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REVIEW

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Phytochemistry, efficacy, and safety of medicinal plants used traditionally for the management of peptic ulcer diseases in Ethiopia: a systematic review

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Abstract

Background Despite significant advances in synthetic medicine, medicinal plants are still widely utilized to treat peptic ulcer disease. This study synthesized evidence on commonly used medicinal plants to manage peptic ulcer disease in Ethiopia.

Methods The evidence was synthesized using electronic databases such as PubMed/Medline, Web of Science, Science Direct, Hinari, and Google Scholar. This review considers all controlled in vivo and ex vivo anti-ulcer studies evaluating Ethiopian medicinal plants with regards to phytochemistry, efficacy, and safety. The search technique covered all published papers using descriptors like Ethiopia, medicinal plants, and anti-ulcer until January 30, 2022. The percentage of ulcer reduction was used to measure the success of the treatment.

Results Anti-ulcer properties were investigated in 13 papers. Twelve in vivo and one ex vivo study were retrieved. *Osyris quadripartita, Plantago lanceolata, Ensete ventricosum, Taverniera abyssinicia, Crotonmacrostachyus Persea Americana and Moringa stenopetala showed effect close to a standard control in difference ulcer induced model. Osyris quadripartite* in the dose of 200 mg/kg, *Ficus thonningii* in dose of 200 and 400 mg/kg, *Plantago lanceolata in* dose of 400 mg/kg, *Trigonella feonum-gracum* in dose of 500 and 1000 mg/kg, *Linum ussitatissimum* in dose of 1000 and 1500 mg/kg, *Urtica simensis 400 mg/kg* have higher activity compared with standard control in difference different models. Phytochemistry studies revealed presence of numerous components, including flavonoids, phenols, tannins, and saponins, which may be responsible for the anti-ulcer activity.

Conclusion This study revealed that there are some promising medicinal plant extracts that have been used in Ethiopia for centuries that could be used as anti-ulcer agents. The most effective anti-ulcer agents in animal models are *Indigofera spicata Forssk*, *Thymus schimperi*, and *Urtica simensis*. Identification of most active pharmacological agents and clinical evaluation of Ethiopian medicinal plants used to treat peptic ulcers are worthy of further investigation.

Keywords Anti-ulcer, Ethiopia medical plant, Ex vivo, In vivo

Introduction

Peptic ulcer disease (PUD) is acid-induced lesions in the stomach and duodenum characterized by denuded mucosa. Inflammatory or necrotizing disorders that affect the esophagus, stomach, and duodenum mucous membranes and are produced by an imbalance between destructive(acid and pepsin secretion) and defensive

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factors (mucus secretion, mucosal barrier, blood flow, cellular regeneration, blood flow, cell renewal and migration, non-enzymatic and enzymatic antioxidants, and some growth factors and endogenous protective chemicals) in the stomach usually aggravates peptic ulcers [5, 7, 11].

Endogenous and exogenous damaging factors that cause mucosal and submucosal erosion can contribute to the etiology of gastric and duodenal ulcers. Endogenous damaging factors in the stomach include HCl, pepsin, biliary reflux, lipid peroxidation, and the generation of reactive oxygen species (ROS). On the other hand, exogenous variables include excessive alcoholic consumption, indiscriminate use of nonsteroidal anti-inflammatory drugs(NSAID), immunosuppressive medications, serotonin reuptake inhibitors, alcohol consumption, stress, smoking, and *Helicobacter pylori infection (H. pylori)* [6, 11, 12, 19].

The majority of peptic ulcer disease occurrences are now most linked to *H. pylori* infection, the use of NSAIDs, or both. *H. pylori* colonizes the gastrointestinal mucosa, causing gastritis, peptic ulcer disease, and possibly gastric cancer [22].

PUD is one of the most common gastrointestinal disorders in the world which affects about 10% of the world population globally [9]. Around 4 million people are affected by these lesions worldwide, and 10–20% of cases develop complications, with a 10–40% mortality rate [2].. PUD affects over 4.5 million people in the United States alone each year, with a lifetime prevalence of about 8.4% [17, 22].

