

Medicinal Plants Used for the Management of Hepatitis Over the Past 15 Years in Ethiopia: A Systematic Review

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Background: Treatment of human and animal ailments using botanical sources has obtained significant attention in Ethiopia. The compounds available in plants comprise a plentiful source of bioactive ingredients able to treat many complications. The review aimed to present an updated list of plants used for managing hepatitis over the past 15 years in Ethiopia.

Methods: Systematic, comprehensive search was undertaken from electronic databases (PubMed, Google Scholar, Science Direct, and Scopus) between September 01 and October 15, 2022, using standard search terms. Original researches carried out in Ethiopia, written and published in English between January 01/2007 and December 31/2021, and reported hepatitis as a disease treated by medicinal plants were included in the review. Plants beyond the list of Ethiopian and Eritrean floral were excluded. Data were extracted from texts and tables of original papers on a Microsoft Excel. Quality was assessed by applying the Joanna Briggs Institute Critical Appraisal Checklist.

Results: A total of 317 papers were obtained from the database search. After removing duplicates and screening, 15 articles fit the inclusion criteria and selected for final review. Of the 24 plants identified, 35.7% were herbs. Leaf and root (35.7% each) were the predominant plant parts used for remedy preparation. Combined use of leaf and root comprised 10.7%. The families Apocynaceae, Asteraceae, Euphorbiaceae, Cucurbitaceae, and Fabaceae comprise the highest number of plant species. About 89.3% of remedies were administered orally.

Conclusion: The majority of plants belong to herbs and the frequently used plant parts are leaf and roots. Evidence generated from the present review indicated that lots of plants have been used to manage hepatitis. Moreover, the findings could serve as preliminary information to formulate new drugs acting against hepatitis. Therefore, it is desirable for scholars to recognize, document, and keep plants and the associated knowledge appropriately.

Keywords: hepatitis, medicinal plant, Ethiopia

Introduction

Herbal medicine has obtained great attention in Ethiopia and continues to be the source to relieve many human and animal ailments.¹ It is believed that the oral and/or written knowledge has been conveyed from a skilled grandparent, parent, or elder in general to the next generation. About 6500–7000 plant species are available in Ethiopia, of which 12–19% are endemic, making the country among the most diverse floristic countries in the world.^{2,3} It is estimated that about 80% of the Ethiopian population and 60% of the world population depend on traditional medicine to treat a variety of health problems. About 25% of the current medicines have compounds from medicinal plants.⁴

The high demand for using traditional medicine is mainly attributed to its minimal cost and ease of accessibility, in addition to serving as a source of knowledge for plant-based synthetic drugs. In Ethiopia, high achievement in the utilization of traditional medicine is believed to be due to a high diversity of plants, rich cultures, beliefs, and language.⁵ Sometimes it becomes the only available and affordable option, especially in

remote or underserved areas. Ayalew et al 2022 reported the ethnomedicinal uses, biological activities, and chemical constituents of Ethiopian endemic medicinal plants.⁶ The global scientific community ranked plants to be investigated and used for human and animal disease treatment. Of which, neem tree (*Azadirachta indica*) was included in the top ten lists and referred to as the tree of the 21st century or miracle tree because of its multipurpose uses and excellent therapeutic potential for all diseases. This tree contains ingredients that have anti-hepatitis activity.^{7,8}

Emerging infectious diseases remain to impose a threat on humans. Of which, viral disease is one of the most life threatening challenging the survival of human beings on earth, followed by bacterial and parasitic diseases.^{9,10} Hepatitis is an inflammation of the liver tissue. The liver is a vital organ that processes nutrients, filters the blood, and fights infections. Some people or animals with hepatitis have no symptoms. Others may develop yellow discoloration of the skin, whites of the eyes, vomiting, and abdominal pain. The common causes of hepatitis are the viruses hepatovirus A, B, C, D, and E. Other common noninfectious causes include heavy alcohol use, certain medications, toxins, and autoimmune diseases. More than one million deaths are recorded due to hepatitis annually.^{11,12}

Screening of plants for the existing bioactive constituents is crucial to discovering and formulating promising drugs that cure hepatitis. Therefore, new drugs of plant origin are urgently needed and drug screening efforts should be encouraged. Despite the excessive role of medicinal plants in primary health care, little work has been conducted in Ethiopia to properly recognize and preserve plants and the associated facts. Therefore, the present review aimed to present an updated list of plants used for managing hepatitis over the past 15 years in Ethiopia.

