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Ethnopharmacological study of traditional medicinal plants used by the people in Metema district, northwestern Ethiopia

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Background: Medicinal plants are used by more than 80% of Ethiopians. The Metema District, shaped by various ethnicities and settlement histories, remains underexplored. This study aimed to document and analyze medicinal plant use and associated traditional knowledge in the local population.

Methods: Data were collected through semi-structured interviews, guided field walks, and focus-group discussions. A total of 110 informants participated in the study, using various sampling techniques. The informant consensus factor (ICF) and direct matrix ranking (DMR) were computed along with descriptive statistics to analyze the basic ethnobotanical data.

Results: In this study, 85 therapeutic plants were utilized to treat 13 disease categories. The three ethnic groups shared 21.18% of their knowledge of medicinal plants. Fabaceae was the most represented family, comprising 11 plant taxa. Herbs were the predominant plant form (42.4%), leaves being the most frequently used (30.5%). Oral administration was the primary method used for the plant extracts (52.3%). Circulatory and blood-related disorders had the highest ICF value (0.91). *Ziziphus spina-christi*, *Ximenia americana*, and *Ficus sycomorus* were ranked as the top multipurpose plants. Fuelwood collection and agricultural expansion have been identified as the major threats to these plants.

Conclusion: This study revealed the rich diversity of medicinal plants and traditional knowledge in the Metema District. The therapeutic potential of the documented plants supports further pharmacological investigations, underscoring the importance of preserving indigenous knowledge and protecting plant resources against ongoing threats.

KEYWORDS

ethnobotany, indigenous knowledge, medicinal plants, Metema, ailments

Background

Medicinal plants have been central to the treatment of various ailments since ancient times and are a vital component of traditional healing systems. Approximately 70%–80% of the global population still depends on these systems for primary healthcare, driven by their proven effectiveness, cultural relevance, and limited access to modern healthcare (Caniago and Siebert, 1998; Kuniyal et al., 2015).

Globally, the transmission of traditional knowledge to subsequent generations is limited, suggesting the need for measures to safeguard existing traditional wisdom and facilitate its dissemination to future generations (Güler et al., 2021; Karaköse, 2022). In Ethiopia, the use of traditional medicinal plants has a well-established history (Yimam et al., 2022), with much of this knowledge being transmitted orally across generations by healers, knowledgeable elders, and community members (Chekole, 2017). It is estimated that over 80% of Ethiopians rely on traditional medicine, with nearly 95% of these remedies originating from plants (Muluye and Ayicheh, 2020).

Plants are served as major natural resources for traditional as well as modern medicinal systems all over the world (Shakya, 2016). Medicinal plants have been integral to human healthcare for centuries, serving as the primary source of therapeutic agents before the advent of modern pharmaceuticals (Mamun and Khan, 2018). With increasing interest in natural remedies, the study of these plants has gained renewed attention, especially in the context of traditional medicine systems and their pharmacological properties (Li and Weng, 2017). The ethnobotanical study of traditional medicinal plants in the Metema district of northwestern Ethiopia is essential for understanding the rich tapestry of local health practices and the reliance on natural resources for medicinal purposes. In this region, traditional medicinal systems are deeply intertwined with cultural practices, reflecting a profound knowledge of local flora.

Despite the crucial role of traditional medicine and medicinal plants in primary healthcare, efforts to document and promote this knowledge in Ethiopia have been limited (Demie et al., 2018). Only a small portion of the country's diverse culture and language has been studied thoroughly, to mention a few; Tadesse et al. (2024), Teka et al. (2020), Tugume et al. (2016), Yimam et al. (2022), and Zemede et al. (2024). There is a need for additional surveys across different regions to capture a broader range of sociocultural groups and to preserve unique knowledge and cultural practices (Giday et al., 2007). Research conducted in various Ethiopian regions (Tefera and Kim, 2019; Tuasha et al., 2018) has shown that medicinal plants are increasingly threatened, and the knowledge possessed by the elderly is at risk of disappearing due to inadequate attention.

Due to the ethnopharmacological study of medicinal plants in the world, newly recorded species and different uses of plants may be reported which will contribute to fields such as phototherapy, chemist's shop, and chemistry (Akbulut et al., 2019; Akbulut et al., 2022; Şen et al., 2022). Thus, the present study will play a role in this regard.

We propose that the sustainable management and conservation of medicinal plants can be achieved when information about their use for treating ailments and traditional herbal practices in specific areas is accessible. It is crucial to preserve this information to benefit both the present and future generations. This study focuses on the Metema district of Northwestern Ethiopia, where we have documented the diversity of ethnomedicinal plants and traditional healing practices among local communities. We anticipate that the qualitative and quantitative insights from this research will support both the conservation and sustainable use of medicinal plants and strengthen the traditional healthcare system. Given Metema's cultural and ecological landscape and the pressing need to protect its traditional plant knowledge, this study aimed to (i) document the medicinal plants and associated indigenous knowledge utilized by the communities, (ii) assess the major threats facing these medicinal plants, and (iii) identify and report any new ethnomedicinal plant species and practices previously unrecorded.

Materials and methods

Description of the study area

This study was conducted in the Metema district of the West Gondar Zone within the Amhara Regional State of Northwestern Ethiopia (Figure 1). Located approximately 925 km northwest of Addis Ababa, Metema comprises 31 kebeles, the smallest administrative units in Ethiopia. Genda Wuha serves as the district's administrative center. The population of the district is 110,231, consisting of the Agew, Amhara, Gumuz, and Kimant ethnic groups (CSA, 2007). The elevation of the area ranges from 550 to 1,608 m above sea level, covering approximately 440,000 ha (Adamu et al., 2012). Metema is characterized by lowland agroecology, with a mean annual rainfall of 1,008 mm and a monomodal rainfall pattern occurring from June to September (Masresha et al., 2023). The mean annual temperature is 26.2°C, ranging from 15.7°C to 41.0°C. The major crops cultivated in the area include sesame, cotton, and sorghum, while goats and cattle are the primary livestock (Masresha et al., 2023).

According to the broad classification of Ethiopia's forests, the lowland dry forests in the Metema district fall under the *Combretum-Terminalia* woodland community. The dominant vegetation in this region consists of mixed dry deciduous woodlands, primarily characterized by abundant *Combretum* spp. and *Terminalia* spp. *Communities* (Friis et al., 2010). Other notable species in these woodlands include *Sterculia setigera* Delile, *Boswellia papyrifera* (Caill.) Hochst., *Terminalia leiocarpa* (DC.) Baill., *Lannea fruticose* Engl., *Stereospermum kunthianum* Cham., *Dichrostachys cinerea* (L.) Wight & Arn. and *Pterocarpus lucens* Lepr. Ex Guill. and Perr. (Adamu et al., 2012; Eshete et al., 2011).

