validate the safety and efficacy of potential therapeutic compounds.
Conclusions: While the cultural and therapeutic value of popular Aizoaceae species have been highlighted in the literature, there remains glaring inconsistencies among other related species. Data deficiency may be ameliorated by further studies focused on taxonomic markers, chemical characterization and underlying molecular mechanisms of activity of a wider pool of species to enhance our knowledge of this hyperdiverse family.

1. Introduction

The socio-economic status of many countries is a limiting factor for the provision of basic healthcare to the general population. The use of traditional remedies sourced from medicinal plants is prevalent in rural communities, mainly due to the inaccessibility, unavailability, and cost of conventional drugs (Mbuni et al., 2020). In recent times, traditional medicine has gained an increasingly large following and is often a preferred component of healthcare by both rural and urban consumers due to its integrated use with ritual and divination for comprehensive and holistic treatment (Mander et al., 2007). The use of succulents and semi-succulents in traditional and/or folk medicine is steeped in the history of many cultural systems worldwide, with information on plant use and preparation being passed down from generation to generation (Smith and Crouch, 1999). An estimated 50% of approved pharmaceutical drugs established within the last 30 years are derived directly or indirectly from botanical resources (Veeresham, 2012). Due to the growing interest in succulent plants by researchers and those in industry, a number of indigenous botanical resources have been screened and evaluated for their pharmacologically important phytocompounds (Street and Prinsloo, 2013).

The Aizoaceae, which constitutes one of the largest succulent families of the Angiosperms, represents a currently underexplored source of potential therapeutic compounds, despite the evidence of some members being used extensively in traditional medicine practices to treat a myriad of health conditions. Moreover, despite growing ethnobotanical and scientific research in recent decades, we have only begun the journey to validate the therapeutic activity of this family. Thus, this review seeks to comprehensively outline the global cultural and traditional uses of the Aizoaceae as well as evaluate the biological activity

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https://doi.org/10.1016/j.jep.2022.115988
Received 19 September 2022; Received in revised form 20 November 2022; Accepted 24 November 2022
Available online 29 November 2022

and pharmacological potential of representative members that occur worldwide.

2. Methods

The current research endeavor included a wide variety of international and local literature sources to comprehensively evaluate foundational and recent information focusing on the global ethnopharmacology, traditional uses, and pharmacological activities of the hyperdiverse Aizoaceae. To this end, full-length research and review articles, *in vivo* and *in vitro* studies, dissertations, and clinical studies, obtained from international databases such as Google Scholar, JSTOR, ScienceDirect, Scopus, Web of Science, and PubMed, were included in this extensive review on global Aizoaceae species. A combination of specific keywords related to the ethnopharmacology and biological activities of Aizoaceae whole plants, extracts, and products were used. Additionally, search terms related to the traditional and cultural uses of species were included either individually or in combination with pharmacology-related terms. Letters and conference proceedings were excluded, as well as data obtained prior to 1940. The literature review search was initially confined to the period between 2000 and 2022 and focused on the most recent articles. However, due to data deficiency, fragmented research records, and the fact that research on this family was primarily conducted during the period 1940–1999, several earlier articles that were pertinent to the review were also included. Scientific names of plant species included the authority at first mention and were screened for any updated changes according to The International Plant Names Index (IPNI) (IPNI, 2022) and cross-referenced with "World Flora Online" (WFO) [(WFO, 2022); previously theplantlist.org]. Comprehensive taxonomic delimitations are beyond the scope of the current review, thus scientific names have been retained as cited in reviewed publications for cross-referencing purposes. However, where possible, alternate, newly revised, or previously accepted scientific names (basionyms) for certain species have been included.

3. Distribution and general characteristics

The Aizoaceae include at least 130 recognized genera and approximately 2000 species occupying diverse subtropical and tropical habitats worldwide (Fig. 1). Despite their wide range, the majority of species are endemic to the southern Africa region, especially the Succulent Karoo biome. However, approximately 25 genera and around 90 species can be found naturalized or introduced to parts of Australasia and the Americas (Morris and Duretto, 2009), wherein they are regarded as weeds. There are reports of *Lampranthus* in Portugal (Smith et al., 2018), *Carpobrotus* across the Mediterranean islands (Fenollosa and Munné-Bosch, 2019) and *Tetragonia* in Chile and Argentina (Taylor, 1994). The Aizoaceae contain annual and perennial succulent herbs and shrubs, rarely trees. Despite a plethora of diverse leaf forms, defining characters of the family include the hygrochastic fruiting capsule, perianth stamen tube and bladder cells which account for the numerous common names associated with these plants (Klak et al., 2003). The light reflective capacity of bladder cells embedded in the foliage is the basis for the common name "ice plant", whilst the South African Afrikaans vernacular term "*vygies*" meaning "little fig" is used due to the resemblance of the fruit capsule to a tiny fig.

4. Taxonomy

The succulent Aizoaceae form a major family within the Caryophyllales and can be divided *sensu stricto* into five sub-families including Aizooideae, Mesembryanthemoideae, Ruschioideae, Sesuvioideae and Tetragonioideae (Hassan et al., 2005). Studies to date have not wholly resolved the debate concerning relationships among these sub-families, with some groups regarded as distinct families (Klak et al., 2013). In fact, Mesembryanthemaceae is frequently used by many researchers to refer to members of the Mesembryanthemoideae and Ruschioideae (Klak et al., 2003) and are colloquially regarded as "mesembs'. Despite the apparent richness and hyperdiversity of the Aizoaceae, there is significant data deficiency pertaining to the majority of taxa. Even within the various sub-families, many genera are being revised and re-circumscribed as new molecular and morphological data becomes available. For instance, the Mesembryanthemoideae previously contained many genera including *Sceletium*, until Klak et al. (2017) provided a revised phylogeny of the sub-family, which resulted in recognition of *Mesembryanthemum* as the sole genus within the Mesembryanthemoideae and members of *Sceletium, Aptenia, Phyllobolus,* and *Psilocaulon* (among others) being reduced to synonymy (Brendler et al., 2021). Von Staden et al. (2013) indicated that at least 55% of taxa in the Aizoaceae require taxonomic revision. Classification discrepancies at species and genera level and rapid evolutionary radiation further add to delimitation woes. In terms of this review, all taxa mentioned are classified under the currently accepted Aizoaceae (Bittrich and Hartmann, 1988; Klak et al., 2003; Klak et al., 2017).

5. Traditional medicinal uses

Notable ethnomedicinal uses of members of the Aizoaceae have been

Fig. 1. Illustrated global distribution of the Aizoaceae (green-shaded regions). Data does not distinguish between endemic, naturalized, or invasive species (Adapted from Hartmann, and Gerbaulet, 2017; Klak et al., 2017). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

documented (Table 1). Among the plant parts used, the leaves and roots appear in various preparatory forms with herbal formulations primarily ingested as juices and decoctions. Decoctions are known to be the most common route of administration, possibly due to its perceived quick absorption and potent action (Yang, 2010). Aizoaceae plants have been used to treat a variety of ailments due to their sedative, analgesic, and antimicrobial activity, amongst others. Hypertension and respiratory, digestive, neurological, and cardiac (to a lesser extent) conditions have been alleviated by traditional remedies derived from plants of the Aizoaceae. The medicinal value of genera such as *Mesembryanthemum, Trianthema* and *Tetragonia* appear to be more widely represented in comparison to others. However, there are many limitations in validating and obtaining reliable conclusions regarding the overall medicinal potential of the Aizoaceae. Much of the earlier literature does not confirm the species used in many reports. Scientific identification of medicinal species may have been hampered by the similar plant morphology shared by different species; whilst some species exhibit varied morphology within the same genus. Further complications arise due to incorrect classification within the family. Genera such as *Gisekia, Glinus* and *Mollugo*, previously included in Aizoaceae, have since been redistributed to their own distinct families. As a result, some published research conducted on these species have incorrectly linked ethnobotanical and pharmacological use to other members of the Aizoaceae based on perceived relatedness (Napagoda et al., 2016). Thus, there is still much to learn regarding the traditional uses of this family.