Conventional drugs currently used in the treatment of PUD (antacids, PPIs, H2 antagonists, anticholinergic, mucosal protective agents, and antimicrobials for *H. pylori*-induced PUD) have no long-term curative effect, and relapse is common after prolonged treatment. Moreover, these conventional drugs produce severe adverse reactions [25, 47]. As much as 50% of the western population uses herbal medicines as a therapy alternative, and about 10% use them to treat or prevent digestive issues [4]. Herbal medicine is used as a primary source of health treatment by an estimated 80 to 90% of Ethiopians [36]. Medicinal plants are one of the most often used drugs in the treatment of peptic ulcers, owing to their low cost, cultural acceptability, accessibility to people of lower socioeconomic position, and lesser side effects [13]. Many rural communities continue to rely on it [8]. Preliminary investigations on the scientific evidence of commonly used medicinal plants for peptic ulcer disease in Ethiopia have been conducted, but no evidence has yet been synthesized. This study was aimed to synthesize evidence on phytochemistry, effectiveness, and safety of medicinal plants used in Ethiopia in the management of peptic ulcers.

Methods

This study is a systematic review that followed the Preferred Reporting Items for Systematic Review and Meta-Analysis and the reporting [37]. PRISMA 2020. It looked at pre-clinical research on the anti-ulcer properties of Ethiopian medicinal herbs.

Information sources, searching, and selection of studies

The search engines used were electronic databases such as Hinari, PubMed/Medline, Web of Science, Medline, Science Direct, and Google Scholar as information sources. The review included published articles and thesis until Jan 2022; all available articles having descriptors were used in the search.

Eligibility criteria

Inclusion criteria

The following studies were included;

Studies conducted in laboratory animals or cell lines as disease models or in an in-vitro and in vivo study. These studies should use medicinal plants as a whole or parts in the experimental groups, with seed, root, flower, bud, and leaf extracts or single or complex medicinal plants, plant extracts, and plant preparations independent of how they were prepared (maceration, decoctions, tablets, capsules, pills, powders, injections, or other types of preparations), but no synthetic compounds were included.

The above studies should be published in English, including articles, thesis, essays, and proceedings, dealing with an anti-ulcer activity in vivo or in vitro research up to January 30, 2022.

Exclusion criteria

Previous reviews are excluded.

Data extraction

Three reviewers (AM and DH) independently conducted a literature search and examined relevant studies, screening their titles and abstracts for eligibility in a sequential manner. The full texts of studies that were considered to be potentially eligible were obtained. Disagreements were resolved after a discussion with other authors (SD and AN). The data were extracted using a pre-designed format. The data extracted includes the first author, study area, scientific, family, and local names, study model, animal type, extraction process, a component of the extract used, treatment time, and change in percentage of protection (from negative control and standard control) A

study is included if the effect on negative control is mentioned; otherwise, it is eliminated.

Results

Characteristics of included studies

The electronic database search resulted in the discovery of 2678 articles. The total number of articles was decreased to 1648 after de-duplication. After screening the titles and abstracts, 13 papers remained. Eleven peer-reviewed articles and 2 M.sc theses were selected for inclusion (Fig. 1).

As shown in Table 1, 12 of the investigations were in vivo, while one was both in vitro and ex vivo. Study plants were collected from different regions of Ethiopia, and seven plants were collected from Amhara, five in Addis Ababa, and one in Oromia. The most obtained in-vivo anti-ulcer model was pylorus ligation anti-ulcer models and ethanol-induced.

Phytochemistry

All medicinal plant tested contained flavonoids, phenols, and saponins. Tannins present in all plant except in *Trigonella feonum-gracum and Linum ussitatissimum.* All except *Cordia Africana* have alkaloids and terpenoids, whereas *Ficus thonningii* exclusively has anthraquinones. *Ficus thonningii, Urtica simensis, Solanum incanum L.*, and *Rumex nepalensis* contain glycosides (Table 2).

