Journal of Ethnopharmacology 256 (2020) 112745

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

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

A review of the ethnobotany, contemporary uses, chemistry and pharmacology of the genus *Thesium* (Santalaceae)

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ARTICLE INFO

Keywords:
Africa
Asia
Medicinal plants
Thesium chinense
Traditional uses
Kaempferol

ABSTRACT

Ethnopharmacological relevance: Many plant species representing the hemi-parasitic genus *Thesium* play important roles in communities around the globe as evidenced by the numerous ethnobotanical and contemporary uses, and pharmacological activities. However, no attempt has been made to amalgamate and analyze all of the available information. A comprehensive survey is needed to highlight knowledge gaps, as well as to determine the economic importance and commercial potential of the genus.
Aims of this review: To provide a comprehensive report on the species diversity, geographical distribution, ethnobotany, contemporary uses, chemistry, pharmacology and toxicology of the genus *Thesium*, as well as to give insights into possible future research opportunities.
Materials and methods: Literature on the ethnobotany, contemporary uses, chemistry and pharmacology of *Thesium* was gathered from standard search engines (Google, Google Scholar, PubMed, SciFinder and Scopus) using the phrase *Thesium,* as well as generic synonyms. Additional information came from relevant books, theses, patents and label information from herbarium specimens in the National Herbarium in Pretoria, South Africa. Information on geographical distributions was compiled from regional floras, regional revisions, original species descriptions and databases (GBIF, IPNI, Plants of the World online and The Plant List). Scientific names and synonyms were validated through www.plantsoftheworldonline.org.
Results: A total of 23 *Thesium* species, 17 from Africa and six from Asia, were found to have traditional and contemporary uses. Despite the near cosmopolitan distribution of the genus, no uses were recorded for Europe, Australia and North America. *Thesium* plants are most commonly used as medicines (18 species), functional foods and beverages (seven species), charms (six species) and crafts (three species), but also have several other minor uses. Charm uses were restricted to southern and East Africa, while several contemporary uses such as functional feeds and fodders, growth mediums and fertilizers and veterinary medicine were unique to Asia. *Thesium chinense* is by far the most utilized and versatile species with a total of 173 uses in nine use categories, followed by *T. longifolium* with 39 uses in six use categories. No specific trends were observed in the plant parts used. As a medicine *Thesium* is used to treat 137 ailments, predominantly reproductive and breast (22), respiratory tract (18), degenerative (11), digestive (11) and urinary (10) ailments. Chemical analyses are available for only eight species, with flavonoids, fatty acids and alkaloids as the main compounds. The potential influence of the host plants on the chemistry and pharmacology remains unexplored. The pharmacological activities of two species, *T. chinense* and *T. viride,* have been studied, while three other species are reported to be poisonous. *Thesium chinense* has analgesic, anti-inflammatory, anti-oxidation, chemopreventive, cytotoxic and other general therapeutic properties, and *T. viride* anti-bacterial activity.
Conclusion: This study has highlighted the ethnobotanical, contemporary and pharmacological importance of *Thesium* and informed possible future research opportunities. While ample information is available on the traditional uses of the richly diverse African *Thesium* species, the few Asian species dominate the literature on contemporary uses and pharmacology, while relevant literature on species in the rest of the world is altogether lacking. In light of the popularity of Asian species as ingredients in contemporary medicines and products, further research is needed into African species and their uses, including potential commercial uses. As an im-

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https://doi.org/10.1016/j.jep.2020.112745
Received 5 December 2019; Received in revised form 5 March 2020; Accepted 5 March 2020
Available online 15 March 2020
0378-8741/

portant medicinal hemi-parasite in both Africa and Asia, the identities of ethnobotanically relevant species and their phytochemistry, pharmacology and toxicology remain underexplored and require more research attention.

1. Introduction

Thesium L. is the largest genus in the Santalaceae, with ± 350 species occurring worldwide (Nickrent and García, 2015). No detailed information is available on the continental distribution of the species, but the majority of them occur in Africa, with smaller numbers in Europe, Asia, Australia, South America and North America.

Thesium represents a taxonomic challenge because species are usually nondescript and therefore often overlooked, and the diagnostic characters are both variable (e.g. habit) and cryptic (e.g. details of the minute flowers). There has not been a comprehensive global revision since the time of De Candolle (1857) and the taxonomy has become outdated. The need for a revision is evident from the recent discovery of 11 species new to science (Visser et al., 2018; García et al., 2018; Lombard et al., 2019; Zhigila et al., 2019a, 2019b). A global approach and broad, multidisciplinary study is required to unravel the systematics and potential uses of this large and poorly known genus.

Since the first published note on the use of *Thesium* (Hill, 1910), several studies have reported traditional medicinal and other uses of *Thesium* species in both Africa and Asia (e.g., Watt and Breyer-Brandwijk, 1962; Adjanohoun, 1989; Neuwinger, 2000; Von Koenen, 2001; Parveen et al., 2006, 2007; Huang et al., 2009; Van Wyk and Gorelik, 2017). For example, *T. viride* plants from Nigeria are used as a treatment for jaundice, liver enlargement, splenomegaly and ulcers (Iwu, 2014; Shehu et al., 2016), while whole plants of *T. wightianum* from India are fastened to the cheek to prevent swelling (Murugesan et al., 2005). *Thesium hystrix* (Fig. 1A) is a traditional southern Africa treatment for various ailments including respiratory, bladder and kidney problems (Watt and Breyer-Brandwijk, 1962), and *T. spicatum* (Fig. 1C) a medicinal herbal tea used by local people from the Cape in South Africa for more than 100 years (Marloth, 1917; Van Wyk and Gorelik, 2017). Numerous contemporary uses have also been reported for the genus. *Thesium chinense* (Fig. 1D) and *T. longifolium* are popular ingredients in contemporary Asian foods and beverages, including several patented recipes (Wang, 2014a, 2018a; Zhang, 2014a; Tong, 2015a), and a plethora of contemporary medicines used to treat an extensive array of ailments (e.g., Yu et al., 2014; Chen, 2015c; Liu, 2016b; Wang, 2017c). Some therapeutic properties such as analgesic, anti-bacterial, anti-inflammatory, chemopreventive and cytotoxic activities have been reported for the genus, mainly from the well-known and widely studied *T. chinense* (e.g., Nam et al., 2003; Parveen et al., 2007; Lee et al., 2009; Liu et al., 2018).

Despite the apparent traditional and contemporary importance of *Thesium* species, no attempt has been made to amalgamate all of the available information. Furthermore, in view of the numerous recorded medicinal uses of *Thesium* species, a comprehensive review of the chemistry and pharmacology of the genus is needed, not only to gain insights into its therapeutic potential, but also to determine gaps in our knowledge. The aim of this study was to provide a comprehensive report on the geographical distribution, ethnobotany, contemporary uses, chemistry and pharmacology of the genus *Thesium*, as well as to give insights into possible future research opportunities.

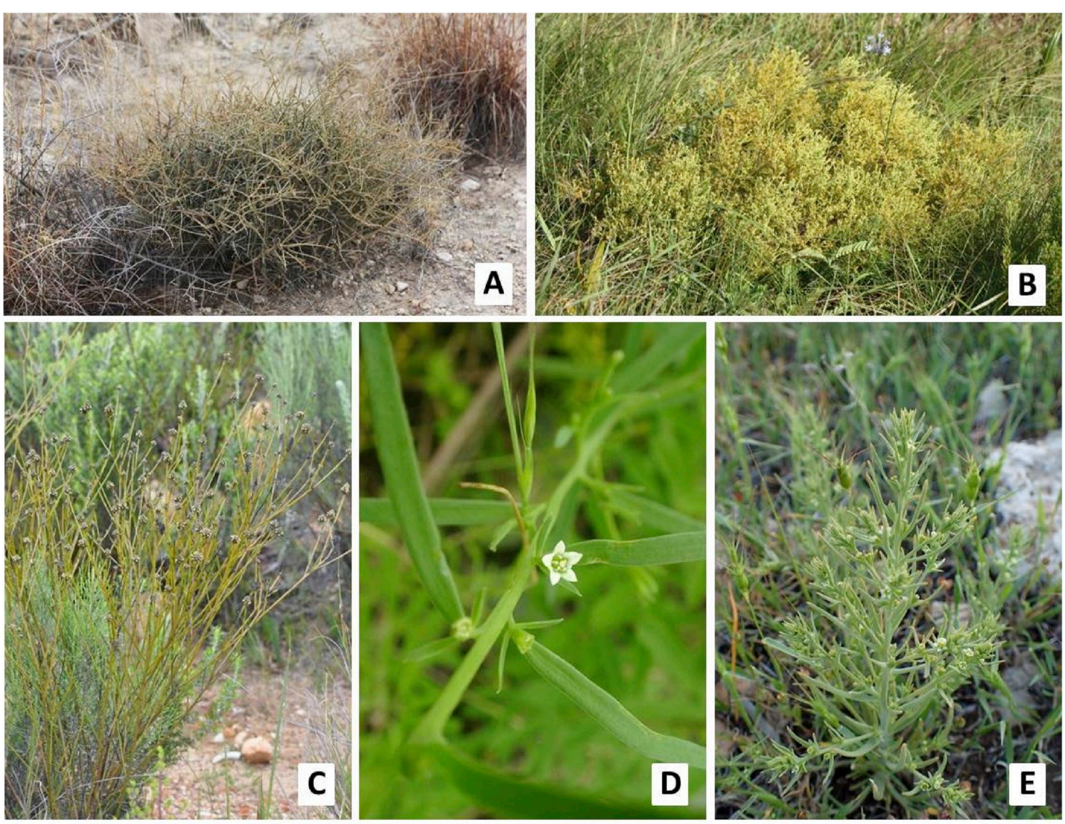

Fig. 1. Some *Thesium* species with traditional and contemporary uses (A-D), and toxicological relevance (E). (A) *T. hystrix*, (B) *T. pallidum*, (C) *T. spicatum*, (D) *T. chinense* and (E) *T. humile*. Photographs by M.M. le Roux (A, B), B.-E. van Wyk (C), Loasa (D) and Krzysztof Ziarnek, Kenraiz [CC BY-SA (https://creativecommons.org/licenses/by-sa/4.0)] (E).

Table 1
A summary of the global distribution of the genus *Thesium*, as well as the numbers of species with traditional and contemporary uses, known phytochemicals and bioactivities in various parts of the world. Species numbers are here summarised for the first time, based on a diversity of literature sources and databases (see Materials and methods).

Geographical region	Total number of species	Species with known uses (% of total diversity)	Species with known phytochemicals (% of total diversity)	Species with known bioactivities (% of total diversity)
Africa	± 260	17 (± 7%)	3 (± 1%)	3 (± 1%)
North Africa	5	0 (0%)	2 (40%)	2 (40%)
West Africa	4	1 (25%)	0 (0%)	1 (25%)
Central Africa	± 45	1 (± 2%)	0 (0%)	1 (± 2%)
East Africa	± 50	3 (± 6%)	0 (0%)	1 (± 2%)
Southern Africa	± 175	12 (± 7%)	1 (< 1%)	1 (< 1%)
Madagascar	7	0 (0%)	0 (0%)	0 (0%)
Australia	1	0 (0%)	1 (100%)	0 (0%)
Eurasia	± 70	6 (± 8%)	6 (± 8%)	3 (± 4%)
Asia	± 45	6 (± 13%)	6 (± 13%)	3 (± 7%)
Europe (incl. the Canary Islands)	± 35	0 (0%)	2 (± 6%)	1 (± 3%)
North America	1	0 (0%)	0 (0%)	0 (0%)
South America	3	0 (0%)	0 (0%)	0 (0%)
Global total	± 350	23 (± 7%)	8 (± 2%)	5 (± 1%)

2. Materials and methods

A first bird's eye view of the global diversity of *Thesium* species (as presented in Table 1) is based on the following major sources as of December 2019: regional floras (e.g., Flora Europaea, Hendrych, 1993; Flora of Australia, George, 1984; Flora of China, Nianhe and Gilbert, 2003; Flora of Siberia, Krasnoborov and Malyschev, 2003; Flora of the U.S.S.R., Bobrov, 1970; Flora of Tropical East Africa, Polhill, 2005; Flora Zambesiaca; Hilliard, 2006), regional revisions (e.g., Hill, 1925), original species descriptions (e.g., De Candolle, 1857; Sonder, 1857; Hill, 1915; Brown, 1932; Bobrov, 1936; Robyns and Lawalrée, 1961; Hedge and Hendrych, 1964; Lawalrée, 1985; Zhigila et al., 2019b) and databases [e.g., African Plant Database (APD), www.ville-ge.ch/musinfo/bd/cjb/africa/recherche.php; Global Biodiversity Information Facility (GBIF), www.gbif.org; International Plant Names Index (IPNI), www.ipni.org; Plants of the World online, www.plantsoftheworldonline.org; The Plant List, www.theplantlist.org]. For some species, circumscriptions were evaluated by studying type specimens (on JSTOR Global Plants, plants.jstor.org) and herbarium collections (e.g., BM, K, NBG, PRE; acronyms as per Thiers, 2019), as part of an ongoing taxonomic study. Geographical divisions in sub-Saharan Africa follow Van Wyk (2015), with the remaining African countries being grouped under North Africa. The Europe-Asia division follows National Geographic (1999).

An extensive search for traditional and contemporary uses, chemistry and pharmacology of *Thesium* was completed using information from books, journal articles, patents, theses and label information from herbarium specimens in the National Herbarium in Pretoria, South Africa (PRE). Searches were also conducted in the Google, Google Scholar, PubMed, SciFinder and Scopus databases using the keyword *Thesium*, as well as current synonyms of the genus: *Austroamericium* Hendrych, *Chrysothesium* (Jaub. & Spach) Hendrych, *Kunkeliella* Stearn and *Thesidium* Sond. Where plant use information was taken from herbarium specimens, the collector name and number, and the herbarium abbreviation are provided. Scientific names and synonyms were validated through www.plantsoftheworldonline.org as it was found to be the most up to date database. Author citations given in Tables 2–4 are not repeated in the text. Only accepted *Thesium* species were included in analyses and summaries. Chemical structures of selected chemical constituents were drawn using ChemDraw Ultra 12.0.2.1076 (© 1986-2010 CambridgeSoft software). All figures and graphs were compiled in Excel and PowerPoint (© 2010 Microsoft Corporation).

Regarding Chinese patents, where original patent information was presented in Chinese, automatic computer translations provided by the SciFinder platform were used. These translations were corroborated through comparison with translations provided by Google Patents (patents.google.com). In the reference list and citations, English translations of patent authors and titles (originally in Chinese) are given, as taken directly from SciFinder or Google Patents. These author names and titles might differ slightly when using alternative electronic translators. English translations of plant parts used were interpreted as follows: “whole plant” as the entire plant; “grass”, “herb” or “herbs” as above-ground parts; “roots” as below-ground parts. Where Latin species names differed between SciFinder and Google Patent translations, or lacking altogether, the species were listed as *Thesium* sp. It is noteworthy that no *Thesium* species are included in classical Chinese texts and pharmacopoeias, including the 3214 monographs of the official Chinese Pharmacopoeia (2005).

3. Results

3.1. Global (continental) diversity

The genus *Thesium* has ± 350 species with the centre of diversity in southern Africa (± 175 species), while the remaining species are distributed throughout Central (± 45 species), East (± 50 species), West (four species) and North Africa (five species), Madagascar (seven species), Asia (± 45 species), Europe (± 35 species), Australia (one species), and North (one species) and South America (three species). A summary of the global distribution of the genus is provided, in Table 1, for the first time since 1857.