Research design

Reconnaissance survey and site selection

The researchers obtained a formal letter from the Vice President for Research and Technology Transfer at the University of Gondar to conduct this study (clearance number 1059/2022). This letter was then presented to the Metema District Administration Office, where we received permission to proceed with a reconnaissance survey and select sample kebeles for the actual study. The reconnaissance survey was conducted from 2nd to 9th July 2022, in Metema district.

Following the reconnaissance survey, 11 kebeles were chosen through stratified random sampling guided by the recommendations of district administrators, local authorities, and elders. These selected kebeles represented 35.48% of the total 31 kebeles in Metema district. The criteria for selecting sample kebeles included the presence of traditional healers, ethnic distribution (Amhara, Agew, and Gumuz), and settlement history (local inhabitants and settlers).

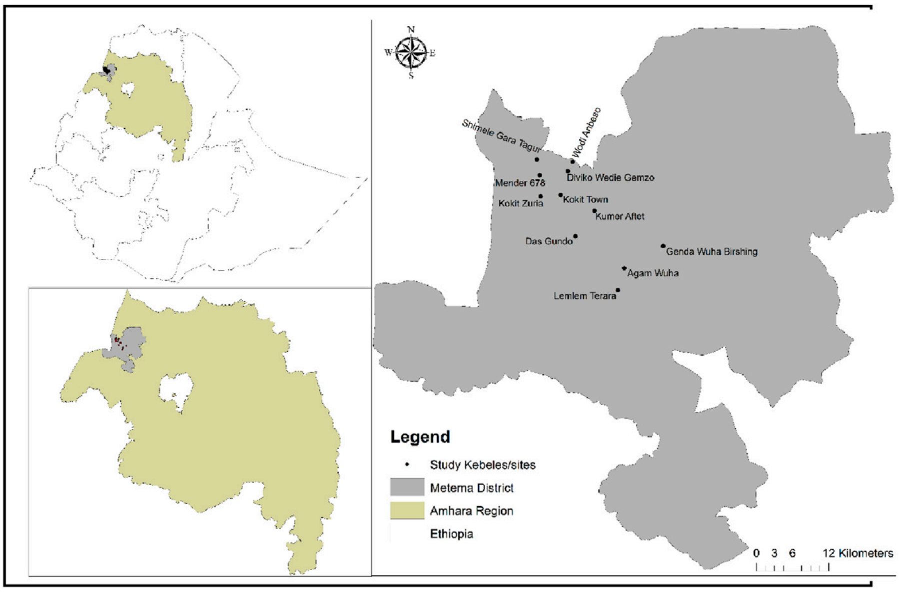

FIGURE 1
Map of Ethiopia showing the Amhara region and the study site.

TABLE 1 Description of study kebeles of data collection, highlighting key geographical and demographical attribute.

Study kebele	Gps coordinates		Elevation (m)	Ecology	NI	Gender		Informant type		Ethnicity		
	Latitude	Longitude				M	F	GI	KI	A	G	Ag
Mender 678	12°57′33″N	36°14′58″E	705	Lowland	6	4	2	3	3	0	0	6
Kokit Zuria	12°51′53″N	36°14′42″E	794	Lowland	11	7	4	9	2	11	0	0
Kokit town	12°52′09″N	36°16′00″E	726	Lowland	14	9	5	10	4	14	0	0
Das Gundo	12°44′19″N	36°11′48″E	838	Lowland	13	8	5	11	2	13	0	0
Kumer After	12°48′14″N	36°21′32″E	742	Lowland	7	6	1	3	4	0	7	0
Agam Wuha	12°43′16″N	36°19′15″E	848	Lowland	8	5	3	6	2	8	0	0
Lemlem Terara	12°40′09″N	36°17′40″E	889	Lowland	4	4	0	3	1	4	0	0
Diviko Wedie Gemzo	12°57′48″N	36°19′17″E	764	Lowland	29	17	12	24	5	29	0	0
Shimele Gara Tagur	13°01′12″N	36°17′00″E	740	Lowland	10	7	3	8	2	10	0	0
Genda Wuha Birshign	12°44′46″N	36°26′38″E	764	Lowland	4	2	2	3	1	4	0	0
Wedi Anbesso	12°58′29″N	36°24′40″E	849	Lowland	4	3	1	3	1	4	0	0
Total					110	72	38	83	27	97	7	6

NI, number of interviewees, Gender (M = male, F = Female), Informant type (GI, general informant; KI, Key Informant), Ethnicity (A = amhara, G = gumuz, Ag = Agew).

Sample size determination and informant selection

Cochran's formula, as cited by Bartlett et al. (2001), was employed to determine representative samples for the study area. A total of 110 informants were selected (72 males and 38 females), as shown in Table 1. Among these, 27 were key informants and 83 were general informants. The key informants were purposefully selected in consultation with local authorities and elders using the snowball sampling method, whereas general informants were chosen through random sampling, taking into account factors such as age, sex, cultural background, and settlement history.

Data collection

Ethnobotanical data were gathered through face-to-face interviews with informants. To ensure consistency, pre-planned semi-structured questionnaires and standardized data collection protocols (Alexiades, 1996; Martin, 2004; Heinrich et al., 2009) were employed. Field trips were conducted between August 2022 and October 2023 to identify and gather therapeutic plant species used within the district. Most interviews were conducted in Amharic, the region's common language; however, local translators assisted when the informants spoke other languages. All collected information was later translated into English. The questionnaire focused on the local names, plant types, parts used, ailments treated, and preparation and administration methods.

For additional on-site data collection, guided field walks were conducted with informants. During these walks, plant specimens were collected, and details of plant names, plant habits, habitats, conservation status, and other relevant attributes were documented. Four focus group discussions were held with seven key informants in each session, addressing topics such as threats to medicinal plants, conservation practices, antidotes, and dosage, following Martin's (1995) approach. These discussions helped validate the data gathered from the individual informants.

Specimen identification

The voucher specimens collected were authenticated by consulting taxonomic literature, reference voucher specimens, and various Flora of Ethiopia and Eritrea books. Specimen identification was performed at the National Herbarium (ETH) of Ethiopia at Addis Ababa University and the Herbarium of the University of Gondar under the guidance of an expert. The names of the species, genera, and families were further validated using the Plants of the World Online website (https://powo.science.kew.org). Finally, the identified specimens were dried, pressed, mounted on herbarium sheets, and deposited at the Herbarium of the Department of Biology, University of Gondar, Gondar, Ethiopia.

Data analysis

This study used a combination of qualitative and quantitative ethnobotanical methods (Martin, 1995; Cotton, 1996). To compare knowledge of medicinal plants across social groups in the Metema district, data analysis was conducted using SPSS (version 29). A t-test was conducted to explore the differences in medicinal plant knowledge based on settlement history (locals vs settlers), gender (men vs women), education level (literate vs illiterate), and healing experience (key informants vs general informants). Additionally, one-way ANOVA was applied to assess significant differences in the mean knowledge of medicinal plants across various age groups and ethnic backgrounds. Medicinal plant knowledge was assessed in terms of the number of medicinal plants mentioned by each informant. Microsoft Excel (2013) was used for calculating totals and percentages, and for creating tables and graphs.

