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REVIEW

Review of Ethnobotanical and Ethnopharmacological Evidence of Some Ethiopian Medicinal Plants Traditionally Used for Peptic Ulcer Disease Treatment

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Abstract: A peptic ulcer is described as the rupture of the mucosal integrity of the stomach, the duodenum, and, in certain cases, the lower esophagus as a result of contact with chloridopeptic secretions. The two most common kinds of peptic ulcer disorders are referred to as "gastric ulcer" and "duodenal ulcer." The name is derived from the location of the ulceration. Despite the promise of a wide range of antiulcer treatments, these therapies are associated with several adverse reactions, including hypersensitivity, arrhythmia, impotence, gynecomastia, galactorrhea, hematological abnormalities, and kidney disease, which are intolerable for many patients. Nowadays, there is a lot of emphasis on finding new and innovative agents. As a result, herbal medicines are commonly utilized in circumstances when drugs are used for long periods and are also cost-efficient, effective, and readily available. In this review paper, a total of 82 medicinal plants have been identified and reported for their use in the treatment of peptic ulcer disease. The majority of these medicinal plants are widely used throughout Ethiopia. However, only the safety and efficacy of *Plantago lanceolata, Osyris quadripartita, Rumex nepalensis, Cordia africana, Croton macrostachyus*, and *Urtica simensis* have been scientifically studied in animal models. Despite this, many medicinal plants' pharmacological effects and chemistry have not been well studied scientifically. As a result, further bioactive compound characterization, efficacy, mechanism of action evaluation, and toxicity evaluation of medicinal plants should be carried out. A study that can improve the documentation of indigenous knowledge and contribute to drug development and future self-reliance is also recommended.

Keywords: ethno pharmacological evidence, Ethiopia, medicinal plants, peptic ulcer disease

Introduction

Ulcers are open sores on the surface of the skin or mucous membrane that are characterized by the sloughing of inflamed dead tissue.[1] Ulcers most commonly occur on the skin of the lower limbs and in the gastrointestinal tract, but they can occur anywhere. A variety of ulcers exist, including mouth ulcers, esophageal ulcers, peptic ulcers, and genital ulcers.[2] Peptic ulcer disease is the most common gastrointestinal disorder, with high morbidity and mortality rates.[3] A peptic ulcer is described as the rupture of the mucosal integrity of the stomach, the duodenum, and, in certain cases, the lower esophagus as a result of contact with chloridopeptic secretions.[2,4] The two most prevalent kinds of peptic ulcers are referred to as "gastric ulcer" and "duodenal ulcer." The name is derived from the location of the ulceration. Both gastric and duodenal ulcers can occur simultaneously in a person. Gastric ulcers are painful ulcers that occur in the stomach. They are more common in those over the age of 50. Eating may aggravate rather than alleviate pain. Nausea, vomiting, and weight loss are some of the other symptoms. Even though patients with gastric ulcers have normal or reduced acid production, ulcers can develop even in the absence of acid.[5] Duodenal ulcers are present at the beginning of the small intestine and cause intense discomfort and a burning sensation in the upper abdomen, waking patients up. Pain is most

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common when the stomach is empty and subsides after eating. A duodenal ulcer is more common in younger people and primarily affects men. Ulcers can occur on both the anterior and posterior walls of the duodenum. Peptic ulcers can be life-threatening in some situations, with symptoms such as bloody stool, severe stomach discomfort, cramping, as well as vomiting blood.[6]

An imbalance between offensive (gastric acid, pepsin, and *Helicobacter pylori*) and defensive (mucin, prostaglandins, bicarbonate ions, growth factors, and nitric oxide) factors are involved in the pathophysiology of peptic ulcer disease.[7,8] Peptic ulcers were once thought to be caused by spicy foods and stress; however, research has revealed that the true causes are bacterial infection (Helicobacter pylori) or a reaction to certain medications, primarily nonsteroidal anti-inflammatory drugs.[9,10] The main etiological variables associated with peptic ulcer disease are *Helicobacter pylori*, nonsteroidal anti-inflammatory medicines, emotional stress, alcohol misuse, tobacco smoking, fatty meals, free radical generation, Zollinger-Ellison syndrome, and an age-related decline in prostaglandin levels.[11] *Helicobacter pylori*, a gram-negative bacterium, lives between the mucous layer and the gastric epithelium and is specifically engineered to thrive in the stomach's hostile environment. At first, *Helicobacter pylorus is* found in the antrum, but it migrates to the stomach's more proximal segments with time.[6]

Peptic ulcer disease is a global health concern because of its high rates of morbidity, mortality, and economic loss, as well as the high frequency of *Helicobacter pylori* infection. It is one of the most common gastrointestinal ailments in the world, affecting 10–15% of the population.[12,13] Duodenal ulcers account for 19 out of every 20 peptic ulcers. Each year, an estimated 15,000 people die as a result of a peptic ulcer. Peptic ulcer bleeding and perforation had annual incidence estimates of 19.4–57 and 3.8–14 per 100,000 people, respectively. The average seven-day bleeding recurrence rate was 13.9%, while the average long-term perforation recurrence rate was 12.2%.[14] Patients in Sub-Saharan Africa who had surgery for peptic ulcer disease revealed that 86% had a duodenal ulcer while the remaining 14% had a gastric ulcer. Major complications like perforation (35%), chronic cases (28%), obstruction (30%), and bleeding (7%) were indicated for surgery, and the overall fatality rate was found to be 5.7%.[15]

Despite the promise of a wide range of antiulcer treatments, these therapies are associated with several adverse reactions, including hypersensitivity, arrhythmia, impotence, gynecomastia, galactorrhea, hematological abnormalities, and kidney disease, which are intolerable for many patients.[10,16] Furthermore, because of rising costs, drug-drug interactions, relapse, and resistance, which limit their usage, novel medications for peptic ulcer therapy are being developed.[17,18] Nowadays, there is a lot of emphasis on finding new and innovative agents. As a result, herbal medicines are commonly utilized in circumstances when drugs are used for long periods and are also cost-efficient, effective, and readily available.[17,18] For the treatment of peptic ulcers, extracts from medicinal plants and other natural products have become widely recognized sources of therapeutic agents.[4,19–23] Many researchers have examined and proven the antiulcer activity of ethno medicinal plants, which are valuable as antiulcer medicines and have been used experimentally.

The purpose of this review was to analyze medicinal plants that have been used in traditional medicine as gastro-protective and healing agents for ulcers, as well as to gather evidence for their usefulness and biological mechanisms in a modern investigation.