In vivo studies

In vivo trials varied significantly in treatment duration, ranging from 1 hour to 20 days. Studies were done using different animals and mice were utilized in four tests, rats in seven, and mice and rat were employed in two investigations. The plant was extracted using methanol in eight experiments, ethanol in one, and aqueous in the remaining four. *Ensete ventricosum* at a dose of 400 mg/kg provided notable ulcer control in pyloric-ligation ulcer

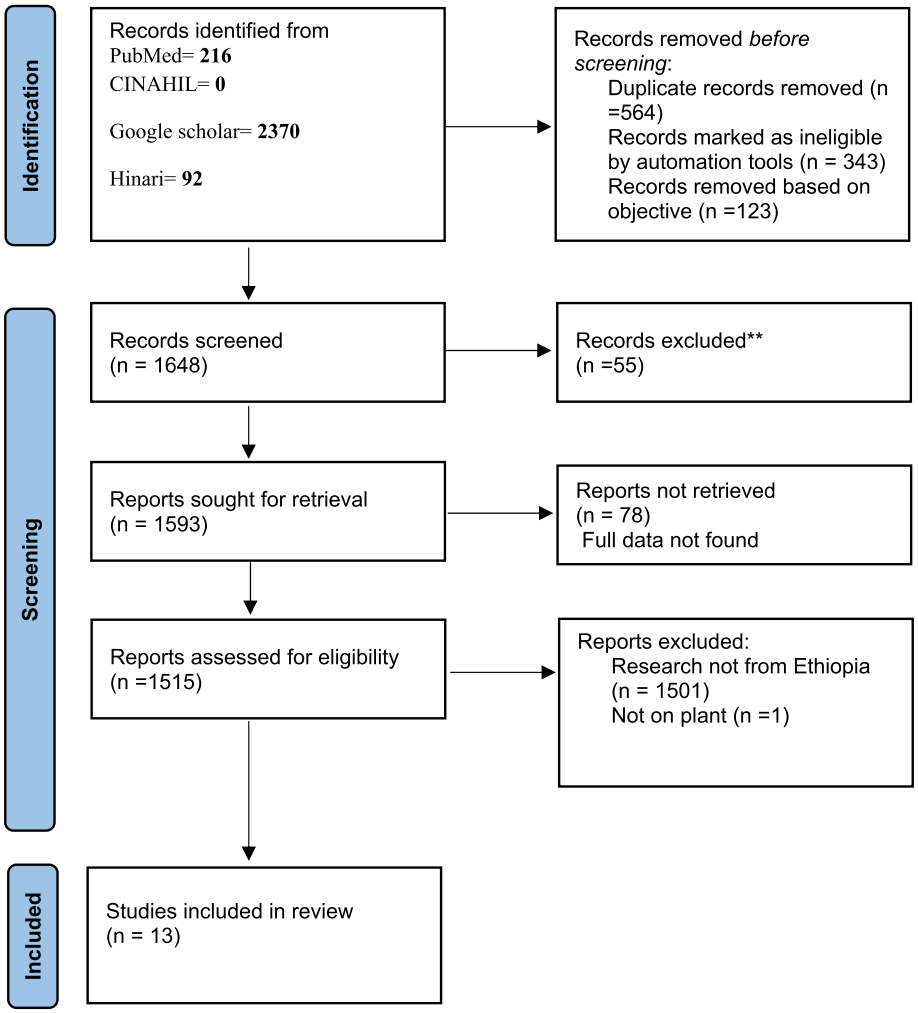

Fig. 1 Flow diagram showing, screened, excluded, and included studies

Table 1 Characteristics of included studies

No	Study	Study area	Name of a plants (Scientific, family, and local)	Model and animal
1	(Abebaw, Mishra et al. 2017) [1]	Gondar area	*Osyris quadripartita Decne. (Santalaceae)* Local name: Qeret	Pylorus ligation-induced and ethanol-induced ulcer models Wistar albino rats
2	(Adane, Atnafie et al. 2021) [2]	Gondar area	*Ficus thonningii(Moraceae)* Local name: Dambii	Pylorus ligation, indomethacin-induced, and ethanol-induced ulcer rodent models
3	(Belayneh, Amare et al. 2021) [9]	Anbessamie town	*Solanum incanum* L. (Solanaceae) Local name: Embuay or Hiddi	Pylorus ligation-induced and ethanol-induced Mice ulcer
4	(Makonnen 2020) [26]	Addis ababa	*Linum usitatissimum (Linaceae) Local name: Telba*	Isolated guinea ileum
5	(Mekonnen, Asrade Atnafie et al. 2020) [27]	Debre Libanos woreda	*Crotonmacrostachyus Hocsht:Ex Del. (Euphorbiaceae)* Local name: bissana or bakanisa	Acidified ethanol-induced Mice ulcer
6	(Melese, Asres et al. 2011) [28]	Addis Ababa	*Plantago lanceolata L* Local name: Gorxobii	Acetic acid-induced, indomethacin-induced gastric ulcer, cysteamine induced duodenal ulcer, and pylorus ligation induced gastric ulcer Female Swiss albino mice and male Sprague Dawley Rats' model
7	(Mequanente, Makonnen et al. 2006) [29]	Addis Ababa.	*Trigonella feonum-gracum* Local name:abish *and Linum ussitatissimum* Local name:telba	Indomethacin-induced Swiss Albino mice model
8	(Noamesi, Mensah et al. 1994) [35]	Addis Ababa	*Taverniera abyssinica A.* Local name = Dingetegna	HCL/ethanol-induced rats
10	(Sisay, Andargie et al. 2021) [44]	Debre Tabor	*Urtica simensis Hochst. ex. A. Rich. (Urticaceae)* Local name = Sama	Pyloric ligation, cold restraint stress, and acetic acid-induced ulcer rat models
11	(Sisay Zewdu and Jemere Aragaw 2020) [45]	Debre Tabor	*Rumex nepalensis* Local name = Tult or shuulti	Pyloric ligation-, cold restraint stress-, and acetic acid-induced ulcer models. Rats