3.2. Overview of uses

A total of 23 *Thesium* species (7% of the genus) were found to have traditional and contemporary uses. Despite the fact that *Thesium* has a near cosmopolitan distribution, use-records were restricted to Africa (17 species, 7% of the total ± 260 species) and Asia (six species, 13% of the total ± 45 species), with no uses being recorded for the remainder of its distribution range (Table 1). Uses were divided into the following ten categories (the corresponding number of species is provided in brackets): medicine (18), functional foods and beverages (seven), charms (six), crafts (three), functional feeds and fodders (two), growth mediums and fertilizers (two), hygiene (two), veterinary medicine (two), plant disease control (one) and other (one) (Fig. 2). Differences in the geographical distribution of use categories were apparent. The use of *Thesium* species as charms was unique to southern and East Africa, while six of the ten use categories (functional feeds and fodders, growth mediums and fertilizers, hygiene, other, plant disease control and veterinary medicine) only had Asian representatives. These six use

Table 2

List of ethnobotanically important species of *Thesium*, their vernacular names, the country of origin of the ethnobotanical information, whether the plant is used singly or in mixtures, use category (underlined) and information, and the plant part used. Abbreviations are as follow: **1)** language of vernacular name, Af = Afrikaans, Ar = Arabic, E = English, C = Chinese, D = Dutch, H = Han, Ha = Hausa, I = Irula, J = Japanese, K = Kimbundu, Ki = Kisafwa, U = Unspecified, S = Sesotho, X = isiXhosa and Z = isiZulu, **2)** plant part used, A = aboveground parts, B = belowground parts, E = entire plants, L = leaves, and S = stems, and **3)** references (in square brackets), A1 = Adjanohoun (1989), A2 = Afolayan et al. (2014), A3 = Ahn (1998), B1 = Baker and Hill (1911), B2 = Belakhdar et al. (2014), B3 = Bosch (2008), B4 = Bossard (1996), C1 = Chekole (2017), C2 = Cunningham (1988), G1 = Gelfand et al. (1985), G2 = Gharbo et al. (1969), G3 = Guillarmod (1971), H1 = Hill (1910), H2 = Hill (1915), H3 = Hill (1925), H4 = Huang et al. (2009), H5 = Hutchings (1996), I = Iwu (2014), K1 = Kepe (2007), K2 = Kose et al. (2015), L1 = Lee (1976), L2 = Lee et al. (2008), L3, = Liu et al. (2018), M1 = Marloth (1917), M2 = Moffett (2010), M3 = Moteetee and Van Wyk (2011), M4 = Moteetee et al. (2019), M5 = Murugesan et al. (2005), M6 = Muschler (1912), N1 = Nam et al. (2003), N2 = Neuwinger (2000), P1 = Parveen et al. (2006), P2 = Parveen et al. (2007), P3 = Philander (2011), Q = Quattrocchi (2000), R = Rood (1994), S1 = Shehu et al. (2016), S2 = Smith (1966), S3 = Stander et al. (2019), S4 = Stephen-Lewis (1936), S5 = Steyn (1935), S6 = Sun et al., (2019), T1 = Thomas (2002), T2 = Thornton-Barnett (2013), V1 = Van Wyk et al. (1997), V2 = Van Wyk et al. (2002), V3 = Van Wyk and Gorelik (2017), V4 = Von Koenen (2001), W1 = Watt and Breyer-Brandwijk (1962), W2 = Welcome and Van Wyk (2019), W3 = Williams et al., 2001, X = Xuan et al., (2012), Z1 = Zhong et al. (2013) and Z2 = Zukulu et al. (2012). Vernacular names and uses recorded for the first time are in bold. Uses specifically indicated as traditional are indicated with an "*".

Scientific name	Vernacular name	Country	Used alone or mixed	Category and use	Plant part used
Thesium angulosum A.DC.	*lentsoe* (S) [K2, M4], *lisiu-lilale* (S) [G3], *marakalle* (S) [G3, M3, T2]	Lesotho, South Africa	Single use	*Charm, used in rituals [T2]. *Medicinal, treatment for digestive ailments [M4], heartburn [G3, M3, W1], internal tumours [K2].	B [K2] E [T2]
Thesium asterias A.W.Hill	*dye-bossie* (Af) [S2]	South Africa	Single use	*Craft, no uses recorded, but the Afrikaans vernacular name suggests that it might be used as a dye.	–
Thesium australe R.Br.	austral toadflax (E) [Q] toadflax (E) [Q]	Australia	–	–	–
Thesium carinatum A.DC.	*jakkalstee* (Af) [V3]	South Africa	–	*Food, herbal tea [V3, W2] (possible adulterant of rooibos tea, *Aspalathus linearis* (Burm.f.) Dahlg.).	L [V3] S [V3]
Thesium chinense Turcz.	*kana-biki-so* (J) [Q]	Japan	–	–	–
	–	Korea	–	Medicinal, treatment for bronchial problems [A3], inflammatory mastitis [A3], tuberculosis [A3] and other unspecified medicinal uses [L1].	–
	chinese bastardtoadflax (E) [H4]	Taiwan	Single use	Medicinal, treatment for common colds [H4], cystitis [H4], dizziness [H4], heat shock [H4], kidney vacuity lumbar pain [H4], lung abscesses [H4], lymphatic tuberculosis [H4], mastitis [H4], pneumonia [H4], seminal emission and efflux [H4], tonsillitis [H4], upper respiratory tract infections [H4]. Root can stabilize "qi" [H4].	B [H4] E [H4]
	bai rui cao (C) [T1], bairui herb (E) [L3]	China	Single use	Medicinal, pharmacological activities: analgesic [P2], anti-inflammatory [P2]. Treatment for coughing [P1], headaches [P1], fever [T1], inflammation [T1, P1], mastitis [T1], pneumonia [P1], sore throat [T1, P1], tonsillitis [T1].	E [P2, T1]
	–	–	Single use	Medicinal, pharmacological activities: anti-bacterial [L3], anti-inflammatory [S6], chemopreventive [N1]. Treatment for nephropathy [X].	
	–	–	Additive in mixture	Medicinal, treatment for laryngopharyngeal reflux disease [Z1], oral diseases [L3].	
Thesium cinereum A.W.Hill	*kangue* (K) [B4]	Angola	Single use	*Medicinal, bronchitis [B4].	B [B4]
Thesium confine Sond.	*teringbossie* (Af) [S2]	South Africa	Single use	*Medicinal, no uses recorded, but the Afrikaans vernacular name suggests a treatment for tuberculosis.	–
Thesium costatum A.W.Hill	*bohoho* (S) [G3, M2, M4, W1], *marakalle* (S) [G3, K2, M4, T2], *marakalle-a-manyenyane* (S) [M2, G3], *sebitsane* (S) [M2, G3, W1], *sebitsoane* (S) [G3], *sebitswane* (S) [M2]	Lesotho, South Africa	Single use	*Charm, used in rituals [T2]. *Medicinal, treatment for asthma [K2], chest colds [M2, G3, W1], digestive ailments [M4], respiratory ailments [M4].	E [K2, T2]
Thesium disciflorum A.W.Hill	white storm (E), *witstorm* (Af)	South Africa	Single use	*Charm, used as an amulet for good luck in court cases [P3]. *Medicinal, treatment for gastric ailments, removes poison from the stomach [P3].	B [P3]
Thesium fastigiatum A.W.Hill *(*= *T. tamariscinum* A.W.Hill)	–	Mozambique	Single use	*Craft, roots used for fish traps [B1, H1].	B [B1, H1]
	inyala (Ki) [*Levett and Kayombo 3401* (PRE)]	Tanzania	Single use	***Craft, plant crushed and added to water to wash children's hair to restore colour** [*Levett and Kayombo 3401* (PRE)].	–

(*continued on next page*)

Table 2 (*continued*)

Scientific name	Vernacular name	Country	Used alone or mixed	Category and use	Plant part used
Thesium himalense Royle	*shanbaizhi* (H) [L2], *siabaiz* (U) [L2]	China	Single use	*Medicinal, decoction as treatment for hepatitis [L2], infant pneumonia [L2].	E [L2]
Thesium humifusum DC.	bastard toadflax (E) [Q]	–	–	–	–
Thesium humile Vahl	*ktitila* (U) [B2]	Morocco	Single use	Poisonous, toxic to animals [B2].	
	habb-el-areysh (Ar) [G2, M6]	Egypt	–	–	–
Thesium hystricoides A.W.Hill	*ystervarkbossie* (Af) [S2]	South Africa	–	–	–
Thesium hystrix A.W.Hill	*kleinswartstorm* (Af) [R, S2, T2], *wit-opslag* (Af) [S4]	South Africa	Single use	*Medicinal, treatment for bladder and kidney infections [N2, R, W1], cough (expectorant) [N2, R, S4, T2, V1, W1], respiratory ailments [R], tuberculosis [N2, R, V1, W1]. May bring on abortion [W1]. Used for blood purification [N2, R, V1, W1].	A [W1] B [N2, R, T2, V1, W1]
Thesium junceum Bernh. var. *junceum*	*motajoane* (S) [G3] *motajwane* (S) [M2]	South Africa	–	–	–
Thesium junceum Bernh. var. *plantagineum* A.W.Hill	***isiqhumiso sentyulube*** (X) [*Van Eeden 401*]	South Africa	Single use	**Medicinal, treatment for intestinal worms in humans and animals** [*Van Eeden 401*].	–
Thesium kilimandscharicum Engl.	–	Ethiopia	Single use	*Medicinal, ash of the burnt plant applied topically to treat dactylitis [C1].	E [C1]
Thesium lacinulatum A.W.Hill	–	Namibia	Additive in mixture	*Medicinal, decoction with *Lacomucinaea lineata* (L.f.) Nickrent and M.A.Garcia is used to treat uterine problems [B3, N2, V4] and venereal diseases [B3].	B [B3, N2, V4]
Thesium namaquense Schltr.	*gifbossie* (Af) [Q, S2, S5], *namakwa-thesium* (A) [Q] namaqua thesium (E) [Q] poison bush (E) [Q, V2]	South Africa	–	Poisonous, harmful or fatal to animals [S5, V2 W1].	A [S5, W1]
Thesium pallidum A.DC.	*umayisaki* (X - isiMpondo) [K1]	South Africa	–	*Medicinal, no specific uses recorded [K1].	–
	umayisake obomvu (X) [Z2], yellow thesium (E) [Z2]	South Africa	Single use	*Charm, love charm administered as a body wash, purgative or steam treatment [Z2].	B [Z2]
Thesium sp. (cf. *T. pallidum*)	red mahesaka (E/Z) [W3], red maisaka (E/Z) [W3], red maseka (E/Z) [V1], red maysaka (E/Z) [W3], red mysaka (E/Z) [W3], *umahesaka-obomvu* (Z) [H5, V1]	South Africa	–	*Medicinal, no specific uses recorded [H5, V1]. Traded in the Witwatersrand umuthi shops [W3].	B [C2, H5, W3]
Thesium racemosum Bernh.	*bohoho* (S) [G3, M2, Q], *marakalle* (S) [G3, M2, T2], *marakalle-a-manyenyane* (S) [G3, M2, W1], *sebitsane* (S) [G3, M2], *sebitsoane* (S) [G3], *sebitswane* (S) [M2]	Lesotho	–	*Medicinal, chest colds [W1]. *Charm, used in rituals [T2].	E [T2]
Thesium refractum C.A.May	–	Korea	–	*Medicinal, no specific uses recorded [L1].	–
Thesium resedoides A.W.Hill (= *T.burkei* A.W.Hill)	*mabelebele* (S) [M2, G3]	Lesotho	–	–	–
Thesium spicatum L. (= *T. macrostachyum* A.DC.)	*lidjes tee* (Af) [M1, V3], *lidjiestee* (Af) [S2, V3], *riettee* (Af) [S3], reed tea (E) [S3]	South Africa	Single use	*Food, herbal tea [V3, S3, W2].	L [V3] S [V3]
Thesium strictum P.J. Bergius	*teringbos* (Af) [M1, S2, V3], *umbiza* (X) [A2]	South Africa	Single use Single use	*Medicinal, paste used to treat boils and wounds [A2]. *Food, herbal tea [V3, W2].	L [A2] S [V3]
Thesium stuhlmannii Engl.	**umwita** (Ki) [*Levett and Kayombo 3402* (PRE)]	Tanzania	Single use	***Charm, shopkeepers chew on the roots to attract customers** [*Levett and Kayombo 3402* (PRE)].	B [*Levett and Kayombo 3402* (PRE)]
Thesium triflorum Thunb.	*gifbossie* (Af) [S2]	South Africa	Single use	Associated with livestock deaths, but was proved to be non-toxic [W1].	–
Thesium utile A.W.Hill	*besembossie* (Af) [S2]	South Africa	Single use	*Craft, used as brooms [H2, H3]. *Medicinal, stem chewed as a treatment for gastric ailments [W1].	A, [H2, H3] S [W1]
Thesium viride A.W.Hill	–	Benin	Single use	*Medicinal, jaundice [A1, N2, B3].	A [A1, B3, N2] L [A1, B3, N2]
	huntu (Ha) [S1]	Nigeria	Single use	*Medicinal, pharmacological properties: anti-bacterial [S1]. Treatment for jaundice [I, S1], liver enlargement [I, S1], splenomegaly [I, S1], ulcers [S1].	A [I, S1]

(*continued on next page*)

Table 2 (*continued*)

Scientific name	Vernacular name	Country	Used alone or mixed	Category and use	Plant part used
Thesium wightianum Wall. ex Wight	*anaikchi* (I) [M5]	India	Single use	*Medicinal, the whole plant is fastened to the cheek to prevent swelling [M5].	E [M5]
Thesium sp.	*lentsoe* (S) [G3], *lisiu-lilale* (S) [G3], *marakalle* (S) [G3], *marakalle-a-manyenyane* (S) [G3], *sehalahala* (S) [G3]	Lesotho	–	–	–
Thesium sp.	*disiudilale* (S) [M2], *lentswe* (S) [M2], *marakalle* (S) [M2], *marakalle-a-manyenyane* (S) [M2], *mofetola* (S) [M2], *sehalahala* (S) [M2]	Lesotho, South Africa	–	–	–
Thesium sp.	*bohoho* (S) [W1], *sebitsane* (S) [W1]	Lesotho, South Africa	Single use	*Medicinal, chest colds [W1].	–
Thesium sp.	*marakalle* (S) [W1]	Lesotho, South Africa	Single use	*Medicinal, chest colds [W1].	–
Thesium sp.	*marakalle* (S) [T2]	South Africa	Single use	*Charm, used in rituals [T2].	E [T2]
Thesium sp.	–	Southern and eastern Africa	Additive in mixture	*Hygiene, refreshing bath decoction mixed with *Afrosciadium magalismontanum* (Sond.) P.J.D.Winter (= *Peucedanum magalismontanum* Sond.) roots and *Polygala rarifolia* DC. roots [W1].	–
Thesium sp.	–	Zimbabwe	Single use	*Medicinal, infusion for the treatment for abdominal pain in infants [G1].	B [G1]
Thesium sp.	–	Zimbabwe	Single use	*Medicinal, treatment for weak joints (applied to cuts made on joins) [G1].	B [G1]

categories resulted from 247 contemporary Chinese, Korean and American patents where either *T. chinense*, *T. longifolium*, *T. ramosoides* or *T. refractum* were used in combination with other species and ingredients. A checklist and a summary of uses of ethnobotanical important *Thesium* species are provided in Table 2. A summary of *Thesium* species included in patents and patent details is provided in Table 3.

3.3. Most utilized species

Thesium chinense (an East Asian endemic) dominated the literature in both number of uses and versatility. A total of 176 uses were recorded for this species across all use categories, except for charms (Figs. 3, 4). The large number of contemporary medicinal uses of this species (94) is in contrast to the lack of recorded history as a medicinal plant and its absence from the Chinese Pharmacopoeia (2005) and other publications on Traditional Chinese Medicine (e.g., Körfers and Sun, 2009). The propagation and cultivation of *T. chinense* has been the subject of numerous studies (e.g., Yuan et al., 2002a; Guo et al., 2011; Luo and Guo, 2012a, 2012b; Guan et al., 2014; Huang et al., 2016; Huang et al., 2018), to ensure a sustainable supply of high quality raw material (Yuan et al., 2002b; Xu et al., 2008, 2009; Luo and Guo, 2011; Song et al., 2017). Similar methodologies may be suitable for African species with commercial potential.