Informant consensus factor (ICF)

The Informant Consensus Factor (ICF) measures the consensus or homogeneity in ethnobotanical knowledge shared by informants (Heinrich et al., 1998). This was calculated using the following formula:

$$ICF = \frac{Nur - Nt}{Nur - 1}$$

Where Nur is the total number of use reports for each disease category and Nt is the number of species used within that category. The ICF value ranges from 0 to 1, where 0 indicates no shared knowledge or exchange of use information among informants and 1 reflects a high level of consensus or knowledge exchange.

Direct matrix ranking (DMR)

The Direct Matrix Ranking (DMR) method was used to compare the multipurpose medicinal plants frequently mentioned by informants. This approach helps score the diversity of uses for selected medicinal plants (Martin, 1995; Cotton, 1996). Eight multipurpose plant species were chosen based on use citations along with eight common uses identified in the study area. Twelve key informants were selected to independently rate each plant's utility and assign scores (5 = best, 4 = very good, 3 = good, 2 = less used, 1 = least used, 0 = not used). The scores from each participant were summed and averaged for each plant and use category. Finally, the aggregate values for each species and use category were calculated and ranked.

Results

Socio-demographics features of the informants

Demographic characteristics were documented based on the information provided by the participants. A total of 110 informants were interviewed: 72 men (65.45%) and 38 women (34.55%). A significant difference ($p < 0.05$) was found between key and general informants regarding the mean number of medicinal plants known and used in the Metema district; key informants demonstrated greater knowledge, averaging 13.6 plants, compared to general informants, who averaged 5.8 plants. Similarly, there was a notable difference ($p < 0.05$) in the mean knowledge of medicinal plants between settlement histories (locals and settlers) and sex (men and women). However, no significant difference ($p > 0.05$) was observed between literate and illiterate respondents. One-way analysis of variance (ANOVA) indicated a significant difference ($p < 0.05$) in the mean number of medicinal plant species reported among different age groups. Additionally, significant differences ($p < 0.05$) were observed in the average number of medicinal plants reported among different ethnic backgrounds, with the Gumuz community mentioning more medicinal plants on average (14.6) than the Agew (10.2) and Amhara (7.1) groups (Table 2).

Medicinal plant diversity

A total of 85 medicinal plant taxa belonging to 71 genera and 33 families were identified and documented for their use in traditional human ethnomedicine across the three ethnic groups studied (Supplementary Table S1). Among these families, 17 (51.5%) included two or more species, whereas the remaining 16 families (48.5%) were represented by a single species. The Fabaceae family

TABLE 2 Medicinal plant knowledge of the informants in Metema district (n = 110).

Parameter	Informant categories	Number of informants	Mean ± SD	Test statistic	*p* value
Healing experience	Key Informants	27	13.6 ± 3.0	145.798	0.000*
	General Informants	83	5.8 ± 2.9		
Settlement history	Local	40	8.6 ± 4.7	6.887	0.010*
	Settlers	70	6.3 ± 3.7		
Gender	Male	72	8.6 ± 4.7	8.018	0.006*
	Female	38	6.1 ± 3.6		
Education level	Illiterate	42	7.6 ± 4.7	0.121	0.729
	Literate	68	7.9 ± 4.3		
Age	20–39	46	5.1 ± 2.1c	19.800	0.000*
	40–59	35	7.6 ± 4.4 b		
	≥60	29	11.2 ± 4.4a		
Ethnic background	Amhara	97	7.1 ± 3.9 b	12.234	0.000*
	Gumuz	7	14.6 ± 5.4a		
	Agew	6	10.2 ± 4.8 b		

*Shows a significant difference at p < 0.05.

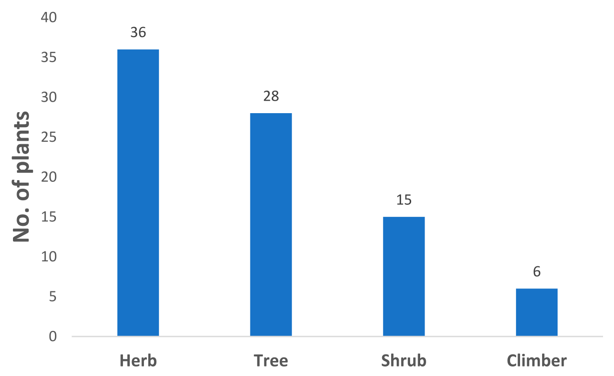

FIGURE 2
Distribution of medicinal plants in different life forms.

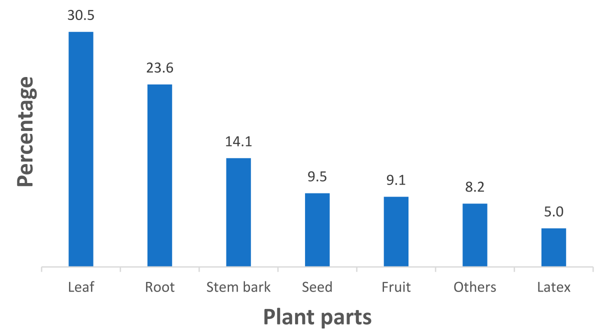

FIGURE 3
Plant part used in the preparation of herbal medicine.

had the highest number of species (11 species), followed by Malvaceae (8 species), and Cucurbitaceae (7 species). Life form analysis revealed that herbs constituted the largest group, with 36 species identified, followed by trees (28 species), shrubs (15 species), and climbers (6 species) (Figure 2).

Plant parts and conditions for preparing remedies

Various plant parts were reported to be utilized in remedy preparation within the district (Figure 3). The most commonly used plant part was the leaves, which accounted for 30.5% of the total, followed by the roots at 23.6%. Other plant parts, including bulbs, tubers, root bark, twigs, seed oil, flowers, gum, and stems collectively constituted 8.2%. Most remedies were prepared using freshly collected plant parts (64.1%), while 22.3% were made using either fresh or dry parts, and 13.6% were prepared exclusively from dry parts.

Ailments treated with medicinal plants

The study identified 67 human ailments treated with 85 medicinal plant species found in the district (Supplementary Table S1). Among these species, the majority (62 species, 72.1%) were reported to address two or more ailments, whereas 24 species (27.9%) were used for single ailments. Notable versatile plants include *Withania somnifera*, which treats nine different ailments; *Moringa stenopetala*, which addresses eight ailments; and *Calotropis procera*, which is effective for seven ailments. Additionally, *Ziziphus spina-christi*, *Securidaca longepedunculata*, and *Azadirachta indica* have been reported to treat six ailments.

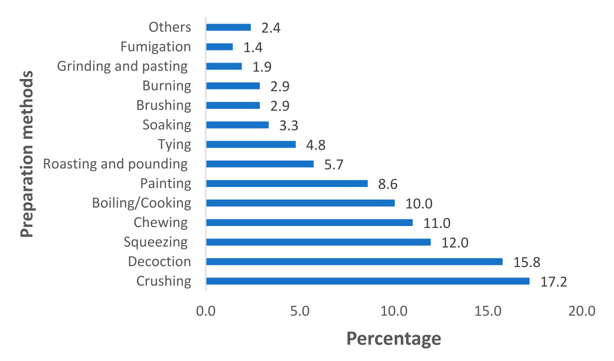

FIGURE 4
Methods of remedy preparation in Metema district.