Methods and Materials

Search Design and Strategy

International electronic databases (PubMed, Google Scholar, Scopus, and Science direct) were systematically searched for published articles about medicinal plants utilized for the treatment of hepatitis over the last 15 years in Ethiopia. All searches were limited to articles published in English between January 01/2007 and December 31/2021. The last search was done on December 31/2021. The search was conducted between September 01 and October 15, 2022. This review has used the Preferred Reporting of Systematic Reviews and Meta-Analysis (PRISMA) guidelines¹³ to assure scientific rigor. Common search terms were “medicinal plants”, “human ailment”, and “Ethiopia”. These search terms were used separately and in combination using Boolean operators like “OR” or “AND”. The reference lists of included studies were screened for additional eligible studies. Grey literature and unpublished data were not included. Search results from different databases were exported to EndNote and then combined after the removal of duplicates.

Procedure for Study Selection

Two researchers (YA, WY) were involved in study selection. After removing duplicate articles, they performed initial screening by reading titles and abstracts of each article for eligibility. Then, the full text of the eligible articles was assessed for inclusion in the review. Articles that did not report the outcome of interest in the full text were removed. Any discrepancy between researchers in inclusion decisions was resolved via discussion. If still not resolved and additional clarification is required, the primary author of eligible studies was contacted via email at least two times.

Study Selection Criteria

Inclusion Criteria

Original articles conducted in Ethiopia, published in English between January 01/2007 and December 31/2021, contain full ethnobotanical information (family name, scientific name, local name, growth form, plant parts used, and route of administration), and reported hepatitis as a disease treated by traditional healers were included in the review.

Exclusion Criteria

Studies without a full text were excluded after contacting the primary author at least two times and no response at all through email. Studies that include only plants of livestock usage were excluded. Plants which are beyond the list of Ethiopian and Eritrean flora were excluded.¹⁴

Data Extraction

Two researchers (YA, BA) extracted all the required data (scientific, family, and local names, growth forms of plants, plant parts used, methods of preparation, and route of administration) independently using a standardized data extraction form adapted from the JBI data extraction format in a Microsoft Excel spreadsheet. Data were extracted from text and tables. If there was a discrepancy between investigators on the data to be extracted, it was resolved via discussion or a third researcher. If still not resolved and additional clarification is required, the primary author of the included studies was contacted via email at least two times. The collected data were analyzed using descriptive statistics to calculate frequency and percentage.

Assessment of Methodological Quality

Two researchers (WY, BA) independently assessed the quality of each original study using a standard quality assessment tool adapted from the JBI Critical Appraisal Checklist. The methodological quality of all 15 papers (Table 1) was therefore checked by applying the Joanna Briggs Institute Critical Appraisal Checklist¹⁵ prior to inclusion. This tool has nine quality items that focus on sample size, methods used for identification of the outcome, and statistical analysis. If disagreement between two assessors occurs, it is resolved by discussion and by contacting the primary author of the included studies via email. Articles assessed with a score of ≥ 6 out of 9 quality items were considered high quality.

