Tuberous plants with active compounds against helminths in livestock: A systematic review

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Review

Abstract

Background: The rise in drug resistance to helminthiases is posing a serious challenge to conventional techniques of controlling parasitic illnesses in livestock. Using less conventional approaches such as plant extracts can improve the situation. This research aims to explore the emerging role of tuberous plants in developing anthelmintics.

Methods: From October 2020 to July 2022, a comprehensive literature search was conducted using the search engines Google Scholar, NISCAIR Online Periodicals Repository, NCBI, Taylor and Francis Online, Wiley Online Libraries, Science Direct, ResearchGate, and Springer Link. The evaluation included only tuberous plants with anthelmintic properties. Qualitative-quantitative analysis techniques were used to analyse the data collected.

Results: Forty-eight ethnobotanical investigations recorded plants with tuber portions that were utilized to combat helminths. There were 43 plants identified, divided into 24 families. Seven plants were found to be the most culturally important in the management of helminths. The common phytochemical classes were phytosterols, tannins, alkaloids, saponins, essential oils, flavonoids, and terpenoids. Twenty-six of these tuberous plants have been tested for their anthelmintic effect against trematodes, cestodes, nematodes, protozoa, coccidian, and eoacanthacephala. Thirty-two plants have been reported to exhibit some toxicity effects. Twelve tuberous plants have been indicated to be endangered.

Conclusions: Dioscorea deltoidea, Dioscorea bulbifera, Dioscorea alata, Gloriosa superba, Curcuma longa, Dioscorea pentaphylla, and *Cyperus rotundus* were the most culturally important plants for controlling helminths. These plants are mostly found in India and Nepal. The review gave more insights into the therapeutic safety of the popular folklore drugs and provided grounds for an assessment of possible measures to be introduced before conducting clinical studies. The article provides public and Government recognition of endangered plants species and spurs conservation efforts toward saving both plants and folk medicinal knowledge. There is a need to investigate other tuberous plants to identify unique compounds that are active against helminths to develop more robust anthelmintic drugs and reduce anthelmintic resistance levels.

Keywords: Anthelmintic, ethnobotanical, tubers, active compound, anthelmintic resistance, livestock

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Background

Helminths are found throughout the world, generating significant losses in ruminant production by exposing animal welfare to risk (Alawa *et al.* 2010). Low reproductive performance, reduced growth rate, low live mass, dull rough coat, organ condemnation, and mortality are all effects of helminths on cattle productivity (Cannel 1998). Helminths are multicellular worms that can be classified into three types: nematodes, cestodes, and trematodes (Duguma *et al.* 2011; Nandhini & Sumathi 2014). Anthelmintics are the most common treatment for helminths. The most commonly used anthelmintics: benzimidazoles, the nicotinic agonists, praziquantel, triclabendazole, and the macrocyclic lactones act either by interfering with target sites unique to the parasite or differ in their structural features from those of the homologous counterpart present in the vertebrate host (Köhler 2001).

Benzimidazole is a broad-spectrum anthelmintic effective against nematodes and trematodes. Levamisole is effective against nematodes and trematodes at higher doses. Mixing benzimidazole and levamisole can reduce resistance to nematodes in sheep (McKenna 1990). The group salicylanilides, contain compounds primarily used against trematodes, praziquantel is effective against cestodes, and ivermectin is primarily used against nematodes (Cezar *et al.* 2010). However, due to their high cost, general toxicity, drug residue concerns in milk and meat, and the development of drug resistance, the utility of current medications for animal health and productivity is being questioned (Mwale *et al.* 2005; Oliveira *et al.* 2009; Zaman *et al.* 2017). Dealing with anthelmintic resistance has also proven problematic due to high costs and long wait times for new compounds to reach the market (Besier 2007).

Because of their accessibility, affordability, and availability, ethnoveterinary plants have become more relevant in managing helminths in the face of the aforementioned obstacles. Furthermore, medicinal plants, including tuberous plants, have been shown to play an important role in drug discovery and development processes (Eloff 1998; Newman & Cragg 2007, McCorkle & Mathias-Mundy 1992; McGaw & Eloff 2010). Dealing with anthelmintic resistance has also proven problematic due to high costs and long wait times for new compounds to reach the market (Besier 2007).

It is thought that livestock farmers have adapted ethnoveterinary remedies used to treat human beingsfor use in animals or vice versa over the millennia. Similar therapies are commonly used to treat similar ailments in humans and their livestock, and the same is true for anthelmintics. (Gakuya 2001) previously stated that human and livestock herbalists are often the same and that there is a need for a collaborative approach when dealing with medicinal plants because most herbs are used to treat both human and animal ailments.

Plants are an important natural supply of a wide range of chemicals, ranging from simple skeleton structures to sophisticated ones. Many well-known components, such as quinine (chloroquine and mefloquine), artemisinin, taxol (paclitaxel), camptothecin, khellin, sodium chromoglycate, galegine, metformin, papaverine, and verapamil, are based on ancient medications (Cragg & Newman 2013; Khan & Ahmad 2019; Koparde *et al.* 2019). Tuberous plants are one of the plant classes being researched for their anthelmintic properties.

Tubers are large fleshy underground structures that form from stems or roots of plants such as potatoes and yams, and they belong to a variety of botanical families. Orchidaceae is one of the largest botanical families that produce tubers, with between 20000 and 35000 species divided into 600-850 genera (Gutiérrez 2010; Hossain 2011). However, leaves, barks, stems, seeds, latex, and flowers were found to be the most regularly employed parts in the treatment of helminths by the majority of researchers (Ataba *et al.* 2020; ba Ndob *et al.* 2016; Kuma *et al.* 2015; Muthee *et al.* 2011). The fact that these parts are easier to collect and process than tubers and roots may explain why they are more commonly used (Ghimire *et al.* 2008; Giday *et al.* 2003). However, their collection may harm regeneration and lead to species extinction. To prevent the loss of ethnobotanical knowledge of these plants, this review study documents species with specific tuber portions employed as anthelmintics as stated in ethnobotanical studies.

Anthelmintic action of Phytochemicals

Tannins, alkaloids, flavonoids, terpenoids, phenols, saponins, and essential oils have all been shown to have anthelmintic properties (Ajah & Eteng 2010; Athanasiadou *et al.* 2001; Wang *et al.* 2010). Phenols affect the decoupling of the oxidative phosphorylation responsible for ATP production interfering with energy production and leading to the death of parasites (Salhan *et al.* 2011). Tannins have ovicidal action related to their interaction with enzymes responsible for the hatching of eggs (Molan & Faraj 2010). In addition, they can interact with metabolites, increasing cell permeability, which leads to their interaction with free proteins or cuticle glycoproteins of parasites hindering nutrient absorption, mobility, reproduction, and consequently causing their death (Botura *et* *al.* 2013). Quinones inhibit cell development by different mechanisms, such as apoptosis induction, intercalation and binding with DNA, and inhibition of the enzyme topoisomerase (Pe´rez-Pertejo *et al.* 2019). Terpenes in essential oils exhibit anthelmintic effects by enhancing suppression effects of many biochemical targets such as tyramine receptors, chloride channels, and acetylcholinesterase (Lynagh *et al.* 2014; Miyazawa *et al.* 2016; Trailović *et al.* 2015). Alkaloids and coumarins effect result from both competitive and non-competitive inhibition of parasitic acetylcholine receptors (Basumatary *et al.* 2020; Dubois *et al.* 2019). Flavonoids cause oxidative stress by increasing the production of the reactive oxygen species (ROS), thus affecting the normal physiology of parasites(Wang *et al.* 2013). Terpenoids inhibit the motility and egg-hatching ability of worms (Ferreira *et al.* 2016; Katiki *et al.* 2017). Anthelmintic effects of saponins are due to their interaction with cell membranes causing changes in cell permeability (Doligalska *et al.* 2011; Tava & Avato 2006; Vo *et al.* 2017).

Materials and Methods

Research questions

i. Which plant species have their tuber parts culturally used as anthelmintics?
ii. What quantitative analysis methods were used in carrying out ethnobotanical surveys?
iii. Which plants and plant families are most represented in ethnobotanical studies?
iv. What are the growth habits of these tuberous plants, and which is the most represented growth habit?
v. Which active compounds were commonly found in most of the identified plants exhibiting anthelmintic properties?
vi. What is the anthelmintic activity of these tuberous plants and which gastrointestinal parasite have they been tested against?
vi. What is the toxicological status of these plants, what are the toxic compounds found in these plants, and the toxic compounds belong to which classes of phytochemicals?
vii. Which tuberous plant with anthelmintics properties are endangered and which ones are not?

Materials

Extensive online literature surveys were done to retrieve relevant data from October 2020 up to July 2022. The identification of tuberous plants used to control helminths was restricted using the following inclusion criterion: i. only ethnobotanical studies articles were considered; ii. articles that indicated a plant with its tuber or tuberous roots used as an anthelmintic, wormicidal vermifuge, and/or vermicide; and iii. only articles that were written in English or that had English translations were considered.

Key search words used were Ethnobotanical survey or study or observations AND tuber or tuberous roots AND anthelmintic or wormicidal or vermifuge or vermicide. Search engines used included Google Scholar, NISCAIR Online Periodicals Repository, NCBI, Taylor and Francis Online, Wiley Online Libraries, Science Direct, ResearchGate, and Springer Link. Data recorded included the scientific name of a plant, vernacular name, voucher number, botanical family, plant growth habit, area of study, country of study, sampling method used, method of data collection, qualitative analysis index, other uses of the plant, and the reference. The identification of the plant's anthelmintic activity was restricted to literature that reported: i. tests against gastrointestinal worms that affect animals but not humans, ii. literature that showed a positive anthelmintic effect of the tuberous plant, and iii. Keywords plant name AND anthelmintic e.g. *Curcuma longa* AND anthelmintic. The toxicological statuses of the plants were researched with the following keywords, plant name e.g., *Curcuma longa* AND toxicity. The endangerment status of the plants, with regards to their conservation, was determined by using the keywords, plant name e.g. *Curcuma longa* AND endangered. To determine phytochemicals found in the culturally important plants, the search involved all articles that indicated phytochemical analysis of the plants with keywords Plant name AND phytochemicals or phytochemistry e.g. *Curcuma longa* AND Phytochemistry. Qualitatiove and quantitative analysis was performed on the gathered data. Tables, radars, and bar graphs were used to display the results.

Data extraction

Data were gathered employing a standardized data collection as follows:
i. General data on studies: number of studies, authors, and date of publication
ii. Data on the survey: country and area of study, sampling method, data collection method, and quantitative analysis index technique used
iii. Data on medicinal plants: scientific name of the plant, vernacular name, voucher number, family, growth habit, phytochemistry, anthelmintic activity, parasites, toxicity, toxic compounds, and plant status

Quali- and quantitative analysis:

Frequency cited (FC), Relative frequency of citation (RFC), and Family importance value (FIV).

Methods used for these calculations were adopted from (Tardío & Pardo-de-Santayana 2008), (Vitalini *et al.* 2013), and (Fakchich & Elachouri 2021) with some modifications. FC was calculated as the frequency of mentioning for a single botanical species by studies. It is the number of times a plant was reported by different studies. RFC was obtained by dividing the FC by the total number of citations (N). FIV is calculated by counting the percentage of studies mentioning a specific family using the formula: FIV= (FC (family)/N). However, this was modified by calculating the number of plants representing each botanical family and dividing it by the total number of plants identified in this study.

Comparative analysis

The Jaccard Index (JI) was used to calculate similarities between studies carried out in the top mentioned countries of study. JI may be expressed as follows:

$$JI = C/(A+B-C)$$

Where A is the number of plants recorded in country A, B is the number of plants recorded in country B, and C is the number of plants common to A and B.

Results and Discussion

Matrix of general data

The data included in this study were acquired through ethnobotanical surveys, as shown in Table 1. The data was compiled using 48 ethnobotanical studies in total. The tubers of 43 plant species from 24 botanical families have been documented to be used as anthelmintics.

As shown in Figure 1, the publications cited were undertaken in India, Nepal, Pakistan, China, Kenya, Turkey, Indonesia, Sudan, Zimbabwe, South Africa, Bangladesh, Ethiopia, and Uganda. The highest numbers of citations were from India followed by Nepal, South Africa, and Pakistan. The reason for high citations in these countries could be that they are developing countries and over 80% of people in developing countries, for example, continue to rely on traditional plant-based medicines for primary health care (Bhat *et al.* 2021; Chauhan 2020). India and Nepal have been reported to be amongst the countries with greatest number of plant species by country in the world (Butler 2020).