12	(Yismaw, Abdelwuhab et al. 2020) [50]	Tinsaye North of Gondar town	*Cordia africana Lam Boraginaceae)* Local name = wanza	Pyloric Ligated Rats
13	(Hailu 2021) [20]	Chelia and Jibat districts of West Shewa Zone	*Ensete ventricosum (Welw.) Cheesman (Musaceae)* Local name: Enset	Pyloric Ligated, Ethanol and indomethacin ulcer induced Rats
14	(Ahmed 2019) [3]	Addis ababa	*Urtica simensis* Local name: Sama	Pyloric Ligated, Ethanol and indomethacin ulcer induced Rats Wistar

induced rats with better ulcer reduction than the negative control. *Osyris quadripartita*, *Plantago lanceolata*, *Ensete ventricosum*, *Taverniera abyssinicia*, *Crotonmacrostachyus Persea Americana* and *Moringa stenopetala* showed effect close to a standard control in difference ulcer induced model. *Osyris quadripartite* in the dose of 200 mg/kg, *Ficus thonningii* in the dose of 200 and 400 mg/kg, *Plantago lanceolata* in the dose of 400 mg/kg, *Trigonella feonum-gracum* in the dose of 500 *and* 1000 mg/kg, *Linum ussitatissimum* in the dose of 1000 and 1500 mg/kg, *Urtica simensis* 400 mg/kg have higher activity compared with standard control in difference model (Table 3).

Ex vivo studies

The aqueous extract of *Linum usitatissimum* seed was found to dramatically reduce the contractile responses of both histamine and carbachol on isolated guinea ileum.

Table 2 Preliminary qualitative phytochemical screening of the studied plants

Test	(Abebaw, Mishra et al. 2017) [1]	(Adane, Atnafie et al. 2021) [2]	(Ahmed 2019) [3]	(Belayneh, Amare et al. 2021) [9]	(Mequanente, Makonnen et al. 2006) [29]	(Sisay, Andargie et al. 2021) [44]	(Sisay Zewdu and Jemere Aragaw 2020) [45]	(Yismaw, Abdelwuhab et al. 2020) [50]
Plant	*Osyris quadripartita*	*Ficus thonningii*	*Urtica simensis*	*Solanum incanum L.*	*Trigonella feonum-gracum and Linum ussitatissimum*	*Urtica simensis*	*Rumex nepalensis*	*Cordia africana*
Flavonoids	+	+	+	+	+	+	+	+
Phenols	+	+	+	+	+	+	+	+
Tannins	+	+	+	+	-	+	+	+
Saponins	+	+	+	+	+	+	+	+
Alkaloids	+	+	+	+	+	+	+	-
Terpenoids	+	+	+	+	+	+	+	-
Glycosides	-	+	+	+	+	-	+	-
Steroids	-	-	-	+	+	-	+	-
Anthraquinones	-	+	-	-	-	-	-	-

With the lengthening of the soaking period, the extract's potency increased significantly. Histamine and carbachol produced reproducible contractions quickly after removing the extract by washing the preparation [26].