Table 1 Characteristics of the Studies Included in This Systematic Review

Authors, and References	Publication Year	Study Area	Study Design	Subjects	Sample Size	Sampling Technique
Gidey et al ¹⁶	2006	Amhara region	Cross-sectional survey	Key informants	38	Purposive sampling
Tedla and Dida ¹⁷	2019	Bale Zone, Southeast Ethiopia	Cross-sectional survey	Key informants (traditional healer)	21	Purposive sampling
Chekole et al ¹⁸	2015	Northwest Ethiopia	Cross-sectional survey	Traditional medicinal practitioners	105	Purposive sampling
Andarge et al ¹⁹	2015	Dawuro Zone, Southern Ethiopia	Cross-sectional survey	Traditional healers	91	Purposive sampling
Eshete et al ²⁰	2016	Oromia region, Ethiopia	Reconnaissance survey	Traditional healers	60	Purposive sampling
Abera ²¹	2014	Southwest Ethiopia	Reconnaissance Survey	Key informants and community members	195	Purposive sampling
Mesfin et al ²²	2009	SNNPR, Ethiopia	Cross-sectional survey	Healers	30	Purposive sampling
Teklay et al ²³	2013	Tigray, Ethiopia	Community based cross-sectional	Healers and knowledgeable informants	72	Purposive sampling
Belayneh et al ²⁴	2012	Eastern Ethiopia	Cross-sectional survey	Traditional medicinal practitioners	50	Stratified random sampling + Purposive sampling
Osman et al ²⁵	2020	Amhara Region, Ethiopia	Cross-sectional survey	Key informants	150	Stratified random sampling
Shimels et al ²⁶	2017	Dire Dawa, Eastern Ethiopia	Cross-sectional survey	Traditional healers	24	Purposive sampling
Amare and Getachew ²⁷	2019	Hararghe, Ethiopia	Cross-sectional	Key informants	48	Judgment and volunteer sampling
Tuasha ²⁸	2018	Sidama Zone, Ethiopia	Reconnaissance survey	Traditional healers	20	Purposive sampling
Tsegay et al ²⁹	2019	Bahir Dar, Ethiopia	Cross-sectional survey	Key and general informants	72	Purposive sampling
Assefa et al ³⁰	2021	Bale Zone, Southeast Ethiopia	Cross-sectional survey	Key informants	90	Random sampling technique

Data Processing and Analysis

The data extracted from Excel spreadsheets were imported to SPSS version-24 software and analyzed using descriptive statistics to calculate mean, range and percentage. The data synthesized were provided from the included studies regarding the frequency of the identified plant family and species, growth form of the plant, plant part used and route of administration.

Results

The search for international databases provided a total of 317 published studies. After the removal of duplicates, 128 remained. Of these, 70 studies were discarded after reading their titles and abstracts since they did not meet the inclusion criteria. Of the 58 studies assessed for eligibility, 43 studies were discarded due to provision of incomplete information. Finally, 15 studies met the inclusion criteria and were selected for final review (Figure 1). In the current review, 24 plants (distributed over 17 families) were identified to be used by the traditional healers to manage hepatitis. The detailed information of each plant recorded from the included original papers is available in Table 2.^{16–30}

Commonly Used Families and Plant Species

The family Apocynaceae, Asteraceae, Euphorbiaceae, Cucurbitaceae, Solanaceae, and Fabaceae had the relatively highest number of plant species. *Acokanthera schimperi*, *Cucumis species*, *Vernonia species*, and *Acacia tortilis* were some of the commonly used plant species (Table 2).

Growth Forms of Medicinal Plants and Plant Parts Used

Of the medicinal plants identified, the majority of them were herbs (35.7%), followed by shrubs (32.1%), trees (25%), and climbers (7.2%) (Figure 2). The commonly used plant parts were leaf and root (35.7% each) followed by a combination of roots and leaves (10.7%) (Figure 3).