Materials and Methods

Traditional Ethiopian medicinal plants used to treat peptic ulcer disease were gathered from available information in scientific publications and MSc thesis reports. For each of the medicinal plants for peptic ulcers, literature was searched in PubMed, EMBASE (Ovid interface), Scopus, MEDLINE, Science Direct, Elsevier, Scifinder, Research Gate, WorldCat, Web of Science, AJOL, and Cite Seerx, as well as other electronic database sources such as Google Scholar, and all retrieved articles were evaluated for any in vitro, in vivo, or clinical evidence for their efficacy and possible mechanisms. To find all relevant documents, no time restriction was set for the search. The studies found either show that these herbs are clearly effective or that they are indirectly effective in the treatment of peptic ulcers. The data was appropriately filtered if it was deemed relevant and related to the topic of interest. This scientific review included information on the use of medicinal plant species to treat peptic ulcer disease in Ethiopia from 63 publications and MSc theses. This review was conducted between August 2021 and December 2021.

Medicinal Plants Used for the Treatment of Peptic Ulcer Disease in Ethiopia

Traditional medicine is important in delivering primary health care all over the world.[24] About 75–80% of people in underdeveloped countries use traditional medicine because of its better cultural acceptability.[10] Plants have been used to treat a variety of ailments for decades, including peptic ulcer disease.[25]

Ethnobotanical investigations in Ethiopia have found a large array of plants belonging to numerous families as antiulcer medicinal plants. As a result, this review article lists a total of 82 medicinal plants that are used in Ethiopia to treat peptic ulcer disease (Table 1).

Medicinal Plants Diversity

For the treatment of peptic ulcer disease, 82 medicinal plant species from 45 families were identified. The Fabaceae family dominated the medicinal plants with nine species, followed by the Lamiaceae and Solanaceae families, each with five species (Table 2).

Habit Diversity of Medicinal Plants

In terms of habit diversity, the majority of the medicinal plants identified were herbs (39 species, 47.56%), followed by shrubs (21 species, 25.61%) (Figure 1).

Parts and Preparation Conditions of Medicinal Plants Used to Treat Peptic Ulcer Disease

Traditional medicines are made by harvesting various plant parts. According to this review, leaves 27 (31.76%) were the most commonly employed plant part in traditional medicine preparation. The other plant parts used were fruits 15 (17.65%), roots 10 (11.76%), and seeds 10 (11.76%) (Figure 2).

Herbal remedies are prepared using 56 (68.29%) fresh plant material followed by 24 (29.27%) dried plant materials (Figure 3).

Methods of Preparation of Medicinal Plants

Traditional remedies were prepared in different methods. Chewing 57 (55.34%) was the most popular method of preparation of traditional medicine from plant material, followed by boiling 21 (20.39%) (Figure 4).

Plants Having Ulcerogenic Activities That Have Been Scientifically Proven

Even though ethnobotanical studies revealed the presence of several traditionally used plants for the treatment of peptic ulcer illnesses in various parts of Ethiopia, only six of these plants were scientifically researched for their in vivo ulcerogenic activities. In this review, six different Ethiopian traditional herbs that are commonly used to treat peptic ulcer disease and have been studied by different researchers at different times and places were presented. Four plants (ie *Cordia africana* Lam, *Urtica simensis* Hochst. ex. A. Rich, *Osyris quadripartita* Decne, and *Plantago lanceolata* L) were evaluated for their anti-ulcer activities using crude extractions of the various plant parts, while the crude extracts, as well as solvent fractions of two of the plants, were evaluated.[4,20,21,23,64,66]

Cordia Africana Lam (Boraginaceae)

The in vivo ulcer healing capabilities of an 80% methanol seed extract of *C. africana* Lam were examined using the pylorus ligation method.[64] The investigators prepared a crude extract from the seed of the study plant using 80% methanol after drying under a shaded area to investigate the plant's traditionally claimed uses of anti-ulcer effect. Then, using an oral acute toxicity test, multiple-dose ranges of crude extract of *C. africana* Lam were found. Following an oral acute toxicity investigation, three separate test dosages of 200 mg/kg, 400 mg/kg, and 600 mg/kg were determined.[64,65]

The major procedures were performed on albino rats of either sexes weighing 230–250g and an oral acute toxicity study was conducted on female Swiss albino mice weighing 25–35 g. The healing abilities of the selected test doses of *C. africana* Lam crude extract were then tested by comparing them to the negative and positive control groups. The rats

Table 1 Traditionally Used Plant Species for Treatment of Peptic Ulcer Disease in Ethiopia

S. No	Scientific Name - Habitat	Local Name	Family	Parts Used	Condition of Plant Part Used	Method of Preparation and Administration	Reference
1.	*Achyranthes aspera* -Herb	Darguu [O]	Amaranthaceae	Root	Fresh	Drink the concoction	[26]
2.	*Afrocarpus falcatus* - Tree	Dagucho [Sd]	Podocapaceae	Leaf	Not stated	Not stated	[27]
3.	*Aloe gilbertii*-Shrub	Irate [A]	Asphodelaceae	Leaf	Fresh	Young leaves are pulverized and the filtrate taken orally	[28]
4.	*Aloe macrocarpa*- Herb	Irate [A]	Aloaceae	Latex	Fresh	Given orally with honey	[29]
5.	*Aloe pubescens* -Shrub	Irate [A]	Aloaceae	Gel	Fresh	Fresh gel is eaten	[28]
6.	*Asparagus africanus* - Herb	Saritii [O]	Asparagaceae	Tuber	Fresh	Drink the concoction	[26]
7.	*Asystasia gangetica* - Herb	Girbia [A]	Acanthaceae	Root	Not stated	Chewing	[30]
8.	*Brassica carinata*- Herb	Koza [Sh]	Brassicaceae	Leaf	Not stated	Oral	[31]
9.	*Brassica oleracea* - Herb	Tikle gomen [A]	Brassicaceae	Leaf	Dry	Powderize, then mix with honey for two days before eating	[32]
10.	*Calpurnia aurea*- Shrub	Chakata [Sd]	Fabaceae	Leaf	Fresh	Chewing	[33]
11.	*Carica papaya* – Tree	Papya [A]	Caricaceae	Seed	Fresh	Oral	[34]
				Seed	Dry	Oral	[26]
				Fruit	Fresh	Oral	[33,35]
12.	*Carissa edulis*- Shrub	Agamsa [O]	Apocynaceae	Flower	Dry	Crushed and dispersed in milk and drink	[36]
13.	*Casimiroa edulis*- Tree	Kazmir [Sd]	Rutaceae	Fruit	Fresh	Eating	[33]
14.	*Catha edulis* – Shrub	Chat [Sd]	Celastraceae	Leaf	Fresh	Eating	[33]
15.	*Caylusea abyssinica* - Herb		Resedaceae	Leaf	Fresh	The leaf is boiled and eaten with roasted powdered barley seeds	[37]
16.	*Centaurium pulchellum* – Herb		Gentianaceae	Not stated	Not stated	Decoction	[38]
17.	*Cicer arietinum* - Herb	Shimbra [A]	Fabaceae	Fruit	Dry	Immersed in water, filtered after one day, mixed with*Allium sativum*, and taken as a meal, chewing andswallowing it	[39]
18.	*Citrus aurantifolia* - Tree	Lomi [A]	Rutaceae	Fruit	Fresh	Eating	[33]
19.	*Citrus sinensis* - Shrub	Burtukan	Rutaceae	Fruit	Fresh	Drink the juice	[35]