Safety

The plant extracts utilized in this study were shown to be quite safe in acute toxicity tests in animals. Eleven plants, including *Osyris quadripartite, Urtica simesis,Solanum incanum, Encete ventricosum,Crotonmacrostachyus hocsht, Plantago laceolata, Trigonella feonum, Linum ussitatissimum, Rumex nepalensis and Cordia Africana,* had LD50 values greater than 2000 mg/kg [1, 3, 9, 20, 27, 28, 29, 44, 45, 50]. *Taverniera abyssinica* has a median lethal dose (LD_{50}) of 1409 mg/ml [35] (Table 4).

Discussion

This study reviewed 13 articles on medicinal plants of Ethiopia that have anti-ulcer properties. The majority of studies were carried out in animal model (12), with only one ex vivo study. *Ensete ventricosum* provided notable ulcer protection over 14 days compared to negative control and lower ulcer reduction compared to the standard control. *Osyris quadripartita*, *Plantago lanceolata*, *Ensete ventricosum*, *Taverniera abyssinicia, Crotonmacrostachyus Persea Americana* and *Moringa stenopetala* showed effect close to a standard control in difference ulcer induced model. *Osyris quadripartite* in the dose of 200 mg/kg, *Ficus thonningii* at dose of 200 and 400 mg/kg, *Plantago lanceolata* at dose of 400 mg/kg, *Trigonella feonum-gracum* at dose of 500 *and* 1000 mg/kg, *Linum ussitatissimum* at dose of 1000 and 1500 mg/kg, *Urtica simensis* 400 mg/kg have higher activity compared with standard control in different models.

The variation between the two studies on *Urtica simensis* could be owing to the geographical locations (Debra tebor versus Addis Ababa), solvents used, soil, or climatic factors.

Compared to studies conducted in India, the number of investigations on the anti-ulcer activity of Ethiopian medicinal herbs was smaller. In India, for example, a review revealed 40 and 64 plants with anti-ulcer efficacy [39, 49] and 58 from America [18]. This is maybe due lower availability of research centers in Ethiopia due to socioeconomic hurdles.

Several medicinal plants have long been utilized in Ethiopia to cure peptic ulcers; however, the number of plants investigated is low. This review evaluated previous research while emphasizing the need for more research. In the old idea, acid secretion was supposed to be the sole cause of ulcer formation, and lowering acid secretion was thought to be the main therapeutic method. However, recent research has led to a shift in this belief. The potentiation of the defensive system and the reduction of acid secretion are now the key goals of ulcer treatment. The world's oldest medicinal systems can lead to the discovery of therapeutically effective plant remedies [39].

The finding of the study done on preliminary phytochemical analysis of selected medicinal plants revealed the presence of secondary phytochemicals. Flavonoids, Phenols, and Saponins were found in *Osyris quadripartite, Ficus thonningii, Urtica simensis, Solanum incanum, Trigonella feonum, Linum usitatissimum, Rumex nepalensis, and Cordia Africana*. Tannins was found in *Osyris quadripartite, Ficus thonningii, Urtica simensis, Solanum incanum, Rumex nepalensis, and Cordia Africana.* Anti-ulcer activities of these medicinal plants could be attributed to one or more of these secondary metabolites.