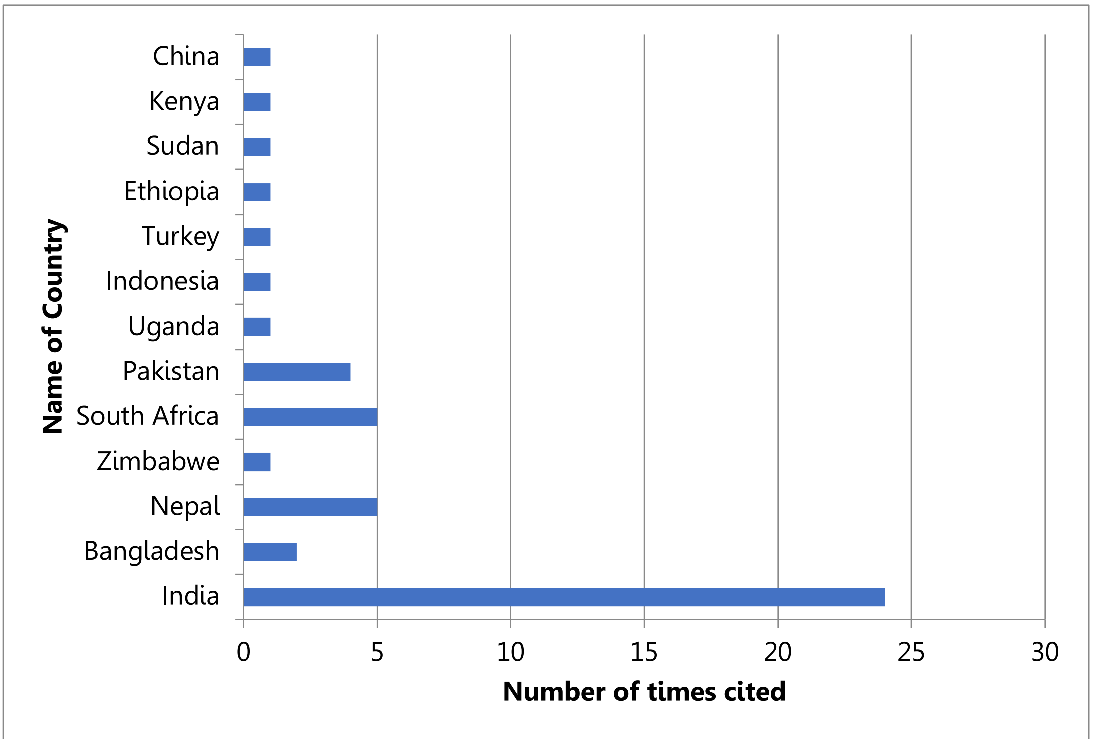

Figure 1. Countries cited to have tuberous plants with anthelmintic properties..

Table 1. Tuberous plants with anthelmintic properties cited in various publications across the world.

Species	Vernacular Name/ Voucher Number	Family/ Habit	Number of participants	Country/ Area	Quantitative Analysis Technique	Other Uses reported	Reference
Aconitum heterophyllum Wall	Sarba wali	Ranunculaceae/ Herb	-	Pakistan/ Dir, Kohistan valley	-	treat fever, gout, rheumatism and pain in body tonic, antiperiodic, vomiting, appetizer, astringent, diarrhea, gastric pain, stomachache and cure cold.	(Hazrat *et al.* 2011)
Albuca setosa Jacq.	Ingwebeba/ MSAN03/2015	Hyacinthaceae/ Herb	53	South Africa/Eastern Cape Province	FL	Not reported	(Sanhokwe 2015)
Allium sativum (L.)	Sambram gufur	Amaryllidaceae/ Herb	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)
Alpinia galangal (L.) Willd.	Pannodara/ Lengkuas	Zingiberaceae/ Herb	-	Indonesia/ South Kalimantan	-	Not reported	(Hatta 2020)
Arisaema consanguineum Schott	Banku	Araceae/Herb	12	Nepal/ Chepang community	-	Not reported	(Rijal 2011)
Arisaema jacuemontii Bume	Sappe didhaud, Sarp	Araceae/ Herb	-	India/ district Kathua (J&K)	-	Remedy for colic	(Kumar & Bhagat 2012)
Asparagus racemosus Willd.	Sansarpali	Asparagaceae/ Shrubby climber	27	India/ Murari Devi and surrounding areas (Mandi district, Himachal Pradesh	-	aphrodisiac, rheumatism, cough, dysentery, febrifuge, gastric complaints gonorrhea, headache, menstrual complaints, snake bite, stomachache, tonic, urine complaints	(Sharma *et al.* 2015)

Asparagus racemosus Willd.	Sansarpali	Asparagaceae/ Shrubby climber	-	India/ Naina Devi Sacred Shrine Rewalsar, Himachal Pradesh, Northwestern Himalaya	-	Medicinal (Anthelmintic, aphrodisiac, rheumatism, bleeding from nose, cough, dysentery, febrifuge, gastric complaints, gonohorrea, headache, menustral complaints, snake bite, stomachache, tonic, urine complaints); Edible	(Marpa *et al.* 2020)
Azadirachta indica A. Juss.	Not reported	Meliaceae/ Tree	-	India/ Paderu division of Visakhapatnam District, AP	-	Not reported	(Padal *et al.* 2010)
Bulbine asphodeloides (L.) Wild.	Not reported	Asphodelaceae/ Herb	30	South Africa/ Nkonkobe Municipality, Eastern Cape Province	-	Not reported	(Wintola & Afolayan 2010)
Bulbine asphodeloides (L.) Wild.	Uyakayakane	Asphodelaceae/ Herb	80	South Africa/ Amathole district municipality of the Eastern Cape province	-	Rashes, dysentery, diarrhea	(Wintola & Afolayan 2015)
Costus speciosus (J. König.) Sm.	Keaw	Costaceae/ Herb	5	Bangladesh/ Daudkandi sub-district of Comilla district	-	Dermatitis, appetizer, leucorrhea, impotency, glassiness of skin.	(Hossain *et al.* 2010)
Costus speciosus (Koen) Sm.	Bogachi	Costaceae/ Herb	-	India/ Visakhapatnam district, Andhra Pradesh	-	Not reported	(Padal *et al.* 2014)
Curcuma amada Roxb.	Jangli haldi/ ZN 04	Zingiberaceae/ Herb	710	India/ Aravalli hill range	-	Not reported	(Bhardwaj *et al.* 2011)
Curcuma aromatica Salisb.	Haldi/ ZN 06	Zingiberaceae/ Herb	710	India/ Aravalli hill range	-	Not reported	(Bhardwaj *et al.* 2011)
Curcuma caesia Roxb.	haldi gaswm/ BUBH0000008	Zingiberaceae/ Herb	710	India/ Chirang District of Assam	-	Not reported	(Swargiary *et al.* 2019)
Curcuma longa L.	Haldi	Zingiberaceae/ Herb	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)
Curcuma longa L.	Haldi/ BUBH2018002	Zingiberaceae/ Herb	27	India/ Udalguri district of Assam	-	Not reported	(Swargiary *et al.* 2019)

Curcuma longa L.	Holud	Zingiberaceae/ Herb	5	Bangladesh/ villages of Natore and Rajshahi districts	-	Gonorrhea, sore throat, hepatitis, appetizer, allergy, eye disorders.	(Hossain *et al.* 2010)
Cyperus rotundus L.	Deela	Cyperaceae/ Herb	250	Pakistan/ District Bahawalpur, Southern Punjab province	-	Astringent, appetizer, stomachic, and leprosy	(Muhammad Farrukh Nisar *et al.* 2014)
Cyperus rotundus L.	Dellia ghas	Cyperaceae/ Herb	90	India/ Panna District, Central India	-	Stimulant, diuretic	(Gwalwanshi *et al.* 2014)
Cyperus rotundus L.	Seida	Cyperaceae/ Herb	-	Sudan/ Southern Blue Nile district	-	TYreat stomach troubles	(El-Kamali & El-Khalifa 1999)
Cyperus rotundus L.	Deela	Cyperaceae/ Herb	-	Pakistan/ Bahawalnagar, Punjab	-	Appetizer, biliousness, pruritis, pain, vomiting, epilepsy, diuretic, diaphoretic, vulnerary ulcers, sores, fevers and dyspepsia	(Nisar *et al.* 2014)
Cyperus rotundus L.	Motha	Cyperaceae/ Herb	-	India/ Bundelkhand region, Uttar Pradesh	-	Tonic and stimulant effect, demulcent, diuretic, diaphoretic, fever, dyspepsia, vomiting cholera, diarrhea, dysentery	(Unial *et al.* 2011)
Cyphostemma adenocaule (A. Rich.) Willd Drummond	Ekimara	Vitaceae/ Herbaceous climber	32	Uganda/ Nakasongola District	_	Not reported	(Nalule *et al.* 2011)
Dioscorea alata L	Not reported	Dioscoraeceae/ Herbaceous climber	-	India/ Chalsa forest range under Jalpaiguri division, West Bengal	F, RF, D, RD, RV, RDo, A, IVI, RH	Used as Diuretic, contraceptive and also useful in diabetes, Leprosy, gonorrhea	(Sarkar *et al.* 2017)
Dioscorea alata L.	Chupri Alu	Dioscoraeceae/ Herbaceous climber	-	India/ Tripura	-	Not reported	(Dey *et al.* 2012)
Dioscorea alata L.	Achuchu	Dioscoraeceae/ Herbaceous climber	40	India/ Sumi Nagas in Zunheboto District, Nagaland, Northeast India	-	Aphrodisiac, Diuretic, it is useful in treating diabetes, piles, leprosy, gonorrhea	(Sumi & Shohe 2018)
Dioscorea alata L.	Pangnang	Dioscoraeceae/ Herbaceous climber	90	Nepal/ chepang community	-	fish poisoning	(Tamang *et al.* 2017)

Dioscorea alata L.	Pangnang	Dioscoreaceae/ Herbaceous climber	12	Nepal/ Chepang community	-	edible	(Rijal 2011)
Dioscorea bulbifera L.	Lak	Dioscoraeceae/ Herbaceous climber	90	Nepal/ chepang community	-	piles, dysentery	(Tamang *et al.* 2017)
Dioscorea bulbifera L.	Metealu, Ram bara	Dioscoraeceae/ Herbaceous climber	-	Bangladesh/ Bilaichari Upazilla, Rangamati District	Factor of informant consensus (FIC) Jaccard index (JI)	Not reported	(Faruque *et al.* 2019)
Dioscorea bulbifera L.	Varahikanda	Dioscoraeceae/ Herbaceous climber	-	India/ Jatasankar region of Girnar forest, Gujarat	-	Diabetes, skin disease,	(Nita & Haresh 2013)
Dioscorea bulbifera L.	Githa/230-91 VN	Dioscoraeceae/ Herbaceous climber	130	Nepal/ Myagdi District	-	Not reported	(Manandhar 1995)
Dioscorea bulbifera L.	Kitthee, Vansittha	Dioscoraeceae/ Herbaceous climber	-	India/ district Samba of Jammu Province, Jammu & Kashmir	-	Tonic, alterative, aphrodisiac, stomachic, expectorant, and astringent	(Pandita *et al.* 2013)
Dioscorea bulbifera L.	Pas	Dioscoraeceae/ Herbaceous climber	12	Nepal/ Chepang community	-	Edible	(Rijal 2011)
Dioscorea deltoidea Wall. ex Griseb.	Goi	Dioscoraeceae/ Herbaceous climber	12	Nepal/ Chepang community	-	Edible	(Rijal 2011)
Dioscorea deltoidea Wall. ex Griseb	Krish	Dioscoraeceae/ Herb	-	India/ Bangus Valley, Kashmir Himalaya	-	Treat ophthalmic infections	(Ishtiyak & Hussain 2017)
Dioscorea deltoidea Wall. ex Griseb	Bhayakur	Dioscoraeceae/ Herb	50	Nepal/ Puranchaur VDC, Kaski District	-	Kill lice and bush poison	(Khatri 2012)
Dioscorea deltoidea Wall. ex Griseb	Kanees	Dioscoraeceae/ Herb	-	Pakistan/ Dir, Kohistan valley	-	Expectorant, diuretic, uterine sedative and homeostatic	(Hazrat *et al.* 2011)
Dioscorea deltoidea Wall. ex Griseb	Kill Dhari	Dioscoraeceae/ Herb	-	India/ District Kathua (J&K)	-	To alleviate constipation and tubers used for washing hairs to kill lice.	(Kumar & Bhagat 2012)