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20.	*Coffea arabica* - Shrub	Qawi habala [H]	Rubiaceae	Leaf	Dry	Crushed, powdered, then thepowder is boiled and drunk	[33,40]
		Buna [A]		Seed	Dry	Cocked, chewed, and swallowed	[35]
21.	*Commiphora hodai* - Herb	Hodai [Sm]	Burseraceae	Stem	Fresh	Drink the fluid from the stem extract with coldwater	[41]
22.	*Commiphora kua* - Tree	Xabaghadi [Sm]	Burseraceae		Not stated	Drink the extract with cold water	[41]
23.	*Cordia africana* - Tree	Wanza [A]	Boraginaceae	Latex	Fresh	Given orally beforefood	[29]
24.	Croton macrostachyus – Tree	Masincho [Sd]	Euphorbiaceae	Fruit	Fresh	Chewing	[33]
25.	*Cucurbita pepo* - Climber	Duba [A]	Cucurbitaceae	Fruit	Fresh	Chop, then boil with water and eat	[42]
26.	*Dichrostachys cinerea* – Tree	Jirmee [O]	Fabaceae	Stem	Dry	Burns stem, make a solution from the ash and take itorally	[43]
27.	*Dodonaea Angustifolia* – Tree	Kitkita [A]	Sapindaceae	Seed	Dry	A small quantity of seed powder is mixed with honey and taken orally on an empty stomach	[44]
28.	*Ekebergia capensis* - Tree		Meliaceae	Root and bark	Dry	In powder form, two teaspoons of infusion into one cup of water are taken before meals	[45]
29.	*Enset ventiricosum* - Tree	Warqee [O]	Musaceae	Root	Dry	Boil and drink the decoction up on cooling	[26]
30.	*Erythrina brucei* - Tree	Walenssu [O]	Fabaceae	Root and bark	Fresh	Drink the concoction	[26]
31.	*Euphorbia abyssinica* – Tree	Kulkual [A]	Euphorbiaceae	Latex	Fresh	Drink the liquidform	[33]
32.	*Flacourtia indica* - Tree	Agnaneshewe [A]	Flacourticaceae	Fruit	Fresh	Eaten as it is	[46]
33.	*Galium simense* - Herb	Jiddha [O]	Rubiaceae	Root	Fresh or dry	Chewing and swallowing juice	[47]
34.	*Girardinia bullosa* - Herb	Dobii [O]	Urticaceae	Root	Fresh	Drink the concoction	[26]
35.	*Girardina diversifolia* – Herb	Dobii [H]	Urticaceae	Leaf	Fresh	The leaf is crushed, filtered and the liquid is taken	[40]
36.	*Guizotia abyssinica* - Herb	Nug [A]	Asteraceae	Seed	Dry	Chew and swallow	[32]
						Roasted, powdered, salted and mixed with one glass ofwater (one or two liters) and drunk per day until relief is obtained	[48]
37.	*Hibiscus cannabinus* - Herb	Wayika [A]	Malvaceae	Fruit	Dry	Taking the decoction	[49]

(*Continued*)

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Table 1 (Continued).

S. No	Scientific Name - Habitat	Local Name	Family	Parts Used	Condition of Plant Part Used	Method of Preparation and Administration	Reference
38.	*Hordeum vulgare* - Herb	Nech gebs [A]	Poaceae	Seed	Dry	The roasted powder is boiled in water and drunk until relief	[34]
						The roasted seed is eaten before the meal	[48]
						Powder mixed with water is given orally	[50]
						Drying the seed on fire and eating it	[51]
39.	*Iphionopsis rotundifolia* – Shrub	Gogobo [Sm]	Asteraceae	Root	Not stated	Chewed	[41]
40.	*Justicia schimperiana* – Shrub	Dhumuga [O]	Acanthaceae	Fruit	Fresh	The fresh fruit is eaten	[36]
41.	*Kalanchoe petitiana* - Herb	Hanshululie [Sd]	Crassulaceae	Bulb	Fresh	Eating	[33]
42.	*Laggera crispata* - Herb	Keskesso [A]	Asteraceae	Leaf	Fresh	Chewing and swallowing the juice	[42]
43.	*Leonotis ocymifolia* - Shrub	Urgo[O]	Lamiaceae	Leaf	Fresh	Chewing and swallowing the juice	[47]
44.	*Lepidium sativum* - Herb	Fecoo [O]	Brassicaceae	Seed	Dry	Crush and steep the plant part in cold water and drink the infusion	[26]
45.	*Leucas jamesii* - Herb	Dahaayanuur [Sm]	Lamiaceae	Leaf	Fresh	Crush leaves and eat them	[41]
46.	*Linum usitatissimum* - Herb	Konter [Ha]	Linaceae	Seed	Dry	Roast, pound and take oral	[43]
		Telba [A]				Boil the seeds with water and, after cooling, drink it	[48,51]
						A few seeds soaked in water overnight and one glass consumed continuously	[34]
						Add water, stay overnight and drink it	[52]
						The seed is crushed, powdered, mixed with water andsugar and then drunk whenfeeling pain	[53]
47.	*Lippia adoensis* - Herb	Kesiy [A]	Verbenaceae	Leaf	Fresh	Chewing	[34]
48.	*Momordica foetida* - Herb	Herassie [Sd]	Cucurbitaceae	Leaf	Fresh	Grinding and eating	[33]
49.	*Myrica salicifolia* - Tree	Barodoo [O]	Myricaceae	Leaf	Fresh	Crush and steep the plant part in cold water and drink the infusion	[26]
50.	*Nigella sativa* – Herb	Tikur azemud [Sd]	Ranunculaceae	Fruit	Fresh	Chewing	[33]
51.	*Ocimum lamiifolium* - Herb	Demakase [A]	Lamiaceae	Leaf	Fresh	Squeeze and drink	[52]