6. Cultural uses

6.1. Rituals and divination

Plants of the Aizoaceae have been utilized by many cultural and ethnic groups for the purposes of divination and ritual, to ameliorate ancestral wrath, and to communicate with the ancestors for guidance to diagnose and treat medical conditions. IsiZulu warriors of South Africa added the ground plant material of *Delosperma saturatum* L. Bolus to a mix of various other unknown plants (called *intelezi* in the IsiZulu language) in water, which was used for cleansing and washing of weapons prior to battle. It was believed to provide "powers" to pre-empt the enemies plan (Burgoyne, 2005). *Bergeranthus artus*, another constituent of *intelezi*, is also used as a protective charm (Dold et al., 2005). The indigenous people of southern Africa, the Khoisan, used pulverized *Mesembryanthemum tortuosum* L. N.E.Br (syn. *Sceletium tortuosum* (L.) N. E.Br) as an intoxicant called "*kanna*" during various divination rituals as well as communal dance and healing ceremonies (Smith et al., 1996). The Nama people, an ethnic derivative of the Khoikhoi, used *Mesembryanthemum* spp. (syn. *Sceletium* spp.) as a narcotic leading to euphoria and heightened sexual desire (Ratsch, 2005).

Many of the Aizoaceae were used in the manufacture of aphrodisiacs and love charms to secure or break relationships. Indigenous African tribes employed *Aptenia cordifolia* (L.f.) Schwantes (now *Mesembryanthemum cordifolium)* as a love charm and protection against witchcraft (van Wyk and Gericke, 2000). In the case of *Lithops lesliei* N.E.Br., its physical resemblance to female genitalia supported its inclusion in charms to recall "lost love" and as a remedy for gynecological disorders (Smith and Crouch, 1999). In Andean culture, *Tetragonia crystallina* L'Hér., colloquially known as "*Hierba de la Señorita*" formed part of a collection of plants and perfumes used in the preparation of a "*baño de florecimiento*" (flowering bath) or "*seguros*" (herbal talisman), created to protect the user against evil and bring good fortune and health (Bussmann et al., 2010).

6.2. Food and beverage

The Bedouin and Tuareg nomadic inhabitants of North Africa and the Arabian Peninsula consume parts of *Mesembryanthemum* spp. (*Mesembryanthemum forskahlii, Mesembryanthemum nodiflorum* L., and *Mesembryanthemum crystallinum* L.) and *Aizoon canariense* L. The green leaves are consumed as a cooked vegetable or included in a salad, whilst the seeds are ground and used in the preparation of porridge and soup, especially in times of famine (Mandaville, 2019; Öztürk et al., 2019). In parts of south-east Asia, Australia, and New Zealand the tangy leaves of *Tetragonia tetragonioides* (Pall.) Kuntze, *Disphyma crassifolium* (L.) L. Bolus and *Trianthema portulacastrum* L. are used as a spinach substitute and eaten raw or cooked (Gaddeyya and Ratna Kumar, 2015). Several of the Aizoaceae are known for their edible fruits including the Australian endemic *Sarcozona* sp. and many *Carpobrotus* spp. [*C. acinaciformis* (L.) L.Bolus*, C. edulis* (L.) N.E.Br.*, C. mellei* (L.Bolus) L.Bolus*, C. deliciosus* (L. Bolus) L.Bolus*, C. dimidiatus* L.Bolus] (Broomhead et al., 2019; Kapitany, 2013). *Carpobrotus* sp. are eaten raw or dried and used in the preparation of fruit preserves and jams in South Africa (Springfield et al., 2003). Welcome and van Wyk (2019) outline many Aizoaceae genera that are used for human consumption as vegetables or snacks in South Africa, including lesser-known species such as *Aizoon glinoides* Eckl. & Zeyh., *Conophytum truncatum* (Thunb.) N.E.Br., *Cleretum papulosum* (L.f.) N.E. Br., *Nananthus aloides* Schwantes, and *Pleiospilos nelii* Schwantes. In the southern African region, many Aizoaceae species are used by local and indigenous people to make alcoholic beverages; either as an ingredient [*Bergeranthus* spp.; *Khadia acutipetala* (N.E.Br.) N.E.Br.*; Glottiphyllum linguiforme* N.E.Br.*; Rhus lancea* L.f.*; Trichodiadema intonsum* (Haw.) Schwantes*; Delosperma mahonia* (N.E. Br.) N.E. Br.] or for fermentation purposes (*Mesembryanthemum* spp. *Delosperma* spp. and *Trichodiadema stellatum* Schwantes) (Dold et al., 2005; Onderstall, 2007; Welcome and van Wyk, 2019). Plant parts of *Khadia*, *Mestoklema* and *Trichodiadema* spp. are used as a leavening agent when making bread.

In addition to humans, animals favour the succulent, arid species of the Aizoaceae. For example, *Mesembryanthemum cryptanthum* Hook.f. (syn. *M. forskahlii)* is a popular forage plant, whilst the aerial parts of *A. canariense* are specially fed to female camels of the Sahrawi nomads to increase milk production (Volpato and Puri, 2014). In parts of Central and South Africa, and Australia, many individual species of *Drosanthemum* are popular grazing plants and are highly palatable to domestic livestock (Haarmeyer et al., 2010), whilst *Ruschia robusta* Schwantes has been known to be semi-palatable (Nenzhelele, 2017). Conversely, *Trianthema*, *Tetragonia* and *Galenia* spp. contain high levels of toxic oxalates, which causes poisoning in poultry, cattle, and horses (Burrows and Tyrl, 2013). Ingestion of *Galenia* spp. by sheep and goats may result in the development of ascites, a condition known colloquially as "*waterpens*" (water belly) in the Western Cape province of South Africa (Botha and Penrith, 2008). Interestingly, some livestock are sufficiently knowledgeable in that they avoid the young and green plants and forage on the dry, older plants that presumably contain lower, more tolerable levels of oxalate.

6.3. Miscellaneous uses

Mesembryanthemum noctiflorum L.*, Galenia africana* L.*, Polymita albiflora* (L.Bolus) L.Bolus and *Stoeberia arborea* van Jaarsv. are some species known for their usefulness as firewood (van Jaarsveld, 2005; Wheat, 2013; Nortje and van Wyk, 2019) whilst *Ruschia* spp. has been used by the Nama indigenous people to build cooking shelters (Wheat, 2013). In New Zealand, the red juice of *T. tetragonioides* berries are used by the Māori people as ink and dye for tattoos (Burton, 2012). However, the majority of Aizoaceae species are used as ornamentals or in the horticulture industry. The vibrant, distinctly colourful flowers of *Carpobrotus, Frithia* and *Erepsia* and the quirky, unusual shape of *Faucaria, Lithops, Conophytum* and *Gibbaeum* make them prized pot plants and succulent collector items.