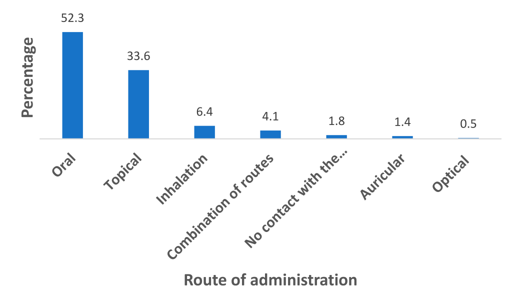

FIGURE 5
Route of administration of medicinal plants in Metema district.

In addition to individual plant species, traditional healers in the study area frequently combine multiple parts to create remedies for various ailments. A total of 16 plant species were used in two or more combinations for this purpose. For example, the roots of *Carissa spinarum* are crushed with the roots of *Ruta chalepensis* and the bulb of *Allium sativum*, and water is added to the mixture and drunk to treat snakebite. To address febrile illness, the leaves of *Ficus sycomorus*, *Cordia africana,* and *Zehneria scabra are* mixed, and boiled, and the filtrate is consumed and used for fumigation. Furthermore, the roots of *S. longepedunculata*, *Tacazzea venosa*, *W. somnifera*, *Sida rhombifolia,* and *Clerodendrum alatum* are pounded, heated, and inhaled to treat evil eyes. The root of *Pterolobium stellatum* is crushed and mixed with the bulbs of *A. sativum* and *Zingiber officinale*, along with the root of *R. chalepensis*, and sniffed as a remedy for the evil eye.

Pharmacological values of selected medicinal plants

The pharmacological values of medicinal plants have garnered increasing attention in traditional medicine, particularly for their diverse therapeutic applications. Among the 85 therapeutic plants reported in this study, the four top-ranked medicinal species included *Z. spina-christi*, *Ximenia americana*, *F. sycomorus*, and *T. leiocarpa*, which had shown important medicinal properties that could be used to treat a wide range of health problems.

Ziziphus spina-christi demonstrates significant pharmacological potential and was widely utilized in traditional medicine for various ailments. It was particularly effective in treating uvulitis; the stem bark was crushed, mixed with cold water, and consumed. For stomachaches, the roots were prepared in a similar manner, providing relief when the fluid was ingested. The leaves were also employed against ringworm, applied directly to the affected area using unripe fruit. For dandruff, the leaves were pounded, the fluid was sieved, diluted with water, and then applied to the scalp. Additionally, the roots can be used to combat malaria by crushing them, mixing them with water, and drinking the solution. Lastly, the leaves served as a remedy for spider poison, where the extracted fluid was painted on the affected area.

Ximenia americana exhibited notable pharmacological properties in treating a variety of conditions. For bleeding wounds, both fresh and dry stem bark can be crushed into a paste for topical application. Eye infections were addressed using the same part of the plant; the bark was crushed and homogenized with warm water to create a fumigating solution. In cases of uvulitis, the fresh stem bark was crushed, mixed with water, and consumed to provide relief. Additionally, fresh leaves were used for treating uvulitis in infants by placing them on the baby's head while reciting the phrase "Return it, return it back" repeatedly, showcasing the plant's cultural significance in traditional healing practices.

Ficus sycomorus presents a range of medicinal applications effective in treating various ailments. For febrile illnesses, fresh leaves were boiled with Cordia africana and *Z. scabra*, and the resultant filtrate was both consumed and used to wash the entire body. In instances of sudden sickness, fresh leaves were boiled with *Z. scabra*, and the mixture was employed for a full-body wash. The fresh latex from the plant served as a topical treatment for wound healing and was also effective against spider poison when applied to the affected area. Furthermore, the fresh stem bark was used for snakebite treatment by crushing it and forming a paste for application.

Terminalia leiocarpa offered a variety of medicinal applications, particularly in traditional healthcare practices. For the treatment of uvulitis, pieces of fresh or dry stem bark were placed on the patient's head while reciting the phrase "put up, put up." To address tapeworms, the fresh stem bark was crushed, mixed with water, and ingested. For dysuria, the fresh stem bark was crushed, boiled with water, and sweetened with sugar before consumption. In cases of jaundice, the crushed fresh stem bark was combined with boiling *Cicer arietinum*, and the filtrate was consumed. Lastly, for amoebiasis, the fresh stem bark was crushed, boiled, and the decoction was ingested once cooled.

Methods of preparation and route of administration of remedies

The communities in the study area have employed a range of methods to prepare and administer traditional medicinal remedies. The most prevalent preparation methods were crushing (17.2%), decoction (15.8%), squeezing (12%), chewing (11%), and boiling/cooking (10%). Five other preparation methods collectively accounted for 2.4% of the remedies used (Figure 4).

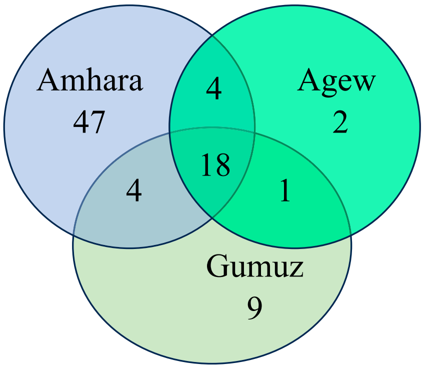

FIGURE 6
Venn diagram of medicinal plants among the studied ethnic groups in Metema district.

Regarding the routes of administration, over half of the remedies (115 preparations, or 52.3%) were administered orally (Figure 5). This was followed by topical application, which accounted for 33.6% of the preparations. Traditional healing practices also involve administering remedies without any physical contact with the ailment, accounting for 1.8% of cases. For example, during the circumcision of a young boy, the removed tissue was covered with the stem bark of *C. africana* to promote wound healing. Similarly, to treat uvulitis, the dried fruit of *Lagenaria siceraria* was hung in a house. Furthermore, certain traditional methods are believed to be effective in dispelling evil spirits. For instance, the root of *Pappea capensis* is burned to fumigate the area with the belief that this will prevent evil entities. Likewise, the root of *S. longepedunculata* is also placed in a fire, under the belief that it will prevent snakes from approaching.

Ethnobotanical knowledge distribution among ethnic groups

The ethnobotanical knowledge of the three ethnic groups—Amhara, Agew, and Gumuz was compared and illustrated using a Venn diagram (Figure 6). The Agew, Gumuz, and Amhara ethnic groups reported 25, 32, and 73 plant species, respectively. Pairwise comparisons indicated that the Amhara and Gumuz groups, as well as the Amhara and Agew groups, exhibited the highest degree of similarity, sharing 4.70% of their medicinal plant species. In contrast, the Agew and Gumuz groups had the least overlap, sharing only 1.18% of their medicinal plant species. Overall, the three ethnic groups collectively utilized 18 species of medicinal plants (21.18%) across the district. Notably, the Amhara ethnic group uniquely used 55.3% of medicinal products, while the Gumuz and Agew ethnic groups accounted for 10.6% and 2.3% of uniquely used species, respectively.