Dioscorea deltoidea Wall. ex Griseb	Kanees	Dioscoraeceae/ Herb	-	Pakistan/ Swat Valley	-	Uterine sedative, homeostatic, diuretic and expectorant. Tubers are also used as fish poison.	(Hamayun 2007)
Dioscorea deltoidea Wall. ex Griseb	Ban goi	Dioscoraeceae/ Herb	90	Nepal/ Chepang community	-	Fish poisoning	(Tamang *et al.* 2017)
Dioscorea deltoidea Wall. ex Griseb	Yams	Dioscoraeceae/ Herb	-	Pakistan/ Chitral District, Malakand Division, NWFP	-	Kill lice, fish poison	(Ahmad 2001)
Dioscorea halmiltonii Hook. F Ban	Not reported	Dioscoreaceae/ Herbaceous climber	-	Nepal/ Kaski District	FIC, UV, FL	Not reported	(Subedi 2017)
Dioscorea pentaphylla	Rani bhyagur, Bhegur;/ Mld.CG. – 022	Dioscoreaceae/ Herbaceous climber	21	India/ Bamangola Block of Malda District, West Bengal	-	Contraceptive, anthelmintic, stomach problems, gastric disorders, pains, allergic fever, veterinary problems	(Ghosh 2017)
Dioscorea pentaphylla L.	Not reported	Dioscoreaceae/ Herbaceous climber	-	Nepal/ Kaski District	FIC, UV, FL	Not reported	(Subedi 2017)
Dioscorea pentaphylla L.	Not reported	Dioscoreaceae/ Herbaceous climber	-	India/ Satpuda Hills	-	Not reported	(Kosalge & Fursule 2009a)
Dioscorea prazeri Prain & Burkill	Jyar	Dioscoreaceae/ Herbaceous climber	12	Nepal/ Chepang community	-	Edible	(Rijal 2011)
Dryopteris setosa (Thunb.) Akas	Pak mo/Mxy72	Dryopteridaceae/ Herb	83	China/ Southwest Guizhou	FIC, UR	Not reported	(Xiong & Long 2020)
Elephantorrhiza elephantina (Burch.) Skeels	Intolwane/ MSAN02/2015	Fabaceae/ Shrub	53	South Africa/ Eastern Cape Province	FL	Not reported	(Sanhokwe 2015)
Flemingia procumbens Roxb.	sohphlang	Fabaceae/ Herb	-	India/ Meghalaya	-	Not reported	(Hynniewta & Kumar 2008)
Flemingia vestita Benth and Hooker	Soh-phlang	Fabaceae/ Shrub	-	India/ Meghalaya	-	Not reported	(Rao 1981)

Gloriosa superba L.	Kalappankizh angu	Colchicaceae/ Herbaceous climber	-	India/ Kolli Malayalis of Nammakkal district, Eastern Ghats, Tamil Nadu	-	anti-inflammatory, alterative, antileprotic. Used for piles, swollen joints, parasitical affections of skin, Uterine stimulant	(Muthuraja *et al.* 2014)
Gloriosa superba L.	Kalihari/ LL 04	Colchicaceae/ Herbaceous climber	710	India/ Aravalli hill range	-	Not reported	(Bhardwaj *et al.* 2011)
Gloriosa superba L.	kalihari	Colchicaceae/ Herbaceous climber	135	India/ Tarai region of Kumaun, Uttarakhand	-	Kill head lice	(Mathur & Joshi 2013)
Gloriosa superba L.	Kukadsira Kadiya-nag	Colchicaceae/ Herbaceous climber	-	India/ district Samba of Jammu Province, Jammu & Kashmir	-	Tonic, stomachic, remedy of gout, neuralgia, colic, chronic ulcers, piles, fever and thirst	(Pandita *et al.* 2013)
Gunnera perpensa L.	Iphuzi (River pumpkin)/ VMAP10/2006	Gunneraceae/ Herb	30	South Africa/Eastern Cape Province	-	Not reported	(Maphosa & Masika 2010)
Gunnera perpensa L.	Iphuzi/ MSAN08/2015	Gunneraceae/ Herb	53	South Africa/Eastern Cape Province	FL	Not reported	(Sanhokwe 2015)
Hypoxis argentea Harv. ex Baker	Inongwe yehashi (Yellow stars)/ VMAP12/2006	Hypoxidaceae/ Herb	30	South Africa/Eastern Cape Province	-	Not reported	(Maphosa & Masika 2010)
Kaempferia galanga L.	Sompera	Zingiberaceae/ Shrub	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)
Melastoma malabatricum L.	tinkur bedor/BUBH0000130	Melastomataceae / Herb	27	India/ Chirang District of Assam	-	Not reported	(Swargiary *et al.* 2019)
Neorautanenia brachypus (Harms) C.A.SM	zhombwe	Fabaceae/ Shrub	83	Zimbabwe/ Sengwe, Chiredzi	-	Feeding animals, Treating bad wounds, Harvesting fish, feed dogs to improve on tracking abilities	(Murungweni *et al*, 2012)
Oroxylum indicum (L) Kurz	Kharong	Bignoniaceae/ Tree	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)

Pelargonium reniforme Curt	Uvendle/ VMAP20/2006	Geraniaceae/ Shrub	30	South Africa/Eastern Cape Province	-	Not reported	(Maphosa & Masika 2010)
Peliosanthes bakeri Hook. f.	sikho bifang/ BUBH2018039	Liliaceae/ Shrub	27	India/ Chirang District of Assam	-	Not reported	(Swargiary *et al.* 2019)
Pueraria tuberosa	Ghora ro bel/ FB 04	Fabaceae/ Shrubby climber	-	India/ Aravalli hill range	-	Relieves pain	(Bhardwaj *et al.* 2011)
Raphanus sativus L.	Karaturp	Brassicaceae/ Herb	43	Turkey/ Çamlıdere	FIC, UV, CI	For asthma, bronchitis, cancer, diabetes, urinary tract diseases, as anthelmintic, antitussive, appetizer, tonic	(Gunbatan *et al.* 2016)
Rhoicissus tridentata (L.f.) Willd. & R.B. Drumm.	Omumara	Vitaceae/ Shrubby climber	160	Uganda/Nakasongola District	_	Not reported	(Nalule *et al.* 2011)
Rhoicissus tridentata (L.f.) Willd. & R.B. Drumm.	Ntagaraga	Vitaceae/ Shrubby climber	32	South Africa/ Madikwe area of the Northwest Province of South Africa	-	Heart water, red water, general ailments, abortion	(Van der Merwe *et al.* 2001)
Rumex usambarensis Dammer.	Enkaisijoi/ JK05	Polyganaceae/ Herb	30	Kenya/ Loitoktok District	UVs, FUV, FIC	Treat constipation	(Muthee *et al.* 2011)
Sauromatum venosum (Ait) Schott	Pebada/ JBA-249	Araceae/ Herb	8	India/Jhabua District of Madhya Pradesh	-	Applied on the pimple and blemishes	(Wagh & Jain 2014)
Stephania glabra Roxb	Nepali-Gurjagano, Lepcha-Burkil-Kunthek-rik	Menispermaceae / Shrubby climber	-	India/ North Sikkim	-	Treatment of diabetes, fever, gastric problem, amoebic dysentery, rheumatic body ache, blood dysentery, leprosy, anticancer	(Maity *et al.* 2004)
Zingiber officinale Roscoe	Haijeng	Zingiberaceae/ Herb	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)
Zingiber zerumbet (L) Roscoe ex Sm.	Bura uth	Zingiberaceae/ Herb	42	India/ Udalguri district of Assam	FC, RFC, FIV	Not reported	(Swargiary *et al.* 2020)

Species number of medicinal plants (families, genera, species, and growth habits)

A total of 24 plant families were recorded with tuber plants that are effective against helminths, and the results are displayed in Figure 2. Zingiberaceae family was most represented with eight plants (33%), Dioscoreaceae six plants (25%), Fabaceae five plants (21%), Araceae three plants 13%), and Polygonaceae two plants (8%). The results on plant families recorded for this study are different from those by Swargiary *et al.* (2019b) where Apiaceae, Araliaceae, Bromeliaceae, Apocynaceae, and Meliaceae families were listed as having plant species with anthelmintic effects. The results were similar to those by Ali *et al.* (2019), who found plants having veterinary effects to belong to the Fabaceae family. This was also similar to those by Sanhokwe *et al.* (2016) where Asphodelaceae, Hyacinthaceae, Fabaceae, and Gunneraceae were represented by plants with anthelmintic effects. However, they reported Apocynaceae, Apiaceae, Araliaceae, and Agapapanthaceae to represent some anthelmintic plants that were not mentioned in the current study. Furthermore, Maphosa and Masika (2010), indicated Anacardiaceae, Capparidaceae, Geraniaceae, Lamiaceae, Loganiaceae, Pittosporaceae, Ptaeroxylaceae, Rhamnaceae, Rutaceae, Sterculiaceae, and Titiaceae families to also represent plants with anthelmintic action.

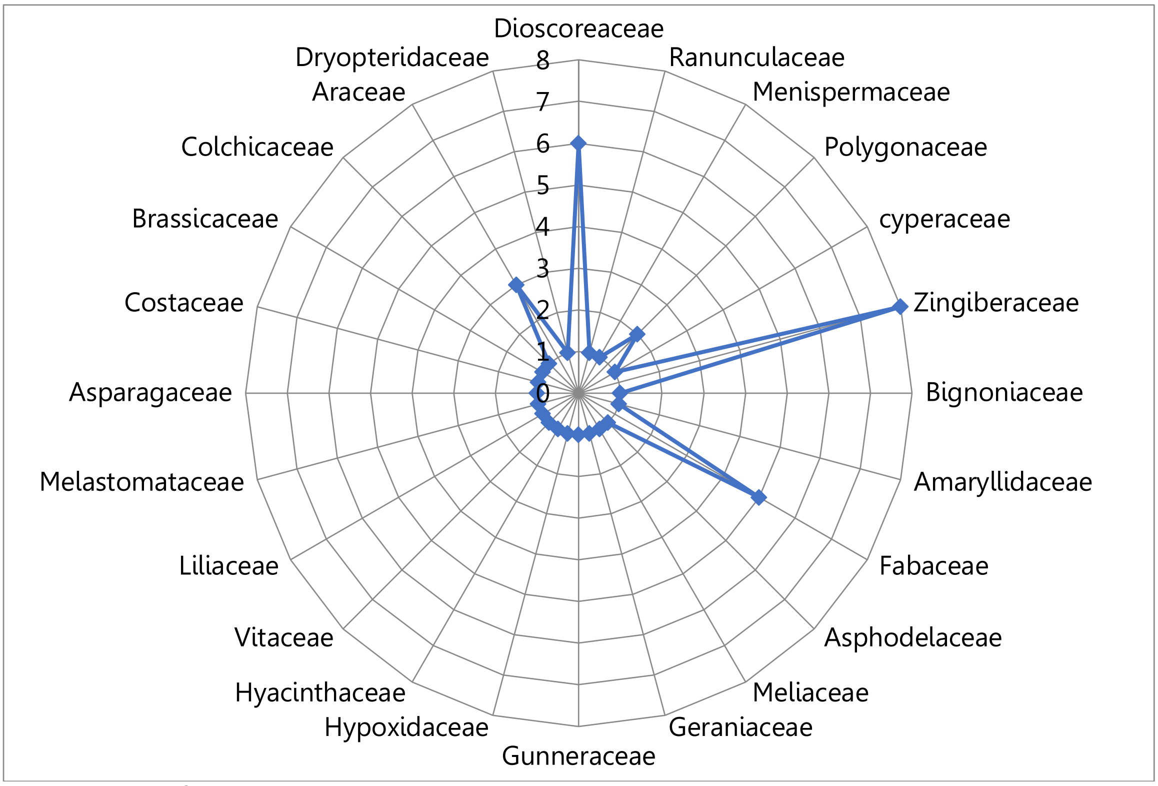

Figure 2. Families of tuberous plants with anthelmintic properties.

Figure 3 depicts the proportions of the tuberous plant species with different growth habits. Twenty-two (51%) of the plants had an herbaceous growth habit, eight plants (19 %) herbaceous climbers, six shrubs (14%), four (9%) shrubby climbers, and three (7%) trees. However, other publications have cited trees and shrubs to represent plants with anthelmintic effects (Gemechu 2021; Mutie *et al.* 2020). The research by Tefera Kim (2019) cited herbs and trees to be the dominant growth habits of medicinal plants

Species Frequency of Citation (FC)

Species Frequency of Citation (FC) was used to identify plants that were frequently mentioned in ethnobotanical research as having tuber portions used as anthelmintics. It therefore represented the most commonly tuberous plants utilized as anthelminthics. The top seven plants with the highest FC value were as follows: *Dioscorea deltoidea* (eight citations) (Ahmad 2001; Hamayun 2007; Hazrat *et al.* 2011; Ishtiyak & Hussain 2017; Khatri 2012; Kumar & Bhagat 2012; Rijal 2011; Tamang *et al.* 2017), *Dioscorea bulbifera* (six citations) (Faruque *et al.* 2019; Manandhar 1995; Nita & Haresh 2013; Pandita *et al.* 2013; Rijal 2011; Tamang *et al.* 2017), *Dioscorea alata* (five citations) (Dey *et al.* 2012; Rijal 2011; Sarkar *et al.* 2017; Sumi & Shohe 2018; Tamang *et al.* 2017), *Cyperus rotundus* (four citations) (El-Kamali & El-Khalifa 1999; Gwalwanshi *et al.* 2014; Nisar *et al.* 2014; Unial *et al.* 2011), *Gloriosa superba* (four citations) (Bhardwaj *et al.* 2011; Mathur & Joshi 2013; Muthuraja *et al.* 2014; Pandita *et al.* 2013), *Curcuma longa* (three citations) (Hossain *et al.* 2010; Swargiary *et al.* 2020; Swargiary *et al.* 2019a), *and Dioscorea* *pentaphylla* (three citations) (Ghosh 2017; Kosalge & Fursule 2009; Subedi 2017). A high FC score indicated that their tuber parts were known to be efficient against helminths in their culture.These findings, however, differed from those of Maphosa Masika (2010). The most reported plants were *Aloe ferox*, *Teucrium trifidum*, *Leonotis leonurus*, and *Strychnos henningsii*. Some common anthelmintic plants indicated in literature are *Carica papaya*, *Butea monosperma*, *Terminalia arjuna*, *Z. officinale*, *Nigella sativa*, *Fumaria parviflora*, *Flemingia vestita*, *Allium sativum*, *Melia azedarach*, *Cucurbita maxima*, *Ocimum sanctum*, *Achyranthes aspera*, *Azadirachta indica*, *Calotropis procera*, and *Artemisia annua* (Nirala 2019). The research by Wintola & Afolayan (2015) found the most common anthelmintic plants to be *Hypoxis hererocallidea*, *Strychonos henningsii*, *Rumex lanceolatus*, *Ozoroa mucronata*, and *Acacia karoo*. The other tuberous plants with anthelmintic effects not indicated in this study are *Strychnos henningsii*, *Corallocarpus epigaeus*, and *Hypoxis hemerocallidea* (Ishnava & Konar 2020; Matyanga *et al.* 2020).