7. Chemistry and pharmacological activities

The sparse literature concerning the identification and characterization of chemical phytocompounds such as alkaloids, flavonoids,

Table 1
Ethnomedicinal properties of the Aizoaceae.

Scientific name[a]	Vernacular/ traditional name	Plant part used	Mode of preparation	Traditional medicine use	Reference/s
Aizoon canariense L.	patilla, pata perro [SP]	whole plant	–	indigestion, hypertension	Adam et al. (2018); Al-Laith et al. (2019)
Aptenia cordifolia (L.f.) Schwantes (=*Mesembryanthemum cordifolium* L.f.)	Ibohlololo [SA[Z]] rooi brakvygie [SA[A]]	stem, leaves	poultice	treatment of nervous complaints, pleurisy, and dropsy	Bhowmik et al. (2014)
Carpobrotus acinaciformis L.Bolus (=*Mesembryanthemum acinaciforme*)	elandvye [SA[A]]	leaves	juice	gargle for mouth infections, laxative	Iwu (2014)
Carpobrotus dimidiatus L.Bolus (=*Mesembryanthemum dimidiatum* Haw)	Natalse suurvy [SA[A]]	leaves	juice	dysentery, sore throat	Iwu (2014)
Carpobrotus edulis (L.) N.E.Br. (=*Mesembryanthemum edule* L.)	suurvygie [SA[A]] igcukuma [SA[X]]	leaves	leaf juice	topical treatment for eczema, wounds, sores, and burns; leaf juice gargled to treat mouth and throat infections	Akinyede et al. (2020)
Chasmatophyllum musculinum (Haw.) Dinter & Schwantes	geelswaelstertvyg [SA[A]]	leaves	–	used to treat swollen feet	Moteetee and van Wyk (2011)
Cleretum bellidiforme (Burm.f.) G.D.Rowley [previously *Dorotheanthus bellidiformis* (Burm.f.) N.E.Br. and *Mesembryanthemum bellidiforme* Burm.f.]	bokbaaivygie [SA[A]]	leaves	juice, decoction of the leaves	antiseptic properties, treatment for dysentery, mild diuretic	Pappe (1847)
Conophytum africana	–	leaves, roots, stems	–	analgesic, anti-infective, sedative	Iwu (1993)
Conophytum bilobum (Marloth) N.E.Br.	pianta sasso [I]	leaves, roots	–	analgesic, anti-infective, sedative	Iwu (2014)
Delosperma herbeum N.E.Br	–	root	–	treatment of the so-called climacteric	Breyer- Brandwijk and Watt (1962)
Delosperma ecklonis Schwantes	–	aerial parts	–	stomach aches	Iwu (2014)
Delosperma resei		leaves	–	anti-ulceritic	Rouibi and Boukrita (2018)
Drosanthemum hispidum (L.) Schwantes	Skaapvygie [SA[A]]	aerial part	decoction	laxative	Iwu (2014)
Galenia africana L.	kraalbos [SA[A]]	leaves, stems	decoction	rheumatism, relieved toothache, wounds and eye infections, tuberculosis treatment, treats skin diseases such as ringworm	van Wyk et al. (2008)
Jordaaniella spongiosa (L.Bolus) H.E.K. Hartmann	ostrich ice plant [ENG]	–	–	skin infections	Iwu (2014)
Khadia acutipetala (N.E.Br.) N.E.Br.	–	root	fermented beverage	remedy for problems linked to the male reproductive system	Monakisi (2007)
Lampranthus elegans (Jacq.) Schwantes (=*Mesembryanthemum elegans*)	–	leaves	infusion	headache	Andrade et al. (2017)
Lampranthus multiradiatus (Jacq.) N.E.Br.	–	essential oils, leaves	decoction	treatment of respiratory tract infections, tuberculosis, dysentery, diabetes mellitus, laryngitis, and vaginal infections	Moyo and Mukanganyama (2015)
Lampranthus francisci L.Bolus	–	leaves	fresh sap	treatment for fungal infections of the scalp	Moyo and Mukanganyama (2015)
Lithops lesliei N.E.Br.	living stones [ENG] beeskloutjies [SA[A]]	leaves	decoction	used to treat issues relating to female reproductive health i.e. prevent bleeding during pregnancy, anti- abortifacient	Smith and Crouch (1999)
Mesembryanthemum crystallinum L.	ice plant [ENG]	leaves	juice, paste	juice ingested to treat dysentery, liver and kidney diseases, pneumonia and as a diuretic, used topically to relieve itching, pain, swelling and redness of the skin	Ibtissem et al. (2012)
Mesembryanthemum nodiflorum L.	slenderleaf ice plant [ENG]	whole plant	decoction	treat gastric disease, used as an emetic in acute poisoning, treatment of eye infection	Doudach et al. (2013)
Mestoklema elatum N.E.Br. ex Glen	–	leaves	–	anti-inflammatory	Iwu (2014)
Opophytum forsskalii (Hochst. ex Boiss.) N.E. Br. (=*Mesembryanthemum forskahlii*)	–	seeds	powdered	controls cholesterol and creatinine levels	Abdel-Farid et al. (2016)
Pleiospilos bolusii N.E.Br.	dumpiesnuif [SA[A]]	leaves	dried and powdered	used for its inebriating properties and as a sedative	Breyer-Brandwijk and Watt (1962)
Polymita albiflora (L.Bolus) L.Bolus	–	leaves	decoction	relieves abdominal cramps	Wheat (2013)
Psilocaulon coriarium N.E.Br. (=*Mesembryanthemum coriarium*)	loogbossie [SA[A]]	–	poultice, infusion	used to treat acne and infections on the scalp	van Wyk et al. (2008)
Rabiea albinota (Haw.) N.E.Br. (=*Nananthus albinotus* (Haw.) N.E.Br.	S'Keng Keng [SA[G]]	whole plant	dried and powdered	used for its reported inebriating properties	Emboden (1972)
Ruschia fredericii (L.Bolus) L.Bolus	vygiebos [SA[A]]	leaves	decoction	leaves are chewed to relieve abdominal pain	Wheat (2013)
Ruschia putterillii (L.Bolus) L.Bolus	Sebabetsi [SA[X]]	leaves	–	used to treat swollen feet	Moteetee and van Wyk (2011)
Ruschia spinosa (L.) Dehn (=*Eberlanzia spinosa* Schwantes)	doringvygie [SA[A]]	aerial parts	leaf decoction	skin infections, treatment for angina	van Wyk et al. (2008); Iwu (2014)
Sceletium emarcidum (Thunb.) L.Bolus (=*Mesembryanthemum emarcidum* Thunb.)	kanna/kougoed [SA[A]]	leaves	powdered, juice	used to treat kidney failure and inflammation, treatment of Crimean–Congo hemorrhagic fever	van Wyk et al. (2008)
Sceletium tortuosum (L.) N.E.Br.(= *Mesembryanthemum tortuosum* L.)	kanna/kougoud [SA[A]]	leaves, whole plants	powdered, juice	toothache, narcotic, sedative	Gericke and Viljoen, 2008

(*continued on next page*)

Table 1 (*continued*)