Informant consensus factor

ICF was calculated to identify the most effective medicinal plants for treating common ailments in the district. ICF values were determined based on disease categories adapted from the International Classification of Diseases (WHO, 2023). In total, 13 disease categories were identified, with ICF values ranging from 0.53 to 0.91, where the maximum possible value is 1.0 (Table 3). The disease categories with the highest ICF values were those related to the circulatory system and blood/blood-forming organs, with an ICF of 0.91. This was closely followed by diseases and symptoms involving the nervous system with an ICF of 0.89. In contrast, the category of diseases and symptoms related to the respiratory system had the lowest ICF value (0.53).

Direct matrix ranking exercise

The DMR exercise was conducted in the Metema district to evaluate and prioritize the most important medicinal plant species utilized by local communities (Table 4). The findings from the DMR exercise revealed that *Z. spina-christi*, *X. americana*, and *F. sycomorus* were the top-ranked medicinal plant species. Furthermore, the DMR exercise assessed various categories of use of these plants in the district. Accordingly, the most common categories of use included medicinal applications, fencing materials, and livestock forage.

Novel ethnobotanical findings

The current ethnobotanical study in the Metema district has revealed several novel findings. Notably, the research team identified six plants that were being used as traditional medicines for the first time in Ethiopia (Table 5). Among these newly documented medicinal plants, five have been recognized for their medicinal uses in other regions of the world. However, one species, *T. venosa*, has not been linked to any known medicinal application prior to this study.

Threats to medicinal plants and conservation efforts

An ethnobotanical study in the Metema district identified several threats to the sustainability of medicinal plant resources and the indigenous knowledge associated with them. During group discussions, participants highlighted seven key threats: the use of herbicides and insecticides, human-induced fires, agricultural land expansion, construction activities, fuelwood collection, the use of plants for agricultural implements, and overgrazing. Additionally, participants noted other threats, including the use of medicinal plants for household utensils, informal cross-border trade to neighboring Sudan, deforestation, seasonal migration patterns, and climate change-related events, such as drought. These discussions also revealed a lack of effective management practices for medicinal plants.

To assess the severity of these threats, we conducted interviews with 12 key informants, who ranked the seven prioritized threats to medicinal plants. The range of values for prioritization was from 23 to 79. The findings indicated that fuelwood collection was the most significant threat, followed by agricultural land expansion and the use of herbicides and insecticides (Table 6).

TABLE 3 ICF values of medicinal and magical plants for treating human ailments in Metema district.

Disease categories	Reported diseases (user reports are in bracket)	No. of species	Use citations	ICF
Diseases of the circulatory system and blood and blood-forming organs	Hypertension (29), Anemia (3), heart disease (2)	4	34	0.91
Diseases and symptoms involving the nervous system	Headache (4), snakebite (27), scorpion sting (14), spider poison (22), febrile illness (168), tendinitis (1)	28	236	0.89
Infectious and parasitic diseases	Rabies (4), tapeworm (8), amoebiasis (4), malaria (71), intestinal parasite (20), ring worm (24), scabies (10), uvulitis (23), wart (8), bacterial infection on the tip of a finger (7), dandruff (7), nail fungus (1)	31	187	0.84
Injury, poisoning, and certain other consequences of external causes	Circumcision wound (8), ear pest (2), wound healing (42), bleeding wound (45), dirt on the eye (1), wound on the penis (3)	18	101	0.83
Endocrine, nutritional, and metabolic diseases and Neoplasms	Diabetes mellitus (18), Cancer (7)	5	25	0.83
Diseases and symptoms involving the digestive system	Toothache (1), stomachache (14), constipation (17), sudden sickness (31), abdominal bloating (16), gastritis (11), diarrhea (11), gum bleeding (5), gum disease (16), jaundice (43), rectal prolapse (2), teething in babies (2)	38	169	0.78
Disease of the skin	Hair loss (3), skin disease (2)	2	5	0.75
Symptoms, signs, and clinical findings not elsewhere classified	Snake repellent (1), evil eye (34), evil spirit (3), to eradicate devil (2)	12	40	0.72
Diseases of the musculoskeletal system or connective tissue	Gout (4), rheumatism (4), back pain (15), stabbing pain (4), Osteoporosis (1), tendon issue (1)	10	29	0.68
Pregnancy, childbirth, and the puerperium	Retained placenta (3), miscarriage (3), uterus sore (1)	3	7	0.67
Urogenital conditions	Male erectile dysfunction (4), satisfying sexual desire (2), Dysuria (2), kidney disease (1)	4	9	0.63
Diseases of the ear or mastoid process and visual system	eye infection (2), ear lesion (4)	3	6	0.60
Diseases and symptoms involving the respiratory system	Asthma (3), cough (7), common cold (7), tonsilitis (2), Covid (1)	10	20	0.53

TABLE 4 DMR of eight multipurpose medicinal plant species in the Metema district.

Medicinal plants	Use categories								Total	Rank
	Co	Fu	LF	Md	Fo	FW	FI	Fe		
Azadirachta indica	3.6	2.2	1.4	4.1	0.9	2.7	2.8	3.4	16.3	8th
Stereospermum kunthianum	1.8	1.9	1.9	4.0	0.0	2.0	3.5	2.6	24.6	5th
Terminalia leiocarpa	5.0	3.0	3.3	1.7	0.0	4.5	3.5	4.0	28.0	4th
Ficus sycomorus	2.8	3.2	4.7	3.4	4.3	3.3	2.1	2.5	29.0	3rd
Carissa spinarum	1.8	0.6	1.3	3.3	3.8	2.8	0.2	4.3	19.8	6th
Ziziphus spina-christi	3.9	4.3	5.0	1.7	4.7	4.1	3.8	5.0	36.3	1st
Ximenia americana	2.2	2.5	2.8	4.1	4.9	3.3	2.5	3.7	30.0	2nd
Moringa stenopetala	0.1	0.1	4.4	4.8	4.3	1.8	0.0	0.9	19.5	7th
Total	21.1	17.7	24.8	27.0	22.8	24.3	18.3	26.3		
Rank	6th	8th	3rd	1st	5th	4th	7th	2nd		

N.B., The scores in the table indicate the average values of ranks given to medicinal plants based on their use diversity. Co, Construction; Fu, Furniture; LF, livestock forage; M, md; Fo, Food; FW, fuel wood; Farm implements = FI, Fence = Fe.

TABLE 5 Plants reported to treat ailments in Metema district for the first time in Ethiopia.