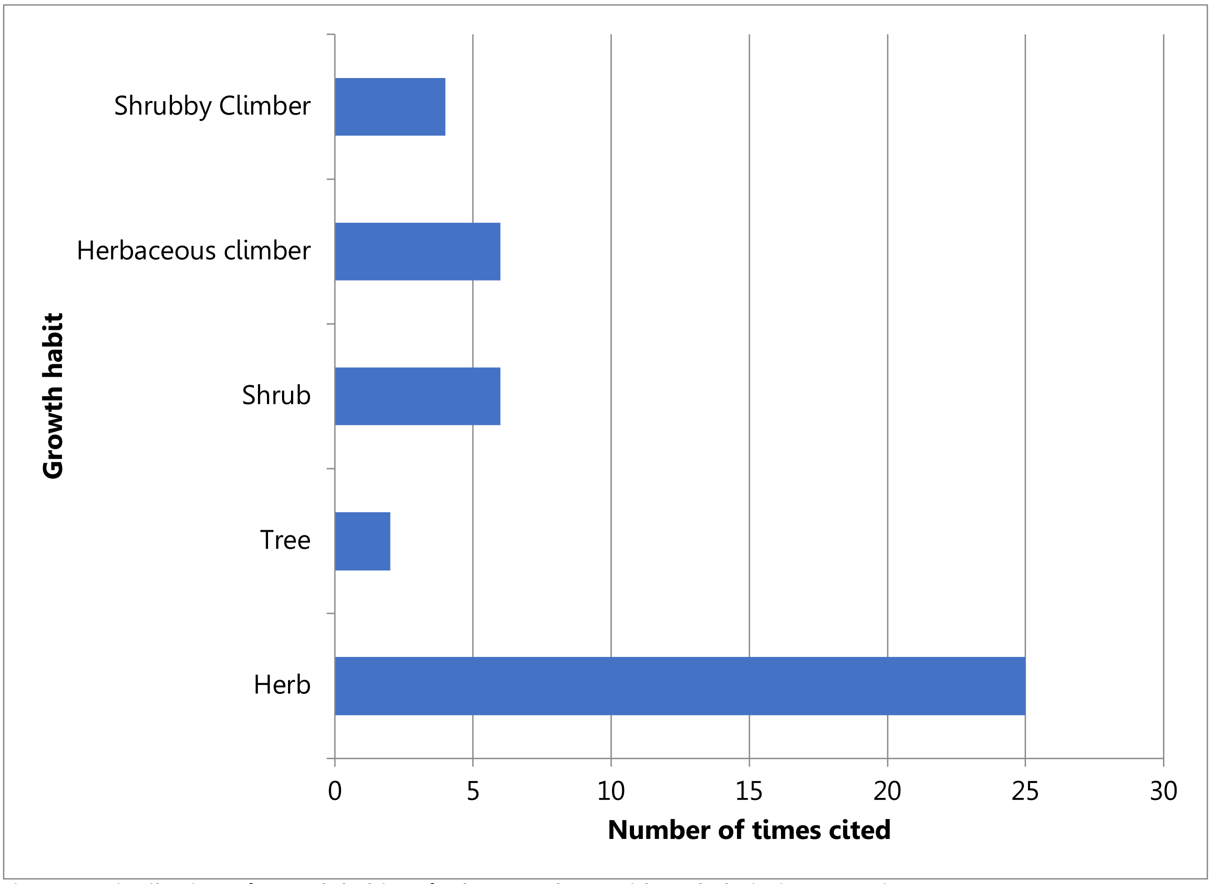

Figure 3. Distribution of growth habits of tuberous plants with anthelmintic properties.

Species Relative Frequency of Citation (RFC)

Relative Frequency of Citation **(**RFC) ranges from zero (no citations indicating that the plant is essential) to one (when all the citations consider a certain plant important). As shown in Figure 4, the greatest RFC value was determined for *Dioscorea deltoidea*, *Dioscorea bulbifera* (0.080), *Dioscorea alata* L., *Cyperus rotundus* (0.067), *Gloriosa superba* (0.053), *Curcuma longa* L., and *Dioscorea pentaphylla* (0.040). The lowest RFC value of 0.013 was found in 31 species and 5 species had a value of 0.027. It was also apparent that plants with a high FC value also had a high RFC value. The plants' high RFC value may be attributed to their abundance in the area, as well as the fact that their tubers were known to have anthelmintic characteristics. Plants with high RFC values, on the other hand, are endangered and should be prioritized for conservation and long-term usage (Amjad *et al.* 2020). The results of this study were different from those by Swargiary *et al.* (2021) who reported *Andrographis paniculata*, *Alstonia scholaris*, *Ananas comosus*, and *Azadirachta indica* to be the dominant anthelmintic plants. Despite having a low RFC value of 0.013 during the investigation, *Flemingia vestita* (Das *et al.* 2009; Toner *et al.* 2008), *Zingiber offficinale* (Ghafar *et al.* 2021; Kiambom *et al.* 2021; Toulah *et al.* 2019), *Azadirachta indica* (Ibekwe 2019; Salma *et al.* 2021; Yamson *et al.* 2019), and *Allium sativum* (Azra *et al.* 2019; Luce 2019; Shirgholami *et al.* 2021) plants' tubers have been widely explored as a source of anthelmintic chemicals against helminths and their important proteins (enzymes). Genistein, the active component derived from *Flemingia vestita* tubers, has been extensively studied for its efficacy against several forms of helminths (Moharm *et al.* 2020; Singla & Kaur 2021)

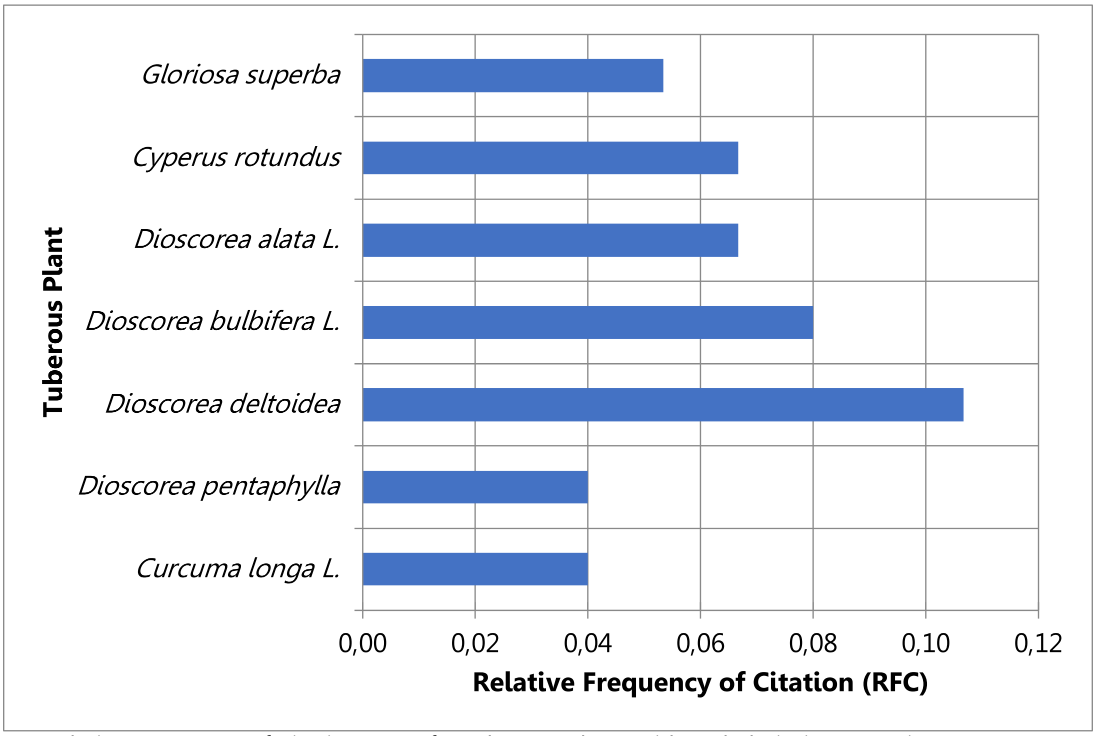

Figure 4. Relative Frequency of Citation (RFC) for tuberous plants with anthelmintic properties.

Phytochemicals found in plants with the highest RFC values

Table 2 below shows the presence of phytochemicals such as essential oils, flavonoids, tannin, saponins, unsaturated triterpenoides, resins, sterols, quinones, coumarins, and alkaloids in *Dioscorea deltoidea, Dioscorea bulbifera*, *Dioscorea alata L.*, *Cyperus rotundus*, *Gloriosa superba*, *Curcuma longa L.*, and *Dioscorea pentaphylla*. The classes of phytochemicals that are common in all these plants are phytosterols, tannins, alkaloids, saponins, essential oils, flavonoids, and terpenoids. Tannins, alkaloids, flavonoids, terpenoids, phenols, saponins, and essential oils have all been shown to have anthelmintic properties*(Busari et al. 2021; Ishnava & Konar 2020; Selvaraju & Dhanraj 2019)*. The tuber extract of *Corallocarpus epigaeus* showed the presence of alkaloids, flavonoids, saponins, phenols, tannins, and steroids (Ishnava & Konar 2020) The bark and stem of *Salsola imbicata* showed the presence of the following anthelmintic phytochemicals, anthraquinones, reducing sugar, tannins, saponins, flavonoids, alkaloids, and cardiac glycosides (Ajaib *et al.* 2019). The leaves of *Termia catappa* revealed the presence of carbohydrates, cardiac glycosides, reducing sugars, alkaloids, triterpenes, saponins, tannins, phenols, and flavonoids (Olukotun *et al.* 2018).

Family Importance Value (FIV)

The Family Importance Value (Figure 5) was utilized in this study to highlight the importance of plant families. The Dioscoreaeceae family has the highest FIV value of 0.320, followed by Zingiberaceae 0.133, Cyperaceae 0.067, Fabaceae 0.067, Cochicaceae 0.0053, and Araceae 0.040. The lowest FIV value of 0.013 was recorded in 12 families and 0.027 in 6 families. A high FIV value showed that the families had plants that were often cited in ethnobotanical studies as anthelminthics, whereas a low FIV value suggested that the families contained species with few citations.

Comparative analysis (Jaccard Index JI)

This was computed between India, South Africa, and Nepal, which had the highest number of plants cited. India and Nepal had the highest JI value (0.15), and there was no relationship between South Africa and the other two countries. Figure 6 depicts the relationship between these three countries using a Venn diagram. Four plants are common in India and Nepal which are *D. deltoidea*, *D. alata*, *D. bulbifera*, and *D. pentaphylla* according to the findings. There was no floristic relationship between South Africa and the two Asian countries. A high similarity rating indicates that the countries share comparable culture, traditions, and vegetation, whilst a low number indicates that the countries do not share any shared cultural values. Ethnobotanical knowledge, on the other hand, is frequently influenced by origin, culture, sample size, vegetation variation, and microclimatic variables (Amjad *et al.* 2020; Kebede *et al.* 2016).

Table 2. Phytochemical constituents of tuberous plants with anthelmintic properties that are culturally important in the control of helminths.