Table 3 In vivo anti-ulcer activity of medicinal plant in Ethiopia

Study	Plant	Animal type and model	Extraction method/ component	Duration of treatment	% Difference From negative Control	% Difference From standard control
(Abebaw, Mishra et al. 2017) [1]	*Osyris quadripartita Decne.(Santalaceae)*	Pylorus ligation induced Wistar albino rats	Methanol	20 days	200 mg/kg = 68.42	200 mg/kg = 1.5%
		Ethanol-induced ulcer models Wistar albino rats		20 days	200 mg/kg = 85.35	200 mg/kg = −4.1%
(Adane, Atnafie et al. 2021) [2]	*Ficus thonningii (Moraceae)*	Pylorus ligation	Hydromethanol	10 days	100 mg/kg = 33.6 200 mg/kg = 59.07 400 mg/kg = 62.1	100 mg/kg = −14.7 200 mg/kg = 10.57 400 mg/kg = 13.6
		Ethanol-induced ulcer rodent models	Hydromethanol	10 days	100 mg/kg = 71.86	100 mg/kg = −1.1
			Chloroform fraction	10 days	200 mg/kg = 39.16	200 mg/kg = −33.2
			Aqueous fraction	10 days	200 mg/kg = 70.76	200 mg/kg = −2.2
		Indomethacin induced	Hydromethanol	4 days	100 mg/kg = 55.02 200 mg/kg = 61.15 400 mg/kg = 63.35	100 mg/kg = − 44.98 200 mg/kg = − 38.85 400 mg/kg = − 36.65
(Belayneh, Amare et al. 2021) [9]	*Solanum incanum L. (Solanaceae)*	Pylorus ligation-induced model	Hydromethanol	10 days	Leaf 100 mg/kg = 5.83 200 mg/kg = 34.17 400 mg/kg = 48.83 Root 100 mg/kg = 27.83 200 mg/kg = 30.5 400 mg/kg = 48.67	Leaf 100 mg/kg = − 48.67 200 mg/kg = − 20.33 400 mg/kg = − 5.67 Root 100 mg/kg = − 26.6 200 mg/kg = − 24 400 mg/kg = − 5.83
		Ethanol-induced Mice ulcer	Hydromethanol	10 days	Leaf 100 mg/kg = 35.43 200 mg/kg = 44.88 400 mg/kg = 52.36 Root 100 mg/kg = 36.02 200 mg/kg = 42.32 400 mg/kg = 52.36	Leaf 100 mg/kg = − 37.4 200 mg/kg = − 27.95 400 mg/kg = − 20.47 Root 100 mg/kg = − 36.81 200 mg/kg = − 30.51 400 mg/kg = − 20.47
(Mekonnen, Asrade Atnafie et al. 2020) [27]	*Crotonmacrostachyus Hocsht:Ex Del. (Euphorbiaceae)*	Acidified Ethanol-induced Mice ulcer	Methanol	7 days	100 mg/kg = 24.44 200 mg/kg = 45.93 400 mg/kg = 62.22	100 mg/kg = − 55.56 200 mg/kg = − 34.07 400 mg/kg = − 17.78
			Chloroform	7 days	100 mg/kg = 53 200 mg/kg = 68.8 400 mg/kg = 78.1	100 mg/kg = − 28.4 200 mg/kg = − 12.6 400 mg/kg = − 3.3
			Ethyl acetate fraction	7 days	100 mg/kg = 18.6 200 mg/kg = 46.6 400 mg/kg = 62.8	100 mg/kg = − 62.8 200 mg/kg = − 34.8 400 mg/kg = − 18.8
			Aqueous fraction	7 days	100 mg/kg = 11.7 200 mg/kg = 11.32 400 mg/kg = 21.4	100 mg/kg = − 69.7 200 mg/kg = − 70.08 400 mg/kg = − 60
(Melese, Asres et al. 2011) [28]	*Plantago lanceolata L*	Indomethacin induced	aqueous extract	4 hrs	200 mg/kg = 27.3 400 mg/kg = 86.4	200 mg/kg = − 40.9 400 mg/kg = 18.2
		cysteamine induced	aqueous extract	24 hrs	200 mg/kg = 40 400 mg/kg = 60	200 mg/kg = − 33.3 400 mg/kg = − 13.3
		Acetic acid-induced	Aqueous extract	10 days	200 mg/kg = 50.9 400 mg/kg = 77.9	200 mg/kg = − 25.3 400 mg/kg = 1.7
Mequanente, Makonnen et al. 2006 [29]	*Trigonella feonum-gracum*	Indomethacin-induced	Aqueous extract	6 hrs	500 mg/kg = 33.6 1000 mg/kg = 59.9 1500 mg/kg = 65.5	500 mg/kg = − 20.8 1000 mg/kg = 5.5 1500 mg/kg = 11.1
	Linum ussitatissimum	Indomethacin-induced	Aqueous extract	6 hrs	500 mg/kg = 42 1000 mg/kg = 58.6 1500 mg/kg = 67.8	500 mg/kg = − 12.4 1000 mg/kg = 4.2 1500 mg/kg = 13.4
(Noamesi, Mensah et al. 1994) [35]	*Taverniera abyssinica A.*	Ethanol induced	Aqueous extract	4 days	125 mg/kg = 54 250 mg/kg = 58 500 mg/kg = 80	

Table 3 (continued)