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52.	*Olea europea* – Tree	Weyira [H]	Oleaceae	Leaf	Fresh	Chewing the leaf and swallowing it	[40]
		Ejersa [O]		Stem	Fresh	A very small amount of the oily liquidproduced from the stem is drunk after each meal for three consecutive days	[54]
53.	*Oncoba spinosa* - Tree	Hargora [Ha], Jilbo [O]	Flacourticaceae	Fruit	Fresh	Its juice is kept for a day before being consumed orally	[43]
54.	*Opuntia ficus-indica* – Shrub	Qulqual [A], Aabashaa [O]	Cactaceae	Fruit	Fresh	Eating	[55]
55.	*Osyris quadripartita* - Herb	Keret [A]	Santalaceae	Leaf	Fresh	The juice of freshly squeezed leaves is mixed with milk and drink	[36]
56.	*Physalis peruviana* - Herb	Nech awut [A]	Solanaceae	Leaf and fruit	Fresh	Fresh leaves and fruit boiled with tea are given orally	[29]
57.	*Plantago lanceolata* - Herb	Kortebi [O]	Plantaginaceae	Leaf	Fresh	The decoction of fresh leaves in water medium is mixed with milk and drink	[36]
		Gorxobii [O]				Crush the leaves and take them three times aday	[56]
58.	*Polygonumsenegalense* – Herb	Gumma mila [H]	Polygonaceae	Whole plant	Fresh	The whole plant was crushed and the juicewas taken	[40]
59.	*Portulaca oleracea* - Herb	Merere hare [O], Siyo [Sm]	Portulacaceae	Whole plant	Fresh	Eat cooked vegetable	[57]
60.	*Psidium guajava* - Tree	Zeytun [Sd]	Myrtaceae	Fruit	Fresh	Eating	[33]
61.	*Pterolobium stellatum* – Shrub	Kanteftef [A]	Fabaceae	Root	Fresh	Root (after removing the cover) boiled together with *Acacia* sp. in water and drunk	[46]
62.	*Rhamnus prinoides* - Shrub	Gesho [Sd]	Rhamnaceae	Leaf	Dry	Chewing	[33]
63.	*Rubus apetalus* - Shrub	Enjory [A]	*Rosaceae*	Leaf and fruit	Dry	Dried leaves and fruit soaked with water are given orally	[29,58]
64.	*Rumex nepalensis* - Herb	Tult [A]	Polygonaceae	Root	Dry	A teaspoon of root powder boiled in 200mL of water to make a decoction. A cup of this decoction is given orally in the morning for five consecutive days on an empty stomach	[44]
		Timijjii [O]				A few roots were chewed and swallowed	[59]
65.	*Rumex nervosus* - Shrub	Dhaangagoo [O]	Polygonaceae	Bark	Fresh	Hold with teeth	[26]
66.	*Saccharum officinarum* – Grass	Shonkora [K]	Poaceae	Stem	Fresh	Chewing	[60]
67.	*Saliva merjamie* - Herb	Jawula [A]	Lamiaceae	Whole plant	Fresh	A fresh whole plant boiled with water is administered orally	[29]
68.	*Senna didymobotrya* – Shrub	Sanamiki [H]	Fabaceae	Leaf	Dry	Crushed, powdered, boiled and drunk	[40]

(*Continued*)

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Table 1 (Continued).

S. No	Scientific Name - Habitat	Local Name	Family	Parts Used	Condition of Plant Part Used	Method of Preparation and Administration	Reference
69.	*Solanum nigrum* - Herb	Tikur awut [A]	Solanaceae	Leaf	Fresh	The washed or cleaned raw leaf is chewed before any meal	[45]
70.	*Solanumschimperianum* – Shrub	Korenet [T]	Solanaceae	Leaf	Fresh	Some leaves were crushed, squeezed, filtered and one coffee cupwas taken	[61]
71.	*Solanum tuberosum* - Herb	Dinich [A]	Solanaceae	Tuber	Fresh	The tuber is taken in the form of juice	[62]
72.	*Stephania abyssinica* – Climber	Kalala or Gura antuta [O]	Menispermaceae	Leaf	Fresh	Boil and drink the decoction up on cooling	[26]
						The fresh leaves are decocted in water medium and drink	[36]
73.	*Teclea nobilis* - Shrub	Sihil [A]	Rutaceae	Bark	Fresh	Chewing and taking the sap from the internal part of the stembark	[48]
74.	*Thymus schimperi* - Herb	Tosign [A]	Lamiaceae	Seed	Dry	Crushed seeds are boiled in water and served as a drink	[63]
				Leaf	Dry	Dried, powdered, and mixed with the seed powder of *Hordeum vulgare* and eaten in the form of "besso"	[48]
75.	*Trigonella foenum-graecum* – Herb	Abish [A]	Fabaceae	Seed	Dry	Grind, then add water and drink	[32,52]
						Putting it in water, drying it, crushing and eating it by mixing it with water and sugar	[51]
76.	*Urtica simensis* - Herb	Gurgubee [O]	Urticaceae	Shoot	Fresh	Eat the plant part (raw/cooked)	[26]
		Sama [A]		Leaf	Fresh	Eaten in the form of stew ("wot")	[48]
						The fresh leaves are collected androasted like "wot" and eaten withinjera	[53]
		Dobi [O]				Boiled leaves are given to eat with injera	[63]
77.	*Vernonia adoensis*- Shrub	Etse Mossie [A]	Asteraceae	Root	Fresh	Crush and powder before drinking with water or chewing and swallowing juice	[42]
		Eras abera [A]				Baking with *Eragrostise teff* and eating, then drinking thedecoction	[49]
78.	*Vicia faba* – Herb	Baaqelaa [O]	Fabaceae	Seed	Dry	Chewing	[59]
		Bakela [A]				Drink roasted and powdered grains soaked in water overnight	[62]
79.	*Vigna sp.* – Climber	Mee chorkaye [Sd]	Fabaceae	Leaf	Fresh	Eating	[33]
80.	*Withania somnifera* - Shrub	Hunzo[O]	Solanaceae	Root	Dry	Decoction, pounding, and then drink	[47]
81.	*Ximenia Americana* - Shrub	Hudha [O]	Oleaceae	Fruit	Fresh	Eating	[36]
82.	*Zingiber officinale* - Herb	Zinjibila [A]	Zingiberaceae	Rhizome	Fresh or dry	Hold with teeth	[26]

Abbreviations: [A], Amharic; [O], Affan Oromo; [T], Tigrigna; [Sm], Somaligna; [Sd], Sidamigna; [Sh], Sheko; [H], Halabenya; [Ha], Harari; [K], Kembatissa.