Scientific name	Ailments treated in the current study	Reports from other parts of the world
Phaseolus lunatus	Wound healing, Spider poison	Magalhãesa et al. (2019)
Cucumis melo	Spider poison, Scorpion sting	Anwar et al. (2024)
Cucumis metuliferus	Wound on penis	Mzena et al. (2018)
Tacazzea venosa	Evil spirit	-
Oryza sativa	Diarrhea	Gedif and Hahn (2003)
Dioscorea dumetorum	Diarrhea, Diabetes mellitus	Bukatuka et al. (2016)

TABLE 6 Ranking of threats to medicinal plants in Metema district.

Threats	Key informants												Total score	Rank
	KI1	KI2	KI3	KI4	KI5	KI6	KI7	KI8	KI9	KI10	KI11	KI12		
Use of herbicides and insecticides	2	2	3	1	6	6	2	3	5	5	6	6	47	3rd
Human-induced fire	3	3	1	3	5	5	4	4	4	4	4	4	44	4th
Agricultural land expansion	7	7	7	7	4	4	6	6	6	7	5	5	71	2nd
Construction	4	5	4	5	1	1	5	5	3	3	3	3	42	5th
Fuel wood	6	6	6	6	7	7	7	7	7	6	7	7	79	1st
Farm implements	1	1	2	2	2	2	3	2	2	2	2	2	23	7th
Over grazing	5	4	5	4	3	3	1	1	1	1	1	1	30	6th

Discussion

Socio-demographics of the informants

This ethnobotanical study in the Metema district provided valuable insights into how socio-demographic factors influence the knowledge and use of medicinal plants within the local community. The findings indicate that men possess greater knowledge of medicinal plants than women do, suggesting that men generally have a broader understanding of these resources. This may be due to the men's increased exposure to social affairs in the study area, which offers more opportunities for knowledge acquisition. This finding aligns with those of Chekole et al. (2015) and Kefalew et al. (2015), who reported similar results. The result may also be attributed to the greater number of males included in the present and cited studies.

Age also plays a significant role in knowledge of medicinal plants. Older informants, particularly those aged 60 years and above, exhibited a higher level of knowledge than younger age groups (20–39 years and 40–59 years). This suggests that firsthand experience and long-term familiarity contribute to the generation's deeper understanding of medicinal plants, a finding that is consistent with that of Tahir et al. (2021), who emphasized the value of accumulated cultural exposure, experience, and exchange over time. However, studies have noted an alarming trend: as older knowledgeable individuals pass away, their wisdom risks are lost because of limited transmission to the next-generation (Demie et al., 2018; Nigussie and Kim, 2019; Karaköse, 2022; Tahir et al., 2023). This loss is compounded by the younger generation's declining interest in learning from elders, endangering the preservation of indigenous knowledge.

The educational background appeared to have a limited impact, as both literate and illiterate individuals exhibited comparable levels of knowledge. However, key informants, such as herbal practitioners, identified more medicinal plants than did general informants, highlighting their specialized knowledge and direct experience with these plants, as supported by Tahir et al. (2023).

Interestingly, local inhabitants cited more medicinal plants than settlers, likely because of their longer residency and greater familiarity with the local flora. Among the ethnic groups in the study area, the Gumuz people have emerged as the most knowledgeable about medicinal plants. This expertise is attributed to their strong reliance on natural resources for health and daily survival, as well as the exchange of indigenous knowledge both within their community and with neighboring groups in Sudan.

Medicinal plant diversity

This study documented a rich diversity of medicinal plants used for treating human ailments in the Metema district, identifying a total of 85 medicinal plant species. Compared to findings from other studies conducted in Ethiopia and internationally, this number was notably higher. For instance, ethnobotanical research by Chekole (2017), Regassa et al. (2017), Tefera and Kim (2019), Tadeyos and Wendawek (2022), and Mekuria and Abduro (2022) recorded 51, 25, 70, 62, and 43 medicinal plant species, respectively, across various regions in Ethiopia. In studies outside Ethiopia, researchers like Ojha et al. (2020), Ishtiaq et al. (2015), Tugume et al. (2016), Wiryono et al. (2019), Al-Robai et al. (2022), and Akbulut et al. (2019), documented 70, 10, 27, 9, 21, and 48 medicinal plant species, respectively, in counties including India, Indonesia, Uganda, Pakistan, Saudi Arabia, and Turkey. The study documented medicinal plants were also found lower than other studied (Karaköse, 2022; Şen et al., 2022).

A study conducted in Quara (Tadesse et al., 2024), which is in close proximity to the current study area, reported 128 medicinal plant species, a number higher than that observed in the present investigation. This discrepancy can be attributed to the fact that Quara district encompasses two agroecological zones, lowland and highland, which contribute to the presence of extensive vegetation cover. In contrast, the current study was limited to lowland areas exclusively.

Among the identified medicinal plants, the Fabaceae family was dominant. This prominence may be attributed to the unique adaptations of Fabaceae species to their local environment, such as their symbiotic relationships, which enable them to thrive in nitrogen-deficient soils. Their extensive root systems also allow these plants to outcompete other plants for resources, giving them a competitive edge in the region (Getaneh et al., 2023; Hedberg et al., 2006). This finding aligns with those of previous ethnobotanical studies conducted in Ethiopia (Kidane et al., 2018; Nigussie and Kim, 2019; Tahir et al., 2023), and other regions of the world (Bhandari et al., 2021; Cordero et al., 2022; Masters, 2023).

In terms of plant habits, herbs were found to be the primary type utilized by the people of the Metema district, likely due to their wide availability, market accessibility, and perceived therapeutic effectiveness. This trend is consistent with the findings reported in other studies (Agize et al., 2022; Faruque et al., 2019; Ojha et al., 2020; Tamene et al., 2024).

Plant parts and the conditions for preparing remedies

The study found that leaves were the most commonly used plant parts for remedy preparation, followed by the roots. This pattern aligns with the findings of other studies in Ethiopia (Ashagre and Lulekal, 2021; Demie et al., 2018; Nigussie and Kim, 2019; Tahir et al., 2021) and globally (Amjad et al., 2020; Cordero et al., 2022; Akbulut et al., 2019; Karaköse, 2022; Şen et al., 2022). Leaves are often preferred owing to their accessibility, abundant availability, and high concentrations of bioactive compounds. Moreover, harvesting leaves has a minimal impact on the survival of plant species, which helps to maintain ecological sustainability. Although roots have been reported as the most frequently used plant part in some studies (Bhandari et al., 2021; Chekole et al., 2015; Teklehaymanot and Giday, 2010) and the second most used plant part in the current study, heavy reliance on roots poses risks to the long-term survival of these medicinal plants (Balde et al., 2015).

Consistent with previous Ethiopian studies (Abera, 2014; Lulekal et al., 2013; Tahir et al., 2023), most remedies in the Metema district were prepared using fresh plant parts. The preference for fresh materials is generally linked to the enhanced efficacy of their bioactive compounds (Chekole et al., 2015). However, given that many medicinal plants in the study area are herbs, remedy availability may be seasonal. Herbs in this dryland region typically grow for only a few months, limiting access to fresh materials outside the growing season.

