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REVIEW

A Systematic Review of Ethnobotanical, Phytochemical, and Ethnopharmacological Studies of *Urtica simensis* (Stinging Nettle)

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Abstract: The Urticaceae family contains 54 genera and more than 2000 species that can be found in tropical, subtropical, and temperate climates all over the world. This family includes the largest genus in the world, *Urtica*, which is also known as stinging nettle. Stinging hairs are present on the lower surface of the leaves and beneath the stems of *Urtica simensis*, also known as the stinging nettle, herbal nettle that is dioecious, upright, and unbranched. For the treatment of conditions like gastritis, heart disease, diabetes, gonorrhea, and malaria, people employ various portions of *Urtica simensis* in a variety of ways in traditional medicine. The *Urtica simensis* leaves are rich in variety of active secondary phytochemical constituents including terpenoids, saponins, tannins, flavonoids, steroids, alkaloids, polyphenols, sterols, oxalate, and ascorbic acid (vitamin C). According to different reports, it possesses a variety of pharmacological properties, including antioxidant, antiproliferative, antidiabetic, cardioprotective, antiulcer, antibacterial, and antifungal actions. The current review summarizes published and unpublished information about the ethnobotanical, phytochemical, ethnopharmacological, and toxicological reports of *Urtica simensis* and summarizes all the research work carried out on this plant to provide updated information for future work.

Keywords: *Urtica simensis*, ethnobotanical uses, phytochemical studies, ethnopharmacological studies, Ethiopia

Introduction

Botanical Source and Characteristics

The Urticaceae family contains 54 genera and more than 2000 species that can be found in tropical, subtropical, and temperate climates all over the world.[1–3] This family includes the largest genus in the world, *Urtica*, which is also known as stinging nettle[4,32] (Table 1). Narrow-leaf nettle is supposed to have sprung from the Anglo-Saxon word "noedl", which means needle. The plant is recognized for its ability to cause long-term pain, burning sensations, and a transient rash by producing an irritant when it comes into contact with human skin.[5–7] The genus *Urtica* is derived from the Latin word "uro", meaning "to burn" or "urere", which means "to sting".[5,7,8] The genus *Urtica* consists of over 80 species distributed throughout the world.[6,9] The Urticaceae family includes the common nettle species *Urtica simensis*, which is native to Ethiopia and indigenous to the country. It has been traditionally used to cure a wide range of illnesses, including infectious and non-infectious diseases, and is consumed as a vegetable in some regions of the country.[5]

Urtica simensis grows year round in Ethiopia's mid- and highlands, particularly the Tigray area, North and South Gondar, North and South Wello, Wag Hamra, Gojam, and North Shewa, as well as the highlands of the Sidama zone in the south and the Arsi zone of the Oromia region.[10–15] It is mainly found in disturbed around grassland areas, is plentiful close to homes, and may be picked whenever needed.[8,12,16–19]

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Table 1 Ethnobotanical Sources and Characteristics of *Urtica simensis*

Botanical Sources and Other Characteristics	A General Description of the Plant	References
Botanical Origin	Order: Urticales Family: Urticaceae Genus: *Urtica* Species name:*Urtica simensis* Common name: Nettle Vernacular names in Ethiopia: Sama (Amharic); Doobii/Gurgubbee (Oromia ethnic community); Amea (Tigray ethnic community); Sanamik (Halaba ethnic community), Dobita (Kembatta ethnic community)	[3,8,10,16,20,32–38]
Morphological Characteristics of Organized Parts	Stem: grows up to 1 m tall Leaves: oval and coarsely serrated leaves are attached in pairs opposite each other to the stem, with stipules fused and interpetiolar 0.5–1 cm long. The leaves' bases are slightly cordate and the apex is broadly acute Flowers: small flowers, each with four petals, sit in dense clusters on elongated inflorescences towards the top of the stem. The flowers are unisexual and regular Fruit: 2 mm long	[8,19,21]
Organoleptic Properties	Leaves: the color ranges from light green to dark green Flowers: greenish to white Roots: the underground roots through which the plant spreads are noticeably yellow	[8,19,21]

The perennial plant known as stinging nettle, *Urtica simensis*, is famous for the stinging hairs on the underside of the leaves and beneath the stems. It is a herb nettle that is dioecious, upright, and unbranched. It varies from other species by being less robust and having smaller stipules and serrated leaf margins[14] (Figure 1).