Scientific name[a]	Vernacular/ traditional name	Plant part used	Mode of preparation	Traditional medicine use	Reference/s
Sesuvium portulacastrum (L.) L. (=*Portulaca portulacastrum* L.)	sea purslane [ENG]	leaves	–	treatment for fever, kidney disorders, scurvy, antidote for venomous fish and infections	Magwa et al. (2006)
Stoeberia utilis (L.Bolus) van Jaarsv.	Gifberg tree-mesemb [ENG]	aerial part	–	fever, skin infections	Iwu (2014)
Tetragonia fruticose L.	kinkelbossie [SA[A]]	leaves	–	leaves are mixed with other plants in a range of different medicinal preparations	Wheat (2013)
Tetragonia tetragonoides (Pall.) Kuntze	kokihi [M] New Zealand spinach [ENG]	whole plant, leaves	tonic	ulcer treatment, anti-inflammatory activity, septicemia, and asthma	Lee and Kang (2014)
Trianthema decandra L. (=*Zaleya decandra* (L.) Burm.f.)	pigweed [ENG]	leaves, root	juice	analgesic, anti-inflammatory, anti-diabetic; relieves skin disorders; the root is used for the treatment of hepatitis, asthma, and leaf juice for headache	Veeresh et al. (2017)
Trianthema portulacastrum L.	horsepurslane [ENG] gadabani [H]	whole plant,	decoction, poultice	analgesic, wound healing, laxative, large doses used as an abortifacient, root applied for corneal ulcers, itching, diminished sight, and night blindness, useful in rheumatism	Gaddeyya and Ratna Kumar (2015)
Zaleya pentandra (L.) C.Jeffrey (=*Trianthema pentandra*)	african purslane [ENG]	whole plant roots, leaves	dried and powdered, decoction	treats Athlete's foot and very septic wounds, used as a stringent, treats snake bite and influenza	Afzal et al. (2015)

ENG: English; H: Hindi; I: Italian; M: Maori; SA[A]: South African-Afrikaans; SA[G]: South African-Griqua; SA[X]: South African-Xhosa; SA[Z]: South African-isiZulu; SP: Spanish.
(–): unknown/not stated in publication.
[a] Scientific names include accepted authorities (at first mention) and synonyms (in parentheses) where available.

steroids, and their related intermediary compounds in the Aizoaceae is concentrated on select species and interspersed throughout the years. Notably, mesembrine alkaloids were earlier isolated from *Mesembryathemum* spp. (syn. *Sceletium* spp.) (Smith et al., 1996) with renewed interest in later publications focusing on mesembrine-type alkaloid derivatives such as mesembranol, mesembrenol, and mesembrenone (Harvey et al., 2011; Krstenansky, 2017). Of interest are the chromoalkaloids, betacyanin and betaxanthin (collectively called betalains), which are plant pigments specific to the Caryophyllales and used as synthetic dye replacements. Betanin pigments such as 2-Descarboxy-betanidin and Lampranthin I and II were isolated from *C. acinaciformis* and *Lampranthus* spp. respectively. Noteworthy betalain content was detected in the flowers of *Erepsia* spp., *Smicrostigma viride* N.E.Br., *Glottiphyllum* spp. and *Lampranthus productus* N.E.Br. (Khan and Giridhar, 2015). Phytochemical evaluation and screening of betalains represents a potential research focus as they are known to exhibit antioxidant, anticancer and anti-inflammatory activity (Gandía-Herrero et al., 2016). While iridoids have yet to be confirmed in the Aizoaceae, a novel, antifungal tetraterpenoid, trianthenol 1 was isolated from the chloroform extract of *T. portulacastrum* (Nawaz et al., 2001) as well as ecdysterone, a potential chemosterilant (Sukalingam et al., 2017). Phytosterols such as sitosterol and stigmasterol were isolated from the ethanol extract of the aerial part of *A. cordifolia*. The presence of beta-sitosterol and campesterol in the seed oil of *M. forskalii* implied its usefulness in attenuating high cholesterol and cardiovascular diseases (Bilel et al., 2020) while the isolated steroidal compound, pentandraol, isolated from *Zaleya pentandra* (L.) C.Jeffrey was implicated in the antibacterial and antioxidant activity of the extract. A novel lignan *N*-2, 3-dihydroxy-3-(3,4-dihydroxyphenol) tyramine was isolated from the aerial regions of *Tetragonia tetragonoides* (Pall.) Kuntze, (Choi et al., 2019). Flavonoids including flavones, flavonols, flavanones, chalcones, and proanthocyanidins have been detected in at least 14 genera of the Aizoaceae. Kaempferol (3,4′,5,7-tetrahydroxyflavone) and/or quercetin was commonly isolated in members of *Mesembryanthemum, Lithops, Lampranthus,* and *Conophytum* (Iwashina, 2015). Recently, Abuzaid et al. (2020) identified a novel kaempferol derivative, kaempferol-3-O-(2''-O–βD-glucopyranosyl)-6''-O-E-feruloyl–βD-glucopyranoside-D-glucopyranosyl)-6''-O-E-feruloyl-β-D-glucopyranoside in *T. portulaca strum*. Proanthocyanidins containing cyanidin were identified in the unripe seeds of *Sesuvium portulacastrum* (L.) L., *A. glinoides, A. cordifolia* and *T. tetragonioides* (Bittrich and Amaral, 1991). Other specific pharmacological effects of the Aizoaceae are discussed further.

7.1. Central and nervous system (CNS)

The activity of psychoactive plants can be attributed to phytocompounds involved in sedative or calming, hallucinogenic, and/or stimulatory effects (Alrashedy and Molina, 2016). Many psychoactive species of *Sceletium/Mesembryanthemum* are widely recognized for their efficacy against multiple CNS conditions. Perhaps one of the most popular poster plants for the treatment of neurological and psychological disorders, *M. tortuosum* (*S. tortuosum*) has been extensively studied for its anxiolytic properties, and usefulness in attenuating cognitive decline (Smith et al., 1996; Gericke and Viljoen, 2008; Patnala and Kanfer, 2013; Krstenansky, 2017; Brendler et al., 2021). The efficacy of the plant extract in both *in vitro* and *in vivo* clinical trials has been attributed to its alkaloid content, specifically the phytocompound, mesembrine and related mesembrine derivatives such as mesembrenol, mesembrenone, mesembranol and epimesembranol (Patnala and Kanfer, 2017; Brendler et al., 2021). These compounds are currently being used in commercially available pharmaceutical preparations for the treatment of anxiety, depression, post-traumatic stress disorder (PTSD) and dementia due to their effectiveness as potent serotonin re-uptake inhibitors in maintaining neurochemical homeostasis (Krstenansky, 2017; Makolo et al., 2019; Brendler et al., 2021). Mesembrine and/or its derivatives are present in related genera of the Aizoaceae including *Lampranthus*, *Bergeranthus, Delosperma*, *Drosanthemum*, *Glottiphyllum*, *Oscularia*, and *Ruschia*, albeit in varying minimal amounts (Smith et al., 1998).