Table 2 Number of Species in Each Family

S.No	Family	Number of Species	Percent (%)
1.	Fabaceae	9	10.97
2.	Lamiaceae	5	6.10
3.	Solanaceae	5	6.10
4.	Asteraceae	4	4.88
5.	Rutaceae	4	4.88
6.	Others	55	67.07
Total		82	100.00

were divided into five groups of six rats each at random. The test group animals received 200 mg/kg, 400 mg/kg, and 600 mg/kg of the crude extract, whereas the negative and positive control groups received a vehicle (2% Tween 80) and a conventional anti-ulcer drug (ranitidine 50 mg/kg, respectively).[64]

As the report revealed all test doses of *C. Africana* Lam possessed significant ulcer healing activity as compared with the negative control. The anti-ulcer activities of the hydroalcoholic seed crude extract of *C. africana* Lam were evaluated using gastric ulcers induced by pylorus ligation, and they were assessed by macroscopic evaluation. With this method, single-dose studies and repeated-dose studies were used to assess ulcer healing effects of the seed crude extract of *C. Africana* Lam. In a single dose study, the crude extract at all test doses (200mg/kg, 400mg/kg, and 600mg/kg) reduced gastric acid secretion to 4.45+0.37, 4.05+0.29, and 3.67+0.23, respectively, when compared to the negative control groups, which produced a gastric acid secretion of 5.92 +0.63. Similarly, the results of the single dose study revealed that *C. africana* Lam significantly increased the pH of the stomach with doses of 400 mg/kg and 600 mg/kg as compared to the negative control group. The lowest dose of the extract (200mg/kg) showed weak acid redaction activity as compared with the standard anti-ulcer drug ranitidine, whereas the middle and the highest doses (400mg/kg and 600mg/kg, respectively) showed comparable elevation of gastric pH to ranitidine. Furthermore, the authors reported that the middle and highest doses of the crude extract demonstrated ulcer protection effects by significantly lowering ulcer scores when compared to the negative control groups.[64]

The presence of active secondary metabolites from hydroethanolic crude seed extract of C. *Africana* Lam, including flavonoids, tannins, saponin, and phenolic compounds, contributes to the ulcer healing and gastric acid secretion reduction of the extract with different proposed mechanisms.[17,64]

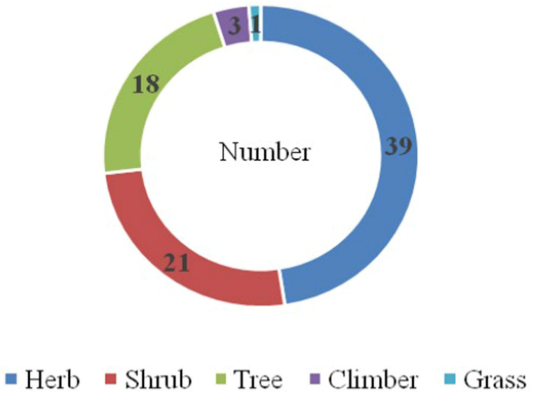

Figure 1 Habit diversity of reported medicinal plants.

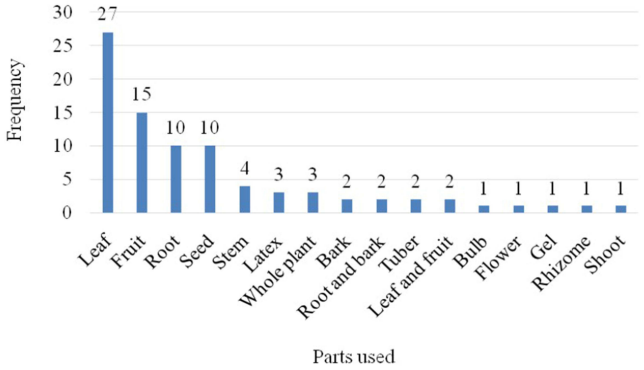

Figure 2 Medicinal plant parts used for the management of peptic ulcer disease in Ethiopia.

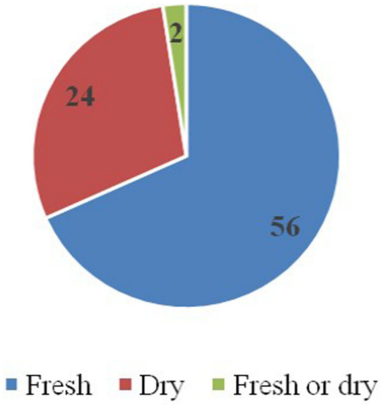

Figure 3 Preparation conditions of herbal remedies.

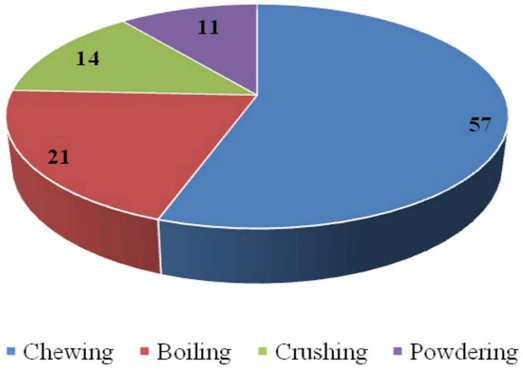

Figure 4 Method of preparation of medicinal plant remedies.

Croton Macrostachyus Hocsht: Ex Del. (Euphorbiaceae)

The anti-ulcer activity of the root crude extract with its derived solvent fractions of *C. macrostachyus* was assessed by.[20] In this experimental study, investigators used adult Sprague Dawley rats (150–200 g, 12–16 weeks) and Swiss albino mice (20–30 g, 10–14 weeks) of either sex to conduct an oral acute toxicity study and to detect the anti-ulcer activities of *C. macrostachyus* hydrometanol crude root extract and different solvent fractions. After determining the test doses of the crude extract and each solvent fraction from the oral acute toxicity study, the anti-ulcer effects of each dose were evaluated by comparing them with the positive control and negative control groups. The test doses of the crude extract

and each solvent fraction determined from the oral acute toxicity study were 100mg/kg, 200mg/kg, and 400mg/kg, and the standard drugs used as positive controls were the proton pump inhibitor anti-ulcer drug (omeprazole 30mg/k) and mucosal protectant (sucralfate 100mg/kg). The negative control group was treated with 2% tween 80.[20]