Methods

Using the keywords "Urtica simensis", "ethnobotanical uses", "phytochemical studies", and "ethnopharmacological studies" in each database, information was systematically gathered from PubMed, EMBASE (the Ovid interface),

Figure 1 Photograph of a stinging nettle (*Urtica simensis*) plant as taken from its natural habitat.

Scopus, MEDLINE, Science Direct, Elsevier, Scifinder, Research Gate, and WorldCat. The extracted information was then appropriately filtered if it was deemed pertinent and related to the topic at hand. About 62 sources were used in this scientific study. The study was conducted from August 2021 to November 2021. Critical analysis of the information gathered in this review way allowed for the discovery of new information gaps that may exist regarding *Urtica simensis*, opening up new avenues for future study.

Ethnobotanical Uses

The various parts of *Urtica simensis* have been used in Ethiopian traditional medicine to treat a variety of human ailments, including gastritis, heart disease, diabetes, gonorrhea, and malaria, using a variety of preparations and administration methods, as listed in Table 2.

Table 2 Ethnobotanical Applications of *Urtica simensis*

Part(s) Used	Description of Preparation	Application	References
Leaves	The fresh leaves of *Urtica simensis* are collected and roasted like "wot" and eaten with injera	Gastritis	[22]
	Roast, grind, and drink juice	Gastritis	[39]
	Cooked leaves are mixed with powder from fried seeds of barley and eaten	Gastritis	[40]
	Boil the leaves and take them as food	Gastritis	[41]
	Pick the leaves of *Urtica simensis* with a protected hand, cut them, and spread them out between two hides on the ground, rubbing them to avoid the leaves burning, then boil and grind them, then salt them and prepare them	Gastritis	[42]
	Boil the semi-crushed leaf and eat it for 2 or 3 days	Peptic ulcer disease	[43]
	Not stated	Stomach ulcer	[44]
	Crushed, powdered, boiled, and taken as a tea	Gastritis, intestinal parasites, sexually transmitted disease	[37]
	Eaten in the form of stew ("wot")	Gastritis, heart disease	[45,46]
	Fresh leaf stem vapor is used nasally to fumigate the whole body	Heart failure	[46,47]
	Fresh leaf juice is applied topically	Wound	[48]
	Grind and cream with butter	Wound, eczema	[39,46]
	Crushed and applied using a gauze strainer/filter	A fresh bleeding wound (livestock)	[49]
	Not stated	Diabetes	[50]
	Leaves are pounded, mixed with water, and given	Gonorrhea	[51]
	Crushed, roasted, and powdered, apply to the affected area	Burns	[45]
	Squeeze the cream onto your skin and rub it in	Warts	[52]
	The leaves of *Urtica simensis* are pounded, squeezed, and then creamed on the affected part	Hemorrhoids	[22]
	The leaves of *Urtica simensis* and *Zehneria scabra* are mashed, powdered, and burned, with the smoke being inhaled	Fibril illness	[22]
	The leaves are boiled in hot water and their aroma is fumigated three times by opening the lid	Night blindness	[53]
	A pounded and squeezed leaf is dropped on the injured eye by the insertion of bad materials	Eye injury	[53,54]
	Boiled the leaves in hot water and fumigated their aroma three times by opening and closing the lid	Nyctalopia	[54]
	Not stated	Rheumatism	[44]
Shoots	Young shoots are cooked and eaten as vegetables	Gastritis	[55]
Sap	The sap was drank	Acute stomach ache	[16]
	Heated and put on the affected part	Body swelling	[16]

(*Continued*)

Table 2 (Continued).