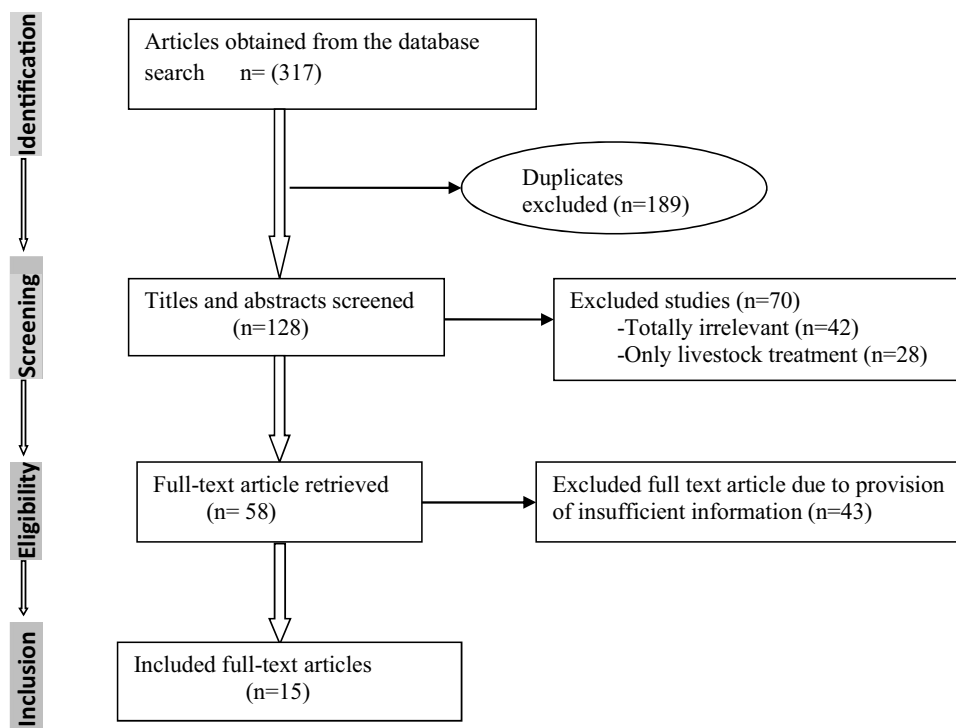


Figure 1 Flowchart of study selection for medicinal plants used for the treatment of hepatitis in Ethiopia.

Table 2 List of Plants Used for the Management of Hepatitis Over the Past 15 Years