SPECIES	PHYTOCHEMICALS
Dioscorea deltoidea	diosgenin, corticosterone, 25-D-spirostan-3,5 diene, smilagenone, stigmasterol, B-sitosterol, dioscorin, dioscin and campastrol, Phytosterols, tannins, starch, alkaloids steroidal glycosides, ascorbic acid, beta-carotene, riboflavin (Tahir *et al.* 2016) flavonoids,0 saponins, unsaturated triterpinoides, resins, sterol (Subhash *et al.* 2012) antroquinone, proteins, carbohydrates (Akalya & Subasri 2016; Chandra *et al.* 2012; Karnick 1971) quercetin, cyanidin, kaempferol, caffeic, p-coumaric, synaptic, ferulic acids (Karnick 1971; Semwal *et al.* 2021) Deltonine, deltoside, diosgenine-3-β-d-gluco1pyranosyl (1→4)-β-d-glucopyranoside (Paseshnichenko & Guseva 1975) Deltostim (Vasil'eva & Paseshnichenko 1996) 3-O-β-d-glucopyranosyl-ergost-5-ene-3β,26-diol-26-O-β-d-glucopyranosyl (1→3)-[β-d-glucopyranosyl(1→2)-β-d-glucupyranosyl(1→6)]-β-d-gluco pyranoside; isonarthogenin-3-O-α-l-rhamnopyranosyl-(1→2)-[α-l-rhamno pyranosyl-(1→4)]-β-d-glucopyranoside; methyl protobioside, protobioside (Shen *et al.* 2002)
Dioscorea alata L	diosgenin, dioscorin, dioscin, phytosterols, alkaloids, tannin, starch, ascorbic acid, beta-carotene, protein, riboflavin (Dutta 2015) hexadecanoic acid, methyl stearate, cinnamyl cinnamate, and squalene (Dey *et al.* 2016) phenols, reducing sugars, flavonoids, glycoside, saponins, triterpenes, coumarins phytosterols, steroids, anthraquinones, proteins, cholin, mucin, allantoin, crude fat, crude fiber, catechins, chlorogenic acids, proanthocyanidins, myricetin, diosbulbin, sapogenin.(Kaur *et al.* 2021; Poornima & Ravishankar 2007; Zhang *et al.* 2008)
Gloriosa superba	Alkaloids such as colchicines and colchicosides (Padmapriya *et al.* 2015) gloriosine, lumicolchicine, 3-demethyl-N-deformyl-N1deacetylcolchicine, 3-demethylcolchicine and N-formyl deacetylcolchcine (Maroyi & Van der Maesen 2011b; Suri *et al.* 2001) benzoic acid, salicylic acid, sterols, resinous substances like as 3-demethyl colchicine, 1,2-didemethyl colchicine, 2,3-didemethyl colchicine, N-formyl, N1deacetyl colchicines, tannins, superbine (Capraro 1984) carbohydrates, flavonoids, vitamin C, vitamin E, phenols, glycosides, saponins (Jagtap & Satpute 2014; Muthukrishnan & Annapoorani 2012; Rehana & Nagarajan 2012) xanthoproteins, triterpenoids, amino acids, carbohydrate, reducing sugar (Jebamalar *et al.* 2019) terpenoids, coumarins (Nikhila *et al.* 2016) 3-demethyl-N-deformyl-N-deacetylcolchi1cine, 3-demethylcolchicine, N-formyl deacetylcolchicine, salicylic acid, (Jana & Shekhawat 2011)
Dioscorea pentaphylla	phenols/polyphenols, flavonoids, terpenoids, tannins, alkaloids, saponins (Prakash & Hosetti 2010) glycosides, phenol, reducing sugars, steroids (Vivek & Prakash 2018) gum protein (Sidde *et al.* 2021)
Dioscorea bulbifera	Kaempferol-3,5-dimethyl ether, Quercetin-3-O galactopyranosid, Myricetin-3-O galactopyranoside, Myricetin-3-O glucopyranoside (Gao *et al.* 2002). 8-epidiosbulbin E acetate (Shriram *et al.* 2008). Bafoudiosbulbin (Kuete *et al.* 2012; Teponno *et al.* 2006) Diosbulbiside (Liu *et al.* 2009) Daucostero, Palmatic acid, Succinic acid, Shikimic acid, 3, 5-dimethoxykaempfero, 3, 5, 3'-trimethoxyquercetin, Caryatin, Myricetin-3-O-β-D galactopyranoside, Myricetin-3-O-β-D glucopyranoside, Hyperoside, Myricetin, Kaempferol-3-O-β-D galactopyrano, Kaempferol-3-O-β-D glucopyranoside Diosbulbin B is a demethyl diterpenoid (Gao *et al.* 2007) β-Sitosterol (Teponno *et al.* 2006) (+)Catechin, Kaempfero, Dioscoreanoside (Tapondjou *et al.* 2013) Protocatechuic acid (Wang *et al.* 2009a)

	Vanillic acid (Tang *et al.* 2006) Quercetin-3-O galactopyranoside, 2,7-dihydroxy-4- methoxyphenanthrene, 3-O-α-L-rhamnopyranosyl- (1→2)-[α-L-rhamnopyranosyl-(1→3)]-β-D-g1ucopyranosyl pennogenin (spiroconazol A), Quercetin-3-O-β-D glucopyranosid (Teponno *et al.* 2006) Demethyl batatasin IV (Wang *et al.* 2009b) 3-hydroxy-5-methoxybenzoic acid, Batatasin III, 1,6-dihydroxy-2,5,7- trimethoxyphenanthrene 2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrene, 2,5,2',5'-tetrahydroxy-3'- methoxybibenzyl, Thunalbene, Flavanthrinin, Isorhamnetin (Liu *et al.* 2011) Pennogenin, Pennogenin-3-O-α-L rhamnopyranosyl-(1→3)-[α L-rhamnopyranosyl-(1→2)]- β-D- glucopyranoside, 26 4-hydroxy-[2-trans-3',7'- dimethyl octa-2',6'-dienyl]-6-methoxy acetophenone, 4,6-dihydroxy-2-O-(4'- hydroxybutyl) acetophenone (Gupta & Singh 1989) Stigmasterol (Wang *et al.* 2009a) Lutein, Neoxanthin, Violaxanthin, Zeaxanthin, Auroxanthin, Cryptoxanthin (Ghosh *et al.* 2015)
Cyperus rotundus	Sesquiterpene, (Chen *et al.* 2011) terpenoids, sesquiterpenes, sitosterol, cyperene, cyperol, nootkatone and valencene (Sonwa & König 2001; Tsoyi *et al.* 2011) α-cyperone. (Jung *et al.* 2013) phenolic acids, ascorbic acids, tannins, alkaloids, essential oils (α-longipinane, β-selinene, cyperene, and caryophyllene oxide), and flavonoids (anthocyanidins, catechins, flavans, flavones, flavanonols, and isoflavane) alkaloids, cyperol, flavonoids, fatty oils, furochromones, glycerol, linolenic acid, myristic acid, nootkatone, starch, saponins, sesquiterpenes, sitosterol, stearic acid, terpenoids, polyphenol, and valencene (Sharma *et al.* 2014; Sivapalan 2013) cyanins, quinones, coumarins, glycosides, steroids terpenoids, (Jeyasheela *et al.* 2014; Madhulika & Varsha 2015; Peerzada *et al.* 2015) alpha-cyperone, beta1selinene, cyperene, cyperotundone, patchoulenone, sugeonol, kobusone, and isokobusone (Lawal & Oyedeji 2009) vitamin C, cardiac glycosides (Nagulendran *et al.* 2007) Cyproterone, cypera-2, 4-diene, a-copaene, cyperene, aselinene, rotundene, valencene, ylanga-2, 4-diene, g-gurjunene, trans-calamenene, d-cadinene, g-calacorene, epi-a-selinene, a-muurolene, g-muurolene, cadalene, nootkatene, cyperotundone mustakone, cyperol, isocyperol,a-cyperone (Pal 2015)
Curcuma longa L	Turmeronol-A (1), turmeronol-B (2), 3,4-dimethoxycinnamic acid (3), 4-hydroxy13-methoxycinnamic acid (4), 4-hydroxybenzaldehyde (5), 2,3,5,6-tetrahydroxyarturmerone (6) and 4-hydroxy1bisabola-2,10-diene-9-one (7) (Khan *et al.* 2009) Turmerin (Hatcher *et al.* 2008) Wenyujinlactone A, neolita1mone A, zedoarondiol, isozedoarondiol, aerugidiol, curcumol, curdione, (1R,10R)-epoxy-(-)-1, 10-dihydrocurdine (Wang *et al.* 2007) parviflorene F4, curcuminoids (Pozharitskaya *et al.* 2008) Alkaloids, Flavonoids, Cardiac glycosides, Saponins, Tannins, Balsams, Terpenes, Phenol, Resins, Carbohydrate, Proteins, Starch, Amino acids, Steroid, Glycoside, (Mohammed *et al.* 2019; Saxena & Sahu 2012) Diarylheptanoids and diarylpentanoids, phenylpropene, monoterpenes, sesquiterpenes, diterpenes, triterpenoids, sterols, Ferulic acid (Sabale *et al.* 2013) Essential oils (Li *et al.* 2009) 8-cineole, 2-bornanol, 2-hydroxy1methyl-anthraquinone, 4-hydroxybisabola-2, 10-diene-9-one; 4-methoxy-5-hydroxybiosabola; 4-hydroxy-cinnamoyl-(Feruloyl)-methane, Alpha-atlantone, Alpha1pinene, Alphaterpineol, Ar-turmerone, Arabinose, Eugenol, Epiprocurcumenol; Eucalyptol; Eugenol; Feruloyl-p-coumaroyl-methane, Gamma-atlantone, Germacrone, Germacrone113-al;Guaiacol, Isoborneol, L-alpha1curcumene(Chanda & Ramachandra 2019)

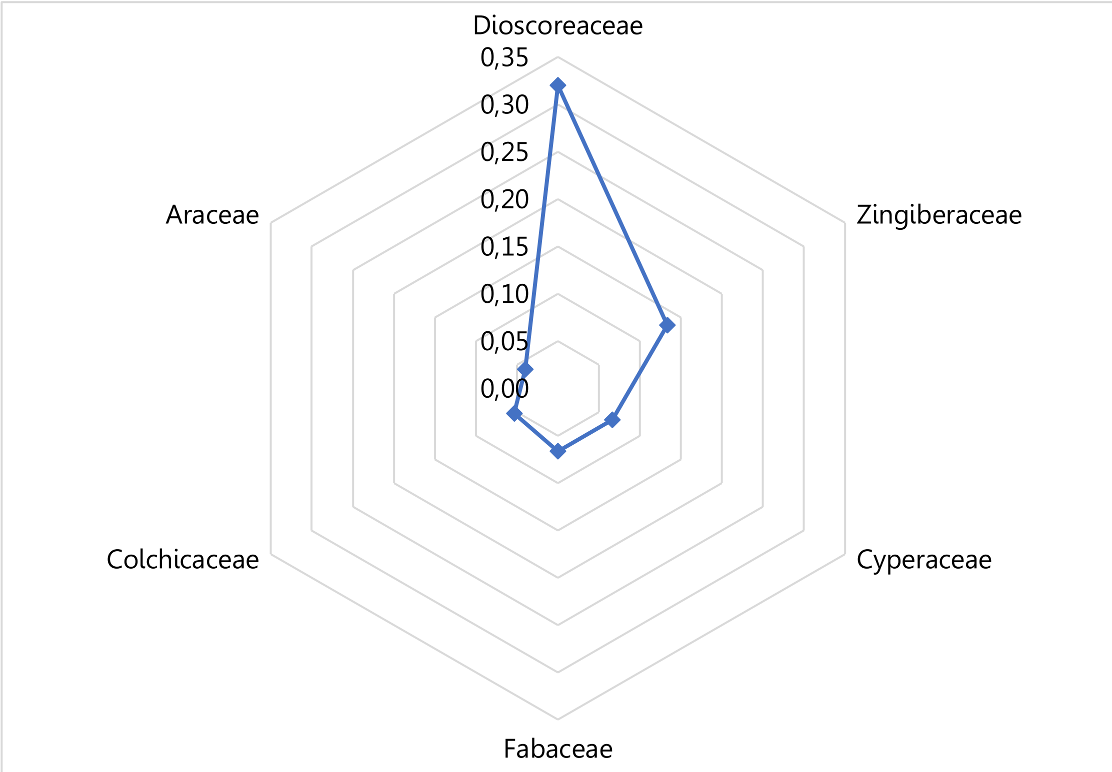

Figure 5. Family Importance Value (FIV) of tuberous plants with anthelmintic properties.

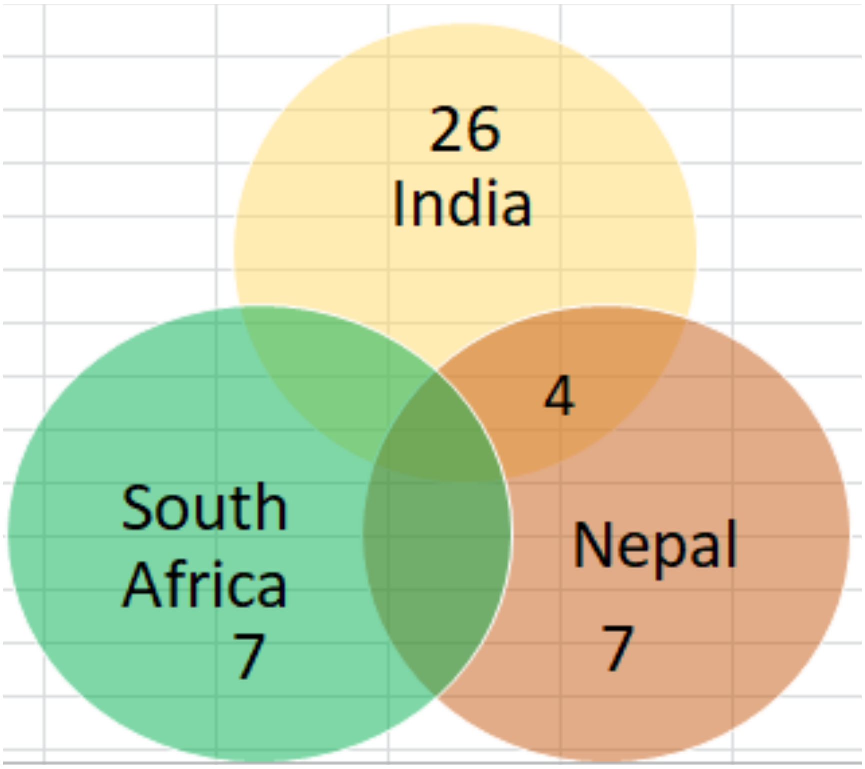

Figure 6. Different types of anthelmintic factors recorded in tuberous plants in different countries.