Part(s) Used	Description of Preparation	Application	References
Rhizomes	It is peeled with a blade; three half-finger size rhizomes are inserted in the vagina	Abortion	[53,54]
Roots	Crushed and dried, then mixed with fresh water, drink one glass of it and drink a large amount of milk	Malaria	[43]
	Water was mixed with mashed *Urtica simensis* root, *Solanum incanum* root, *Croton macrostachyus* root, *Grewia beguinoti* leaf, and aloe leaf, and drank	Milking phobia	[56]
	Chewing the roots of *Urtica simensis* and/or pounding the root with water and drinking it	Erectile dysfunction	[56]
	A finger-sized root was chewed and drunk for 3–5 consecutive days	Scorpion venom	[36]
	An infusion of the root is prepared and the genital organ is washed with it once daily	Gonorrhea	[57]
	The root of *Urtica simensis* is crushed and mixed with powders of barley, then cooked and eaten	Skin disease	[58]
	Crushed, packed with a piece of cloth, and filter through the nasal cavity	Bleeding	[49,59]
	Roots are collected and tied to the patient's arm	Cut/bleeding	[60]
	Not stated	Cold	[38]
Leaves and shoots	Prepared in the form of a stew and eaten with bread ("Injera")	Gastritis	[61]
Roots and leaves	This plant's roots and leaves are powdered, mixed with water, and drank as a filtrate.	Gonorrhea	[16]
	The roots and leaves of this plant, along with the bark of *Croton macrostachyus*, are mashed, powdered, mixed with a small amount of water, filtered, and then a cup of the filtrate is drunk every morning for 3–5 days	Gonorrhea	[16]
	The roots and leaves of this plant, along with the bark of *Croton macrostachyus*, are mashed, powdered, mixed with a small amount of water, filtered, and then a cup of the filtrate is drunk every morning for 5 days	Gonorrhea	[22]
	This plant's roots and leaves are crushed and mixed with wheat or barley powder, then cooked and eaten for 7 days	Gonorrhea	[58]

Phytochemicals

Terpenoids, saponins, tannins, flavonoids, steroids, alkaloids, polyphenols, sterols, oxalate, and ascorbic acid (vitamin C) are all present in significant amounts in *Urtica simensis* leaves.[14,20–26] Aromatic hydrocarbons like *p*-xylene (12.16%), *o*-cymene (7.84%), and *p*-cymene (7.83%) as well as organosulfur compounds like 3,5-dimethyl-1,2,4-trithiolane (10.24%), 2,4,6-trimethyl-1,3,5-trithiane (1.26%), and 3,6-dimethyl-1,2,4,5-trithiolane (1.26%) are also the main components.[27]

Ethnopharmacological Studies

The different traditionally asserted uses of *Urtica simensis*, which has a long history of usage in Ethiopian folk medicine, were assessed. *Urtica simensis* is frequently used to treat a wide range of human illnesses. Scientifically proven activities with plausible theorized mechanisms of action were present in the various plant parts and summarized as follows.

Antioxidant Activity

The antioxidant potential of *Urtica simensis* leaf extract, extracted in 80% methanol was evaluated using DPPH free radical scavenging methods. The test doses of *Urtica simensis* leaves extract was made in a variety of concentrations, ranging from 40, 80, 160, 320, 400, 600, 800, 1600, and 2400 mg/L.[28,29] In the other investigation, ascorbic acid was used as a reference. A DPPH radical scavenging experiment was used to determine the antioxidant activity after that. The results were reported

by the authors in terms of milligrams of ascorbic acid equivalents per gram (mg AAE/g) of the sample's dry weight. The quantity and placement of hydrogen-donating hydroxyl groups on the aromatic ring of phenolic compounds determined their ability to scavenge free radicals and act as antioxidants (flavonoids and tannins). Other secondary metabolites, such as the glycosylation of aglycones and other H-donor groups, also have an impact (-NH and -SH).[28] At this observation, it can be generalized that the test plant possessed strong anti-oxidant effects and free radical scavenging capabilities.[28–30]

Antiproliferative Effect

The essential oil isolated from *Urtica simensis* aerial extract showed a significant anti-proliferative activity when it was assessed in vitro against human ovarian (A2780) and leukemia (MV4-11) cancer cells using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and resazurin assays. In this procedure, the essential oil was found to be active against human ovarian (A2780) and leukemia (MV4-11) cancer cells. The result obtained was achieved by reducing the growth of MV4-11 and A2780 cells, with GI50 values of 0.299 ± 0.086 and 1.856 ± 0.066 L/mL, respectively. It is postulated that the essential oil of *Urtica simensis'* aerial extract's antiproliferative action was due to the presence of naphthalene derivative components such eugenol and organosulfur compounds.[27]