The ulcer was induced on the test animals using HCl/ethanol-induced ulcer model and the anti-ulcer effects of each test dose were detected using different methods namely, Pyloric Ligation-Induced Ulcer Model, Macroscopic Evaluation of Stomach, and Determination of Gastric Volume and pH, Determination of Total Acidity, Acidified Ethanol-Induced Ulcer Model, and Determination of Gastric Mucus Content.[17,20]

According to the report, all test doses of the crude extract of *C. macrostachyus* showed a dose-dependent anti-ulcer activity on Pyloric Ligation-Induced Ulcer in Rats as compared with the negative control group. As the pyloric ligation procedure caused the accumulation of gastric secretions, the anti-ulcer effects of the different doses of the crude extract were expressed in terms of lowering gastric volume.[20] As detected from the experiment, the middle dose (200mg/kg), and the highest dose (400mg/kg) showed a significant lowering of gastric volume as compared with the lowest dose (100mg/kg) of *C. macrostachyus* crude extract while 400mg/kg *C. macrostachyus* crude extract showed comparable gastric volume reduction with the standard drug (omeprazole 30mg/kg).

The authors' report revealed that gastric acidity in 200mg/kg and 400mg/kg pretreated groups was lowered than that of the negative control group and 100mg/kg pretreated groups, whereas 100mg/kg pretreated groups showed no acid-reducing activity as compared to the negative control group. Based on this it can be concluded that only the middle and highest doses (200mg/kg and 400mg/kg respectively) showed significant acid reduction activities as compared with the negative control. Besides, as reported[17,20] the crude extract at the dose of 200mg/kg and 400mg/kg elevated gastric pH significantly as compared with the negative control, but the crude extract at the dose of 100mg/kg showed no pH elevation as compared with the negative control. On the other hand, as per the report pyloric ligation-induced gastric ulceration was reduced with *C. macrostachyus* crude extract in a dose-dependent manner. The highest dose (400mg/kg) showed a significant reduction in gastric ulceration than the middle dose (200mg/kg) and the lowest dose (100mg/kg) as compared with the negative control.[20] Furthermore, *C. macrostachyus* crude extract at the dose of 400mg/kg and 200mg/kg possessed a significant ulcer protection activity by increasing gastric mucus as compared with the negative control and this effect was found to be comparable with the standard drug (omeprazole 30mg/kg), while the lowest dose of the extract (100mg/kg) possessed no significant effect on mucus content.[20]

The authors also detected anti-ulcer effects of the crude extract using Acidified Ethanol-Induced Ulcer in Mice. In this model, the investigators induced superficial ulcer and hemorrhage using acidified ethanol (0.15 M HCl/ethanol) at a dose of 5 mL/kg in mice. The crude extract at the dose of 200mg/kg and 400mg/kg showed a significant antiulcerogenic effect as compared with the negative control while 100mg/kg showed no antiulcerogenic effect. The antiulcerogenic effect showed by the highest dose (400mg/kg) was comparable with the standard drug (sucralfate).[20]

The effects of different solvent fractions of *C. macrostachyus* were also evaluated using Acidified Ethanol-Induced Ulcer in Mice. As detected by the investigators, chloroform fraction significantly prevented ulcer formation at the test dose applied (100mg/kg, 200mg/kg, and 400mg/kg) as compared with the negative control group. The results obtained from each dose were comparable with the standard drug (sucralfate 100mg/kg). Likewise, the middle doses (200mg/kg) and highest doses (400mg/kg) of ethyl acetate fractions significantly prevented the occurrence of ulcer formation as compared to the negative control group.

According to the report, the result obtained from 200mg/kg and 400mg/kg of ethyl acetate fractions were comparable with the standard drug (sucralfate 100mg/kg), while the lowest dose of ethyl acetate fraction (100mg/kg) showed no ulcer protection effect. And it is reported that all tested doses of the aqueous fraction showed no significant antiulcer activity as compared to negative control group mice.[20]

In this experimental study, the authors conducted a qualitative phytochemical screening test and it was confirmed that *C. macrostachyus* crude extract has as components different active secondary metabolites including phenolic compounds, tannins, flavonoids, saponins, and polyterpenes. The presence of each active secondary metabolite contributes to the anti-ulcer activities of each dose of the crude extract and active solvent fractions with different proposed mechanisms.[17,20,64]

Urtica Simensis Hochst. Ex. A. Rich. (Urticaceae)

Hydromethanolic Crude Extract of the Leaf of *U. simensis* was evaluated[21] for its anti-ulcer activity to validate the traditionally claimed uses of the plant to heal gastric ulcer in Ethiopian folk medicine. According to[21] hydromethanolic crude leaf extract of *U. simensis* was assessed for its anti-ulcer effect using different models namely, Pylorus Ligation-Induced Ulcer, Cold Restraint Stress-Induced Ulcer, and Acetic Acid-Induced Chronic Ulcer. On each model, the investigators used Healthy adult Wistar albino rats of either sex weighing 150–250 gm.

For Pylorus Ligation-Induced Ulcer in Rats, the investigators used to detect the effects of different test doses of *U. simensis* crude extract on decreasing gastric secretion and elevation of gastric pH by comparing with the negative control group. As the result showed, gastric acid secretion was significantly decreased while gastric pH was elevated by the tested doses of *U. simensis (*100mg/kg, 200mg/kg, and 400mg/kg) in a dose-dependent manner as compared with the negative control group. As the report revealed, the highest dose of *U. simensis* extract (400mg/kg) produced comparable ulcer protection with the standard drug (omeprazole 20mg/kg).[21]

Similarly, the Effects of the test doses of *U. simensis* crude extract on Cold Restraint Stress-Induced Ulcer was detected by considering ulcer score. Accordingly, the crude extract reduced ulcer score significantly as compared with the negative control in a dose-dependent manner. The maximum dose (400mg/kg) comparably reduced the ulcer score with the standard drug (Cimetidine 100mg/kg). The investigators also observed that ulcer index reduction was statistically significant on 200mg/kg and 400mg/kg doses of *U. simensis* leaf crude extract as compared with the negative control group.[21]

The test doses of the crude extract were also found to possess anti-ulcer activity on Acetic Acid-Induced ulcers. In this model, the investigators reported that the crude extract cured gastric mucosal ulcerations in a dose-dependent manner as compared to the negative control. The report also revealed that the test doses of *U. simensis* leaf crude extract possessed curative potential in both ulcer surface area and ulcer depth as compared with the negative control group.[21]