Thesium longifolium, also from Asia, had the second most uses (39) included in five use categories: functional foods, growth mediums and fertilizers, hygiene, medicine and veterinary medicine (Figs. 3, 4). In contrast, the majority of species all had less than seven uses and each formed part of two or less use categories (Figs. 3, 4).

3.4. Plant parts used

For this analysis, patents were excluded as translations of the plant parts used were often dubious or entirely absent. Plant part data were only available for four of the ten use categories (charms, crafts, functional foods and beverages and medicines), and more information is therefore needed for a complete picture. Available data showed that in the majority of species (10), below-ground parts (including roots and rhizomes) were utilized, followed by entire plants (eight species), leaves and stems (four species each) and above-ground parts (including stems, leaves, flowers and fruits) (eight species) (Fig. 5). There was a general lack of trends between use categories and plant parts utilized, with the possible exception of leaves and stems, which were only used as functional foods and beverages.

3.5. Uses

3.5.1. Medicine

A total of 18 *Thesium* species (12 from Africa and six from Asia) were used, both singly and as part of mixtures, to treat 137 ailments throughout the body. Recorded ailments were divided into 10 categories according to the affected body parts. *Thesium* species were most commonly used to treat reproductive and breast-related ailments (22 ailments, five species), followed by respiratory tract ailments (18 ailments, seven species), degenerative diseases (11 ailments, three species), digestive ailments (11 ailments, eight species), urinary ailments (10 ailments, four species), nervous system disorders (eight ailments, two species), oral ailments (eight ailments, three species), skin ailments and wound healing (eight ailments, three species), liver, spleen and pancreas-related ailments (five ailments, four species), as well as 36 miscellaneous ailments not included in these categories (Figs. 6, 7). Each ailment category is discussed below, first for African species, followed by Asia species.

3.5.1.1. Reproductive and breast ailments. Five *Thesium* species, *T. chinense*, *T. hystrix*, *T. lacinulatum*, *T. longifolium* and *T. refractum* were used to treat 22 ailments related to the breasts and reproductive organs.

Table 3

Thesium species included in patents, with their uses and use categories (underlined), as well as the plant parts used. Species are used in combination with other plants and ingredients unless stated otherwise. Abbreviations are as follow: **1)** plant part used, A = aboveground parts, B = belowground parts, E = entire plants, L = leaves and S = stems, and **2)** patent references (in square brackets), A1 = An et al. (2019), A2 = An and Meng (2016), B1 = Bai (2015a), B2 = Bai (2015b), B3 = Bai (2015c), B4 = Bi and Qing (2016), B5 = Bu et al. (2017), C1 = Cao and Zhou (2015), C2 = Cen (2017), C3 = Chang et al. (2008), C4 = Chen (2015a), C5 = Chen (2015b), C6 = Chen (2015c), C7 = Chen (2016a), C8 = Chen (2015d), C9 = Chen, 2015e, C10 = Chen (2014a), C11 = Chen (2017a), C12 = Chen (2017b), C13 = Chen (2013a), C14 = Chen (2014b), C15 = Chen (2016b), C16 = Chen (2016c), C17 = Chen (2013b), C18 = Chen et al. (2016a), C19 = Chen and Liao (2017), C20 = Chen et al. (2016b), C21 = Choi et al. (2018), D1 = Ding et al. (2017), D2 = Dong et al. (2017), F1 = Fan and Tang (2016), F2 = Fan (2015a), F3 = Fan (2015b), F4 = Fan (2015c), F5 = Fan (2018), F6 = Fang (2017), F7 = Fang et al. (2015), F8 = Feng et al. (2018), G1 = Gan (2014a), G2 = Gan (2014b), G3 = Ge (2016), G4 = Ge (2014), G5 = Guan (2014), G6 = Guan (2006), G7 = Gui (2014), G8 = Guo (2017), H1 = Han (2016a), H2 = Han (2016b), H3 = Han (2015a), H4 = Han (2015b), H5 = Han (2016c), H6 = Hou (2015), H7 = Hu (2008), H8 = Hu (2016), H9 = Hu et al. (2017a), H10 = Hu et al. (2017b), H11 = Hu et al. (2015), H12 = Hu and Yang (2017a), H13 = Hu and Yang (2017b), H14 = Huang (2016), H15 = Huang (2018), J1 = Jeong et al. (2002), J2 = Jiang (2015), J3 = Jiang (2014a), J4 = Jiang (2014b), J5 = Jiang (2018), J6 = Jin (2014a), J7 = Jin (2014b), J8 = Jin (2017), J9 = Jin et al. (2016), J10 = Ju (2014), K1 = Kong (2013), L1 = Lei et al. (2019), L2 = Li (2016a), L3 = Li (2014a), L4 = Li (2018a), L5 = Li (2016b), L6 = Li (2018b), L7 = Li (2016c), L8 = Li (2018c), L9 = Li (2012), L10 = Li (2015a), L11 = Li (2016d), L12 = Li (2014b), L13 = Li, 2016e, L14 = Li (2015b), L15 = Li, 2016f, L16 = Li and Lu (2016), L17 = Li et al. (2014), L18 = Lian (2017a), L19 = Lian (2017b), L20 = Lin (1999), L21 = Lin (2009), L22 = Lin (2016), L23 = Lin (2000), L24 = Liu (2016a), L25 = Liu (2016b), L26 = Liu (2017a), L27 = Liu (2017b), L28 = Liu (2017c), L29 = Liu (2015a), L30 = Liu (2017d), L31 = Liu (2019), L32 = Liu (2016c), L33 = Liu (2014), L34 = Liu (2015b), L35 = Liu (2015c), L36 = Liu and Qu (2016), L37 = Liu et al. (2017), L38 = Liu et al. (2016a), L39 = Liu and Li (2016), L40 = Liu et al. (2015a), L41 = Liu et al. (2015b), L42 = Liu and Han (2015), L43 = Liu et al. (2016b), L44 = Liu and Li (2015), L45 = Lu (2015a), L46 = Lu (2015b), L47 = Lu (2015c), L48 = Lu and Lu (1998), L49 = Lu and Wang (2015), L50 = Luo and He (2015), M1 = Ma (2018), M2 = Ma (2014), M3 = Ma (1997), M4 = Ma and Li (2005), M5 = Meng and Bai (2016), M6 = Min (2006), N1 = Nashun and Han (2006), N2 = Ni (2014), P1 = Pan (2017), P2 = Pan (2018), P3 = Peng (2015), Q1 = Qi (2016), Q2 = Qian (2013), Q3 = Qin (2016a), Q4 = Qin (2016b), S1 = Shi (2018), S2 = Shin et al. (2015), S3 = Song (2014), S4 = Song (2015), S5 = Song (2016), S6 = Song et al. (2013), S7 = Su et al. (2007), S8 = Sun (2016a), S9 = Sun (2016b), S10 = Sun and Ma (2016), S11 = Sun et al. (2018), T1 = Tang (2017), T2 = Tang (2007), T3 = Tang et al. (2016), T4 = Tian (2011), T5 = Tong (2015a), T6 = Tong (2015b), T7 = Tong (2015c), U1 = Unknown author(s), 2014, U2 = Unknown author(s), 2015, U3 = Unknown author(s), 2016a, U4 = Unknown author(s), 2016b, U5 = Unknown author(s), 2016c, U6 = Unknown author(s), 2016d, U7 = Unknown author(s), 2016e, U8 = Unknown author(s), 2016f, U9 = Unknown author(s), 2016g, W1 = Wang (2017a), W2 = Wang (2017b), W3 = Wang (2013), W4 = Wang (2015a), W5 = Wang (2014a), W6 = Wang (2016a), W7 = Wang (2016b), W8 = Wang (2016c), W9 = Wang (2016d), W10 = Wang (2015b), W11 = Wang (2015c), W12 = Wang, 2016e, W13 = Wang (2018a), W14 = Wang (2018b), W15 = Wang (2014b), W16 = Wang (2015d), W17 = Wang (2017c), W18 = Wang, 2016f, W19 = Wang, 2016g, W20 = Wang (2017d), W21 = Wang, 2015e, W22 = Wang, 2015f, W23 = Wang, 2015g, W24 = Wang (2012), W25 = Wang, 2015h, W26 = Wang, 2015i, W27 = Wang et al. (2016a), W28 = Wang and Li (2016a), W29 = Wang and Li (2016b), W30 = Wang et al. (2015), W31 = Wang et al. (2016b), W32 = Wang et al. (2016c), W33 = Wang et al. (2014), W34 = Wang and Xie (2015), W35 = Wang et al. (2016d), W36 = Wang et al. (2017), W37 = Wei (2015a), W38 = Wei (2015b), W39 = Wu (2017), W40 = Wu (2016), W41 = Wu (2015a), W42 = Wu (2015b), X1 = Xiang (1995), X2 = Xie et al. (2015), X3 = Xin (2016), X4 = Xu (2018), X5 = Xu (2016), X6 = Xu (2015a), X7 = Xu (2015b), X8 = Xu (2017a), X9 = Xu (2017b), X10 = Xu et al. (2013), X11 = Xue (2016), Y1 = Yan and Yao (2016), Y2 = Yang (2016), Y3 = Yang (2015), Y4 = Yang and Xu (2016), Y5 = Ye and Zhou (2017), Y6 = Yin (2016), Y7 = Yin and Wang (2018), Y8 = Yin and Gao (2016), Y9 = Yu (2016a), Y10 = Yu (2016b), Y11 = Yu (2015), Y12 = Yu (2017), Y13 = Yu and Xu (2015), Y14 = Yu and Wu (2017), Y15 = Yu et al. (2014), Y16 = Yue (2018), Z1 = Zang (2016), Z2 = Zhang (2014a), Z3 = Zhang (2017a), Z4 = Zhang (2018a), Z5 = Zhang (2017b), Z6 = Zhang (2015a), Z7 = Zhang (2015b), Z8 = Zhang (2015c), Z9 = Zhang (2015d), Z10 = Zhang (2017c), Z11 = Zhang (2017d), Z12 = Zhang (2018b), Z13 = Zhang (2016), Z14 = Zhang (2014b), Z15 = Zhang, 2015e, Z16 = Zhang and Zhao (2015), Z17 = Zhang and Gu (2015), Z18 = Zhang and Li (2014), Z19 = Zhang et al. (2016), Z20 = Zhang et al. (2017), Z21 = Zhang et al. (2010), Z22 = Zhang and Wang (2014), Z23 = Zhang et al. (2015), Z24 = Zhao (2016), Z25 = Zhao (2015a), Z26 = Zhao (2015b), Z27 = Zhao (2015c), Z28 = Zhao (2017), Z29 = Zhao et al. (2016), Z30 = Zheng et al. (2014), Z31 = Zhou (2015a), Z32 = Zhou (2015b), Z33 = Zhou (2005), Z34 = Zhou et al. (2018), Z35 = Zhu (2015a), Z36 = Zhu (2012), Z37 = Zhu (2013), Z38 = Zhu (2008), Z39 = Zhu (2015b), Z40 = Zhu (2016), Z41 = Zhuang (2016).

Scientific name	Category and use	Plant part used
Thesium chinense Turcz.	Craft, aromatic stick (may prevent cough and asthma, treat dizziness and headaches) [W1], ink powder (prevents hay fever, fragrant) [W6], material for medicinal use (antibacterial) [J9, S1], part of a wastewater treatment method [P2], part of silk quilt core (may improve skin quality) [J5], rattan treatment (protects against sun damage, anti-microbial, insect resistant) [X8], shirt fabric (anti-wrinkle, good anti-bending performance, enhances sweat volatility, flame retardant, UV resistant, water resistant) [W9], temporary medicinal filler for the pocket left after tooth extraction (possibly substituted or combined with *T. longifolium* Turcz., *T. himalense* Royle, *T. longiflorum* Hand.-Mazz., *T. refractum* C.A.Mey.) [H6], water-based paint (abrasion resistant, high radiance, strong adhesion, calms mental anxiety) [L39].	A [B1, B2, B5, C6, C20, F2, F3, F4, H3, H4, H14, J6, L17, L22, L32, L33, L37, L43, Q2, S3, S9, T4, T5, W12, W17, W26, W27, W30, W32, W37, X3, X11, Y14, Y15, Z8, Z24, U2, U3, U4, U6, U8, U9] B [L4, L9, L28, M2, Q1, W40, Z6, Z13, Z14] E [B3, C4, C5, C17, F1, F8, L12, L13, L14, L15, L50, W29, W38, X9, Z9, Z22, Z26, Z27, Z31, Z37]
	Functional feeds and fodders, black guinea pig feed (prevents common diseases, promotes growth) [Z10], chicken feed (improves disease resistance and immunity [F6, W39, H8, L27, Y14, Z35], better meat quality [F6], increased egg laying rate [F6, L27], higher growth rate [F6, H8]), duck feed (promotes growth, improves immunity and disease resistance) [H15], eel feed (promotes growth) [H9, H10], feed additive for bamboo rat (Rhizomyidae) breeding (prevents and treats common diseases, promotes growth, increases	

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Table 3 (*continued*)

Scientific name	Category and use	Plant part used
	appetite) [Z11], feed additive for piglets (anti-diarrhoea, increased survival rate) [X10], feed for lactating female cats (improves appetite and increases milk yield) [L28], peafowl feed (high protein content, increased disease resistance, improved immunity) [G5], pheasant feed (prevents coccidiosis, mycoplasmosis, and colibacillosis, increases growth rate) [L40, L41], silver carp feed (arouses appetite [Q2], increases growth rate [Q2, Z12], improves disease resistance [Z12]).	
	Functional food and beverages Health beverages (antibacterial [F8], calms [W41], clears heat [U7, W5], clears sinuses [W5], detoxifies and nourishes kidneys and liver [Y7, W2], fights fatigue [T5], improves sleep quality [T5], increases appetite [T5, W5], inhibits cancer [W2], invigorates blood [T5, W41], invigorates stomach and spleen [Y7], lowers blood sugar [F8], nourishes stomach yin [F8, U7], prevents and treats cardiovascular and cerebrovascular diseases [W2], promotes metabolism [U7], promotes salivation [U7], promotes skin health [W2], relieves throat irritation [W5], removes dampness [W5], replenishes qi [T5, W41, Y7], strengthens immunity [T5, W2], strengthens the brain [W41], tonifies liver [W41], treats constipation [W5], treats swelling in gums [W5]). Functional foods, health additive to rice (clears heat, detoxifies, lowers internal heat) [S9], health cereal [Q1, W40], health oils (clears heat [G2, G1], detoxifies [G2, G1], increases absorption by the body [G2], treats coughing [G2, G1]), health sauce (anti-inflammation, anti-septic, clears heat, detoxifies, improves immunity, increases disease resistance) [P3], health soup (eliminates cold, promotes blood circulation, relaxes tendons, relieves pain) [A2], "hot pot" (Chinese cooking method) seasoning (clears heat [W14, W13], eliminates dampness [W13], nourishes yin [W14], promotes diuresis [W13], promotes salivation [W14], quenches thirst [W14], relieves fever [W13], relieves swelling [W13], tonifies stomach [W14]), noodle dishes (beautifies [W26], boosts immunity [W26, Z2], clears heat [Z2], detoxifies [Z2], enriches and activates blood [Z2], invigorates spleen [W26], lowers blood pressure [Z2], nourishes kidneys [W26, Z2], nourishes qi [W26], prevents skin ageing [Z2], promotes sleep [W26]), rice cake (clears heat, detoxifies, enriches yin, invigorates and replenishes blood, nourishes kidneys, strengthens tendons and bones) [G7], rice dish (beautifies, benefits kidneys, calms, clears heat, delays ageing, detoxifies, nourishes (general), nourishes liver, replenishes energy) [W15], Selenium-enriched health product (benefits qi, replenishes blood) [L13], soft-shelled turtle dishes (aids fatigue prevention [J6], anti-aging [J6], increases immunity [J6], invigorates spleen and stomach [J6], nourishes and invigorates kidneys [J7, J6] and liver [J6], nourishes yin [J7, J6], prolongs life [J7], promotes metabolism [J7]), other health dishes (aids digestion [Z16], anti-fatigue [Z16], assists weight loss [L45], benefits qi [L45], clears heat [L45], clears lungs [L45], detoxifies [L45], increases metabolism [Z16], invigorates spleen [L45], nourishes blood [L45], promotes postpartum lactation [M2], reduces blood pressure [L45], stimulates appetite [Z16], tonifies spleen [Z16], treats constipation [Z16]).	
	Growth mediums and fertilizers, aquatic plant fertilizer [F5, Y12], culture medium for *Burcella* [L37], foliar pear fertilizer [B5], growth medium for *Agaricus* mushrooms (increases growth rate, prevents diseases) [Z14], growth treatment for rice seeds [L18], tomato fertilizer [Y16], treatment for enhanced wheat seed-germination [L19].	