Family Name	Scientific Name	Local Name	Growth Form	Part Used	Method of Preparation	RoA	Reference
Apocynaceae	<i>Acokanthera schimperi</i>	Merenz (Am)	Tree	Leaf & root	Fumigation	Oral	[16]
	<i>Acokanthera schimperi</i>	Merenz (am)	Tree	Leaf	Fresh leaf juice with honey is eaten	Oral	[17]
	<i>Acokanthera schimperi</i>	Merz (Am)	Shrub	Leaf	Crush, dry then fumigate	Nasal	[18]
Solanaceae	<i>Nicandra physaloides</i>	Puqaqiya (Daw)	Herb	Leaf	Crushed and taken cup of it	Oral	[19]
	<i>Solanum spp.</i>	Puk'ek'iya (Daw)	Shrub	Root	Washed/crushed mixed with water and taken orally 3 cup before breakfast for three days	Oral	[19]
Acanthaceae	<i>Justicia schimperiana</i>	Ciiggaa (Or)	Shrub	Leaf	Chopping young leaves, making solution and drinking half of water glass at once	Oral	[20]
Moraceae	<i>Ficus sycomorus</i>	Odaa (Or)	Tree	Bark	Sap is collected from bark surface of and creamed on skin	Dermal	[21]
Asclepiadaceae	<i>Kanahala laniflora</i>	Wundiffo (Ged)	Shrub	Root	Fresh/dry root powder mixed with honey taken orally before breakfast for three days.	Oral	[22]
Caryophyllaceae	<i>Stellaria sennii</i>	Papaya (Ged)	Herb	Root	Decoction root	Oral	[22]
Cucurbitaceae	<i>Cucumis ficifolius</i>	Ramboambo (Tig)	Herb	Whole part	Crush, add water, filter and drink or Chew and swallow the product	Oral	[23]
	<i>Cucumis dipsaceus</i>	Hare goge (Or)	Herb	Root	Concoction	Oral	[24]
	<i>Cucumis dipsaceus</i>	Yemdir embuay (am)	Herb	Whole plant	Chewing or crushing after adding water and then filtering	Dermal	[25]
Aloaceae	<i>Aloe yavellana</i>	Hargiissa (Or)	Herb	Latex	Taking the latex and drinking one coffee cup for humans	Oral	[20]
Fabaceae	<i>Abrus precatorius</i>	Badaluwa (Daw)	Climber	Seed	Crushed and concocted with <i>Maesa lanceolata</i> and taken	Oral	[19]
	<i>Acacia tortilis</i>	Assel (Or)	Tree	Root	Crushed and mixed with water and consumed like tea (decoction)	Oral	[26]
Euphorbiaceae	<i>Acalypha villicaulis</i>	Wak'ak'uwa (Daw)	Herb	Root	Crushed and mixed with water taken	Oral	[19]
	<i>Phyllanthus reticulatus</i>	Wusiwisiya mala(Daw)	Shrub	Leaf & root	Crushed both parts taken	Oral	[19]
	<i>Clutia lanceolata</i>	Kutta dhigaa (Or)	Herb	Root	Crushing the root, boiling it and giving one water glass	Oral	[20]
Thymelaeaceae	<i>Gnidia glauca</i>	Migra (Daw)	Shrub	Root	Crushed and leave it for overnight mixed with water and taken orally	Oral	[19]
Asteraceae	<i>Vernonia spp.</i>	Yesheshuwa (Daw)	Herb	Root	Powdered and press then mixed with the root of <i>Abrus precatorius</i> and milk	Oral	[19]
	<i>Vernonia amygdalina</i>	Eebicha (Or)	Shrub	Leaf	Pounding the leaves of and mix it with water and drink it	Oral	[27]
	<i>Galinsoga paruiifolia</i>	Ematiya/bizdiya (Or)	Tree	Leaf & root	Crushed root and leaf together taken orally within three days interval until heal	Oral	[19]
Boraginaceae	<i>Cordia africana</i>	Wanza (am)	Tree	Leaf	Chewing after mixing it with <i>Sorghum bicolor</i>	Oral	[25]
Menispermaceae	<i>Stephania abyssinica</i>	Kalaala (Or)	Climber	Leaf	The leaf part is boiled, and about 1 cup is drunk	Oral	[28]
Polygonaceae	<i>Rumex nervosus</i>	Embuacho (Am)	Herb	Leaf	A leaf is pounded and boiled and drink a cup of it before breakfast	Oral	[29]
Rhamnaceae	<i>Rhamnus staddo</i>	Qadiidaa (Or)	Shrub	Leaf	Boil with water and drinking	Oral	[30]
Anacardiaceae	<i>Rhus vulgaris</i>	Dabobechaa (Or)	Shrub	Leaf	Pounding the young leaves and mix with water and drinking it for seven consecutive days	Oral	[27]

Abbreviations: Am, Amharic; Or, Oromifa; Tig, Tigrigna; Ged, Gedogna; Daw, Dawrogn; RoA, route of administration.

Method of Preparation and Route of Administration

Traditional medicinal practitioners use simple compounding procedures like drying, crushing, concoction, and decoction, and remedies are given using honey and water as an additive and/or solvent (Table 2). They prefer the oral route as the best administration route (89.3%). Other routes, even if minimal, were also used to administer remedies (dermal=7.1%, nasal=3.6%) (Figure 4).

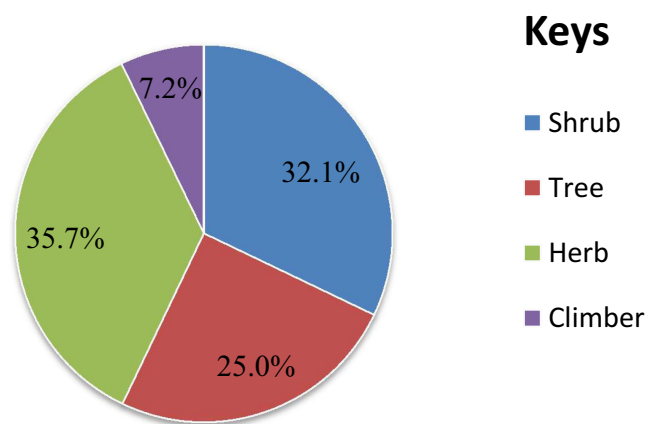


Figure 2 Growth forms of medicinal plants used for the treatment of hepatitis.