Serotonergic hallucinogens such as tryptamines and tryptamine derivatives - N, N-dimethyltryptamine (DMT) and 5-MeO-DMT/5-methoxy-N,N-dimethyltryptamine have been shown to induce mood changes, euphoria and provide the user with an altered or distorted view of objects and reality (Schifano et al., 2016). These compounds have been found to occur at high levels in many *Delosperma* spp. Studies show that other plants, such as *A. cordifolia*, *Plinthus sericeus* Pax and *Psilocaulon coriarium* N.E.Br (previously known as *Psilocaulon absimile* N.E.Br, now also known as *Mesembryanthemum coriarium*) contain appreciable levels of currently unidentified alkaloids which may be of therapeutic value (Said et al., 2019; Smith et al., 1998) and thus serve as a potential avenue of future research.

A few studies have highlighted the efficacy of Aizoaceae extracts in treating neurodegenerative diseases such as Alzheimer's. The dichloromethane crude extract and currently unidentified compound GA2 from *G. africana* inhibited acetylcholinesterase activity (Phungula et al., 2014). Silver nanoparticles synthesized from the aqueous extract of *Lampranthus coccineus* (Haw.) N.E.Br. (LC) and *Malephora lutea* (Haw.) Schwantes (ML) showed greater acetylcholinesterase inhibition in comparison to crude aqueous extracts (LC: 0.82 ± 0.03 ng/mL vs. 1.23 ± 0.01 ng/mL, ML: 1.36 ± 0.01 ng/mL vs. 1.95 ± 0.01 ng/mL) despite poor activity against the standard drug Rivastigmine (0.79 ± 0.01 ng/mL, $p < 0.05$) (Youssif et al., 2019). The leaves of *C. edulis* showed an affinity to treat cognitive impairment due to the AChE- and BuChE-inhibitory activity of their dichloromethane and methanol extracts (Rocha et al., 2017). However, the fruit peel of *C. edulis* demonstrated little to no acetylcholinesterase activity (Castañeda-Loaiza et al., 2020).

7.2. Antimicrobial activity

Many members of the Aizoaceae have been used as part of traditional medicine practices for the treatment of infections and related microbial diseases. This has led to the evaluation of the antimicrobial activity of a select few plants (Table 2). Various conventional methods, such as disc or agar diffusion and microdilution assays have been used for the preliminary screening of plants with potential microbial-inhibitory effects. Whilst most studies indicated broad-spectrum antimicrobial activity, gram-positive bacteria in comparison to gram-negative bacteria, appeared to have greater susceptibility to the bactericidal and inhibitory effects of Aizoaceae plant extracts and oils. This may be attributed to the lipopolysaccharide-enriched outer membrane of Gram-negative bacteria that serve as a permeability barrier to antimicrobial agents. Interestingly, many studies have focused on the identification and isolation of specific compounds or secondary metabolites involved in microbial inhibition. For example, Nawaz et al. (2001) isolated an antifungal triterpenoid, Trianthenol 1 from the chloroform extract of *T. portulacastrum.* Neubauerová et al. (2011) isolated low molecular weight peptides from the leaves of *T. tetragonioides* which demonstrated moderate antimicrobial activity, detected by a 9 mm and 7 mm inhibition zone, against *Staphylococcus aureus* and *Pseudomonas aeruginosa,* respectively. In a study by Ticha et al. (2015), two compounds, a flavonoid ((S)-5,7-dihydroxy-2′-methoxyflavanone) and a chalcone ((E)-2-hydroxy-3′,6′-dimethoxychalcone) were isolated from the leaves of *G. africana*. The latter compound presented a MIC_{99} of 5 μM against *Mycobacterium tuberculosis* necessitating further investigation of the chalcone as an effective antimycobacterial compound. In another study evaluating the antituberculotic activity of flavonoids isolated from *G. africana* leaves by Mativandlela et al. (2009), the synergistic combination of (2S)-5,7,2′-trihydroxyflavanone, isolated from the ethanolic fraction, and an existing antituberculotic drug, isoniazid, reduced the initial minimum inhibitory concentration 16-fold against *Mycobacterium tuberculosis.* Further studies would be required to fully evaluate the combined effects and potential toxicity of these compounds in *in vivo* models.

The use of *Carpobrotus* spp. (most commonly *C. edulis* and *C. acinaciformis*) for the traditional treatment of oral infections, insect bites, and toothache is well documented in southern Africa (Springfield et al., 2003; van Wyk et al., 2008). As a result, there are numerous studies evaluating the antimicrobial activity and efficacy of *C. edulis* crude extracts and isolated fractions against a range of Gram-positive and Gram-negative microorganisms (van der Watt and Pretorius, 2001; Springfield and Weitz, 2006; Ibtissem et al., 2012). This activity has been attributed to various flavonoids, such as rutin, hyperoside, neohesperidin, catechin and ferulic acid, and tannins isolated from the plant (van der Watt and Pretorius, 2001). The crude leaf extracts of *Carpobrotus muirii* L.Bolus*, C. mellei*, and *Carpobrotus quadrifidus* L.Bolus also showed antimicrobial activity against *S. aureus* and *Mycobacterium smegmatis* in the disc diffusion assay (Springfield et al., 2003; Springfield and Weitz, 2006). Interestingly, the authors pointed out that *C. edulis* and *C. mellei* were morphologically congruent to each other and widespread in the Western Cape region of South Africa. It is surmised that these species may have potentially been utilized interchangeably in traditional medicine preparations. However, Akhalwaya et al. (2018) evaluated the *in vitro* antimicrobial efficacy of 139 South African medicinal plants and found that the dichloromethane extract of *C. edulis* showed noteworthy activity for only one out of nine tested oral pathogens (*Fusobacterium nucleatum,* MIC: 0.50 mg/mL). According to existing ethnobotanical literature, traditional healers utilize water and alcohol decoctions derived from the aerial parts and roots of *Carpobrotus* spp. to treat fungal and HIV-related infections (Otang et al., 2012). However, the aqueous and ethanol extracts were inactive against various strains of *Candida* spp. and *Cryptococcus neoformans* in comparison to the antibiotics, Nystatin and Amphotericin B (Springfield et al., 2003; Omoruyi, 2014). Subsequently, *C. edulis* was disregarded as a hospital and home-care remedy for the treatment of oral candidiasis affecting HIV patients in KwaZulu-Natal, South Africa (Motsei et al., 2003). Moreover, fungal growth was promoted, like that of *C. albicans* and *C. krusei* in the aqueous extracts of *Lampranthus francisci* L.Bolus (Moyo and Mukanganyama, 2015). It is important to note that solvent polarity and the extract concentration may affect antifungal activity as herbal practitioners often prescribe remedies in multiple doses, prepared via different methods and which may, or may not contain other plant extracts derived from various plant organs (Omoruyi, 2014).

7.3. Antioxidant activity

Oxidative stress occurs when reactive oxygen species (ROS) production exceeds intrinsic antioxidant mechanisms, resulting in cell damage and degradation of macromolecules, which further leads to chronic and degenerative diseases such as diabetes, cardio-vascular conditions, cancers, and neurodegenerative disorders (Szymanska et al., 2016). Current research trends indicate the effectiveness of exogenous antioxidants, especially plant-derived extracts, or compounds, for free radical scavenging, chelation of transition metals, and inhibition of peroxidation. The *in vitro* antioxidant activity of some members of the Aizoaceae is outlined in Table 3. Most studies utilized the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay to determine the antioxidant capacity of selected samples. Whilst no single method can comprehensively describe and evaluate the mechanism of action of antioxidants *in vitro*, the DPPH assay is useful for the preliminary screening of plants with free radical scavenging capabilities and identification of novel compounds with antioxidant value.