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Table 3 (*continued*)

Scientific name	Category and use	Plant part used
	Hygiene, cosmetic facial mask (clears toxins, cools and refreshes, nourishes skin, delays aging, whitens, preserves moisture) [Z15], decontaminating laundry liquid (fragrant) [X4], female sanitary pad (anti-bacterial) [Y4], filler for shoe insole (anti-microbial, deodorizing) [L8], general antiseptic and anti-bacterial solutions [W16, Z3], hand-wash liquids (anti-bacterial [P1], sterilizes [J10], moisturizes [J10, P1], kills insects [P1]), medical air sterilization spray for operating rooms [W24], preoperative hand sterilizer [Z36], refrigerator disinfecting solution (anti-bacterial [L30, X7], deodorizing [L30, X7]), sanitary ware detergent (sterilizes) [W25], washing solution (promotes blood and qi circulation, relieves swelling) [L12].	
	Medicinal, proposed pharmacological activities: anti-bacterial [G6], anti-biotic properties [L31], anti-cancer effect [A1, Z24], anti-inflammatory [Z33], inhibits tumour proliferation [A1], improves immunity [X9], anti-influenza virus activity [C3].	
	Treatment for acute cystitis [H5, L16, Y15], acute jaundice [B2], acute mastitis [J4], adverse reactions after anaesthesia [L42], arteriosclerosis [C9], bromhidrosis [U3, U4, U6], asthma [M3], bronchial pneumonia in children [W28], bronchitis [M3], cancer related anaemia [Y13], cervical erosion [S6], chronic epididymitis [H14], chronic obstructive emphysema [L25], chronic pyelonephritis [Z19, L32], common colds [C6, T1], common oral diseases (used singly) [W36], constrictive pericarditis [C17], cough (expectorant) [M3, W17, Z33], flattened nipples [N1], gastric ulcer [W7], genital warts [X11], gout [C12, Y10, Z27], hangovers [C21], gynaecological inflammation [S6], gynaecological problems [W4], haemorrhoids [U8, U9], haemostatic effect [L33], heat induced strangury [X3, Z1], heat stroke [Z29, Z7, Z9, Z8], hepatitis A [B2], hives [S3, W21, Y1], hydrocephalus [W27], hydrothorax [S8], hysteromyoma [L14], infantile pinworm infection [D2], infection at the outlet of a peritoneal dialysis tube [W32], insomnia [H4, H3, L10, X9], irregular menstruation [K1], lymph node swelling [F4, F3, F2, L50], malnutrition [S5], mammary gland hyperplasia [Z18], menopausal symptoms [X2], migraine [T6], mumps in children [C20], neurasthenia [W29], night sweat [L25], oesophagitis [Z37], oral ulcers [Z31], osteoarthritis [F1], osteoporosis [L49], pancreatitis [B4, B3, B1, L2], perianal abscesses [L22], pinkeye [W23], pitted breast skin [N1], pleural effusion [H1], prolapse of lumbar intervertebral disc [L46], postoperative adhesive intestinal obstruction [Z41], post-operative (prostate) bladder spasm pain [W34], postpartum depression [L43], premature ovarian failure [Z40], puerperal mastitis [W11], pulmonary abscesses [C19, W17], pulmonary embolism [Z26], purpura [C4], purulent meningitis [W30], rheumatoid arthritis [W8, Y11], sleep improving sachet [L7], stenocardia [Z6], tonsillitis [L24, L17, W38, W37], tuberculosis [C5, M3, W35], ulcerative colitis [W12], upper respiratory tract infections [Z4, Z20, C1], urethritis [X5, H2], uterine prolapse [Z39], uterine (womb) coldness [S6], vaginal itching [T4], vascular headaches [L4]. Also used as an anaesthetic drug for gastroscopies [U2], a contrast agent for ultrasounds [L5, L34, L35, U5], to enlarge breasts [L15, N1], lower blood pressure [T7], promote bone development in children (used singly) [S11] and promote postpartum lactation [Z13, Z22]. Promotes the flow of qi and harmonizes qi [L4].	
	Plant disease control, control agent for lawn patch disease [Y2], pest and	

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Table 3 (*continued*)

Scientific name	Category and use	Plant part used
	disease control agent for *Paris polyphylla* Sm. (general [C2], leaf spot [H12], anthracnose [H13]).	
	Veterinary uses, treatment for bovine mastitis [W10, Z23, Z21].	
	Other, carp summerling aquaculture (increased breeding quality and amount, increased disease resistance, increased growth and survival) [Z5].	
Thesium longifolium Turcz.	Functional feeds and fodders, sheep feed (increases feed intake amount, rapid growth and development) [N2].	A [C8, C18, H11, L29, M5, S10, W19, Y8, Z17, Z25] B [L20] E [C7, C8, F7, W20, Z7, Z17, Z32]
	Functional food and beverages Health beverages, internal uses: calms liver [L20, T2], disperses dampness [L20, T2], dissolve stones in the body [L21], dredges meridian [T2], improves eyesight [T2], improves gastrointestinal functions [L21], increases metabolism [L21], maintains and refreshes spirit [L21], promotes overall health [L20], supplements microelements [L21]. External uses: good for the skin [L21], reduces inflammation [L21], refreshing [L21], relieves pain [L21], sterilizes [L21], stops bleeding [L21].	
	Functional foods, bean curd dish (clears heat, detoxifies) [C10], caramel treat (increases immune function, invigorates qi and blood, nourishes liver and kidneys) [L3], flavoured oil (often substituted with *Thesium himalense* Royle) [Z38], health dumpling (activates blood circulation, clears heat, detoxifies, eliminates dampness, promotes urination to treat strangury) [G3], health soups (clears heat [W20, Y6], dispels wind [W20, Y6], relieves fever and pain [Y6], treats common colds [Y6]), rice dish (clears heat, detoxifies, improves digestion, improves eyesight, improves stomach and kidney health, increases disease resistance, increases immune function, protects liver, strengthens stomach) [G4], seasoned trotters (anti-fatigue effect, benefits bile, clears heat, moistens, nourishes yin, protects liver) [W22], walnut kernel powder (enhances memory) [W3].	
	Growth mediums and fertilizers, organic fertilizer (promotes healthy bacterial growth, restrains harmful bacterial growth) [Y3].	
	Hygiene, medicinal plaster (promotes circulation, relieves stasis, relieves pain and swelling) [J3].	
	Medicinal, treatment for acne [C11], Alzheimer's disease [L23], blood stasis [Z32], burns [M1], diarrhoea [W33], epilepsy [L44], haemorrhoids and other anorectal diseases [C16], heat-induced cramps and dizziness [L29], hepatitis [C8], herpes simplex keratitis [Q4], insomnia [J2], jaundice [C8], *Mycoplasma pneumoniae* [T3], non-gonococcal urethritis [Z25], postpartum eclampsia [C7], prosopospasm [W19], sciatica [F7], senile dementia [L23], spinal cord injuries [L26], tetanus [Z17], vaginal leukoplakia [L47]. Assists neonatal umbilical wound healing [C18, Y8]. Preoperative medicine for diabetic patients (prevents wound disunion) [M5, S10]. Throat lozenges [Z30].	

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Table 3 (*continued*)

Scientific name	Category and use	Plant part used
	Veterinary uses, treatment for bovine coccidiosis (might also be substituted with *T. himalense* Royle ex Edgew.) [H11].	
Thesium ramosoides Hendrych	Functional food and beverages, Health beverage (nourishes yin, treats pneumoconiosis) [U1].	–
Thesium refractum C.A.May	Medicinal, contrast agent for ultrasounds [L38]. Functional food and beverages, Functional food, health dish (cancer-preventing agent, treats atopic dermatitis and various allergic diseases, treats diseases of digestive organs) [M6].	–
Thesium spp.	Medicinal, treatment for necrospermia [Y9]. Craft, storage bag that prevents insect and other pest infestations [L1].	A [C14, S4] B [W42]
	Functional food and beverages Health beverages (clears heat [J8, L48], clears throat [L48], detoxifies [J8, L48], dispels wind [Y5], eliminates dampness [Y5], improves digestion [J8], promotes diuresis [J8], protects vocal cords [L48], relieves swelling from rheumatoid arthritis [Y5], treats and prevents upper respiratory tract infections [L48]).	
	Functional foods, soybean milk (clears heat, diuretic detoxification effects, enhanced immune function, increases nutrient absorption, probiotic) [C14].	
	Growth mediums and fertilizers, fertilizer (enhances plant growth, prevents plant disease) [J1].	
	Hygiene, deodorant body powder (anti-inflammatory, antipruritic, arrests sweating, prevents bromhidrosis, athlete's foot, body odour and sterilizes) [M4].	
	Medicinal, anaesthesia for gastroscopy [D1], apoplexy sequela [L11], brain atrophy symptoms [Z28], cough [X1, X6, Z34], detoxifies kidneys [G8], headaches [H7], keratitis [Q3], malaria [L6], nephropathy [C15], primary trigeminal neuralgia [C13, L36], osteoarthropathy [S2], pancreatic encephalopathy [W18], promotes postpartum lactation [L9, W42], relieves lumbar pain [G8], rheumatoid arthritis [S2], upper respiratory tract infection [S4], urinary tract infections [W31].	
	Other Prevents and treats foulbrood (anti-bacterial) [S7].	

Table 4
Chemical constituents isolated from *Thesium* species, along with the geographical distribution of each species, the constituent class and plant part used. Abbreviations are as follow: **1)** plant part used, A = aboveground parts, B = belowground parts, E = entire plants, F = fruit, L = leaves, and S = stems, and **2)** references (in square brackets): A = Arendaruk et al. (1960), B1 = Belakhdar et al. (2014), B2 = Belakhdar et al. (2015), G = Gharbo et al. (1969), H1 = Hatt et al., (1960), H2 = Hopkins et al., (1969), K1 = Kim et al. (2019), K2 = Kuttan et al. (1974), L1 = Lee et al. (2009), L2 = Le Scao et al., (1975), L3 = Liu et al., (2006), L4 = Liu et al. (2009), L5 = Liu et al. (2018), L6 = Lu and Wang (2004), M = Mashkovskii (1944), P1 = Parveen et al. (2006), P2 = Parveen et al. (2007), S1 = Stephen-Lewis (1936), S2 = Sun et al. (2019), W = Wang and Li (2006), Z = Zou et al. (2016).

Scientific name	Distribution	Constituent class	Constituent name	Plant part
Thesium australe R.Br.	Australia	Fatty acids	octadecenediynoic acid [H1]	B, L, S (somatic lipids) [H1]
Thesium chinense Turcz.	Eastern Asia	Alkaloids	*N*-methylcytisine [W]	-
			lupanine [W]	-
			sophocarpine [W]	-
		Fatty acids	(12E) - heptadec-12-en-8, 10-diynoic acid [L5]	E [L5]
			dodec-9,11-diynoic acid [L5]	E [L5]
			exocarpic acid [L5]	E [L5]
		Phenolics	methyl-*p*-hydroxycinnamate [L1]	A [L1]
			methyl caffeate [L1]	A [L1]
			kaempferol [L1, L5, P2]	A [L1], E [L5, P2]
			kaempferol-3-O-*β*-D-glucopyranoside [L1]	A [L1]
			kaempferol-3,7-di-O-*β*-D-glucopyranoside [L1, L5]	A [L1], E [L5]
			kaempferol-3-O-*β*-D-glucopyranoside-6"-(3-hydroxy-3-methylglutarate) [L1]	A [L1]
			kaempferol-3-*O*-glucoside [L3, L4, L5, L6, P1, P2]	E [L5, P1, P2]
			kaempferol-3-*O*-neohesperidoside [L5, S2]	E [L5], Pure compound sourced [S2]
			quercetin-3-*O*-neohesperidoside [L5]	E [L5]
			kaempferol-3-*O*-rhamnopyranosyl-(1→2)-[6-*O*-acetyl]-glucopyranoside [L5]	E [L5]
			naringenin-4-*O*-glucoside [L6]	-
			apigenin-7-*O*-glucoside [L6, Z]	-
			luteolin-7-*O*-glucoside [L4, L6, Z]	-
			rutin [L4, L6]	-
			kaempferol-3-O-rutinoside? [Z]	-
			apigenin-8-C-α-L-arabinopyranoside [Z]	-
			homoplantaginin [Z]	-
			pectolinarin [Z]	-
			acacetin-7-O-β-d-rutinoside? [Z]	-
			apigenin-7-O-β-D-glucopyranuronide [Z]	-
			chrysoeriol 7-O-glucuronide [Z]	-
			chrysoeriol [Z]	-
			kaempferyl 5-methyl ether [L4]	-
			apigenin-5-*O*-neohesperidoside [L4]	-
			kaempferol 3-rhamnoside [K1]	-
		Terpenes	5,6-epoxy-3-hydroxy-7-megastigmen-9-ene [L1]	A [L1]
			(−)-loliolide [L1]	A [L1]
Thesium divaricatum Jan ex Mert. & W.D.J.Koch	Mediterranean	Phenolics	isorhamnetin-3-*O*-galactoside [L2]	S [L2]
			isorhamnetin-3-*O*-galactorhamnoside [L2]	S [L2]
			isorhamnetin-3-*O*-galactorhamnoglucoside [L2]	S [L2]
Thesium himalense Royle ex Edgew.	Southeast Asia	Other	*cis*-4-hydroxy-L-proline [K2]	L [K2]
Thesium humile Vahl	Northern Africa, southern Europe, south eastern Asia	Alkaloids	1-hydroxymethylpyrrolizidine [B1, B2]	A [B2]
				A [B2]
		Alkanes	undecane [B2]	A [B2]
			3-3dimethyl hexane [B2]	A [B2]
			eicosane [B2]	A [B2]
			docosane [B2]	A [B2]
			cyclotetradecane [B2]	A [B2]
		Alkenes	1-hexadecene [B2]	A [B2]
			1-octadecene [B2]	A [B2]
		Fatty acids	dodecanoic acid methyl ester [B2]	A [B2]
			n- tridecanoic acid methyl ester [B2]	A [B2]
			n-tetradecanoic acid methyl ester [B2]	A [B2]
			pentadecanoic acid methyl ester [B2]	A [B2]
			hexadecanoic acid methyl ester [B2]	A [B2]
			10-octadecenoic acid methyl ester [B2]	A [B2]

(*continued on next page*)

Table 4 (*continued*)

Scientific name	Distribution	Constituent class	Constituent name	Plant part
			9-octadecenoic acid (Z) methyl ester [B2]	A [B2]
			octadecanoic acid methyl ester [B2]	A [B2]
			hexadecanoic acid, butyl ester [B2]	A [B2]
			ximenynic acid [H2]	F (seed oil) [H2]
			exocarpic acid [H2]	F (seed oil) [H2]
		Phenolics	phenol, 2,4-bis(1,1-dimethylethyl) [B2]	A [B2]
			phenol 4,6-di(1,1-dimethylethyl)-2-methyl [B2]	A [B2]
		Other	B-sitosterol [G]	A [G]
			tricosanol-12 [G]	A [G]
			D-mannitol [G]	A [G]
			1-octadecanol [B2]	A [B2]
			1,2 benzene dicarboxylic acid dibutyl ester [B2]	A [B2]
Thesium hystrix A.W.Hill	Southern Africa	Phenolics	quercitrin [S1]	B [S1]
Thesium minkwitzianum B.Fedtsch.	Eastern-central Asia	Alkaloids	thesine [A, M]	A [A]
			thesinine [A]	A [A]
			thesinicine [A]	A [A]
			D- isoretronecanol [A]	B [A]
		Other	D-mannitol [A]	B [A]
			succinic acid [A]	B [A]
Thesium wightianum Wall. ex Wight	India	Other	*cis*-4-hydroxy-L-proline [K2]	L, S [K2]

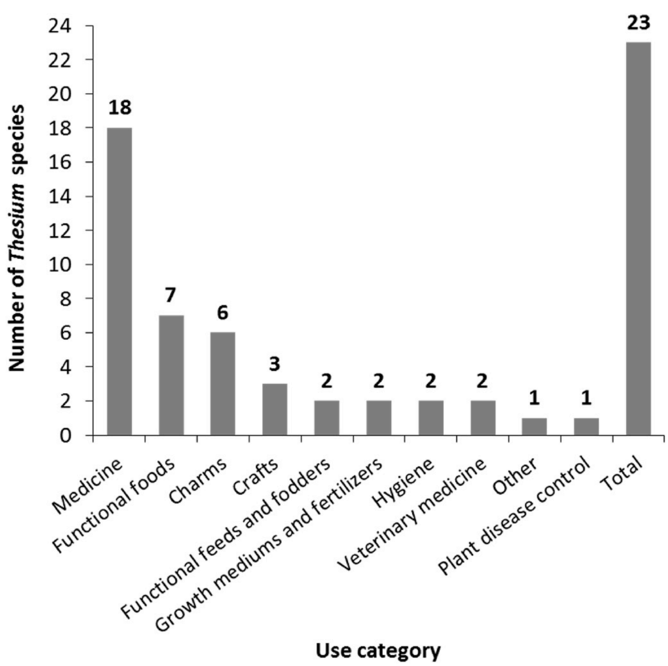

Fig. 2. Ethnobotanical and contemporary uses of *Thesium* species in all parts of the world, arranged according to ten different use categories.