Anthelmintic activity of the tuberous plants

Table 3 shows that 26 of the tuberous plants had their anthelmintic activity reported and 17 have not been reported. *Zingiber officinale*, *Azadirachta indica*, *Flemingia vestita*, *Allium sativum*, and *Curcuma longa* were the most studied plants for their anthelmintic activity. However, common anthelmintic plants indicated in literature are *Carica* *papaya*, *Butea monosperma*, *Terminalia arjuna*, *Z. officinale*, *Nigella sativa*, *Fumaria parviflora*, *Flemingia vestita*, *Allium sativum*, *Melia azedarach*, *Cucurbita maxima*, *Ocimum sanctum*, *Achyranthes aspera*, *Azadirachta indica*, *Calotropis procera*, and *Artemisia annua* (Nirala 2019). The other tuberous plants with anthelmintic effects not indicated in this study are *Strychnos henningsii*, *Corallocarpus epigaeus*, and *Hypoxis hemerocallidea* (Ishnava & Konar 2020; Matyanga *et al.* 2020).

Table 3. Anthelmintic activity of the tuberous plants with anthelmintic properties cited in various publications.

Tuberous Plant	Anthelmintic Activity
Aconitum heterophylum	*Pheretima postuma* (Pattewar *et al.* 2012)
Albuca setosa	Not reported
Allium sativum	nematodes (Ahmed *et al.* 2014; Amin *et al.* 2008b; Kanojiya *et al.* 2015), *Giardia lamblia* (Mirelman *et al.* 1987), gastrointestinal worms (Nadkarni 1954; Sunada *et al.* 2011), *H.gallinarum*, A. *galli* (Kavindra & Shalini 2000; Raza *et al.* 2016), *H. contortus* (Ahmed *et al.* 2013; Azra *et al.* 2019; Iqbal *et al.* 2001; Luce 2019; Navaneetha & Veerakumari 2009; Palacios-Landín *et al.* 2015; Perry 1980; Shalaby & Farag 2014; Veerakumari & Lakshmi 2006; Worku *et al.* 2009) , *A. suum* (Chybowski 1997; Urban *et al.* 2008), strongyloids (Lakshmi *et al.* 2011; Sutton & Haik 1999; Tavassoli *et al.* 2018), *Fasciola gigantica* (Jeyathilakan *et al.* 2012; Kumar *et al.* 2016; Singh *et al.* 2007; Singh *et al.* 2009), *Gigantocotyle explanatum* (Singh *et al.* 2007; Singh *et al.* 2008), *Neoechinorhynchus buttnerae* (de Oliveira *et al.*, 2021), *Pheretima posthuma* (Dubey *et al.* 2010a; Ittiyavirah *et al.* 2012; Kadam *et al.* 2015), *Trichostrongylus colubriformis* (Urban *et al.* 2008), *T. canis* and *A. caninum* (Orengo *et al.* 2016), Coccidia (Worku *et al.* 2009), Echinococcus granulosus (Mohammadi *et al.* 2018; Shirgholami *et al.* 2021), *Aspiculuris tetraptera* (Ayaz *et al.* 2008), whipworm (Lucido 2014), *Moniezia expansa* (Shalaby & Farag 2014), hookworm (Ambriani 2012), *Dipylidium camnum* and *Taenia hydatigena* (Sblivanova-yartseva 1959), Trichostrongylous (Hayajneh *et al.* 2019).
Alpinia galanga	*Pheretima posthuma* (Babu *et al.* 2017; Subash *et al.* 2012), *Ascardia galli* (Subash *et al.* 2012), earthworms (Patil *et al.* 2014)
Arisaema consanguineum	Not reported
Arisaema jacuemontii	Not reported
Asparagus racemosus	*F. gigantica* (Vishwakarma & Kumar 2021), *Gastrothylax crumenifer* (Soren & Yadav 2021), *Pheretima posthuma* (Kiranmayi *et al.* 2012)
Azadirachta indica	*H. contortus* (Akhter *et al.* 2015; Azra *et al.* 2019; Costa *et al.* 2008; Iqbal *et al.* 2014; Iqbal *et al.* 2012; Iqbal *et al.* 2010; Nawaz *et al.* 2014; Perry 1980; Radhakrishnan *et al.* 2010; Rahman *et al.* 2011; Sakti *et al.* 2018; Swarnkar *et al.* 2008; Tomar & Preet 2017; Zahoor-ul-Hassan *et al.* 2012), gastrointestinal worms (Ajabe *et al.* 2018; Chandrawathani *et al.* 2000; Prasad *et al.* 2011; Premaalatha *et al.* 2013; Sarker *et al.* 2016; Sivashanmugapillai 2016; Vikram *et al.* 2019), *Pheretima posthuma (Naidu et al. 2016; Nazneen et al. 2017; Rabiu & Subhasish 2011; Salma et al. 2021; Singh et al. 2018b)*, *Raillietina spiralis(Rabiu & Subhasish 2011)*, *Ascaridia galli* (Ali *et al.* 2006; Hellawi & Ibrahim 2021; Hogade *et al.* 2013; Rabiu & Subhasish 2011), *Fasciola gigantica* (Kushwaha *et al.* 2004), *Setaria cervi* (Kausar 2017; Mishra *et al.* 2005) , Trichostrongylus (Iqbal *et al.* 2010), strongyle (Das *et al.* 2015; Jamra *et al.* 2015; Suhaimi & Mossadeq 2016), *Gastrothylax indicus* (Aggarwal & Bagai 2014; Aggarwal *et al.* 2016), *Paramphistomum cervi* and *Fasciola hepactica* (Ibekwe 2019), Fasciola spp. (Sunita *et al.* 2013; Yamson *et al.* 2019), *Eudrilus eugeniae* (Hogade *et al.* 2013; Priya & Santhi 2015), nematodes (Alam *et al.* 2014; Amin *et al.* 2008a; Bhattacharjee *et al.* 2021; Jamnah *et al.* 2006; Priscilla *et al.* 2014; Yakubu *et al.* 2006; Zapata Salas *et al.* 2013), *Eisenia foetida* (Priya & Santhi 2015), *Heligmosomoides polygyrus* (Githiori *et al.* 2003), *Teladorsagia (Ostertagia) circumcincta* (Al-Rofaai *et al.* 2012), *Toxocara vitulorum* (Chamuah *et al.* 2014),
Bulbine asphodeloides	Not reported
Costus speciosus	*Pheretima posthuma* (Srivastava *et al.* 2011). *Eisenia foetida* and *Taenia saginata* (Kosalge & Fursule 2009b)
Curcuma amada.	*Pheretima posthuma* (Rakh *et al.* 2014), Eisenia foetida (Gill *et al.* 2011)
Curcuma aromatic.	Not reported
Curcuma caesia.	Earthworms (Chadalavada & Budala 2017), *Eisenia foetida* (Randeep *et al.* 2011), *Pheretima posthuma* (Chadalavada & Budala 2017; Karim *et al.* 2017)
Curcuma longa	*Echinococcus granulosus* (Almalki *et al.* 2017), *Pheretima posthuma* (Nirmal *et al.* 2009; Raul *et al.* 2012), *Toxacara canis* (Kiuchi *et al.* 1989), gastrointestinal worms (Bannerjee *et al.* 1978; Sivashanmugapillai 2016), *Raillietina cesticillus* (El-Bahy & Bazh 2015), Eimeria species (Ashraf *et al.* 2020; Cervantes-Valencia *et al.* 2015), Haemonchus spp. (Nasai *et al.* 2016; Pandey *et al.* 2018b), *F. gigantica* (Ullah *et al.* 2017), *Neoechinorhynchus buttnerae* (de Oliveira *et al.* 2021), nematodes (Amin *et al.*

	2008b; Nath *et al.* 2019), *Ascaridia galli* (Bazh & El-Bahy 2013), Strongyles (Nasai 2012; Ramdani *et al.* 2021)
Cyperus rotundus	tapeworms and earthworms (Mishra *et al.* 1979), *Pheretima posthuma* (Kasala *et al.* 2016)
Cyphostemma adenocaule	Gastrointestinal worms (Tumwesigye 2011)
Dioscorea alata	*Dactyogyrus intermedius* (Wang *et al.* 2010a)
Dioscorea bulbifera	earthworms and liver flukes (Adedapo & Mubo 2013), *Eisenia foetida, Raillietina spiralis* and *Ascardia galli* (Kosalge & Fursule 2009c), *Fasciola gigantica* and *Pheretima posthuma* (Patel & Galani 2017)
Dioscorea deltoidea	Not reported
Dioscorea hamiltonii	Not reported
Dioscorea pentaphylla	Not reported
Dioscorea prazeri	Not reported
Dryopteris setosa	Not reported
Elephantorrhiza elephantina	*Haemonchus contortus* (Maphosa & Masika 2012a; Maphosa *et al.* 2010b), *Paramphistomum cervi* (Mazhangara *et al.* 2020), Trichuris spp.(Maphosa & Masika 2012b)
Flemingia procumbens	Not reported
Flemingia vestita	*Raillietina echinobothrida* (Das *et al.* 2009; Das *et al.* 2004a, b, 2006; Das *et al.* 2007; Pal & Tandon 1998a; Tandon & Das 2007; Tandon *et al.* 2003; Tandon *et al.* 1997), *Fasiolopsis buski* (Kar & Tandon 2000; Kar *et al.* 2002; Kar *et al.* 2004; Pal & Tandon 1998b; Roy & Tandon 1996), *Fasciola hepatica* (Toner *et al.* 2008), *E. multiloculoris* and *E. granulous* (Naguleswaran *et al.* 2006), *Artyfechinostomum sufrartyfex* (Kar & Tandon 2000; Roy & Tandon 1996),
Gloriosa superba	*Pheretima posthuma* (Pawar *et al.* 2010), *Eisenia foetida* (Suryavanshi *et al.* 2012)
Gunnera perpensa	*Heterakis gallinarum* (Mwale & Masika 2015), nematodes (Fomum & Nsahlai 2017), gastrointestinal worms (Mhlongo 2018)
Hypoxis argentea	Not reported
Kaempferia galanga	*Pheretima posthuma* (Dash *et al.* 2017)
Melastoma malabatricum	*Haemonchus contortus* (Suteky 2019).
Neorautanenia brachypus	strongyloid (Murungweni *et al.* 2012b)
Oroxylum indicum	*Hymenolepis diminuta* (Deori & Yadav 2016), strongyle (Downing 2000), *Pheretima posthuma* (Islam *et al.* 2016).
Pelargonium reniforme	not reported
Peliosanthes bakeri	Not reported
Pueraria tuberosa	Not reported
Raphanus sativus	*Pheretima posthuma* (Robertson & Thamizharasi 2016; Shetty *et al.* 2011), *Raillietina spiralis* and *Ascaridia galli* (Shetty *et al.* 2011)
Rhoicissus tridentata	*Ascaris suum* (Innocent & Deogracious 2006; Nalule *et al.* 2012), *Haemonchus contortus* (Mdletshe 2018),
Rumex usambarensis.	Not reported
Sauromatum venosum	Not reported
Stephania glabra	*Raillietina echinobothrida* (Das *et al.* 2009; Das *et al.* 2004a; Das *et al.* 2013)
Zingiber officinale	*Dirofilaria immitis* (Datta & Sukul 1987), Anisakis larvae (Goto *et al.* 1990), *Fasciola gigantica* (Jeyathilakan *et al.* 2010; Sunita & Singh 2011; Toulah *et al.* 2019), *Setaria cervi* (Ghosh *et al.* 1992), *Pheretima posthuma* (Dubey *et al.* 2010b; Korukola *et al.* 2014; Nirmal *et al.* 2009; Raul *et al.* 2012), *Toxocara vitulorum* (Shalaby *et al.* 2017), *Haemonchus contortus* (Iqbal *et al.* 2001), nematodes (Iqbal *et al.* 2006), *Angiostrongylus cantonensis* (Lin *et al.* 2010), *Lumbricus rubellus* (Dhiman 2017), *Strongyloides ransomi*, *Hyostrongylus rubidus*, *Trichostrongylus axei* and *Globocephalus urosubulatus* (Kiambom *et al.* 2021), *Raillietina cesticillus* (El-Bahy & Bazh 2015), Fasciola miracidia (Ghafar *et al.* 2021), *Echinococcus granulosus* (Almalki *et al.* 2017), gastrointestinal worms (Adeniji *et al.* 2017), *Toxocara canis* (El-Sayed 2017), *Fasciola hepatica* (Moazeni & Khademolhoseini 2016), Eimeria species (Ashraf *et al.* 2020).
Zingiber zerumbet	*Pheretima posthuma* (Goswami *et al.* 2011; Pandey *et al.* 2011a; Raul *et al.* 2012; Sahu *et al.* 2018),

Parasites tested against during anthelmintic activity studies

The reported tuberous plants with anthelmintic properties have been tested against nematodes, trematodes, cestodes, protozoa, eoacanthacephala, and coccidia that affect animals and fish as shown in Table 4 below. The tuberous plants have been tested against 41 different parasites that were indicated in literature and are subdivided into 21 nematodes, nine cestodes, nine trematodes, one protozoan, and one eoacanthacephala. The top five parasites that were tested for efficacy of anthelminthics derived from the tuberous plants were *Pheretima posthuma*

(33 citations), *Haemonchus contortus* (31 citations), *Raillietina echinobothrida* (12 citations), *Fasciola gigantica* (11 citations), and *Ascardia galli* (10 citations). These results agree with Patil *et al.* (2019) who reported *Haemonchus contortus* to be the most commonly employed test agent for anthelmintic potential. Twenty parasites had more than one citation (number of times it has been indicated to be used as a model during research using the tuberous plants). Of the 41 parasites indicated four are non-parasitic earthworms which are *Lumbricus rubellus*, *Eudrilus eugeniae*, *Pheretima posthuma*, and *Eisenia foetida*. They are used as test worms because of their anatomical and physiological resemblance to gastrointestinal tapeworms and because they are easily available (Choudhary *et al.* 2021a; Salma *et al.* 2021).