As noticed by the investigators, the presence of various active phytoconstituents might contribute to the antiulcerogenic activity of the crude extract with different proposed mechanisms. In Preliminary Phytochemical Screening, the existence of terpenoids, saponins, tannins, flavonoids, alkaloids, and phenolic compounds was confirmed.[21] These active secondary metabolites contribute the ulcer healing, decrease gastric secretion, raise gastric pH, and increase mucus secretion with a variety of proposed mechanisms.[17,20,21,64]

Osyris Quadripartite Decne. (Santalaceae)

The traditionally claimed uses of *O. quadripartite* for healing peptic ulcer disease by traditional healers in Ethiopian folk medicine were evaluated scientifically upholding its traditionally claimed uses.[4] As stated by the investigators, anti-ulcer activities of hydrometanolic crude extract of the leaf of *O. quadripartite* were evaluated in experimental rats. The effects of the extract on healing peptic ulcer disease were evaluated using different models namely, pylorus ligation-induced and ethanol-induced models. Depending on the models, the authors detected the effects of test doses of *O. quadripartite* extract in different parameters which include, volume and pH of gastric fluid, total acidity, ulcer score, the percent inhibition of ulcer score, ulcer index as well as percent inhibition of ulcer index by comparing with negative control groups.[4]

For the Pyloric ligation-induced ulcer model, the effects of the test doses (100mg/kg, 200mg/kg, and 400mg/kg) of the extract were detected using single-dose and repeated dose study. In a single-dose study, all test doses (100mg/kg, 200mg/kg, and 400mg/kg) of *O. quadripartite* extract statistically reduced the volume of gastric secretion, whereas a statistically increased in gastric pH was noted with 200mg/kg and 400mg/kg as compared with the negative control group.[4]

As reported, 400mg/kg of *O. quadripartite* extract showed a comparable effect in reducing gastric secretion as the standard drug (ranitidine 50mg/kg). Ulcer index was also significantly reduced by *O. quadripartite* 200mg/kg and *O. quadripartite* 400mg/kg doses where ulcer index reduction and percent inhibition ulcer score potential of 400mg/kg *O. quadripartite* extract were found to be better than the standard drug (ranitidine 50mg/kg).[4]

In a repeated-dose study; the investigators used to detect the effects of the test doses of *O. quadripartite* extract for 10 days and 20 days of pretreatment method. As the result obtained revealed, from 10 days of pretreatment groups, only 200mg/kg of *O. quadripartite* exhibited a significant reduction in test parameters such as volume of gastric secretion and total acidity, ulcer score, and ulcer index similar to the standard drug (ranitidine 50mg/kg) as compared to the negative control. In addition, for 20 days of pretreatment groups, only 200mg/kg of *O. quadripartite* extract exhibited a significant reduction in the volume of gastric secretion and total acidity, ulcer score, and ulcer index similar to the standard drug as compared to the negative control.[4]

On ethanol-induced ulcer, the effects of the test doses of *O. quadripartite* extract were evaluated using single dose and repeated dose study as stated above. In a single-dose study, both the ulcer score and ulcer index were significantly reduced by 200 mg/kg and 400 mg/kg of *O. quadripartite* extract as compared with the negative control group. As the result obtained revealed the effect exhibited with a 400mg/kg dose of *O. quadripartite* extract was comparable to the standard drug (ranitidine 50mg/kg) regarding percent reduction in ulcer scores. On the other hand, repeated-dose study evaluation was carried out by 10 days and 20 days pre-treating groups. In both cases, it is reported that only 200mg/kg dose of *O. quadripartite* extract showed a significant effect on reduction in ulcer score and ulcer index as compared to the negative control group. The reduction in ulcer score and ulcer index was very high to the extract and sucralfate. In both cases, the results obtained were compared with the standard drug (sucralfate 100 mg/kg).[4]

In preliminary phytochemical screening, the investigators assured the presence of the following active secondary metabolites in *O. quadripartite* leaf crud extract, flavonoids, saponins, tannins, phenols, terpenoids, and alkaloids. The presence of these active metabolites contributed to the anti-ulcer activities of the extract with different proposed mechanisms (64, 66, 67, 69, 70,).

Plantago Lanceolata L. (Plantaginaceae)

The aqueous leaf extract of *P. lanceolata* at the doses of (140mg/kg, 280mg/kg, 200mg/kg, and 400mg/kg) was assessed for its anti-peptic ulcer activity in rodents using different models of gastroduodenal ulcer namely, acetic acid-induced chronic gastric ulcer, indomethacin induced gastric ulcer, cysteamine induced duodenal ulcer and pylorus ligation induced gastric ulcer. In each of the aforementioned models, the authors revealed the effects of each test dose of the extract on gastric secretion and cytoprotection by comparing it with the negative control.[23]

The researchers used acetic acid to create large penetrating and/or deep ulcers on the serosal surface of the stomach of experimental rats in an acetic acid-induced ulcer model. The ulcer created in rats was quite comparable to the ulcer induced in humans. When compared to the negative control group, both doses (200mg/kg, 400mg/kg) of *P. lanceolata* leaf aqueous extract exhibited a substantial reduction in ulcer index. Even though both dosages of the leaf extract reduced the ulcer index, only the 400 mg/kg dose resulted in a statistically significant reduction in ulcer score, not the 200 mg/kg dose. The typical anti-ulcer drug (ranitidine 70mg/kg) showed a similar pattern of decline as 400mg/kg of PL extract, as the report validated in both ulcer index and ulcer score. While the difference was not statistically significant, the drop in ulcer index appeared to be slightly smaller than that seen with the leaf extract. Similar to what was observed with the leaf aqueous extract, the mucilage was capable of reducing the ulcer index as well as the ulcer score when compared to the negative control group.[23]

The effects of *P. lanceolata* aqueous leaf extract on indomethacin-induced ulcers were also investigated, with the results revealing that at doses of 280 mg/kg and 400 mg/kg, *P. lanceolata* extract demonstrated a statistically significant reduction in ulcer score compared to the negative control group. When compared to the negative control on cysteamine HCl generated ulcer, *P. lanceolata* extract resulted in a considerable reduction in ulcer score at a dose of 400 mg/kg. The results revealed that *P. lanceolata* dosages of 200mg/kg and 400mg/kg reduced the ulcerated area significantly.[23]

The effects of *P. lanceolata* leaf extract at the test doses were also investigated on a pylorus ligation-induced ulcer model, with the results revealing that the extract at the dose of 280mg/kg showed a significant reduction in ulcer score when compared to the negative control group score, with the 280mg/kg dose of *P. lanceolata* providing better protection than ranitidine 50mg/kg. The leaf extracts significantly increased mucin secretion at 140mg/kg and 280mg/kg doses compared to the negative control, according to the findings. The results from these doses were better than ranitidine at this stage. In comparison to the control values, both doses of the extract lowered overall acidity.[23]