For example, a strong root decoction of *T. hystrix* is used by the Griqua and Batswana people of South Africa as a blood purifier (Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 1997; Rood, 1994; Neuwinger, 2000), and is also thought to bring on abortion (Watt and Breyer-Brandwijk, 1962). In Namibia, a decoction made from the crushed roots of *T. lacinulatum* and *Lacomucinaea lineata* (formerly *Thesium lineatum* L.f.) is used as a treatment for venereal diseases (Bosch, 2008).

In Taiwan, entire plants of *T. chinense* are used singly to treat problems relating to seminal emission (Huang et al., 2009). *Thesium chinense* is also included in mixtures patented for the treatment of cervical erosion (Song et al., 2013), chronic epididymitis (Huang, 2016), genital warts (Xue, 2016), gynaecological inflammation (Song et al., 2013), other gynaecological problems (Wang, 2015a), hysteromyoma (Li, 2015b), irregular menstruation (Kong, 2013), menopausal symptoms (Xie et al., 2015), premature ovarian failure (Zhu, 2016), uterine (womb) coldness (Song et al., 2013) and vaginal itching (Tian, 2011). It is also a popular Chinese medicine (used both singly and in mixtures) for breast-related problems such as mastitis (Lee, 1976; Thomas, 2002; Huang et al., 2009; Jiang, 2014b; Wang, 2015c) and mammary gland hyperplasia (Zhang and Li, 2014). *Thesium chinense* forms part of medicines used to promote postpartum lactation (Zhang and Wang, 2014; Zhang, 2016), as well as remedies said to improve cosmetic breast problems, for example, flattened nipples and pitted breast skin (Nashun and Han, 2006). *Thesium longifolium* is used in Chinese medicines for postpartum eclampsia (Chen, 2016a) and vaginal leukoplakia (Lu, 2015c), and *T. refractum* in a Korean medicine for necrospermia (Yu, 2016a).

3.5.1.2. Respiratory tract ailments. Seven *Thesium* species, *T. chinense*, *T. cinereum*, *T. costatum*, *T. himalense*, *T. hystrix*, *T. longifolium*, *T. racemosum* and *T. strictum* were used to treat 18 respiratory-related ailments. In Africa, a decoction of *T. cinereum* roots is used by the Ambundu people of Angola to treat bronchitis (Bossard, 1996). This remedy is known locally as *kangue* (Bossard, 1996). Similarly, a root decoction of *T. hystrix* is used to treat cough (as expectorant) (Stephen-Lewis, 1936; Watt and Breyer-Brandwijk, 1962; Rood, 1994; Van Wyk et al., 1997; Neuwinger, 2000; Thornton-Barnett, 2013), tuberculosis (Watt and Breyer-Brandwijk, 1962; Rood, 1994; Van Wyk et al., 1997; Neuwinger, 2000) and other respiratory ailments (Rood, 1994) in South Africa. Although no specific medicinal use has been recorded for *T. confine*, the Afrikaans name from South Africa, *teringbossie* (Smith, 1966), also implies its use as a treatment or remedy for tuberculosis. The Basotho people of South Africa and Lesotho use several *Thesium* species to treat respiratory ailments. For example, *T. costatum* plants are a remedy for asthma (Kose et al., 2015), chest colds (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Moffett, 2010) and other respiratory ailments (Moteetee et al., 2019), while *T. racemosum* and two unidentified *Thesium* species are also used to treat chest colds (Watt

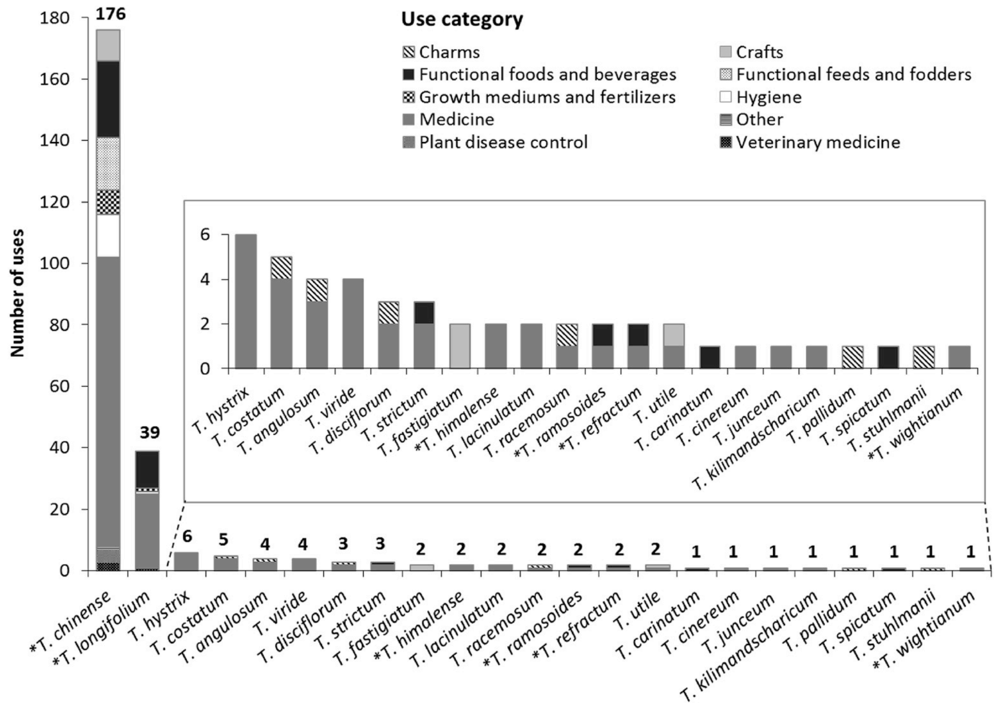

Fig. 3. The total number of ethnobotanical and contemporary uses (values above each bar) for 23 *Thesium* species, as well as the proportion of applications from 10 different categories of use (shown by different shades). Species from Asia are indicated with an *, the remainder of species are from Africa.

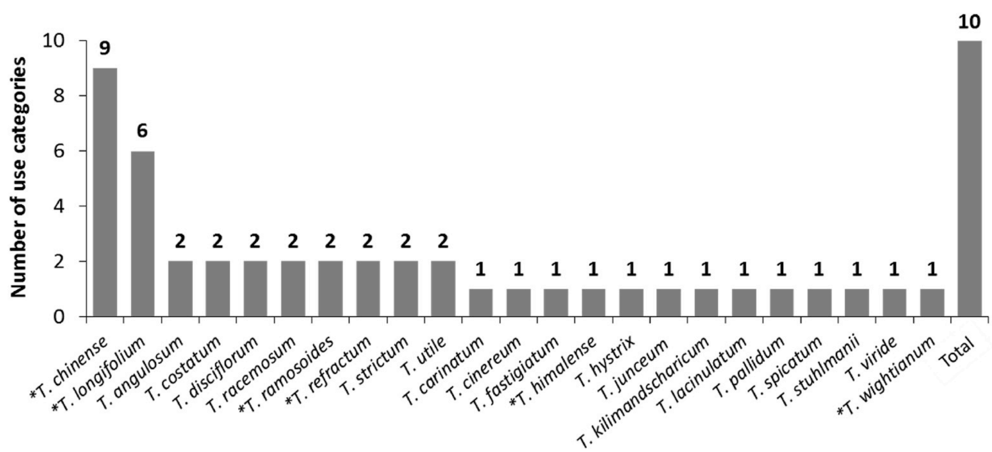

Fig. 4. The versatility of ethnobotanical and contemporary uses of 23 *Thesium* species. The number of use categories recorded for each species is presented (value above each bar), as well as the total number of use categories included in this study.

and Breyer-Brandwijk, 1962). There is likely some confusion in species identity here as *T. costatum*, *T. racemosum* and the unidentified species are all referred to as *bohoho* (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Quattrocchi, 2000; Moffett, 2010; Moteetee et al., 2019), *marakalle* (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Moffett, 2010; Thornton-Barnett, 2013; Kose et al., 2015; Moteetee et al., 2019) and variations of the name *sebitsane* (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Moffett, 2010). Since the two named species are similar in distribution, appearance and use, it is possible that *marakalle* refers to *T. racemosum*, while *marakalle-a-manyenyane* (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Moffett, 2010), meaning a smaller version of *marakalle*, refers to *T. costatum*. Some work is however needed to provide clarity on these species' identities.

In China, *T. chinense*, also known as *bai rui cao* (Chinese), is used singly to treat coughing and pneumonia (Parveen et al., 2006). Similarly, it is a Korean medicine for bronchial problems, tuberculosis (Ahn, 1998) and other unspecified medicinal uses (Lee, 1976), as well as a Taiwanese remedy for common colds, lung abscesses, pneumonia and upper respiratory tract infections (Huang et al., 2009). *Thesium chinense* is furthermore used in mixtures to treat, amongst others, asthma (Ma, 1997), bronchial pneumonia in children (Wang and Li, 2016a), bronchitis (Ma, 1997), chronic obstructive emphysema (Liu, 2016b), common colds (Chen, 2015c; Tang, 2017), cough (expectorant) (Ma, 1997; Zhou, 2005; Wang, 2017c), hydrothorax (Sun, 2016a), laryngopharyngeal reflux disease (Zhong et al., 2013), pleural effusion (Han, 2016a), pulmonary abscesses (Chen and Liao, 2017; Wang, 2017c), pulmonary embolisms (Zhao, 2015b), tuberculosis (Ma, 1997; Chen, 2015b; Wang et al., 2016d) and upper respiratory tract infections (Cao and Zhou, 2015; Zhang et al., 2017; Zhang, 2018a). *Thesium longifolium* also forms part of a Chinese patented medicine used against *Mycoplasma pneumoniae* bacteria (Tang et al., 2016). Similarly, entire plants of *T. himalense* are used to treat infant pneumonia in China (Lee et al., 2008).

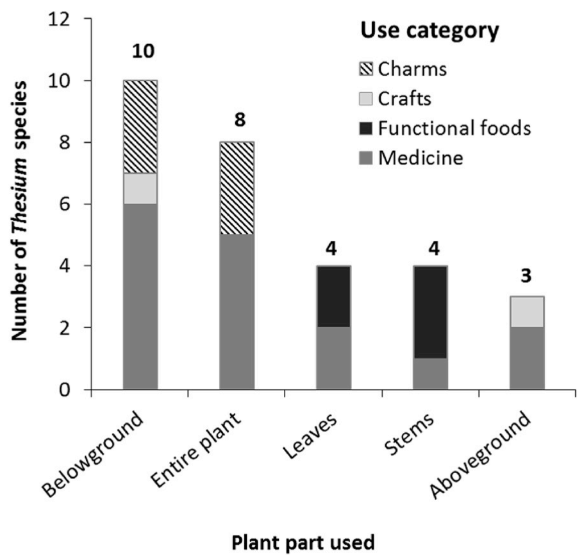

Fig. 5. Utilized plant parts of *Thesium* species. The number of species (value above each bar) of which each plant part is used is presented, as well as the corresponding categories of use.

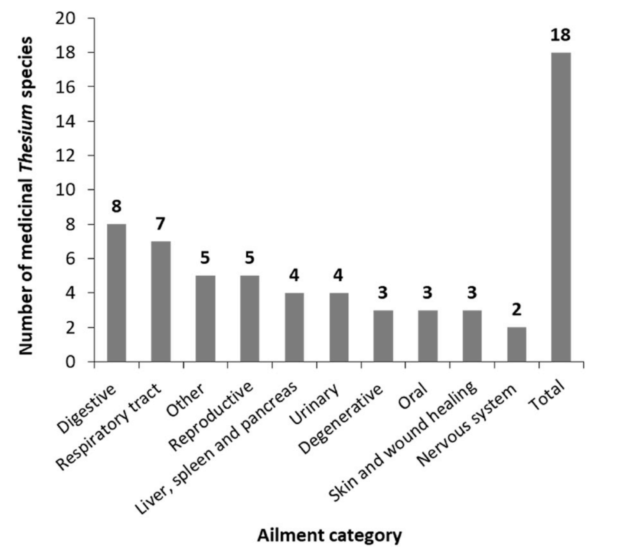

Fig. 7. The numbers of *Thesium* species used to treat ailments in 10 different categories (value above each bar), as well as the total number of *Thesium* species used as medicines.

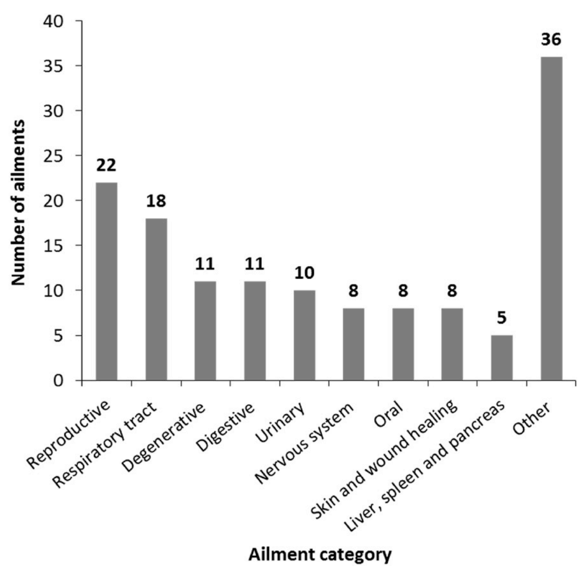

Fig. 6. The numbers of medical ailments treated with *Thesium* species (value above each bar) in each of ten ailment categories.

3.5.1.3. Degenerative diseases. Three *Thesium* species, *T. angulosum*, *T. chinense* and *T. longifolium*, were used to treat 11 types of degenerative diseases. Degenerative diseases relate to progressive degenerative changes in tissues, such as arthritis, cancers and osteoporosis, as well as degeneration in mental health. The Basotho people in Lesotho use the roots of *T. angulosum*, also called *lentsoe*, as a treatment for internal tumours (Kose et al., 2015).