Oxidative stress is one of the primary mechanisms that facilitates the progression of HIV to AIDS and increases patient susceptibility to opportunistic infections (Kapewangolo et al., 2016). Some members of the Aizoaceae have demonstrated significant antioxidant activity and have been indirectly implicated in reducing the viral load in infected individuals. For example, Omoruyi et al. (2012) identified significant radical scavenging activity in *C. edulis* extracts (DPPH IC_{50} of aqueous and ethanolic extract: 0.018 mg/mL and 0.016 mg/mL respectively, $p < 0.05$) thereby supporting the traditional use of the plant in managing HIV and AIDS related infections. The ethanol and ethyl acetate crude extracts of *M. tortuosum* (*S. tortuosum*) were found to inhibit HIV-1 enzymes, reverse transcriptase (RT) and protease (PR). Both extracts demonstrated values of $IC_{50} < 50$ μg/mL and $IC_{50} < 100$ μg/mL for RT and PR inhibition respectively, suggesting further monitoring of *M. tortuosum* (*S. tortuosum*) as a potential therapeutic agent (Kapewangolo et al., 2016).

Many halophytic members of the Aizoaceae have demonstrated enhanced ROS scavenging as an adaptive mechanism in response to abiotic stresses. Noteworthy examples include *M. crystallinum* (Agarie et al., 2009) and *Trianthema triquetra* Willd. ex Spreng (Sharma and

Table 2
List of studies evaluating the antimicrobial activity of the Aizoaceae.

Plant name[a]	Part used	Extraction solvent	Method/assay	Test organisms	Key findings/responses	Reference/s
Aizoon canariense L.	aerial parts	MeOH	agar well diffusion and broth dilution assay	*Pseudomonas syringae* pv tomato DC3000	*Aizoon canariense* inhibition zone of 21 mm, MIC: 4.0 mg/mL	Elkhalfi et al. (2013)
Carpobrotus edulis (L.) N.E. Br. *(=Mesembryanthemum edule* L.*)*	leaves	water	broth dilution	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*	*S. aureus* (MIC 0.4%), *P. aeruginosa* (MIC 6.6%) and *E. coli* (MIC 1.6%)	Ibtissem et al. (2012)
Carpobrotus muirii L.Bolus (*Mesembryanthemum muirii* L. Bolus), *Carpobrotus quadrifidus* L.Bolus	whole plant whole plant	MeOH MeOH	disc diffusion assay and TLC direct bioautography	*S. aureus, P. aeruginosa, Candida albicans, Mycobacterium smegmatis.*	Both *Carpobrotus* spp. showed antimicrobial activity against *S. aureus* and *M. smegmatis* by clear zones of inhibition in both methods	Springfield et al. (2003)
Galenia africana L.	leaves	EtOH	broth dilution assay	*Propionibacterium acnes*	MIC of 125 μg/mL against tested bacterium	Sharma and Lall (2014)
Mesembryanthemum nodiflorum L.	aerial parts	MeOH, water	disc diffusion and microdilution assay	*Micrococcus luteus, S. aureus, Bacillus subtilis, Klebsiella pneumoniae, P. aeruginosa, E. coli*	Methanol extracts active against all strains except *B. subtilus* (MIC: 3.12–6.25 mg/mL) Poor antibacterial activity of aqueous extract against all tested bacteria	Doudach et al. (2013)
Mesembryanthemum crystallinum L.	whole plant	EtOH	agar well diffusion	*S. aureus, B. subtilis, P. aeruginosa, Salmonella enterica* serotype *typhi (S.typhi), E. coli, C. albicans, Aspergillus fumigates, Penicillium italicum, Fusarium* solani f. sp. *cucurbitae, Fusarium niveum, Botrytis cinerrea*	Inhibition zone of 27-22 mm against *B. subtilis*, *S. aureus*. No activity against *P. aeruginosa* or *B. cinerrea*. Poor activity of polar extracts	Mohammed et al. (2012)
Sesuvium portulacastrum (L.) L. (=*Portulaca portulacastrum* L.)	leaves	essential oils	antibacterial: agar well diffusion antifungal: mycelium growth inhibition assay	*Acetobacter calcoacetica, B. subtillis, Clostridium sporogenes, Clostridium perfringens, E. coli, S. typhi, S. aureus, Yersinia enterocolitica. C. albicans, Aspergillus niger, Aspergillus flavus, Penicillium chrysogenum (previously Penicillium notatum)*	The oil exhibited antibacterial and antifungal activity against all tested strains	Magwa et al. (2006)
Sesuvium portulacastrum (L.) L. (=*Portulaca portulacastrum* L.)	aerial parts	DCM, EtOH, water	agar well diffusion	*S. aureus, E. coli*	Ethanolic extract showed antimicrobial activity against both microorganisms	Al-Azzawi et al. (2012)
Tetragonia tetragonoides (Pall.) Kuntze	leaves	MeOH, HX, DCM, EA, BuOH	agar well diffusion	*Listeria monocytogenes, M. luteus, Bacillus cereus, K. pneumoniae, Proteus mirabilis, Proteus vulgaris* and *Shigella sonnei*	Relatively high antibacterial activity against most of the tested bacteria with inhibition zones (9.0–15.4 mm) MIC values for active fractions were 15.63-1000 μg/mL	Choi et al. (2008)
Trianthema decandra L. (=*Zaleya decandra* (L.) Burm.f.)	essential oil from leaves	–	disc diffusion and broth dilution assay	*S. aureus, Streptococcus faecalis, Enterococcus faecalis, E. coli, P. aeruginosa, S. typhi, Vibrio cholera, P. vulgaris, B. subtilis, Y. enterocolitica, C. albicans, Cryptococcus neoformans*	MIC of essential oil against all microbial strains ranged between 625 and 1250 μg/mL	Geethalakshmi and Sarada (2013)
Trianthema decandra L. (=*Zaleya decandra* (L.) Burm.f.)	whole plant	–	agar well diffusion	*B. subtilis, S. aureus, E. coli, P. aeruginosa, E. aerogenes, Raoultella planticola, C. albicans, A. niger, A. flavus, Trichophyton rubrum, P. chrysogenum*	Ethyl acetate extract showed potent activity against all test strains with an MIC 125 μg/mL in all cases	Jain et al. (2012)
Trianthema decandra L. (=*Zaleya decandra* (L.) Burm.f.)	leaves	–	disc diffusion assay	*E. faecalis, S. aureus, S. faecalis, E. coli, P. aeruginosa, S. typhi, V. cholera, P. vulgaris, B. subtilis, Y. enterocolitica*	Potent activity of isolated compounds against all the tested microorganisms	Geethalakshmi and Sarada (2018)
Trianthema portulacastrum L.	whole plant	EtOH	disc diffusion assay	*E. coli, Vibrio harveyi, S. aureus* and *B. cereus*	Notable activity against all four strains of bacteria compared to the aqueous extract, with *B. cereus* noted as most susceptible (12 mm zone of inhibition)	Vohora et al. (1983)
Zaleya pentandra (L.) C. Jeffrey *(=Trianthema pentandra)*	whole plant	–	agar well diffusion assay	*E. coli, S. typhi, Bacillus spizizenii, S. aureus, Staphylococcus epidermidis*	*S. typhi*, with zone of inhibition 13 mm and 11 mm at concentration 3 mg/100 μL and 1.5 mg/100 μL, respectively. *S. aureus* with zone of inhibition 17.5 mm at concentration 3 mg/100 μL	Afzal et al. (2016)

MIC: minimum inhibitory concentration.
(–): unknown/not stated in publication.