Ailments treated with medicinal plants

Analysis of medicinal plant diversity in the Metema district showed that nearly three-quarters of the identified species were used to treat multiple diseases. This widespread application suggests a high level of adoption and reliance on these plants within the local community, consistent with the findings of Pala et al. (2019). The versatility of these medicinal plants in treating various health conditions may be due to the combined action of multiple bioactive constituents. Supporting this idea, Mahomoodally (2013) noted that the synergistic effects of diverse medicinal components can enhance the catalytic activity and improve the absorption of beneficial compounds in the human body. These findings highlight the importance of further scientific investigation of the phytochemical profiles and pharmacological properties of these versatile plants. Understanding the mechanisms that enable certain medicinal plants to treat a broad range of ailments could significantly advance traditional medicine practices and offer more effective and holistic treatment options. Such insights have the potential to improve the overall health and wellbeing of the local population by preserving and enhancing indigenous health practices.

Pharmacological values of some selected plants

The study's four highest-ranked medicinal species have been documented as therapeutically effective in other studies as well. *Ziziphus spina-christi* leaves have been shown to be effective against dandruff (Yimam et al., 2022). *Ximenia americana* fruit has been found to alleviate fever, toothache, and common cold symptoms (Zemede et al., 2024). *Ficus sycomorus* leaves have demonstrated efficacy in treating stomachache (Zemede et al., 2024). The root of *T. leiocarpa* has been utilized to address scorpion stings and malaria, while its stem bark has been employed in the treatment of jaundice, scorpion stings, and uvulitis (Tadesse et al., 2024).

A review of the eight multipurpose medicinal plants selected for the direct matrix ranking exercise was conducted, focusing on their *in vivo* experiments as documented in the literature (Table 7). The findings indicate that *in vivo* experiments have been performed for all selected species, aligning with the traditional medicinal uses reported in the current study. This consistency underscores the compatibility between the scientific research and the traditional knowledge identified.

Methods of preparation and route of administration of remedies

This study found that the most common methods of preparing medicinal remedies in the Metema district included crushing,

TABLE 7 Review of an *in vivo* experiment with selected medicinal plants.

Medicinal plants identified	Review of an *in vivo* experiment
Azadirachta indica	Anti-plasmodial activity of both aqueous and ethanolic leaf extracts were studied *in vivo* using *Plasmodium berghei* infected mice and demonstrated significant anti-plasmodial activity (Oseni and Akwetey, 2012). This is in agreement with our report of the use of this species for treatment of malaria
Stereospermum kunthianum	Maceration the stem bark in 80% v/v methanol extract was analyzed for its acute toxicity profile in rats for its effects on wound healing and found significant reduction of wound area (Nwinyi et al., 2021). This is in agreement with our report of the use of this species for treatment of wound healing
Terminalia leiocarpa	The root bark extract therapeutic activity was carried out against *E. coli* in experimentally infected rats, and found a significant reduction of defecation frequency, water content of faeces, weight and volume of diarrheic faeces, and *E. coli* load of faeces (Adrien et al., 2018). This is in agreement with our report of the use of this species for treatment of amoebiasis whose major symptom is diarrhea
Ficus sycomorus	An *in vivo* toxicological analysis of the fruit of the plant on Wistar rats showed positive results as enzymatic examination of the liver, kidney and blood of the Wistar rats did not indicate any serious damage (Braide et al., 2018). Additionally, an *in vitro* analysis of the fruit extract showed bactericidal effect on multi drug resistant bacteria. This is in agreement with our report of the use of this species for treatment of wound healing by preventing bacterial growth
Carissa spinarum	An *in vivo* methanolic extract of root was evaluated on burn wound model in mice, showed significant wound healing activity. Besides, an *in vitro* antimicrobial activity of the methanolic root extract against the bacterial and fungal strain using agar dilution method also exhibited significant antimicrobial activity against all the tested microorganisms (Sanwal and Chaudhary, 2011). This is in agreement with our report of the use of this species for treatment of snakebite, as it helps to heal the wound caused by the bite
Ziziphus spina-christi	The root bark was evaluated for *in vivo* anti plasmodial activity against Plasmodium berghei in mice. It showed a potent activity against the parasite suggesting the plant as promising agent for malaria treatment (Adzu et al., 2007). This agrees with our report of the use of this species for treatment of malaria
Ximenia americana	An *in vivo* extract of stem bark induces a decrease in mast cell concentration leading to the healing process of skin wound contraction in rats (Castro Souza et al., 2017). This agrees with our report of the use of this species for treatment of bleeding wound
Moringa stenopetala	Crude aqueous leaf extract of the plant in an *in vivo* experiment carried out on male guinea Pigs had shown blood pressure lowering effect substantiating the use of the plant in traditional medicine (Mengistu et al., 2012). This agrees with our report of the use of this species for treatment of hypertension

decoction, squeezing, and chewing. These preparation methods align with the findings of previous ethnobotanical studies in various regions (Alemu et al., 2024; Amsalu et al., 2018; Atnafu et al., 2018). Informants reported that no standardized approach exists for administering remedies; instead, the method varies based on factors such as patient age and health condition. This observation is consistent with Ahmad et al. (2014), who noted the flexible, patient-specific nature of traditional medicine practices.

Oral administration was identified as the primary route for delivering herbal remedies in the Metema district, a trend observed in other ethnobotanical studies that also reported that the oral route was predominant in traditional medicines (Regassa, 2013; Tahir et al., 2023). The range of preparation techniques and administration routes highlights the depth of traditional knowledge within the local community. Healers are likely to adapt their methods based on the specific needs and conditions of each patient, drawing on a rich body of experiential knowledge accumulated over generations.

Ethnobotanical knowledge distribution among ethnic groups

This study revealed that 21.18% of medicinal plants were mentioned across all three ethnic groups. However, the Amhara ethnic group reported a higher number of unique medicinal plant species than the Agew and Gumuz groups. This may be due to the large population size and greater agricultural land coverage in the area. Additionally, the seasonal movement of the Amhara people from neighboring highland districts to Metema for farming and livestock rearing may have fostered knowledge sharing of medicinal plants within their community. In contrast, the Agew ethnic group reported fewer medicinal plants, possibly because of the secretive nature of their traditional knowledge, a characteristic commonly observed in many indigenous communities. These findings, along with those of previous studies (Haq et al., 2022; Sop et al., 2012; Teka et al., 2020), highlighting that the diversity of medicinal plant knowledge is often shared by ethnicity and cultural backgrounds. These insights emphasize the importance of considering ethnic and cultural contexts when documenting and interpreting traditional medicinal plant knowledge.