Thesium chinense is an ingredient in two Chinese patents stating anti-cancer effects (Zhao, 2016; An et al., 2019), as well as tumour proliferation inhibition effects (An et al., 2019). *Thesium chinense* has indeed been suggested to have chemo-preventative effects (Nam et al., 2003; see *Pharmacology*). This species furthermore forms part of several mixtures used to treat ailments such as arteriosclerosis (Chen, 2015e), cancer-related anaemia (Yu and Xu, 2015), gout (Zhao, 2015c; Yu, 2016b; Chen, 2017b), osteoarthritis (Fan and Tang, 2016), osteoporosis (Lu and Wang, 2015) and rheumatoid arthritis (Yu, 2015; Wang, 2016c). Regarding degenerative mental diseases, *T. chinense* is included in a medicine for treating brain atrophy symptoms (Zhao, 2017) and *T. longifolium* in a medicine for Alzheimer's disease and senile dementia (Lin, 2000).

3.5.1.4. Digestive ailments. Eight *Thesium* species, *T. angulosum*, *T. chinense*, *T. costatum*, *T. discifolium*, *T. junceum* var. *plantagineum*, *T. longifolium*, *T. utile* and *T. viride*, were recorded as treatments for 11 ailments related to the stomach and intestines. In Lesotho and South Africa, both *T. angulosum* and *T. costatum* are Basotho remedies for digestive ailments (Moteetee et al., 2019), and a species believed to be *T. angulosum* is also used to treat heartburn (Watt and Breyer-Brandwijk, 1962; Guillarmod, 1971; Moteetee and Van Wyk, 2011). *Thesium disciflorum* A.W.Hill is a South African endemic of which the roots are used to treat gastric ailments and remove toxins from the stomach (Philander, 2011). The stems of another species from South Africa, *T. utile*, are chewed as a treatment for gastric ailments (Watt and Breyer-Brandwijk, 1962). *Thesium junceum* var. *plantagineum*, known as *isiqhumiso sentyulube* by the Xhosa people of South Africa, is used as a remedy against intestinal worms in both humans and animals [*Van Eeden 401* (PRE)]. The aboveground parts of *T. viride* are used as a treatment for ulcers by the Hausa people living in northern Nigeria (Shehu et al., 2016). In Zimbabwe, an infusion of the roots of an unknown *Thesium* species is used to relieve abdominal pain in infants (Gelfand et al., 1985).

In China, *T. chinense* is included in mixtures prescribed to treat gastric related ailments such as gastric ulcers (Wang, 2016b), infantile pinworm infection (Dong et al., 2017), perianal abscesses (Lin, 2016) and ulcerative colitis (Wang, 2016e). *Thesium longifolium* is similarly incorporated into Chinese medicines used to treat diarrhoea (Wang et al., 2014), haemorrhoids and other anorectal diseases (Chen, 2016c).

3.5.1.5. Urinary problems. Four *Thesium* species, *T. chinense*, *T. hystrix*, *T. lacinulatum* and *T. longifolium*, were recorded as treatments for 10 ailments related to the urinary system, including the kidneys and bladder. In South Africa, a strong decoction of the roots of *T. hystrix* is taken by European, Griqua and Batswana people to treat bladder and kidney problems (Watt and Breyer-Brandwijk, 1962; Rood, 1994; Neuwinger, 2000). A similar decoction made from the crushed roots of *T. lacinulatum* and *L. lineata* is used to treat uterine problems in Namibia (Von Koenen, 2001; Neuwinger, 2000; Bosch, 2008).

Huang et al. (2009) reported the use of entire *T. chinense* plants in Taiwan to treat cystitis and kidney vacuity lumbar pain. *Thesium chinense* is furthermore used alone as a treatment for nephropathy (Xuan et al., 2012), and as part of mixtures to treat acute cystitis (Yu et al., 2014; Han, 2016c; Li and Lu, 2016), chronic pyelonephritis (Liu, 2016c; Zhang et al., 2016), post-operative bladder (prostate) spasm pain (Wang and Xie, 2015), uterine prolapse (Zhu, 2015b) and urethritis (Han, 2016b; Xu, 2016). *Thesium longifolium* is an ingredient in a Chinese remedy for non-gonococcal urethritis (Zhao, 2015a), while another *Thesium* species from China forms part of mixtures used to detoxify the kidneys (Guo, 2017) and treat urinary tract infections (Wang et al., 2016b).

3.5.1.6. Nervous system disorders. Two Asian endemics, *T. chinense* and *T. longifolium* are used in various mixtures to treat eight nervous system disorders, for example headaches, mental illnesses and epilepsy. *Thesium chinense* is a traditional Chinese medicine for treating headaches (Parveen et al., 2006). Chinese patents furthermore include *T. chinense* in medicines for headaches (Li, 2018a), migraines (Tong, 2015b), postpartum depression (Liu et al., 2016b) and purulent meningitis (Wang et al., 2015). An unidentified *Thesium* species is similarly included in medicines for headaches (Hu, 2008) and primary trigeminal neuralgia (Chen, 2013a; Liu and Qu, 2016), and *T. longifolium* in medicines for epilepsy (Liu and Li, 2015), sciatica (Fang et al., 2015) and tetanus (Zhang and Gu, 2015).

3.5.1.7. Oral diseases. The use of *Thesium* species to treat oral ailments is restricted to Asia. Three species, *T. chinense*, *T. longifolium* and *T. wightianum*, have been recorded as treatments for eight ailments of the mouth, throat and oesophagus. The Irula people of India place whole *T. wightianum* plants (known locally as *anaikchi*) in a cloth that is then fastened to the cheek to prevent swelling (Murugesan et al., 2005). *Thesium chinense* is a popular remedy for tonsillitis in both China (Thomas, 2002) and Taiwan (Huang et al., 2009). It is also included in several Chinese patents for tonsillitis remedies (Li et al., 2014; Wei, 2015a,b; Liu, 2016a). It is furthermore used singly and as a part of medicines to treat mumps in children (Chen et al., 2016b), oesophagitis (Zhu, 2013), oral ulcers (Zhou, 2015a), other oral diseases (Wang et al., 2017; Liu et al., 2018) and throat soreness (Thomas, 2002; Parveen et al., 2006), while *T. longifolium* is an ingredient in throat lozenges (Zheng et al., 2014).

3.5.1.8. Skin ailments and wound healing. Three *Thesium* species, *T. chinense*, *T. longifolium* and *T. strictum*, were used to treat eight skin-related ailments, and also to aid wound healing. For example, the Xhosa people of South Africa use a paste made from the leaves of *T. strictum* to treat boils and other topical wounds (Afolayan et al., 2014).

In China, mixtures containing *T. chinense* are used to treat hives (Song, 2014; Wang, 2015e; Yan and Yao, 2016) and purpura (Chen, 2015a), and to prevent adhesive intestinal obstructions in postoperative patients (Zhuang, 2016). *Thesium longifolium* is used in mixtures to treat acne (Chen, 2017a) and burns (Ma, 2018), as well as to prevent wound disunion in diabetics (Meng and Bai, 2016; Sun and Ma, 2016) and to assist neonatal umbilical wound healing (Chen et al., 2016a; Yin and Gao, 2016).

3.5.1.9. Liver, spleen and pancreas-related ailments. Four *Thesium* species, *T. chinense*, *T. himalense*, *T. longifolium* and *T. viride*, were recorded as treatments for five types of ailments related to the liver, spleen and pancreas. In the only African species in this category, *T. viride*, the aboveground parts are taken whole, as a seasoning with other food such as rice, or as an oral decoction to treat jaundice (Hutchings, 1996; Bosch, 2008). In Nigeria, the aerial parts of this species are also used to treat jaundice, in addition to liver enlargement and splenomegaly (Iwu, 2014; Shehu et al., 2016). Shehu et al. (2016) showed that *T. viride* has anti-bacterial properties (see Pharmacology).

In South West China, a decoction of entire *T. himalense* plants is taken orally as a remedy for hepatitis (Lee et al., 2008). Both *T. longifolium* and *T. chinense* are furthermore included as part of Chinese medicines for hepatitis and jaundice (Bai, 2015b; Chen, 2015d). *Thesium chinense* is also a popular ingredient in patented mixtures used to treat pancreatitis (Bai, 2015a,c; Bi and Qing, 2016; Li, 2016a).

3.5.1.10. Other ailments. In South Africa, *T. pallidum* (Fig. 1B) has been noted as a Xhosa and Zulu medicinal plant, but no specific medicinal uses have been recorded (Hutchings, 1996; Van Wyk et al., 1997; Williams et al., 2001; Kepe, 2007). An unidentified *Thesium* species from Zimbabwe is used to treat weak joins by applying roots to cuts made on the joins (Gelfand et al., 1985). Ash from burnt *T. kilimandscharicum* plants is applied topically to treat dactylitis in Ethiopia (Chekole, 2017).

In Asia, *T. chinense* and *T. longifolium* are commonly used to treat fevers (Thomas, 2002), night sweat (Liu, 2016b), heat stroke (Huang et al., 2009) (Zhang, 2015b,c,d; Zhao et al., 2016) and related ailments such as heat-induced strangury (Xin, 2016; Zang, 2016) and heat-induced cramps and dizziness (Huang et al., 2009; Liu, 2015a). Both these species are included in medicines for treating insomnia (Han, 2015a,b; Jiang, 2015; Li, 2015a; Li, 2016c; Xu, 2017b) and spinal cord injuries (Lu, 2015b; Liu, 2017a). *Thesium chinense* is furthermore used singly to treat inflammation (Thomas, 2002; Parveen et al., 2006) and lymphatic tuberculosis, to stabilize *qi* (Huang et al., 2009) and to promote bone growth in children (Sun et al., 2018).

3.5.2. Functional foods and beverages

Three *Thesium* species from Africa and four from Asia are consumed by humans. In the majority of cases they are prepared as beverages, or ingredients or seasoning in other dishes. All seven species in this category, excluding *T. carinatum*, are classified as functional foods (products that are ingested as much for their beneficial physiological and medicinal activities as for their nutritional value).

The three African species, *T. carinatum*, *T. spicatum* and *T. strictum*, all from the Cape region in South Africa, are taken as teas (Van Wyk and Gorelik, 2017). The leafy stems of *T. carinatum*, also known as *jakkalstee* in Afrikaans, has been used as an adulterant of rooibos tea, which is made from *Aspalathus linearis* (Van Wyk and Gorelik, 2017; Welcome and Van Wyk, 2019). The Afrikaans name for *T. strictum*, *teringbos* (Marloth, 1917; Smith, 1966; Welcome and Van Wyk, 2019), implies its use as a treatment against tuberculosis, while its isiXhosa name, *umbiza* (Afolayan et al., 2014), indicates its use as an internal purge or cleanse. The stems of *T. spicatum* (*lidjiestee* or *riettee*) are used as a medicinal tea (Smith, 1966; Van Wyk and Gorelik, 2017; Stander et al., 2019; Welcome and Van Wyk, 2019).

It is important to note that the four Asian *Thesium* species which are used as foods are always consumed in combination with various other plants. Consequently, the health benefits reported are apparently a culmination of several ingredients and not just of the *Thesium* species. For instance, *T. chinense* is prepared as part of numerous health beverages, with the function of amongst others detoxifying and nourishing the kidneys and liver (Wang, 2017b; Yin and Wang, 2018), nourishing stomach *yin* (Feng et al., 2018), replenishing *qi* (Tong, 2015a; Wu, 2015a; Yin and Wang, 2018) and strengthening the immune system (Tong, 2015a; Wang, 2017b). This species is also included in dishes such as a type of rice cake, other rice dishes, noodle dishes, “hot pots” (Chinese cooking method), soups, sauces, soft-shelled turtle dishes and other health dishes with a plethora of health benefits (a detailed summary is provided in Table 3). These dishes have been reported to, amongst others, clear heat (Gan, 2014b; Peng, 2015; Sun, 2016b; Wang, 2018b), enhance the metabolism (Jin, 2014b; Zhang and Zhao, 2015), lower blood pressure (Zhang, 2014a; Lu, 2015a), and relieve pain and fever (Peng, 2015; An and Meng, 2016; Wang, 2018a). Another unspecified Chinese species is included in three health beverages and a type of soybean milk, with similar health benefits as *T. chinense* (Lu and Lu, 1998; Chen, 2014b; Jin, 2017; Ye and Zhou, 2017). *Thesium longifolium* is an ingredient in three health beverages with health benefits including, but not limited to, having a calming effect on the liver, dispersing dampness (Lin, 1999; Tang, 2007), improving gastro-intestinal functions and reducing inflammation (Lin, 2009). It is also included in various health dishes said to detoxify (Chen, 2014a; Ge, 2016), dispel wind (Yin, 2016; Wang, 2017d) and promote urination (Ge, 2016), to name a few. *Thesium ramosoides* forms part of a health beverage which nourishes *yin* and can be used to treat pneumoconiosis (unknown author(s), 2014), while *T. refractum* is an ingredient in a health food said to treat atopic dermatitis, various other allergic diseases and diseases of the digestive organs (Min, 2006).

3.5.3. Charms

Following medicine, charms were the second most common use of *Thesium*. Interestingly, the use of *Thesium* species as charms was unique to southern and East Africa with six species recorded. In South Africa, the roots of *T. pallidum* are commonly used as a love charm (Zukulu et al., 2012). The roots are crushed and boiled and administered as a body wash, purgative or steam treatment, all of which are believed to increase a person's attractiveness and sexual appeal (Zukulu et al., 2012). *Thesium pallidum* is known as *umayisaki* (isiMpondo dialect; Kepe, 2007) and *umayisake obomvu* (Zukulu et al., 2012) in isiXhosa, as *umahesaka-obomvu* in isiZulu (Hutchings, 1996; Van Wyk et al., 1997) and yellow *Thesium* (Zukulu et al., 2012) or variations of red mahesaka in English (Van Wyk et al., 1997; Williams et al., 2001). The Basotho people in South Africa use entire plants of *T. angulosum*, *T. costatum*, *T. racemosum* and an unidentified *Thesium* species (all known locally as *marakalla* or *marakalle*) in unspecified rituals (Thornton-Barnett, 2013). The roots of two other South African species, *T. disciflorum* and *L. lineata*, are used as amulets for good luck in court cases (Philander, 2011). Similarly, Safwa shopkeepers in Tanzania chew on the roots of *T. stuhlmannii* (*umwita*) to attract costumers [*Levett and Kayombo 3402* (PRE)].

3.5.4. Crafts

Two African and one Asian *Thesium* species had recorded craft uses. In South Africa, *T. utile* plants are used as brooms (*besems*), as indicated by the Afrikaans name "*besembossie*" (Hill, 1915, 1925). Although not confirmed, the Afrikaans name of *T. asterias*, *dye-bossie* (Smith, 1966) possibly refers to the use of the plant as a dye. In Tanzania, the Safwa people produce a wash which restores the colour to children's hair by crushing *T. fastigiatum* (formerly *T. tamariscinum*) plants and adding it to water [*Levett and Kayombo 3401* (PRE)]. This plant is known locally as *inyala* [*Levett and Kayombo 3401* (PRE)]. The roots of *T. fastigiatum* are also used to make fish traps in Mozambique (Hill, 1910; Baker and Hill, 1911).

Contrary to the single species craft uses of *Thesium* in Africa, the Asian species *T. chinense* is used in combination with other species for (primarily contemporary) craft purposes. For example, this species is included in anti-bacterial materials for medicinal use (Jin et al., 2016; Shi, 2018), a silk quilt core which may improve skin quality (Jiang, 2018), a UV-, water-, and fire resistant shirt fabric with anti-wrinkle properties (Wang, 2016d), a hypoallergenic printer ink powder (Wang, 2016a) and a temporary medicinal filler for the pocket left after tooth extraction (Hou, 2015). In the latter, *T. chinense* might be substituted or combined with *T. himalense*, *T. longiflorum*, *T. longifolium* or *T. refractum*. Other craft uses of this species include a part of a wastewater treatment method (Pan, 2018), an aromatic stick used to prevent and treat cough, asthma, dizziness and headaches (Wang, 2017a), an anti-microbial, insect resistant and UV-resistant treatment for rattan (Xu, 2017a) and a water-based paint with high radiance, strong adhesion and abrasion resistance which calms mental anxiety (Liu and Li, 2016). An Asian species of uncertain identity is also used as part of a storage bag that prevents insect and other pest infestations (Lei et al., 2019).