Table 4. List of parasites that were used as helminths models in anthelmintic studies of tuberous plants with anthelmintic properties.

Parasite	Number of citations	Parasite Class
Pheretima posthuma	33	Nematode
Haemonchus contortus	31	Nematode
Raillietina echinobothrida	12	Cestode
Fasciola gigantica	11	Trematode
Ascardia galli	10	Nematode
Eisenia foetida	6	Nematode
Fasciolopsis buski	5	Trematode
Echinococcus granulosus	4	Cestode
Ascaris suum	4	Nematode
Raillietina spiralis	3	Cestode
Setaria cervi	3	Nematode
Toxocara canis	3	Nematode
Fasciola hepatica	3	Trematode
Neoechinorhynchus buttnerae	2	Eoacanthacephala
Heterakis gallinarum	2	Nematode
Toxocara vitulorum	2	Nematode
Artyfechinostomum sufrartyfex	2	Trematode
Gastrothylax indicus	2	Trematode
Gigantocotyle explanatum	2	Trematode
Paramphistomum cervi	2	Trematode
E. multiloculoris	1	Cestode
Hymenolepis diminuta	1	Cestode
Moniezia expansa	1	Cestode
Raillietina cesticillus	1	Cestode
Taenia hydatigena	1	Cestode
Taenia saginata	1	Cestode
Ancylostoma caninum	1	Nematode
Angiostrongylus cantonensis	1	Nematode
Aspiculuris tetraptera	1	Nematode
Eudrilus eugeniae	1	Nematode
Globocephalus urosubulatus	1	Nematode
Heligmosomoides polygyrus	1	Nematode
Hyostrongylus rubidus	1	Nematode
Lumbricus rubellus	1	Nematode
Strongyloides ransomi	1	Nematode
Teladorsagia circumcincta	1	Nematode
Trichostrongylus axei	1	Nematode
Trichostrongylus colubriformis	1	Nematode
Giardia lamblia	1	Protozoa
Dactyogyrus intermedius	1	Trematode
Gastrothylax crumenifer	1	Trematode

Toxicological indications of tuberous plants and their active compounds

The results displayed in Table 5 showed that 11 (26%) of the anthelmintic tuberous plants indicated have not been subjected to any toxicological studies. The other 32 were reported to be cytotoxic, hepatotoxic, mutagenic, carcinogenic, embryogenic, teratogenic, hemotoxic, cardio toxic, and cause mortality, pathological changes of organs, paralysis, diarrhea, and vomiting. The differences in toxic effects exhibited by these plants might have been because of differences in animal species on which the toxological tests were carried out, the dosage of plant extract, and duration of exposure. One study mentioned the following plants to be poisonous to livestock *Manihot spp. 78.3%, S. coriaceum 55%, Brachiaria spp. 43.3%, E. contortisiliquum 41.7%, M. pseudoglaziovii 25%, D. mollis Benth*

14.3%, M. indica 7.1% e D. ecastophyllum (de Sousa *et al.* 2019).. *Tribulus terrestris*, *Narthecium ossifragum*, *Agave lecheguilla*, *Trifolium hybridum*, and *Lantana camara* have been reported to cause hepatotoxicity in livestock (Clayton *et al.* 2020). It is common that large doses are responsible for major deleterious effects (Maroyi & Van der Maesen 2011). This information shows the therapeutic safety of the cited anthelmintic tuberous plants before conducting clinical studies.

The results in Table 5 show that 22 compounds produced by the cited anthelmintic tuberous plants that have been reported to exhibit toxic effects. These compounds belong to the following classes of phytochemicals essential oils (12 compounds), alkaloids (four compounds), flavonoids (two compounds), terpenoids (two compounds, phenols (one compound), and organic acids (one compound). These results showed most toxic compounds in tuberous plants are essential oils. However, alkaloids are cited as the most important plant-derived toxins in livestock (Clayton *et al.* 2020).

Endangerement status of tuberous plants

Since many of the plants used in ethnoveterinary systems are native to specific geographic locations they may be endangered. Medicinal plants are frequently endangered because of overexploitation, dwindling natural habitat, unselective harvesting, and less production (Umavathi *et al.* 2020). Seven tuberous plant species were indicated as the most culturally important plants that are potentially endangered plants in this study. These are *Dioscorea deltoidea, Dioscorea bulbifera*, *Dioscorea alata L., Curcuma longa L., Dioscorea pentaphylla, Gloriosa superba,* and *Cyperus rotundus*. However, Table 5 below lists 12 plants (28%) that have been reported to be endangered and 31 tuberous anthelmintic plants are not endangered. Other endangered tuberous plants are *Corallocarpus epigaeus* (Vemula *et al.* 2020), , , etc. Other anthelmintic plants that have been reported to be endangered are*Ilek khasiana* (Lalnunfela *et al.* 2020), *Picrorhiza kurroa* (Mehta *et al.* 2021), *Potentilla fulgens* (Kumar *et al.* 2020), *Embelia ribes* (Choudhary *et al.* 2021b).

There is an urgent need for biogeopgraphical and ecological studies of endangered plants to facilitate their conservation before they become highly endangered or totally extinct (Singh & Geetanjali 2016). The use of leaves is less damaging when compared to the use of roots, tubers, and bark, which negatively affects the conservation of medicinal plants (Odongo *et al.* 2018). However, roots, tubers, and bark are sometimes preferred by traditional healers due to their easy storage and transport when compared to leaves.

Conclusions

Forty-two plants have been recorded to have their tuber parts used in the control of helminths. Analysis indicated seven plants to be the most culturally important plants in the control of helminths. These were *Dioscorea deltoidea, D. bulbifera*, *D. alata L., D. pentaphylla, Curcuma longa L., Gloriosa superba,* and *Cyperus rotundus*. The classes of phytochemicals that are common in these plants are phytosterols, tannins, alkaloids, saponins, essential oils, flavonoids, and terpenoids. These plants are mostly found in India and Nepal. Twenty-six of these tuberous plants have been tested for their anthelmintic effect and 17 have not. These plants have been tested against trematodes, cestodes, nematodes, protozoa, coccidian, and eoacanthacephala. The most commonly used helminth species for testing anthelminthic activity *Pheretima posthuma*, *Haemonchus contortus*, *Raillietina echinobothrida*, *Fasciola gigantica*, and *Ascardia galli*. Eleven of the anthelmintic tuberous plants indicated have not been subjected to any toxicological studies. The other 32 were reported to be cytotoxic, hepatotoxic, mutagenic, carcinogenic, embryogenic, teratogenic, hemotoxic, cardiotoxic, and cause mortality, pathological changes of organs, paralysis, diarrhea, and vomiting. Twenty-two compounds produced by the cited anthelmintic tuberous plants have been reported to exhibit toxic effects. Twelve tuberous plants have been indicated to be endangered.

Therefore, there is a need for conservation programs for these culturally important plants to prevent extinction. In addition, there is a need to investigate other tuberous plants, especially those found in Africa, and to identify unique compounds that are active against helminths and combine them to develop more robust anthelmintic drugs. These drugs will have the potential to effectively control helminths and reduce the rate at which anthelmintic resistance occurs. The results of the present investigation add more information about the therapeutic safety of these popular folklore drugs and provide grounds for an assessment of possible measures to be introduced before conducting clinical studies. It is hoped that this research will lead to wider public and Government recognition of endangered plants species and spur conservation efforts toward saving both plants and folk medicinal knowledge.

Table 5. Toxicological indications, toxic compounds, and endangerment status of tuberous plants with anthelmintic properties.

Plant	**Positive Toxicology results**	**Negative Toxicology results**	**Toxic compound**	**Class of toxic compound**	**Status**
Aconitum heterophylum	Aconitine (Wani *et al.* 2022)	non-toxic (Kumar & Chauhan, 2016; Prasad, Jain, Patel, Sahu, & Hemalatha, 2014)	Aconitine (Wani *et al.* 2022)	Alkaloid	Endangered (Beigh *et al.* 2006)
Albuca setosa	*Albuca setosa* silver nanoparticles are cytotoxic (Odeyemi & Afolayan 2019)	aqueous extracts not cytotoxic (Odeyemi *et al.* 2015)	Not reported	-	Not endangered
Allium sativum (L.)	Mortality occurred in rabbits given the extract at 3200 and 4200 mg/kg with other behavioral signs like loss of appetite and partial paralysis (Mikail 2010), Garlic-derived di allyl sulfide (DAS) caused death at 1600 mg/kg (1/5 male) and 1920 mg/kg (2/5 female and 3/5 male) doses. DAS also induced marked pathological changes in the lungs, liver, and reproductive organs. DAS highest dose had genotoxicity (Dutta *et al.* 2021) toxic at high doses to the liver, heart, kidney, spleen, and lungs, cause loss of appetite and anemic conditions (Fowotade *et al.* 2017; Gatsing *et al.* 2005)	No acute and sub-acute toxicity (Lawal *et al.* 2016; Njue *et al.* 2015), no hepatotoxicity (Samson *et al.* 2012)	Garlic derived di allyl sulfide (DAS)	Essential oil	Not endangered
Alpinia galanga	2000 mg/kg of extract was highly toxic to Wistar rats when administered intraperitoneally (Karunarathne *et al.* 2018), causes cytotoxicity, Apoptosis and DNA Damage (Muangnoi *et al.* 2007), caused an increase in the relative weight of the heart, liver, spleen, and kidney. Hematological studies revealed a fall in the red blood cells and white blood cells level as well as hemoglobin and platelets (Alajmi *et al.* 2018)	No acute toxicity and mortality observed (Qureshi *et al.* 1992; Unnisa & Thahera 2011) did not produce significant changes in the general behavior, body weights, feed intake (Karunarathne *et al.* 2018)	Not reported	-	Endangered (Shetty & Monisha 2015)