Using the more delicate A2780 cell line approach, the authors supported their hypothesized pathways for how *Urtica simensis* oil inhibits cell proliferation. It was postulated that the essential oil of *Urtica simensis* inhibits the proliferation of A2780 cells by inducing cell cycle arrest during the G1/S phase in the cell cycle analysis method that was utilized to identify the hypothesized mechanisms. The apoptotic potential of *Urtica simensis* essential oil was also assessed utilizing co-staining techniques with Annexin V and PI. Based on the results observed from each assay, it can be concluded that, the test plant induced apoptotic cell death in a dose-dependent manner. The presence of active metabolites like 1.8-cineole and eugenol contributes for the significant anti-proliferative effects of the test plant. However, the induction of apoptosis and cell cycle arrest brought on by the aerial extract of *Urtica simensis* essential oil may be also attributed to the combined actions of its phytoconstituents. Based on the outcomes of these observations, it can be stated that the oil derived from the aerial extract of *Urtica simensis* is hoped to be a future chemotherapeutic agent for treating cancer. Induction of apoptosis is an essential anticancer therapy method.[27]

Antidiabetic Activity

In streptozotocin-induced diabetic mice, *Urtica simensis* methanol crude extract, and derived aqueous fraction showed statistically significant hypoglycemic effects. However, the petroleum ether, chloroform, and acetone fractions were not able to show a statistical significant antidiabetic effect. Streptozotocin-induced diabetic mice model was applied to determine the anti-diabetic potentials of the crude extract and the solvent fractions of the test plant in different doses. Thus, healthy Swiss albino mice of either sexe were employed that had been starved overnight. Before diabetes had been induced on each mouse, the weight and fasting blood glucose levels of each mouse were measured. A single intraperitoneal injection of 150 mg/kg of streptozotocin was then administered to each mouse to induce diabetes. After giving the medication to the mice for 30 minutes, food and water were then given to them. After streptozotocin induction, the mice were maintained for 72 hours. Each mouse's fasting blood glucose level was then measured, and mice with fasting blood glucose levels over 200 mg/dl were taken into consideration for the commencement of the main procedures.[13]

The anti-diabetic potentials of the test doses of hydro-alcoholic leaf crude extract and derived solvent fraction of *Urtica simensis* were then evaluated in comparison with the standard medication (glibenclamide), which was used as a positive control, and to distilled water, which was used as a negative control. The authors grouped the mice into treatment, positive and negative control groups six mice each to compare the anti-diabetic effects of the test doses of the test plant. The treatment groups received the smallest, middle, and highest doses of the extract and solvent fractions. The negative and positive control groups were treated with distilled water and the standard anti-diabetic drug (glibenclamide), respectively. The test doses of the crude extract and each solvent fraction of *Urtica simensis* that had been employed into the mice were determined from oral acute toxicity study conducted before the commencement of the main procedure. As reported from the finding, the crude extract and the aqueous fractions of the test plant showed statistical significant blood glucose lowering effect in a dose-dependent manner. The results obtained from the study demonstrated that at a dose of 300 mg/kg of body weight, the aqueous fraction of *Urtica simensis* reduced blood glucose levels more effectively

(32.3%) than the 80% methanol extract (25.1%). Three hours after the petroleum ether, chloroform, and acetone fractions of *Urtica simensis* were administered orally, the blood glucose level did not decrease significantly. On the other hand, the aqueous and methanol fractions showed a considerable drop in blood glucose levels after oral administration of 300 mg/kg. Blood glucose levels decreased significantly in the aqueous fraction in a dose-dependent manner as well. It is clear from the outcomes of each procedure that the active components of *Urtica simensis'* hydro-alcoholic leaf extract have considerable ant diabetic properties.[13]