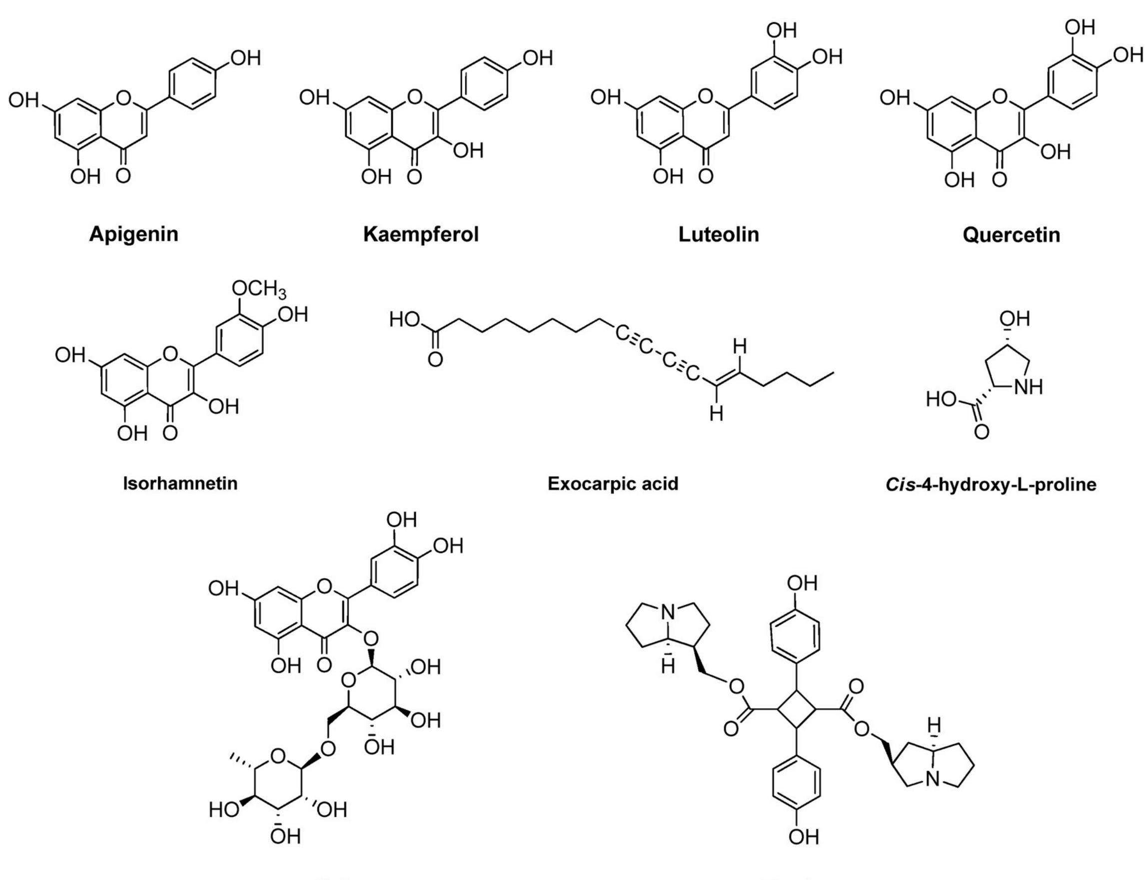

Fig. 8. Chemical structures of common compounds isolated from *Thesium* species.

3.5.5. Functional feeds and fodders

The Asian species *T. chinense* and *T. longifolium* are often found in functional feeds and fodders. *Thesium chinense* is included in bamboo rat feed (Zhang, 2017d), black guinea pig feed (Zhang, 2017c), chicken feed (Zhu, 2015a; Liu, 2017b; Wu, 2017), duck feed (Han, 2015a), eel feed (Hu et al., 2017a), lactating cat feed (Liu, 2017c), peafowl feed (Guan, 2014), pheasant feed (Liu et al., 2015a), piglet fodder (Xu et al., 2013) and silver carp feed (Qian, 2013), with the primary purpose of enhancing disease resistance, growth and immunity (e.g., Liu et al., 2015b; Hu, 2016; Fang, 2017; Hu et al., 2017b; Zhang, 2018b). Similarly, *T. longifolium* forms part of a sheep feed said to promote growth and development (Ni, 2014).

3.5.6. Growth mediums and fertilizers

Thesium chinense and *T. longifolium* are not only popular ingredients in functional feeds and fodders, but also commonly included in growth mediums and fertilizers. Mixtures including *T. chinense* are used to fertilize aquatic plants (Yu, 2017; Fan, 2018), pears (Bu et al., 2017), and tomatoes (Yue, 2018). Similarly, *T. longifolium* forms part of an organic fertilizer which promotes the growth of healthy bacteria (Yang, 2015), and another unidentified *Thesium* species from Korea is used in a general fertilizer and is said to enhance plant growth and prevent plant disease (Jeong et al., 2002). *Thesium chinense* is used in mixtures to improve the germination of wheat seeds (Lian, 2017b) and growth of rice seeds (Lian, 2017a). It is also included in a culture medium for *Burcella* (Liu et al., 2017) and a growing substance for *Agaricus* mushrooms (Zhang, 2014b).

3.5.7. Hygiene

The two popular species from Asia, *T. chinense* and *T. longifolium*, as well as two unknown species are used in combination with other plants and ingredients to produce traditional and contemporary hygiene-related products. In their treatment of the medicinal and poisonous plants of southern and eastern Africa, Watt and Breyer-Brandwijk (1962) mentions the use of an unidentified *Thesium* species as a refreshing bath. The bath is prepared as a decoction of *Thesium* sp., and the roots of *Afrosciadium magalismontanum* (formerly *Peucedanum magalismontanum*) and *Polygala rarifolia*.

In Asia, *T. chinense* is included in Chinese patents for anti-bacterial and moisturizing hand-wash liquids (Ju, 2014; Pan, 2017), a fragrant and decontaminating laundry liquid (Xu, 2018), a preoperative hand sterilizer (Zhu, 2012), a sanitary ware detergent (Wang, 2015h), a washing solution which relieves swelling and promotes both blood and *qi* circulation (Li, 2014b), refrigerator disinfecting solutions (Xu, 2015b; Liu, 2017d) and other general antiseptic and anti-bacterial solutions (Wang, 2015d; Zhang, 2017a). Other patented hygiene products containing *T. chinense* include an anti-microbial and deodorizing filler for shoe insoles (Li, 2018c), anti-bacterial female sanitary pads (Yang and Xu, 2016), a medical air sterilization spray for operating rooms (Wang, 2012) and a cosmetic facial mask that clears toxins, cools and refreshes, nourishes the skin, delays aging, whitens the skin and preserves moisture (Zhang, 2015e). Another *Thesium* species is used in a Chinese deodorant body powder with sweat arresting, sterilizing, anti-inflammatory and antipruritic properties (Ma and Li, 2005). The body powder also prevents bromhidrosis, athlete's foot and body odour (Ma and Li, 2005). *Thesium longifolium* forms part of a Chinese medicinal plaster which promotes circulation, and relieves pain, stasis and swelling (Jiang, 2014a).

3.5.8. Veterinary medicine

Three patents from China list *T. chinense* as an additive in medicinal mixtures used to treat bovine mastitis (Zhang et al., 2010, 2015; Wang, 2015g), while one patent lists a mixture including *T. longifolium* (might be substituted with *T. himalense*) as a treatment for bovine coccidiosis (Hu et al., 2015).

3.5.9. Other

One unspecified species from China (possibly *T. chinense*) is an ingredient in a traditional anti-bacterial solution used to prevent and treat foulbrood (Su et al., 2007).

3.5.10. Plant disease control

Chinese medicinal preparations containing *T. chinense* are used to prevent anthracnose (Hu and Yang, 2017b), leaf spot (Hu and Yang, 2017a) and other pests and diseases in *Paris polyphylla* (Cen, 2017), a popular Chinese medicinal plant (the product is known as Rhizoma Paridis; Duan et al., 2018). It is also used as a control agent for lawn patch disease (Yang, 2016).

3.6. Phytochemistry

More than 70 chemical constituents have been isolated from eight *Thesium* species (2% of the genus), *T. australe*, *T. chinense*, *T. divaricatum*, *T. himalense*, *T. humile* (Fig. 1E), *T. hystrix*, *T. minkwitzianum* and *T. wightianum*, since the first phytochemical investigation of the genus by Stephen-Lewis in 1936. Isolated constituents are primarily phenolics, fatty acids and alkaloids (e.g., Arendaruk et al., 1960; Wang and Li, 2006; Lee et al., 2009; Belakhdar et al., 2015; Zou et al., 2016; Liu et al., 2018), and to a lesser extent terpenes (Lee et al., 2009), alkanes (Belakhdar et al., 2015), alkenes (Belakhdar et al., 2015), amino acids (Kuttan et al., 1974), fatty alcohols (Gharbo et al., 1969; Belakhdar et al., 2015), sugar alcohols (Arendaruk et al., 1960; Gharbo et al., 1969), phytosterols (Gharbo et al., 1969) and aromatic dicarboxylic acids (Belakhdar et al., 2015). The presence of quinones (anthraquinones), cardiac glycosides, resin, saponins, tannins and volatile oil has also been reported (Stephen-Lewis, 1936; De Kock and Rapson, 1938, 1939; Shehu et al., 2016). A summary of the compounds isolated from *Thesium* is provided in Table 4 and the associated structures of selected compounds provided in Fig. 8.

Thesium chinense (the most utilized *Thesium* species; Fig. 3) and *T. humile* (known for its toxicity; Belakhdar et al., 2014) have been the main species investigated with 34 and 26 compounds isolated, respectively. The second most utilized species, *T. longifolium* (Fig. 4), remains chemically unstudied despite its use in contemporary medicines, foods, beverages, feeds and fodders (e.g., Lin, 2000; Lin, 2009; Ni, 2014; Chen, 2015d; Zhao, 2015a; Yin, 2016). The chemistry of 14 *Thesium* species used as traditional and contemporary medicines and products (Table 2) has not been studied.

Many of the chemical constituents found in *Thesium* are bioactive. Bioactivities are primarily therapeutic (e.g., Parveen et al., 2007; Shehu et al., 2016; Liu et al., 2018; Kim et al., 2019; Sun et al., 2019), but some toxicity has been reported (Mashkovskii, 1944; Arendaruk et al., 1960; Belakhdar et al., 2014).

3.6.1. Phenolics

Thesium is rich in phenolics with 32 compounds such as flavanones, flavones, flavonols and phenylpropanoids isolated thus far from the aboveground and belowground parts. Apigenin, kaempferol, luteolin, quercetin and isorhamnetin derivatives, and rutin (Fig. 8) are the most common flavonoids found in *Thesium* species and are likely linked to their therapeutic properties, as these flavonoids are known for various beneficial biological activities including anti-cancer, anti-inflammatory, anti-microbial and anti-oxidant properties (e.g., Lopez-Lazaro, 2009; Calderón-Montaño et al., 2011; D'Andrea, 2015; Yan et al., 2017) (also see Pharmacology).

3.6.2. Fatty acids and amino acids

A total of 14 acetylenic, saturated and unsaturated fatty acids, have been isolated from *T. australe*, *T. chinense* and *T. humile*. The presence or absence of selected seed oil derived acetylenic acids has been proposed to be of taxonomic importance in genera of Santalaceae (Hopkins et al., 1969). Indeed, the hypothesis of Hopkins et al. (1969) that *Thesium* should be most closely related to *Buckleya* (among the 12 genera studied), due to the presence of exocarpic acid (Fig. 8) and ximenynic acid in both, was subsequently supported by molecular data (Der and Nickrent, 2008). To date, exocarpic acid has been isolated within *Thesium* from *T. chinense* and *T. humile*, ximenynic acid from *T. humile* and an unidentified acetylenic acid from *T. australe*. A wider survey of species may yield interesting results. Another compound of possible taxonomic significance is the amino acid *cis*-4-hydroxy-L-proline (Fig. 8), which has only been reported in the free state from four genera, *Osyris* L., *Santalum* L., *Scleropyrum* Arn. and *Thesium*, in the family Santalaceae (Kuttan et al., 1974, 2015). Due to the restricted distribution of *cis*-4-hydroxy-L-proline, its presence may serve as a chemotaxonomic marker within the family (Kuttan et al., 1974, 2015). Further examination of acetylenic acids and *cis*-4-hydroxy-L-proline in both *Thesium* and Santalaceae might provide valuable insights into the chemosystematic relationships within the genus. This is especially important in *Thesium* where current phylogenetic groupings are not supported by morphology (Moore et al., 2010) and additional lines of evidence are required to inform an infrageneric classification for this taxonomically problematic genus.

3.6.3. Alkaloids

Eight quinolizidine- and pyrrolizidine alkaloids have been isolated from the aboveground and belowground parts of three *Thesium* species, *T. chinense*, *T. humile* and *T. minkwitzianum* (Mashkovskii, 1944; Arendaruk et al., 1960; Wang and Li, 2006; Belakhdar et al., 2014, 2015). Since *Thesium* plants are hemi-parasitic it is likely that these alkaloids were absorbed from neighbouring host plants, or even from the soil, rather than being synthesised by the plants themselves (Stermitz, 1998). The pyrrolizidine alkaloids reported from *T. minkwitzianum* appears to have their origins from *Borago officinalis* L. (Boraginaceae), known to produce thesinine and related alkaloids (Dodson and Stermitz, 1986; El-Shazly and Wink, 2014). On the other hand, thesine (Fig. 8) and thesinicine appear to be known only from *T. minkwitzianum* (Azimova and Yunusov, 2013), suggesting that these may be derivatives synthesised by *Thesium* plants. However, parasitic plants typically have the same combination of alkaloids as their host plants (Stermitz, 1998), so that it may be worthwhile to repeat the original study of *T. minkwitzianum* by Mashkovskii (1944). Similarly, the quinolizidine alkaloids found in *T. chinense* almost certainly came from a member of the Fabaceae (Wink, 1987). More studies are clearly needed to determine to what extent parasitism influences the alkaloid chemistry of *Thesium.*

3.6.4. Other

Belakhdar et al. (2015) isolated five alkanes, undecane, 3-3dimethyl hexane, eicosane, docosane and cyclotetradecane, and two alkenes, 1-hexadecene and 1-octadecene from the aboveground parts of *T. humile*. Anti-bacterial, anti-fungal, anti-oxidant and anti-larva activities have been reported for the alkenes, while the alkanes docosane and eicosane have anti-bacterial, anti-fungal, anti-tumor and cytotoxic properties. Alkanes and alkenes have only been reported from this *T. humile* within the genus (Belakhdar et al., 2015). Lee et al. (2009) isolated two nor-sesquiterpenes, 5,6-epoxy-3-hydroxy-7-megastigmen-9-ene and (−)-loliolide, which showed moderate and minor cytotoxic activities respectively, from the aerial parts of *T. chinense*. These two compounds are the only terpenes isolated from the *Thesium* to date.

3.7. Pharmacology

Thesium has been shown to possess several pharmacological properties including analgesic, anti-bacterial, anti-inflammatory, chemopreventive and cytotoxic activities (e.g., Parveen et al., 2007; Shehu et al., 2016). As with chemistry, the majority of pharmacological studies in this genus focussed on the widely used and versatile *T. chinense* (e.g., Nam et al., 2003; Lee et al., 2009; Sun et al., 2019). To our knowledge the only other *Thesium* species that has been pharmacologically investigated is *T. viride*. There is a striking lack of pharmacological data for 16 *Thesium* species used as traditional and contemporary medicines to treat a wide array of ailments. The therapeutic potential of the genus necessitates further pharmacological and pharmacokinetic research attention. In addition, the limited toxicological and clinical studies should be addressed. Three species, *T. humile*, *T. minkwizianum* and *T. namaquense* are known for their toxic potential.