Study	Plant	Animal type and model	Extraction method/ component	Duration of treatment	% Difference From negative Control	% Difference From standard control
(Sisay, Andargie et al. 2021) [44]	*Urtica simensis Hochst. ex. A. Rich. (Urticaceae)*	pylorus-ligated rats.	Hydromethanolic	10 days	100 mg/kg = 50.34 200 mg/kg = 59.88 400 mg/kg = 67.68	100 mg/kg = − 16.96 200 mg/kg = − 7.32 400 mg/kg = 0.38
		Cold restraint stress-induced ulcerated rats.	Hydromethanolic	3 hrs	100 mg/kg = 33.77 200 mg/kg = 49.93 400 mg/kg = 53.22	100 mg/kg = −8.08 200 mg/kg = − 12.37 400 mg/kg = − 27.53
		acetic acid-induced ulcer in rats	Hydromethanolic	20 days	100 mg/kg = 33.54 200 mg/kg = 58.34 400 mg/kg = 67.07	100 mg/kg = − 30.79 200 mg/kg = − 6 400 mg/kg = 2.76
(Sisay Zewdu and Jemere Aragaw 2021) [45]	*Rumex nepalensis*	Pyloric ligation Rats	Hydromethanolic	10 days	100 mg/kg = 51.17 200 mg/kg = 59.78 400 mg/kg = 67.52	100 mg/kg = − 16.18 200 mg/kg = − 7.57 400 mg/kg = 0.17
			Chloroform Fraction	10 days	100 mg/kg = 2.54 200 mg/kg = 4.4 400 mg/kg = 8.6	100 mg/kg = − 67.36 200 mg/kg = − 65.5 400 mg/kg = − 61.3
			Ethyl acetate Fraction	10 days	100 mg/kg = 53.26 200 mg/kg = 61.4 400 mg/kg = 69.26	100 mg/kg = − 16.64 200 mg/kg = − 8.5 400 mg/kg = − 0.64
			Aqueous fraction	10 days	100 mg/kg = 45.69 200 mg/kg = 55.6 400 mg/kg = 58.23	100 mg/kg = − 24.21 200 mg/kg = − 14.3 400 mg/kg = − 11.67
		Acetic acid-induced ulcer Rats	Hydromethanolic	15 days	100 mg/kg = 26.1 200 mg/kg = 51.82 400 mg/kg = 54.59	100 mg/kg = − 36.94 200 mg/kg = − 9.82 400 mg/kg = − 8.45
(Yismaw, Abdelwuhab et al. 2020) [50]	*Cordia africana Lam Boraginaceae)*	Pyloric Ligated Rats	Methanol	10 days	600 mg/kg = 59.73	600 mg/kg = − 0.28
(Hailu 2021) [20]	*Ensete ventricosum (Welw.) Cheesman (Musaceae)*	Indomethacin induced Rat	Aqueous extract	6 hrs	100 mg/kg = 25.8 200 mg/kg = 42.3 400 mg/kg = 71.7	100 mg/kg = − 73.5 200 mg/kg = − 57 400 mg/kg = − 27.6
		Ethanol-induced Rat	Aqueous extract	1 hr.	100 mg/kg = 24.24 200 mg/kg = 41.6 400 mg/kg = 55.04	100 mg/kg = − 46.08 200 mg/kg = − 28.72 400 mg/kg = − 15.28
		Pyloric Ligated Rats	Aqueous extract	4 hrs	100 mg/kg = 40.07 200 mg/kg = 60.38 400 mg/kg = 98.53	100 mg/kg = − 59.53 200 mg/kg = − 39.22 400 mg/kg = − 1.07
(Ahmed 2019) [3]	*Urtica simensis*	Pyloric Ligated Rats	Aqueous extract	6 hrs	100 mg/kg = 33.7 200 mg/kg = 52.5 400 mg/kg = 65.5	100 mg/kg = − 35.8 200 mg/kg = − 17 400 mg/kg = − 4.2
			Methanol extract	6 hrs	100 mg/kg = 34.8 200 mg/kg = 55.3 400 mg/kg = 67	100 mg/kg = − 34.7 200 mg/kg = − 14.2 400 mg/kg = − 2.5
		Ethanol ulcer induced	Aqueous extract	5 days	200 mg/kg = 72.3	200 mg/kg = − 1
			Methanol extract	5 days	200 mg/kg = 72.8	200 mg/kg = − 0.5
		Indomethacin ulcer induced	Aqueous extract	5 days	200 mg/kg = 73.21	200 mg/kg = − 2.29
			Methanol	5 days	200 mg/kg = 74.4	200 mg/kg = − 1.2

Medicinal plants are rich in bioactive compounds and have a wide range of pharmacological effects, including anti-ulcer activity. The activity could be attributed to a single phytochemical or a combination of phytochemicals. Alkaloids, phenolics, flavonoids, saponins, and tannins are some of the phytochemicals that could exert anti-ulcer activities [31, 38, 40].