Rumex Nepalensis

A root extract in 80% methanol and solvent fractions of *R. lanceolata* was investigated for its anti-ulcer activities by[66] using different models, namely, pyloric ligation, cold restraint stress, and acetic acid-induced ulcer models in rats. As the investigators notified, the extract and each solvent fraction were assessed at the doses of 100mg/kg, 200mg/kg, and 400mg/kg, and all the experiments were conducted on Wistar rats of either sex weighing 150–250.[66]

As notified by the investigators, at dosages of 100, 200, and 400 mg/kg, *R. lanceolata* extract statistically reduced the volume of stomach secretions as compared with the negative control group, on a pylorus ligation-induced ulcer. At doses of 100, 200, and 400 mg/kg/day of hydromethanolic crude extract *R.lanceolata*, the pH of the digestive fluid was considerably elevated in a dose-dependent manner as compared with the negative control. Furthermore, as compared to the negative control, overall acidity was lowered significantly. Additionally, pyloric ligation generated stomach ulcers, which were considerably decreased in a dose-dependent manner after pretreatment with *R. nepalensis* root extract was observed. In this model, *R. lanceolata* extract at the dose of 400mg/kg exhibited comparable percent inhibition of gastric ulceration as the standard drug (omeprazole 20mg/kg).[66]

Investigators confirmed that at doses of 200mg/kg and 400mg/kg of *R. lanceolata* crude extract, both ulcer index and ulcer score were considerably reduced when compared to the negative control on Cold Restraint Stress-Induced Ulcer. In comparison to the negative control group, *R. lanceolata* extract at doses of 200 and 400 mg/kg cured ulcers after 15 days of treatment.[66]

The researchers also looked into the anti-ulcer effects of different *R. lanceolata* solvent fractions on a Pylorus Ligation-Induced Ulcer model. The results showed that the chloroform fractions of 200mg/kg and 400mg/kg caused a percent reduction in ulcer score when compared to the negative control group, while the chloroform fraction of 100mg/kg caused no percent reduction in ulcer score. Ethyl acetate and aqueous fractions of *R. lanceolata*, on the other hand, caused increasing percent inhibition of ulcer score in all test doses (100mg/kg, 200mg/kg, and 400mg/kg). The researchers also confirmed that in all test doses, both ethyl acetate and aqueous fractions significantly reduced ulcer index and ulcer score when compared to the negative control. At 400 mg/kg/day, the ethyl acetate fraction exhibited high protection as compared with all test doses of other fractions.[66]

In terms of gastric secretion reduction, all test doses of ethyl acetate and aqueous fractions (100mg/kg, 200mg/kg, and 400mg/kg) produced a significant reduction in gastric secretion when compared to the negative control, whereas the chloroform fraction only showed a percent reduction in gastric secretion at the dose of 400mg/kg.[66]

As indicated in Table 3, 80% methanolic extract of the root of *R. lanceolata* proved positive for flavonoids, saponins, tannins, phenols, terpenoids, anthraquinones, glycosides, and alkaloids in a qualitative phytochemical study conducted.[66]

Table 3 Pharmacologically Evaluated Plants for Ulcerogenic Effects, Parts Used and Active Secondary Metabolites

Plant Name and Parts	Secondary Metabolite	References
Cordia africana Lam Seed extract	Tannins, flavonoids, saponins and phenols	[64]
Croton macrostachyus Hocsht root extract	Phenols, tannins, flavonoids, coumarins, saponins, and polyterpenes	[67]
Urtica simensis Hochst Leaf extract	Terpenoids, saponins, tannins, flavonoids, alkaloids, and phenols	[21]
Osyris quadripartita Decne leaf extract	Alkaloids, phenols, terpenoids, tannins, saponins and flavonoid	[4]
Rumex nepalensis root extract	Flavonoids, saponins, tannins, phenols, terpenoids, anthraquinones, glycosides, and alkaloids	[66]
Rumex nepalensis chloroform fraction	Alkaloids, anthraquinones, and glycosides,	
Rumex nepalensis ethyl acetate fraction	Flavonoids, saponins, tannins, phenols, terpenoids, anthraquinones, glycosides, and alkaloids	[66]
Rumex nepalensis aqueous fraction	Flavonoids, saponins, tannins, phenols, terpenoids, anthraquinones, and glycosides	[66]

A preliminary phytochemical investigation of each solvent fraction revealed that the chloroform fraction was rich in alkaloids, anthraquinones, and glycosides, whereas all secondary metabolites reported in the crude extract were detected in the ethyl acetate solvent fractions. Except for alkaloids, all secondary metabolites found in the crude extract were found in the aqueous solvent fractions (Table 3). The presence of these active secondary metabolites contributed to the anti-ulcerogenic effects of the crude extract and each solvent fraction with different proposed mechanisms.[4,17,20,21,23,64,66]

Conclusion and Recommendations

In general commercial antiulcer drugs are becoming increasingly difficult to use due to their high costs, drug-drug interactions, and associated adverse reactions to the health of the patient. Both developing and developed countries are increasingly turning to medicinal plants to treat disorders like peptic ulcer disease. In this review paper, a total of 82 medicinal plants have been identified and reported for their use in the treatment of peptic ulcer disease. The majority of these medicinal plants are widely used throughout Ethiopia. However, only the safety and efficacy of *Plantago lanceolata, Osyris quadripartita, Rumex nepalensis, Cordia africana, Croton macrostachyus*, and *Urtica simensis* have been scientifically studied in animal models. Many researchers have found that the bioactive compounds found in plants have beneficial effects, such as reducing the volume of gastric secretions and stimulating the production of gastro-protective mucus. Despite this, many medicinal plants' pharmacological effects and chemistry have not been well studied scientifically. As a result, further bioactive compound characterization, efficacy, mechanism of action evaluation, and toxicity evaluation of medicinal plants should be carried out. A study that can improve the documentation of indigenous knowledge and contribute to drug development and future self-reliance is also recommended.

Data Sharing Statement

The data sets used and or analyzed during the current work are available from the corresponding author upon a reasonable request.

Author Contributions

All authors made a significant contribution to the work reported; participated in the conception, study design, execution, and acquisition of data, analysis, and interpretation; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work. TYT conceived the idea and drafted the proposal. MMZ and SBD prepared and critically reviewed the final manuscript for publication. All authors read and approved the final version of the manuscript.

Disclosure

The authors report no conflicts of interest in this work.

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