3.7.1. Analgesic and anti-inflammatory activity

An ethyl acetate extract of whole *T. chinense* plants, as well as two flavonoids (kaempferol and kaempferol-3-*O*-glucoside) isolated from *T. chinense*, showed analgesic and anti-inflammatory activity in a study by Parveen et al. (2007), while a chloroform extract was inactive. Anti-inflammatory activity was shown in mice where carrageenan-induced hindpaw edema was significantly reduced ($p < 0.01$) at all concentrations (50, 100 and 200 mg/ml) and all time intervals (60, 120, 180, 240 min) for the ethyl acetate extract and both flavonoids (Parveen et al., 2007). A control group was treated with 3% (v/v) Tween-80 in normal saline solution as a negative control and indomethacin as a reference drug (Parveen et al., 2007). Similarly, xylene-induced ear edema was also reduced significantly at 100 and 200 mg/ml of ethyl acetate extract, and 50 and 100 mg/ml of both flavonoids (Parveen et al., 2007). Analgesic activity was shown, also in mice, using an acetic acid-induced writhing test. Writhing was reduced by up to 79% using the ethyl acetate extract ($p < 0.01$; 200 mg/ml), 64% using kaempferol ($p < 0.01$; 100 mg/ml) and 52% using kaempferol-3-*O*-glucoside ($p < 0.01$; 100 mg/ml) (Parveen et al., 2007). Control groups for both the ear edema and writhing tests were treated with 3% (v/v) Tween-80 in normal saline solution as a negative control and aspirin used as a reference drug (Parveen et al., 2007). No acute toxicity was observed during this study (Parveen et al., 2007).

Sun et al. (2019) studied the anti-inflammatory activity of the flavonoid kaempferol-3-*O*-glucorhamnoside (derived from *T. chinense*) on *Klebsiella pneumoniae* infected mice and cell cultures. The flavonoid had a significant inhibitory effect on the expression of four inflammatory cytokines (IL-1β, IL-6, PGE2 and TNF-α) compared to the phosphate buffered saline negative control group (Sun et al., 2019). A similar inhibition of the MAPK and NF-κB pathways in cultured murine RAW 264.7 cells and mice was observed, also indicating an anti-inflammatory effect (Sun et al., 2019). Dexamethasone was used as a positive control. Kaempferol-3-*O*-glucorhamnoside furthermore lowered reactive oxygen species (ROS) levels and oxidative stress in cultured cells exposed to the anaerobe. Oxidative stress in the lungs was also reduced while lung edema was improved, suggesting that kaempferol-3-*O*-glucorhamnoside is a promising therapeutic agent against *K. pneumoniae* and possibly its antibiotic drug resistant phenotypes (Sun et al., 2019).

Kim et al. (2019) recently showed the anti-inflammatory and anti-oxidation properties of the flavonoid kaempferol-3-rhamnoside, also known as afzelin. The anti-inflammatory effect of this compound isolated from *T. chinense* was tested on HaCaT cells (human keratinocytes) that were exposed to 1649b particulate matter (Kim et al., 2019). Gene and protein expression was investigated by means of reverse transcription-quantitative polymerase chain reaction for the former and western blot analysis for the latter (Kim et al., 2019). They also assessed cell viability using a water-soluble tetrazolium salt-1 assay and the generation of reactive oxygen species using a dichloro-dihydro-fluorescein diacetate assay (Kim et al., 2019). Lastly, the level of secreted inflammatory cytokines was tested with an enzyme-linked immunosorbent assay (Kim et al., 2019). Kim et al. (2019) found that afzelin suppressed the 1) mRNA expression of proinflammatory cytokines, 2) protein secretion in HaCaT cells, 3) generation of intracellular reactive oxygen species, as well as the activation of 4) p38 mitogen-activated protein kinase and 5) transcription factor activator protein-1 component c-Fos and c-Jun (Kim et al., 2019). These results indicate that afzelin may be used to treat and prevent inflammatory skin ailments caused by particulate matter (Kim et al., 2019).

3.7.2. Anti-bacterial activity

An aqueous ethanol extract of *T. viride* plants from Nigeria proved active against several bacteria including *Escherichia coli* and *Staphylococcus aureus*, but inactive against *Corynebacterium ulcerans* and *Salmonella typhi*, compared to a ciprofloxacin control (Shehu et al., 2016). Minimum inhibitory concentrations (MIC) were 5 and 10 mg/ml and minimum bactericidal concentrations (MBC) 10 and 20 mg/ml (Shehu et al., 2016). This study reported the presence of flavonoids, anthraquinones, alkaloids and cardiac glycosides as possible anti-bacterial agents, but studies are needed to isolate and identify the active compounds. The presence of unidentified cardiac glycosides in this species necessitates toxicity studies, as a cardiac glycoside (of the bufadienolide type) in the closely related *L. lineata* has caused the occasional poisoning of livestock (Anderson et al., 1987; Van Wyk et al., 2002).

Liu et al. (2018) tested the anti-bacterial activities of six flavonoids and three acetylenic acids isolated from an ethanol extract of *T. chinense* against three oral pathogens: *Fusobacterium nucleatum*, *Porphyromonas gingivalis* and *Streptococcus mutans*. Exocarpic acid was the only compound that inhibited *S. mutans* (MIC of 13.7 μg/ml), compared to the solvent blank control group (Liu et al., 2018). *Fusobacterium nucleatum* was inhibited by all three acetylenic acids (MIC of 26 μg/ml or less), but none of the six flavonoids had inhibitory effects at the maximum concentration of 200 μg/ml (Liu et al., 2018). *Porphyromonas gingivalis* was inhibited by all three acetylenic acids (MIC of 1.6 μg/ml or less), three of the flavonoids (MIC of 119 μg/ml or less) and an ethanolic extract (MIC of 200 μg/ml) (Liu et al., 2018).

3.7.3. Chemopreventative activity

A study by Nam et al. (2003) indicated that *T. chinense* may have chemopreventative effects. An ethanolic extract of *T. chinense* (90 and 150 mg/ml) significantly inhibited the activity of the cytochrome P450 1A1 enzyme (Nam et al., 2003), which is known for its ability to activate carcinogenic compounds (Androutsopoulos et al., 2009). The *T. chinense* extract furthermore induced quinone reductase activity (implicated in detoxification pathways; Spitsberg and Coscia, 1982) at concentrations between 3 and 150 mg/ml (Nam et al., 2003). Increased glutathione S-transferase (detoxification enzymes; Townsend and Tew, 2003) activity, as well as higher levels of the antioxidant glutathione were observed in cultured murine (Hepa1c1c7) hepatoma cells treated with *T. chinense* extract (Nam et al., 2003). Lu and Wang (2004) furthermore identified kaempferol-3-*O*-glucoside as the strongest antioxidation component isolated from *T. chinense* and gave its optimum concentration as 1 × 10~(-4) mol/L.

3.7.4. Cytotoxic activity

Lee et al. (2009) tested the cytotoxic activities of eight compounds (four flavonoids, two norsesquiterpenes and two phenylpropanes) isolated from the aboveground parts of *T. chinense*. The compounds were tested against four *in vitro* cancer cell lines A549 (non small cell lung adenocarcinoma), HCT15 (colon cancer cells), SK-MEL-2 (skin melanoma) and SK-OV-3 (ovarian cancer cells) using a sulforhodamin B bioassay (Lee et al., 2009). The norsesquiterpene 5,6-epoxy-3-hydroxy-7-megastigmen-9-one had moderate cytotoxic effects on all four cancer cell lines at ED_{50} of 20.19, 26.07, 21.56 and 21.83 μM respectively, while the other norsesquiterpene, four flavonoids and two phenylpropanes only had minor cytotoxic effects in all treatments with ED_{50} above 100 μM (Lee et al., 2009).

3.7.5. General therapeutic activity

Xuan et al. (2012) investigated the therapeutic effects of a *T. chinense* decoction on rats with Adriamycin-induced nephrotic syndrome (excessive excretion of protein in the urine; Hull and Goldsmith, 2008). Rats were divided into a normal control group, a model control group (administered water), a low-dosage experimental group [1 g/(kg.d)] and a high-dosage experimental group [6 g/(kg.d)] with the latter two being administered the *T. chinense* decoction intragastrically (Xuan et al., 2012). For both experimental groups the volume of urine produced in 24 h was significantly higher than the control after two weeks of treatment, while the 24 h urine protein concentrations were significantly lower than the control after three weeks (Xuan et al., 2012). After five weeks the serum albumin and total serum protein levels of the low-dosage group were significantly higher than the control and the total cholesterol and triglyceride levels significantly lower than the control (Xuan et al., 2012). In addition, other symptoms of the disorder, such as edema and tail-rot disease were relieved in both experimental groups (Xuan et al., 2012). *Thesium chinense* had a marked therapeutic effect on several symptoms associated with nephrotic syndrome.

In a clinical study by Zhong et al. (2013), patients with laryngopharyngeal reflux were successfully treated with Bairui tablets. Bairui tablets, named after the Chinese name for *T. chinense*, *bairui cao*, are sugar tablets containing pure *T. chinense* which are sold commercially (e.g., Baimeixing® Bairui Tablets). Zhong et al. (2013) showed that symptoms associated with laryngopharyngeal reflux were significantly ($p < 0.01$) reduced after eight weeks of treatment in an experimental group given Bairui tablets and Omeprazole capsules, compared to a control group only administered Omeprazole capsules. Given the variety of therapeutic activities reported for *T. chinense* and its associated phytochemicals in both cell and animal models, more clinical studies are needed for this species.

3.7.6. Poisonous and toxic species

Only three of the ± 350 *Thesium* species are known to be poisonous. *Thesium humile* (widespread through northern Africa and the Mediterranean) has been implicated in acute poisonings and death in cattle and ruminants (Curasson, 1957; Belakhdar et al., 2014). Belakhdar et al. (2014) identified a pyrrolizidine alkaloid (1-hydroxymethylpyrrolizidine) as the likely cause, but alkaloids with a saturated necine base are usually non-hepatotoxic. Symptoms of *T. humile* poisoning include abdominal pain, convulsions and severe meteorism (Fennane et al., 2007).

The alkaloid thesine has been isolated from the aboveground parts of *T. minkwizianum* (from western Asia) and is known to be very toxic at high concentrations (Mashkovskii, 1944; Arendaruk et al., 1960). Mashkovskii (1944) showed that high concentrations of thesine isolated from *T. minkwizianum* depressed motor centres of the brain, causing a loss of skeletal muscle tone, decreased activity of the intestines and lowered blood pressure.

Thesium namaquense (poison bush), a species endemic to South Africa, was shown to be toxic to animals (rabbits and sheep), with symptoms including apathy, anorexia, generalized cyanosis and laboured breathing (Steyn, 1935; Watt and Breyer-Brandwijk, 1962). Toxicity tests showed that a dosage of 200 mg of dry material was fatal when ingested by sheep, but further research is needed to elucidate the active compound(s) (Watt and Breyer-Brandwijk, 1962).

4. Discussion

This review provides the first comprehensive report on the global diversity, traditional and contemporary uses, chemistry and pharmacology of *Thesium* species, which are of medicinal importance in Africa and Asia. Of the ± 350 *Thesium* species in the world, 23 have traditional and contemporary uses and are most commonly used as medicines (18 species), functional foods and beverages (7 species), charms (6 species) and crafts (3 species), as well as several other minor uses. Use records mirror the geographical distribution of the genus but are restricted to Africa (17 species) and Asia (6 species) despite the presence of *Thesium* on all continents except Antarctica. A striking contrast in use patterns between African and Asian *Thesium* species has become apparent. A noteworthy number of patents (247) for contemporary products, mainly foods and medicines, containing Asian *Thesium* species (predominantly *T. chinense* and *T. longifolium*) have been recorded but none for African *Thesium* species. This complete lack of scientific information on the possible contemporary applications of the large number of African species (± 260) deserves more research attention, especially in light of the popularity of the less diverse Asian *Thesium* species (± 45) as ingredients in contemporary products. The 17 African *Thesium* species with a history of traditional use reported in this review (Table 2) would be a logical starting point for the development of new products, particularly medicinal and food products.

As a medicine, *Thesium* is a valuable resource used in the traditional and contemporary treatment of a remarkable number (137) of ailments related mainly to the reproductive, respiratory and digestive systems, as well as degenerative problems. Several therapeutic properties such as analgesia, anti-bacterial, anti-inflammation, chemoprevention and cytotoxicity have been reported for species of the genus but substantial knowledge gaps remain.

The majority of chemical and pharmacological research on *Thesium* has focussed on *T. chinense* and despite the large number of medicinal uses and wide range of pharmacological activities reported for the genus, there is an extreme paucity of information on basic chemistry and pharmacology, especially for African species. Only four of the 18 medicinally used species (*T. chinense*, *T. himalense*, *T. hystrix* and *T. wightianum*) have published data on chemical compounds and two species (*T. chinense* and *T. viride*) data on pharmacology. To date about 70 chemical compounds, mainly phenolics and fatty acids have been isolated and identified from *Thesium*. The flavonoids kaempferol and quercetin and their associated derivatives isolated from *T. chinense*, have shown multiple therapeutic activities (analgesic, anti-bacterial, anti-inflammatory and anti-oxidation) both *in vitro* and *in vivo*. Furthermore, a norsesquiterpene and three acetylenic acids isolated from *T. chinense* respectively showed cytotoxic and anti-bacterial activities when tested *in vitro*. An aqueous ethanol extract of *T. viride* also showed anti-bacterial properties but as with the majority of medicinal *Thesium* species, the phytochemistry and mode of action of this plant remains unknown. The therapeutic potential of *Thesium* is apparent even from limited studies and necessitates further research attention on phytochemistry, pharmacology and pharmacokinetics to validate its medicinal uses. Such studies may yield bioactive compounds, or combinations that can be used in the development of new and novel therapeutic drugs. Clinical experiments and toxicity studies are furthermore limited and should be addressed, especially since several toxic compounds have been isolated from plants of the genus. To this end, evaluations of the effect of host species on the chemistry and possible uptake of harmful chemical compounds by this parasitic group of plants is needed to ensure safety and efficacy. Chemosystematic studies are also limited and could potentially shed light on relationships within this taxonomically problematic genus.

5. Conclusions

There is substantial scope for new scientific and developmental work to be done on *Thesium*, especially on the African species, against the background of the widely traded and scientifically well-known *T. chinense*. The information presented in this review offers baseline data for such much-needed future studies.

Future research priorities include detailed investigations on: 1) species delimitations and relationships in the genus; 2) further refinements of the geographical distribution patterns that are summarised for the first time in this paper; 3) the identity and traditional uses of ethnobotanically relevant *Thesium* species, several of which have hitherto remained unidentified and only known by their local vernacular names; 4) phytochemistry and chemosystematics, including parasite-host relationships and potential chemical discontinuities of taxonomic value – hardly any comparative data is available for the African species; 5) pharmacology and pharmacokinetics, including clinical experiments and toxicity studies – only *T. chinense* has thus far been studied to any extent; 6) crop development, to explore methods of sustainable production of raw materials as is already done with *T. chinense*; 7) product development, to create new medicinal and functional food products for local and international markets – species with a history of use would be a logical starting point.

Author's contribution

Natasha Lombard did all the literature searches and wrote the first rough draft; Ben-Erik van Wyk conceptualised the study and suggested numerous conceptual improvements to the first and later drafts, and Marianne le Roux contributed editorial comments and corrections.

Declaration of competing interest

The authors declare that there is no conflict of interest regarding publication of this paper.

Acknowledgements

The following people and organizations are thanked: the University of Johannesburg and the South African National Biodiversity Institute (SANBI) for funding and hosting this study, the National Research Foundation for funding the Research Chair in Indigenous Plant Use at the University of Johannesburg (NRF Grant no. 84442), the Pretoria National Herbarium (under SANBI) for access to their collection, Professor Henok Kinfe from the University of Johannesburg for assistance with the search database SciFinder, the staff of the Mary Gunn Library (under SANBI) for their valuable assistance in obtaining information for this study and three anonymous reviewers for suggestions which greatly improved the manuscript.

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