Flavonoids are hypothesized to raise mucosal prostaglandin content, limit *H. pylori* growth, function as free radical scavengers, and inhibit H+/K+-ATPase, as well as decrease histamine production from mast cells by inhibition of histidine decarboxylase [10, 41].

Saponins may activate mucous membrane protective factors, while tannins make the mucosa's outermost

Table 4 Bioactive components responsible for Antiulcer activities

No	Classes of compound with Antiulcer activities	Isolated compound with antiulcer activity	Reference
1	Flavonoids	Quercetin,chalcones,Garcinol,Rutin and Naringenin	[21, 33, 42]
2	Terpenes	Limonene,Pinene,Citral,Lupeol,Ursolic acid and Nomilin	[21, 23]
3	Alkaloids	Rutaecarpine, Phenylquinoline, Rohitukine, ethoxycanthin-6-one, Chelerythrine, Piplartine Piplartine and Peganine	[15, 21, 34]
4	Phenols	*p*-Coumaric acid, Gallic acid	[43, 46]
5	Tannins	Acutissimmin, Acutissimmin, Alienanin B, Castalagin, Casuarictin, Casuarinin, Corilagin, Elagic acid, Geraniin,Nobotanin B, Pedunculagin, Procyanidin B5	[14, 16]
6	Saponin	Theasaponin A2	[32, 48]

layer less receptive to chemical irritants [10]. Furthermore, terpenoids and alkaloid compounds have been shown to have powerful anti-ulcer action [24, 30].

To isolate, define, and standardize the active ingredients from herbal sources, ethno-medical knowledge supplemented by modern research is required. By combining traditional and current knowledge, improved anti-ulcer medications with fewer adverse effects can be developed. Although the experimental evaluation of herbal medications for peptic ulcers is excellent, there is no clinical trial on Ethiopian medicinal plants for anti-ulcer activity. This demonstrates that the advantages of study are not reaching the individuals who are the focus of medical research, so time, energy, and resources are being wasted. As a result, pharmacologists must devote more time to investigating herbal medications for possible anti-ulcer action and standardizing such herbal drugs for them to be clinically efficacious and globally competitive.

Numerous therapeutic plants can be found worldwide, but less than one-third of them have had their medical properties determined. More thorough and trustworthy scientific investigations are still required to assess and guarantee the efficacy of medicinal plants and their potential metabolites in the treatment of ulcers. The research included in this paper was conducted entirely using crude plant extract. Future research can use the findings of this study to isolate the active components and turn them into conventional drugs.

Conclusions

According to the findings of this study, some medicinal plants that have been used in Ethiopia for centuries were found to be a promising compound as anti-ulcer agents. The most effective anti-ulcer agents in animal models were *Indigofera spicata Forssk*, *Thymus schimperi*, and *Urtica simensis*. This study found that medicinal plants used in Ethiopia to treat peptic ulcers are worthy of additional research into pharmacologically active components and clinical trials. To collaborate the stated effectiveness of commonly used medicinal plant species, more in vitro, in vivo, and clinical research are needed.

Abbreviations

ARRIVE	Animal Research: Reporting of In vivo Experiments
H.Pylori	Heliobacter pylori
LD_{50}	Median lethal dose
NSAID	Nonsteroidal anti-inflammatory drug
PPI	Proton pump inhibitors
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
PUD	Peptic ulcer disease
SYRCLE's	Systematic Review Centre for Laboratory Animal Experimentation

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Disclosure

The authors declare no competing interests.

Authors' contributions

AM was the one who came up with the concept and designed the study. SD, AN, and DH conducted literature searches, gathered data, and drafted the manuscript. The manuscript was written by AM. The final text was reviewed and approved by all authors.

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Declarations

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