[a] Plant names include accepted authorities (at first mention) and synonyms (in parentheses) where available.

Table 3
Studies evaluating antioxidant activity and free radical scavenging capability of the Aizoaceae.

Plant name[a]	Plant part tested/used	Solvent used for extraction	Antioxidant assay	Results	reference
Aizoon canariense L.	whole plant	MeOH	FRAP, DPPH and ABTS	DPPH: $IC_{50} = 66.56$ mg/mL; poor activity and not significantly different from other tested species ($p > 0.05$)	Al-Laith et al. (2019)
Aizoon hispanicum L.	aerial parts	MeOH	DPPH	$IC_{50} = 292.3$ μg/mL	Khettaf et al. (2016)
Carpobrotus dimidiatus L.Bolus (=*Mesembryanthemum dimidiatum*)	leaves	MeOH, water	DPPH	MeOH extract: IC_{50} value of 240 μg/mL and water extract had an IC_{50} value of 1125 μg/mL	Hurinanthan (2009)
Carpobrotus edulis (L.) N.E.Br. (=*Mesembryanthemum edule* L.)	leaves	Water extract	DPPH	94.6% DPPH inhibition at 2 mg/mL	Ibtissem et al. (2012)
Carpobrotus edulis (L.) N.E.Br. (=*Mesembryanthemum edule* L.)	aerial parts	MeOH	DPPH, ABTS, Beta carotene-linoleic bleaching and superoxide anion assay	IC_{50} value of 29.8 μg/mL for MeOH extract against DPPH. IC_{50} value of 431.76 μg/mL for antiradical activity against ABTS synthetic radical, compared to 355 μg/mL for BHT	Hanen et al. (2009)
Galenia africana L.	leaves, root, bark, and twigs	EtOH	DPPH	EC_{50} value of 90.92 μg/mL	Sharma and Lall (2014)
Mesembryanthemum crystallinum L.	leaves	Water extract	DPPH	75.5% DPPH inhibition at 2 mg/mL	Ibtissem et al. (2012)
Mesembryanthemum crystallinum L.	aerial parts	MeOH	DPPH, ABTS, β carotene-linoleic bleaching, iron chelating and superoxide anion assay	DPPH activity: $IC_{50} = 160$ μg/mL Iron chelating activity with EC_{50} value of 2.13 mg/mL	Hanen et al. (2009)
Mesembryanthemum nodiflorum L.	aerial parts	MeOH	DPPH, ABTS, β carotene-linoleic bleaching and superoxide anion assay	DPPH: $IC_{50} = 112.5$ μg/mL	Hanen et al. (2009)
Opophytum forsskalii (Hochst. ex Boiss.) N.E.Br. (=*Mesembryanthemum forskahlii*)	shoots, seeds, fruit	MeOH	DPPH	Radical scavenging activity (%) decreased in the order, shoots (14%), seed (10%) and fruit (2%) at 400 μg/ml	Abdel-Farid et al. (2016)
Sceletium tortuosum (L.) N.E.Br. (= *Mesembryanthemum tortuosum* L.)	not stated	EA, EtOH	DPPH	IC_{50} values of the EtOH and EA extracts were 49 μg/ml and 64.7 μg/mL respectively	Kapewangolo et al. (2016)
Sesuvium portulacastrum (L.) L. (=*Portulaca portulacastrum* L.)	leaves	PE, MeOH, EtOH, EA, Benzene	DPPH, superoxide anion, ABTS radical scavenging and reducing power assay	IC_{50} value of MeOH extract in DPPH assay was 31.53 μg/mL. Hydroxyl superoxide: IC_{50} value of MeOH extract was 19.17 μg/mL. Potent scavenging activity of methanolic extract (94.70%) in ABTS assay, compared to the standard Trolox (70.29%)	Paulpriya et al. (2013)
Trianthema decandra L. (=*Zaleya decandra* (L.) Burm.f.)	whole plant	PE, EtOH, chloroform, EA, and water	DPPH	EtOH extract showed highest activity (DPPH inhibition) of 46.9% at 100 μg/mL	Geethalakshmi et al. (2010)
Zaleya pentandra (L.) C.Jeffrey (=*Trianthema pentandra*)	whole plant	MeOH	DPPH	73% radical scavenging at concentration 161 μL/mL	Afzal et al. (2016)

DPPH: 2,2-diphenyl-1-picrylhydrazyl.
ABTS: 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid).
MeOH: Methanolic extract, EtOH: Ethanol extract, EA: Ethyl Acetate, PE: Petroleum ether.
(−): unknown/not stated in publication.
[a] Plant names include accepted authorities (at first mention) and synonyms (in parentheses) where available.

Ramawat, 2014) which exhibited increased antioxidant activity in response to elevated levels of NaCl. In addition, there was a corresponding increase in the production of polyols and phenolic compounds, which are recognized as osmoregulants and potent natural antioxidants respectively (Agarie et al., 2009). Phenolic compounds are significant contributors to the radical scavenging capability in many Aizoaceae species. For example, high levels of polyphenolics in *M. crystallinum* and *M. nodiflorum* extracts correlated to greater antioxidant activity (Hanen et al., 2009). Similar results were obtained with *C. edulis* (Omoruyi et al., 2012) and *C. rossi* (Geraghty et al., 2011).

In addition to biological and environmental factors, the choice of solvents for chemical extraction affects phenolic content and antioxidant activity. For instance, the methanolic extract of *M. edule* (*C. edulis*) contained higher levels of polyphenols than the ethanolic extract (Ksouri et al., 2008). Whilst there are a plethora of preliminary studies assessing the *in vitro* antioxidant activity of Aizoaceae extracts, few, if any, have evaluated the *in vivo* effects. Consideration must be given to the fact that significant *in vitro* antioxidant activity does not necessarily pre-empt *in vivo* activity.

7.4. Cosmetic use

Traditional methods have seen the incorporation of plant extracts into poultices, lotions, and topical ointments for the treatment of a variety of skin ailments including aging, inflammation, and pigmentation (Mabona and van Vuuren, 2013). Moreover, the cosmetic industry has seen a shift in consumer demand toward more eco-friendly and natural treatments, with many recent skin care products being supplemented with plant extracts (Lall and Kishore, 2014). Members of the Aizoaceae that display wound-healing, anti-inflammatory, antioxidant, antimicrobial, antimutagenic and anti-aging properties, can be used to alleviate the effects of various skin conditions (De Beer and van Wyk, 2011; Martins et al., 2011). For example, *C. edulis*, used traditionally as an antiseptic and astringent against itching, insect bites and wounds has shown to exhibit antioxidant and antibacterial activity (Falleh et al., 2012; Ibtissem et al., 2012). This served as the basis of its use in a commercial patent as a cosmetic agent to enhance skin brightness and texture (Laperdrix et al., 2013). Kim et al. (2017) related the use of *M. crystallinum* alcohol extracts to delays in skin cell aging and enhanced skin whitening. Additionally, ferulic acid isolated from *T. tetragonioides*, has been evaluated for its whitening effect and anti-wrinkle activity on mouse melanoma cell lines and human dermal fibroblast cell lines respectively (Park et al., 2018).