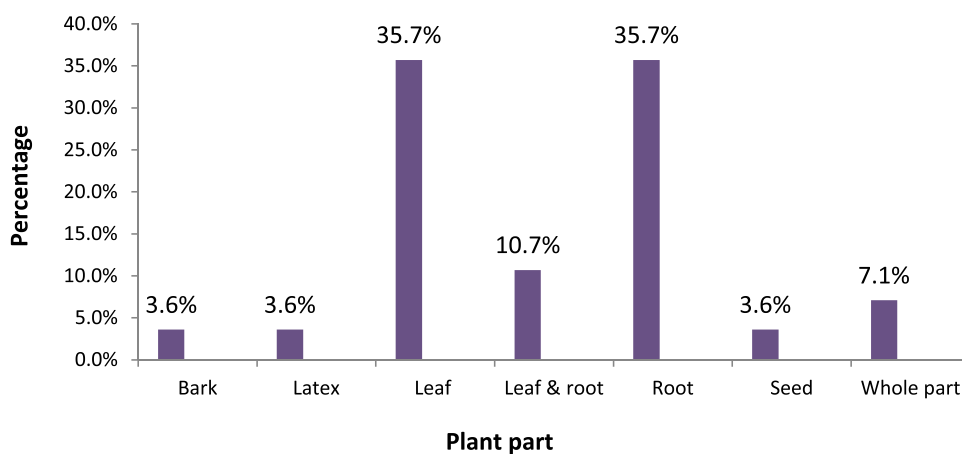


Figure 3 Plant parts used for the treatment of hepatitis in Ethiopia.

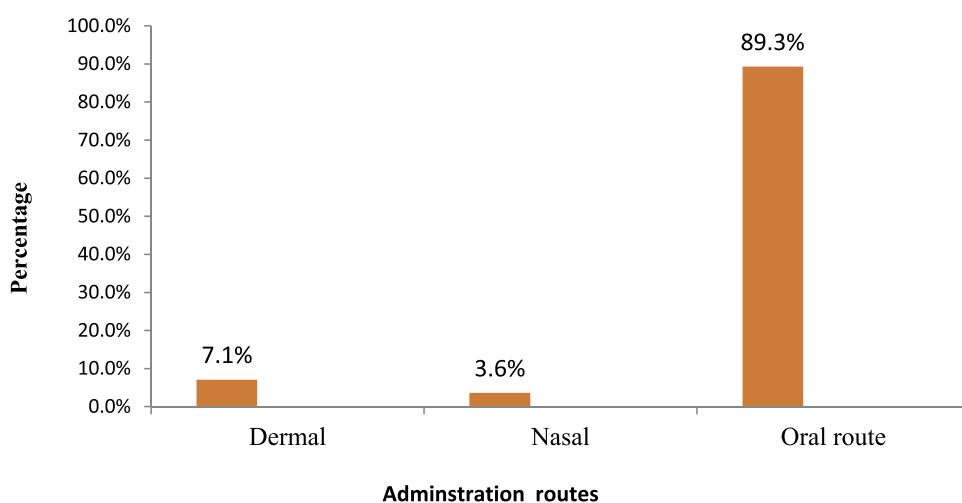


Figure 4 Route of administration of medicinal plants used for the treatment of hepatitis.

Discussion

Ethnobotany is a useful scheme for pharmaceutical research and novel drug discovery. Claimed medicinal plants play a great role in this purpose. Their outstanding therapeutic effect along with ease of formulation results in their widespread usage in the management of infectious and non-infectious diseases. The reasons for choosing drugs from herbal/botanical sources over traditional/conventional drugs are their minimal side effects, efficacy and multi-target activities. The current review identified 24 plant species having been applied by traditional healers to manage hepatitis. This shows the level of knowledge existing in the diverse communities of Ethiopia. High species diversity of plants was observed, which might be due to differences in climate in Ethiopia. The family Apocynaceae, Asteraceae, Euphorbiaceae, Cucurbitaceae, Solanaceae, and Fabaceae had the relatively highest number of plant species. A study done in Spain and Korea revealed the dominance of Family Asteraceae.^{31,32} Another study conducted in the Hawassa Zuria district³³ showed the dominance of the family Fabaceae, which might be attributed to their extensive distribution and abundance and plenty of bioactive ingredients.