Informant consensus factor

This study reported ICF values ranging from 0.53 to 0.91, indicating a strong consensus among the informants regarding the therapeutic uses and effectiveness of specific medicinal plant species, which is consistent with the findings of Tuttolomondo et al. (2014). The highest ICF value (0.91) was observed under conditions related to the circulatory system and blood/blood-forming organs. This high level of agreement aligns with the findings of previous studies (Cheng et al., 2022; Ralte et al., 2024; Zemede et al., 2024) and suggests that the local community holds strong confidence in the efficacy of certain plants for treating these conditions, specifically hypertension, anemia, and heart disease. The second-highest ICF value was recorded for ailments related to the nervous system, which is consistent with the findings of Zemede et al. (2024), who reported a high consensus for conditions such as headaches and febrile illnesses in this category. The third highest ICF value was observed for infectious and parasitic diseases, consistent with Al-Robai et al. (2022), who reported high ICF values for medicinal plants used to treat viral, fungal, bacterial, and other parasitic infections.

High ICF values often indicate that plants have potentially effective therapeutic properties (Heinrich et al., 1998). These findings suggest that the local community has a well-established and shared knowledge base regarding the therapeutic efficacy of certain medicinal plants, particularly for circulatory and blood-related conditions. This consensus not only helps prioritize these plants for further phytochemical and pharmacological investigations but also highlights their potential role in culturally relevant healthcare interventions.

Direct matrix ranking

The DMR exercise was instrumental in identifying the most heavily used multipurpose plant species in the Metema district as well as the key threats to their sustainability. The three most utilized species were *Ziziphus spina-christi*, *X. americana,* and *F. sycomorus*, which are predominantly harvested for their medicinal properties rather than for non-medicinal uses. This finding aligns with previous research (Alemneh, 2021), which indicates that medicinal use is the primary threat to many plant species among the eight threats assessed in the DMR exercise.

The specific parts of these plants that are used for medicinal purposes significantly influence their vulnerability. For example, the root, root bark, and stem bark of *Z. spina-christi* have been harvested to treat various ailments, thereby increasing the susceptibility of plants to overexploitation. The frequent use of *X. americana* stem bark for medicinal purposes places additional pressure on this species. The DMR findings suggest that overharvesting of these multipurpose plants for medicinal applications poses a considerable threat to their long-term sustainability in the Metema district. These insights underscore the need for conservation strategies that balance the medicinal and non-medicinal uses of valuable plant resources.

Novel ethnobotanical findings

Of the 85 medicinal plant species identified in this study, 79 had already been reported as traditional medicinal plants in Ethiopia, although the plant parts used, ailments treated, and mode of remedy preparation may vary from area to area as well as culture to culture. This high overlap suggests a strong cultural exchange of plant-based healthcare knowledge among the Ethiopian communities (Agize et al., 2022). However, six species have been documented for the first time as medicinal plants in Ethiopia, highlighting the biodiversity and ethnobotanical richness of the study area. To the best of our knowledge, *the medicinal use of T. venosa has not been reported elsewhere*, marking a novel discovery on a global scale. The identification of this plant as a new medicinal species highlights the unique health practices of the Metema district, including the use of plants unrecognized for their therapeutic potential elsewhere.

The findings of this study expand the understanding of traditional plant-based medicine in Metema, achieved through an ethnically focused approach and exploration of less studied areas. Similarly, other studies (Subba et al., 2016) have shown that studying under-explored ethnic communities can reveal new medicinal plant species. The discovery of these previously undocumented medicinal plants in Metema highlights the importance of the continued documentation of traditional ethnobotanical knowledge in Ethiopia. Further phytochemical research on these newly reported plants and their uses is essential to validate their medicinal efficacies. This line of research has the potential to contribute valuable insights to medical sciences (Iwu, 2002) while strengthening traditional healthcare practices passed down through generations (Subba et al., 2016).

Threats to medicinal plants and conservation efforts

The primary threats to medicinal plants in the Metema district include the use of fuelwood, agricultural land expansion, and the application of herbicides and insecticides, consistent with findings from previous research in Ethiopia (Zemede et al., 2024). Additional threats identified include the use of pant parts for construction, human-induced fires, and overgrazing. The unsustainable exploitation of specific species such as *X. americana*, *C. spinarum*, *S. longepedunculata*, and *B. papyrifera* further jeopardizes their survival. To mitigate these threats, it is essential to implement awareness programs and conservation education programs that engage stakeholders and local communities. However, currently, the study area has limited conservation and management practices for medicinal plants. Reported local conservation efforts include cultivating medicinal plants in home gardens and preserving them on agricultural lands.

In addition to their medicinal uses, the plant species documented in this study serve multiple vital purposes in local communities. They are cultivated for their aesthetic value, are used as living fences, and provide food, shade, and fuelwood. This diverse range of uses underscores the cultural and ecological significance of natural resources. Strengthening the conservation and management practices surrounding these medicinal plants is essential to ensure their long-term sustainability and continued availability to the local population. Protecting these invaluable natural resources is essential not only for preserving traditional medicine knowledge and practices but also for enhancing food security within the area.

Conclusion

The ethnobotanical study conducted in Metema district has yielded valuable insights into the intricate relationship between local communities and their use of medicinal plants. The findings revealed that knowledge of medicinal plants is predominantly held by older male informants, indicating a concerning trend: traditional knowledge is at risk of erosion as the older generation passes away without adequately transferring this wisdom to younger community members. This trend highlights the urgent need for strategies to preserve and document indigenous knowledge before it can be lost.

This study identified and documented 85 medicinal plant species across the three ethnic groups, emphasizing the rich biodiversity present in the study area. Notably, the Fabaceae family was the most represented among medicinal plants, reflecting their adaptability and ecological significance. The predominant use of leaves for medicinal preparations demonstrates a sustainable approach that minimizes the impact on plant populations. However, there are concerns about the overharvesting of roots, which could threaten the long-term survival of some species.

Moreover, the findings suggest that a considerable portion of medicinal plants are utilized to treat various ailments, indicating the community's deep reliance on these resources for healthcare. The identification of new medicinal plants, including *T. venosa*, shows the potential for further exploration of ethnobotanical diversity. However, the study also identified significant threats to medicinal plants, primarily due to unsustainable practices, such as fuelwood collection and agricultural expansion. Efforts to conserve these plants and associated indigenous knowledge are currently limited.

To address these challenges, awareness programs should be developed to educate local communities on the importance of conserving medicinal plants and the risks associated with overharvesting. Involving community stakeholders in conservation efforts can foster a sense of ownership and responsibility toward local resources. Promoting sustainable harvesting techniques for medicinal plants, particularly those with a high demand for roots and other vulnerable parts, is also essential.

Furthermore, phytochemical and pharmacological studies are recommended to validate the medicinal properties of the newly identified plants. Supporting and expanding local conservation practices, such as cultivating medicinal plants in home gardens, could also play a crucial role. By implementing these recommendations, the local community can safeguard its rich ethnobotanical heritage, while ensuring the sustainability of medicinal plant resources for future generations.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

DT: Writing–original draft, Writing–review and editing. EL: Supervision, Writing–original draft, Writing–review and editing. GM: Supervision, Writing–original draft, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2025.1535822/full#supplementary-material

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