Of interest was the detection of gamma linolenic acid (GLA), a fatty acid found primarily in seed oils, at appreciable levels in the leaves of *A. canariense* (Freije et al., 2013). Gamma linolenic acid is widely used as a homeopathic remedy for inflammatory skin conditions such as psoriasis and eczema. Additionally, the appreciable inhibitory effect of *M. forskahlii* seed oil extract on *P. chysogenum* and *A. fumigatus* underpinned its usefulness for the treatment of fungal infections of the scalp and hair (Bilel et al., 2020). The increasing prevalence of botanical derived skin care products requires further scientific and clinical exploration. Health and safety implications should be a significant consideration when evaluating the *in vitro* and *in vivo* efficacy of plant extracts on dermatological conditions.

7.5. Cytotoxicity/anti-cancer agents

Due to the high incidence and aggressive nature of many cancers globally, it has become imperative to evaluate plants and naturally derived products to ameliorate current cancer strategies. There is growing evidence of the use of plant-derived compounds for adjuvant treatment during chemo- and radio-therapy as well as for their anti-mutagenic and antitumorigenic activity. The anti-cancer potential of the ethanolic and chloroform fractions of *T. portulacastrum* was evaluated in n-diethylnitrosoamine (DENA)-induced rat hepatocarcinogenesis (Bhattacharya and Chatterjee, 1999) and 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat mammary tumorigenesis models (Mandal and Bishayee, 2015). In the earlier study, a marked reduction in the size and distribution of nodules and liver focal lesions was observed, with no apparent toxic side-effects. *T. portulacastrum* suppressed (DMBA)-initiated mammary tumor incidence without any toxicity due to the regulation of NF-κB and Nrf2 signaling pathways involved in inflammation responses.

Efflux pumps, such as P-glycoprotein are known to confer multidrug resistance to cancer by extruding chemotherapy drugs as well as other drugs to which cancers have become refractory (resistant). Currently, compounds used to block these efflux pumps are toxic at active levels and may lead to increased cancer risk overall. However, a study conducted by Martins et al. (2010) demonstrated the antiproliferative activity of the chloroform and ethyl acetate soluble fractions from *C. edulis* on mouse lymphoma cell lines. All isolated compounds, especially Uvaol, were effective in the reversal of multidrug resistance in cancer and displayed no toxicity at concentrations evaluated in the study. Whilst this basic study supports the potential use of plant derived compounds to indirectly supplement anti-cancer therapies, much research is required to evaluate the chemo-preventative efficacy of such compounds in humans.

Other members of the Aizoaceae that have demonstrated promising anti-carcinogenic and immunomodulatory effects include *Z. pentandra* (Mughal et al., 2020) and *Trianthema decandra* L. (Gajjala et al., 2019) extracts against breast adenocarcinoma cell line MCF-7, and *M. crystallinum* against HCT116 human colon cancer cells (Seo and Ju, 2019). The cytotoxic potential of *T. portulacastrum* and *A. canariense* fractions against human hepatocellular carcinoma (HepG2) cell lines was evaluated by Abuzaid et al. (2020), with noteworthy cytotoxic activity of the n-hexane and n-butanol extracts of *A. canariense* (24.7 ± 3.5 and 55.3 ± 4.9 μg/mL, respectively). Conversely, *M. nodiflorum* did not exhibit any significant cytotoxic activity on breast cancer (MCF7) and cervix adenocarcinoma (HeLa) cells, at concentrations ranging from 31.25 to 1000 μg/mL ($p > 0.05$) (Doudach et al., 2013). Furthermore, mesembrenone isolated from *M. tortuosum* (*S. tortuosum*) and cannabidiol from *Cannabis sativa* were tested for their anti-cancer activity against three breast cancer cell lines, MCF12A, MCF7 and MDA-MB-231. Unfortunately, not only did mesembrenone show insignificant activity against the three cancer cell lines in comparison to cannabidiol, but it also demonstrated high levels of toxicity in healthy breast cells at all tested concentrations, which could not be alleviated by co-treatment with cannabidiol (Tunstall, 2019).

7.6. Other pharmacological activities

Moawad et al. (2020) evaluated the acaricidal activity of *T. portulacastrum* L. and *A. canariense* against *Rhipicephalus annulatus* tick using adult and larval immersion tests at increasing concentrations. While the crude hydroalcoholic extract of *T. portulacastrum* demonstrated 100% adult and larval mortality, *A. canariense* did not show appreciable acaricidal effects (<25% adult and larval mortality, $p \geq 0.05$). The anthelminthic activity of the aqueous methanolic extract of *T. decandra* Linn. against female *Haemonchus contortus* and their eggs was assessed by Hussain et al. (2011). Significant anthelmintic activity ($p < 0.05$) on live worms as well as egg hatching was noted.

Various ethanolic extracts of *M. tortuosum* (*S. tortuosum*) were evaluated for their anti-malarial activity and three extracts demonstrated potent *in vitro* anti-malarial activity against a chloroquine-sensitive *Plasmodium falciparum* strain (Setshedi et al., 2012). The methanol extract of *T. portulacastrum* and *Zaleya decandra* (L.) Burm.f. roots produced dose-dependent hypoglycemic, hypolipidemic, and anti-hyperglycemic activity in alloxan-induced diabetic rats, which was comparable to a standard oral hypoglycemic agent, glibenclamide (Anreddy et al., 2010; Meenakshi et al., 2010).

8. Conclusion and future research

The present review evaluated the traditional uses and pharmacological activities of representative members of the Aizoaceae. Most species are used as ornamentals and form part of specialist succulent collections. The traditional uses of popular genera such as *Mesembryanthemum, Sesuvium, Trianthema* and *Carpobrotus* are well documented in South African and Indian traditional medicine systems for their antidepressant, anxiolytic, antimicrobial, anti-inflammatory, and antioxidant effects. However, few scientific studies have comprehensively validated their clinical efficacy or safety. Lesser-known genera like *Ruschia, Lithops* and *Delosperma* have been used in traditional medicine, especially in the southern Africa region, without any significant scientific validation of therapeutic activity. Hence, isolation and chemical characterization of therapeutic compounds of interest are a potential research focus for further studies. It was noted that the taxonomic discrepancies within the family add to existing confusion regarding species delimitation and reliable evaluation of most taxa. For this reason, evidence of biological activity based on species relatedness should be carefully reviewed. Moreover, incorrect and/or duplicated species nomenclature, and morphological changes which have contributed to the taxonomic irregularities within the Aizoaceae may be resolved by future studies focusing on genomic analyses and chemotaxonomic markers. It is apparent that the findings of most studies on the Aizoaceae are inconsistent and cannot be used to make accurate conclusions regarding the family. Moreover, a sparse number of publications in recent years have comprehensively addressed the ethnobotany, pharmacognosy and chemical constituents of the hyperdiverse Aizoaceae, thus these focus areas are worthy of further investigation.

Funding

This study was supported by funding received from the National Research Foundation, South Africa.

CRediT authorship contribution statement

B. Kalicharan: Conceptualization, Investigation, Writing – original draft. **Y. Naidoo:** Supervision, Writing – review & editing. **J. van Staden:** Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that there is no conflict of interest.

Data availability

Data will be made available on request.

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