Arisaema consanguineum	Not reported	Not reported	Not reported	-	Not endangered
Arisaema jacuemontii	classified as poisonous plant (Ali & Yaqoob 2021)	Not reported	Not reported	-	Not endangered
Asparagus racemosus.	partial teratogenic effects have been observed in pre- and postnatal studies with methanol extract (Goel *et al.* 2006), alcoholic extract of the root produces positive ionotropic and chronotropic effects on frog's heart with lower doses, and cardiac arrest with higher doses (Goyal *et al.* 2003), cytotoxicity (Karmakar *et al.* 2012; Singh *et al.* 2018a)	No acute toxicity (Kumar *et al.* 2010; Ngeny *et al.* 2013), no reproductive, sub-acute, and sub-chronic toxicity (Bhandary *et al.* 2017; Goel *et al.* 2006; Goyal *et al.* 2003)	Not reported	-	Endangered (Bopana & Saxena 2008)
Azadirachta indica	Acute toxicity, mortality after 24hr (Saravanan *et al.* 2011) root bark aqueous extract was considered moderately toxic using the Brine shrimp lethality test (Mwangi *et al.* 2015) chronic toxicity of BioneemTM (Botelho *et al.* 2010; Maranho *et al.* 2014) genotoxicity (Chandra & Khuda-Bukhsh 2004) oil neem oil showed sub-chronic toxicity (Wang *et al.* 2013a)	no acute toxicity and sub-acute toxicity in mammals (Dorababu *et al.* 2006; Kingsley *et al.* 2012), no reproduction and Teratogenicity(Babalola & Areola 2010; Da Silva *et al.* 2015)		Essential oil	Not endangered
Bulbine asphodeloides	Not reported	No cytotoxicity (Otang-Mbeng & Sagbo 2021)	Not reported	-	Not endangered
Costus speciosus	Cytotoxicity (Jha *et al.* 2010)	No sub-acute toxicity (Sari & Nurrochmad 2016)	Not reported	-	Endangered (Pandey *et al.* 2011b)
Curcuma amada	showed brine shrimp lethal activity (Krishnaraju *et al.* 2006)	non-toxic by cytotoxicity tests (Nag *et al.* 2021; Policegoudra *et al.* 2010; Prema *et al.* 2014)	Not reported	-	Not endangered
Curcuma aromatic	Not reported	Not reported	Not reported	-	Not endangered
Curcuma caesia	Not reported	non-toxic by cytotoxicity tests (Nag *et al.* 2021)	Not reported	-	Endangered (Borah *et al.* 2020)
Curcuma longa	Out of 200 *C. longa* compounds, 184 compounds were predicted as toxigenic, 136 compounds were	No acute, sub-acute, oral toxicity, and chronic toxicity (Ibukun & Oluwadare 2021; Qureshi *et al.*	Curcumin, ar-turmerone, R-	Phenol, Essential oils	Endangered (Patel 2015)

	mutagenic, 153 compounds were carcinogenic, and 64 compounds were hepatotoxic, curcumin and its derivatives may cause dose-dependent hepatotoxicity (Balaji & Chempakam 2010; Deshpande *et al.* 1998), cytotoxicity and apoptotic effects of ar-turmerone, R-turmerone, and β-turmerone (Aratanechemuge *et al.* 2002; Ji *et al.* 2004) Embryotoxicity, and Teratogenic (Alafiatayo *et al.* 2019)	1992), No acute, subchronic and genotoxicity of turmeric essential oil Ar-turmerone (Liju *et al.* 2013), nonmutagenic (Soleimani *et al.* 2018) curzerene has limited toxicity and side effects in vivo and cytotoxicity (Wang *et al.* 2017)	turmerone, and β-turmerone		
Cyperus rotundus	Cytotoxic (Susianti *et al.* 2018), the hematological parameters showed an increase in white blood cells count and Hemoglobin level after administration of ethanolic extracts to rats. The kidney function and liver function didn't change even after long term exposure (Jebasingh *et al.* 2012). humulene epoxide and caryophyllene oxide exhibited moderate cytotoxicity (Samra *et al.* 2020) Cyperene, α-cyperone, isolongifolen-5-one, rotundene, and cyperorotundene had cytotoxicity effects (Kilani *et al.* 2008)	No sign of toxicity at 10, 100 and 1000mg/kg doses of ethanolic extract (Ahmad *et al.* 2012), Acute and Subacute toxicities tests showed no cause changes in terms of general behaviors, mortality, weight gain, Hematological and clinical blood chemistry parameters. The results of gross and pathological examinations showed a normal appearance of the internal organs as compared to those of the control group (Thanabhorn *et al.* 2005) Sub-chronic toxicity study revealed that food, water consumption, and body weight of animals didn't vary significantly. The kidney function and liver function didn't change even after long-term exposure (Jebasingh *et al.* 2012).	humulene epoxide,, caryophyllene oxide, Cyperene, α-cyperone, isolongifolen-5-one, rotundene, and cyperorotundene	Essential oils	Not endangered
Cyphostemma adenocaule	Not reported	Not reported	Not reported	-	Not endangered
Dioscorea alata	Cytotoxicity	Not reported	Not reported	-	Not endangered

	(Bhandari & Kawabata 2005; Raju & Mehta 2008; Wallace *et al.* 2021)				
Dioscorea bulbifera	Hepatotoxicity (Guan *et al.* 2017; Tan *et al.* 2003; Wang *et al.* 2010c), Cytotoxicity (Nur & Nugroho 2018; Yu *et al.* 2004)	No form of blood toxicity (Princewill-Ogbonna *et al.* 2015), No acute toxicity (Webster *et al.* 1984)	Diosbulbin B and D	Terpenoid	Not endangered
Dioscorea deltoidea	Cytotoxicity effects (Mohammad *et al.* 2017; Shen 2002)	No acute toxicity (Ali *et al.* 2020; Povydysh *et al.* 2021)	oxalate (Bhandari & Kawabata 2005)	-	Endangered (Mandal & Dixit-Sharma 2007; Nazir *et al.* 2021)
Dioscorea halmiltonii	Not reported	Not reported	Not reported	-	Not endangered
Dioscorea pentaphylla	Not reported	toxicity test demonstrated that the starch was safe and can be classified as non-toxic (Lazim *et al.* 2021)	Not reported	-	Not endangered
Dioscorea prazeri	Not reported	Not reported	Not reported	-	Endangered (Thankappan & Morawala-Patell 2011)
Dryopteris setosa	Not reported	Not reported	Not reported	-	Not endangered
Elephantorrhiza elephantina	Is harmful when used at an excessive dosage (Gelfland *et al.* 1985; Hutchings 1996; Watt & Breyer-Brandwijk 1962), root infusions have constipating effects seeds are strongly irritant and have been suspected of causing human death when used as herbal medicine (Hutchings 1996). Seeds are toxic to sheep with a lethal dose 250 g and rabbits (lethal dose 5–7.50 g/kg) causing gastroenteritis and pulmonary edema (Jansen & Cardon 2005) Root extracts caused changes in body weight and hematological and serum biochemical parameters between the control and treated animals were observed. In acute tests, decreased respiratory rate was observed at higher doses and in sub-acute tests, the root extract caused an	Root extract showed no physiological and behavioral changes in the animals and also no mortalities were recorded (Maphosa *et al.* 2009)	Not reported	-	Not endangered

	increase in white blood cells, monocytes, and serum levels of creatinine at higher doses. In chronic toxicity, caused increase in lymphocytes and platelets and changes were also noted in the body and organ weights in both sub-acute and chronic toxicities (Maphosa *et al.* 2010a) showed cytotoxicity effects (Mpofu *et al.* 2014)				
Flemingia procumbens	Not reported	Not reported	Not reported	-	Not endangered
Flemingia vestita	the administration of high doses of isoflavones could induce potentially adverse effects (Sirtori 2001). Genistein causes cell death by inducing apoptosis and other cytotoxic processes (Klein & King 2007). Genistein showed significant negative impacts on ovarian differentiation, estrous cyclicity, and fertility in the rodent model (Jefferson & Williams 2011; Spagnuolo *et al.* 2015)	No toxicity to was observed in postmenopausal women after a single dose that exceeded normal dietary intakes of purified unconjugated isoflavones (Bloedon *et al.* 2002)	Genistein	Isoflavone, Flavonoid	Not endangered
Gloriosa superba	Poisoning is indistinguishable from alkaloid colchicine overdose (Mendis 1989), Causes gastrointestinal and haematological abnormalities, hepatic and renal insufficiency, cardiotoxicity and hair loss (Khanam *et al.* 2015), acute respiratory distress syndrome and sustained multiple organ dysfunction following ingestion of tubers (Peranantham *et al.* 2014), fatal (Joshi 1993), The study of colchicine on rats and monkeys has been shown to induce epileptic foci in rats, causing generalized seizures and death in animals (Eddleston 2000), causes diarrhea, depressant action on bone	Not reported	colchicine	alkaloid	Endangered (Sivakumar & Krishnamurthy 2000)

	marrow and alopecia (Gooneratne 1966), tubers are extremely poisonous (Aleem 1992; Angunawela & Fernando 1971), causes vomiting, purging, stomachache and burning sensation (Roberts *et al.* 1987), use of colchicine has been shown to induce epileptic foci in rats, causing generalized seizures and death (Dasheiff & Ramirez 1985; Sechi *et al.* 2003), Causes acute renal failure (Badwaik *et al.* 2011)				
Gunnera perpensa	Cytotoxicity to brine shrimp (McGaw *et al.* 2005b; Simelane *et al.* 2010) 200 mg/kg dose of chronic test was 20% potentially toxic when used consecutively for a long period (Mwale & Masika 2011)	Neither rat mortality nor changes in behavior were noted for acute test and rat mortality for 400 mg/kg dose of sub-acute (Mwale & Masika 2011) nonmutagenic (Ndhlala *et al.* 2011)	Not reported	-	Not endangered
Hypoxis argentea	Not reported	Not reported	Not reported	Not reported	Not endangered
Kaempferia galanga	Essential oil toxic to brine shrimp (AlSalhi *et al.* 2020) cytotoxic (Dash *et al.* 2014; Omar *et al.* 2017) Ethanolic extracts cause central nervous system depression, decreased motor activity and respiratory rate, loss of screen grip and analgesia in rats (Kanjanapothi *et al.* 2004; Koh *et al.* 2009),	No oral acute and sub-acute toxicity (Amuamuta *et al.* 2017; Kanjanapothi *et al.* 2004), its essential oils namely ethyl p-methoxycinnamate, trans-ethyl cinnamate and trans-cinnamaldehyde were safe to aquatic fauna (AlSalhi *et al.* 2020) 1,8-cineole showed weak acute toxicity (Liu *et al.* 2014), Hexane fraction when applied on skin of rabbits, showed no sign of dermal irritation (Kanjanapothi *et al.* 2004)	Not reported	Essential oils	Endangered (Kalpana & Anbazhagan 2009)
Melastoma malabatricum	Cytotoxicity (Kamsani *et al.* 2019; Kumar *et al.* 2013)	extract is safe even at a high dose of 5,000 mg/kg and has no oral toxicity (Alnajar *et al.* 2012) no acute, sub-acute, and sub-chronic	Not reported	-	Not endangered

		toxicity (Kumar *et al.* 2013; Reduan *et al.* 2020a)			
Neorautanenia brachypus	Not reported	Not reported	Not reported	-	Not endangered
Oroxylum indicum	toxic for the brine shrimp (Chowdhury *et al.* 2005), Mortality was observed for 72 hours after administration to mice (Tripathy *et al.* 2011), fruit extracts caused hepatotoxicity in rats (Konsue & Katisart 2021), cytotoxicity (Buranrat *et al.* 2018)	No acute oral toxicity and sub-acute oral toxicity (Joshi *et al.* 2011; Reduan *et al.* 2020b; Tamboli *et al.* 2011) not toxic to humans and experimental animals even up to high doses (Siddiqui *et al.* 2012), stem bark extracts showed non-mutagenic, non-cytotoxic, and non-genotoxic (Singh *et al.* 2017)	Not reported	-	Endangered (Tiwari *et al.* 2007)
Pelargonium reniforme	Not reported	aqueous root extract is not toxic (Adewusi & Afolayan 2009)	Not reported	-	Not endangered
Peliosanthes bakeri	Not reported	Not reported	Not reported	-	Not endangered
Pueraria tuberosa	Sub-chronic toxicity (Santosh *et al.* 2010) Puerarin and Genistein have potent inhibitory effects on the metabolic activities of cytochrome enzymes (Burnett *et al.* 2011; Kim *et al.* 2014)	Acute and sub-acute test of tuber extract was found to be safe in rats (Pal & Mishra 2019; Pandey *et al.* 2018a; Shukla 1995)	Puerarin, Genistein	Isoflavone-Flavonoids	Not endangered
Raphanus sativus	Not reported	Not reported	Not reported	-	Not endangered
Rhoicissus tridentata	Cytotoxicity (Tshikalange *et al.* 2016)	Not reported	Not reported	-	Not endangered
Rumex usambarensis	Not reported	Not reported	Not reported	-	Not endangered
Sauromatum venosum	Not reported	Not reported	Not reported	-	Not endangered
Stephania glabra	Gindarine (1) shows some toxic effects on pregnant rats (Arzamastsev *et al.* 1983)	No acute toxicity (Semwal *et al.* 2010; Semwal *et al.* 2011)	Gindarine (1) (Arzamastsev *et al.* 1983)	Alkaloid	Endangered (Chhetri *et al.* 2005)
Zingiber officinale Roscoe	toxic by causing severe hypotension and bradycardia with induction of pre-necrotic changes in cardiac tissue (Elkhishin & Awwad 2009), Findings	no sub-acute toxicity, no acute toxicity, no chronic toxicity (Elkhishin & Awwad 2009;	β-phellandrene, 6-gingerol	Essential oils, Alkaloid	Not endangered

	suggest caution on chronic use of ginger oils (Idang *et al.* 2019), cytotoxicity (Plengsuriyakarn *et al.* 2012), β-phellandrene showed genetic toxicity in spleen cells evaluated by comet assay (Cheng *et al.* 2017), 6-gingerol induces DNA strand breaks in Hepatoma G2 cells evaluated by comet assay (Yang *et al.* 2010)	Plengsuriyakarn & Na-Bangchang 2020)			
Zingiber zerumbet	Zerumbone showed selective cytotoxicity (Latif *et al.* 2019; Matthes *et al.* 1980; Sharifah Sakinah *et al.* 2007)	No acute toxicity, no chronic toxicity (Chang *et al.* 2012b; Rahman *et al.* 2014), poses no risk of genotoxicity (Chang *et al.* 2012a)	Zerumbone	Terpenoid	Not endangered

Declarations

List of abbreviations: FC: Frequency of citation, RFC: Relative frequency of citation, FIV: Family importance value, N: number of citations, JI: Jaccard index

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