According to this review, most plants belong to herbs, followed by shrubs and trees. Other studies conducted elsewhere in Ethiopia also showed the dominance of herbs.^{33–38} Herbs are periodical that require storing and/or farming in a restricted area. However, shrubs are not periodical (easily available throughout the year) and do not need storage. Use of shrubs and trees in the preparation of remedies is therefore beneficial over herbs. Leaf and root (alone and in combination) were the predominant plant parts used for remedy preparation. This was in agreement with other research work.^{33,39,40} The frequent use of leaves in most preparations might be due to the presence of bioactive compounds in variety and abundance, ease of accessibility and formulation into different dosage forms. Collecting leaves is preferable for mother plant survival than other plant parts (root and stem) which might pose a serious threat. Removal of up to 50% of plant leaves does not significantly affect their growth. However, root and stem harvesting if not performed carefully, may cause harmful effect on the mother plant.

Simple methods (crushing, powdering, pounding, and wetting) were commonly employed to prepare remedies. This might be due to poor training and lack of processing equipment which are important for drug formulation processes. Similar studies conducted earlier reported crushing, grinding, or pounding as the most common remedy preparation.^{41–43} Lulekal et al⁴⁴ reported boiling as the most frequently used method of remedy preparation. Honey and water, which are vital for improving odor, solubility, and taste, were commonly used during remedy preparation. Water has a high ability to extract different phytochemicals from plant origins. This finding is consistent with other studies conducted elsewhere.^{16,40,45,46}

As shown in Figure 4, practitioners prefer the oral route as a principal mode of administration. Nasal and dermal routes were minimal. This might be due to the relative easiness of the oral route, inability to administer preparations via parenteral ways, and fear of associated adverse effects. This finding agrees with a study conducted in Dega Damot District,⁴⁵ Tigray Region,²³ Hawassa Zuria district,³³ Addis Ababa,⁴⁷ Gemad District,⁴⁸ and Kenya.⁴⁹ However, other studies conducted in Southern Ethiopia revealed that most medicinal plant preparations were administered cutaneously.⁵⁰ Eshete et al²⁰ reported that both oral and dermal routes allow the rapid physiological reaction of remedies to agents of diseases to increase potency. Depending on the type of ailment treated, patients are instructed to be careful during and after intake of remedies. They might be restricted from drinking tella, tej, and milk and/or eating meat and eggs as such practices are believed to interfere with, potency of the remedies. The action of these medicinal plants is generally supposed to have a direct effect on the virus particle and is able to inhibit cell-to-cell spread.

Limitations of the Study

This systematic review has considered only studies conducted in English, which may have restricted some reports/articles from being included. This systematic review also did not summarize the dosage schedule of the remedies given as it was not reported by the original studies. Moreover, the restriction in the study period might exclude studies conducted earlier.

Conclusions and Recommendations

In this ethnomedicinal review, a total of 24 plants, belonging to 17 families, have been identified to be used for managing hepatitis. Though the majority of the remedies are prepared from leaves, it does not cause the reduction of plant biodiversity. Oral route is the principal mode of remedy administration. Evidence generated from the present review could serve as preliminary information to formulate new drugs that can treat hepatitis. Efforts should be made to protect these important plants using any available means. Therefore, it is desirable for scholars to recognize, document, and keep plants and the associated knowledge appropriately and test for safety and efficacy.

Data Sharing Statement

The datasets used and/or analyzed during the current study are included in this article.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas, took part in drafting, revising, or critically reviewing the article, gave final approval to the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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