Cardioprotective Effect

Anatomical, biochemical, and histopathological techniques were used to evaluate the cardioprotective activity of *Urtica simensis* crude leaf extract as well as its aqueous and hexane fractions. It was proved that each solvent fraction and the crude extract both significantly impacted cardioprotection in each procedure. The animals were divided into groups of six rats each for the treatment and control. Then, cyclophosphamide-induced myocardial damage was used to assess the cardioprotective efficacy of the crude and solvent fractions of *Urtica simensis* leaves. The extract and solvent fractions were administered to the rats at the calculated doses for 10 days with their respective groups. On the 11th day, the rats received an intraperitoneal injection of cyclophosphamide (200 mg/kg). After all, the cardio protective effect of the test plant was assessed by comparing with the control groups. In comparison to the positive control group, all doses of *Urtica simensis* crude extract and solvent fractions significantly reduced body weight as a percentage of starting weight. Additionally, compared to the positive control group, significant weight loss was observed with the 100 mg/kg, 200 mg/kg, aqueous, and hexane fractions.[31]

The ratio of heart weight to body weight significantly increased after cyclophosphamide treatment. Nevertheless, all test doses of the crude extract and solvent fractions of *Urtica simensis* leaves significantly decreased the heart weight to body weight ratio when compared to the cyclophosphamide-treated groups when the rats were pretreated with a standard medication. The authors evaluated the effects of *Urtica simensis* crude extracts and solvent fractions on cardiac biomarkers. As a result, they saw that the rats given cyclophosphamide had much higher troponin I levels than the positive control groups. However, troponin I level was dramatically reduced in the rats after pretreatment with the 200 mg/kg dose of the crude extract and all doses of the aqueous fractions of *Urtica simensis*. Additionally, the troponin I level was markedly decreased by the 400 mg/kg crude extracts and EN treatment.[31]

The plasma ALT value was elevated in the cyclophosphamide-treated group and decreased in *Urtica simensis*, crude extract, and solvent fractions-treated groups as compared to the positive and negative control groups, respectively. Even yet, when compared to the enalapril-treated and positive control group, the 200 mg/kg and 400 mg/kg hexane fraction-treated rats showed a higher ALT level. A 400 mg/kg dose of crude extract, as confirmed by the authors, considerably decreased the elevation of plasma AST levels brought on by cyclophosphamide when compared to the negative groups. Furthermore, the 200 and 400 mg/kg aqueous fractions of plasma AST were lower than those of the negative control group when compared to those of the fractions-treated rats.[31]

The effects of the crude extract and the solvent fractions on the lipid profiles were also statistically significant. The reduction of cyclophosphamide-induced increase of triglycerides by *Urtica simensis* crude extract and an aqueous fraction at doses of 200 and 400 mg/kg was also demonstrated. In addition, the triglyceride level was decreased in the cyclophosphamide-treated group in relation to the 100 mg/kg crude extract, 200 mg/kg, and 400 mg/kg hexane fractions, respectively. The study found that the crude extract of *Urtica simensis* and its solvent fractions significantly decreased the rise of plasma cholesterol brought on by cyclophosphamide.[31]

Antiulcer Effect

At all test doses employed, *Urtica simensis* demonstrated considerable antiulcer effectiveness against rat models of pylorus ligation-induced ulcer, cold-restraint stress-induced ulcer, and chronic ulcer caused by acetic acid in a dose-dependent manner. *Urtica simensis* leaf extract effectively lowered gastric secretions and raised stomach pH in pylorus ligation-induced ulcers at all dosages. Furthermore, it was noted that the full acidity had significantly decreased in *Urtica simensis*-treated mice. At the higher dose used in this procedure (400 mg/kg), *Urtica simensis* leaf extract exhibited antiulcer activity that was comparable to that of the standard medication. Additionally, this approach guaranteed *Urtica*

simensis leaf extract's dose-dependent antiulcer capability. The ulcer score was also found to be significantly decreased with *Urtica simensis* crude extract in a cold=restraint stress-induced model. On the other hand, the statistical ulcer index reduction was observed at the 200 mg/kg and 400 mg/kg dose ranges. Furthermore, it was assessed that *Urtica simensis* leaf crude extract cured gastric mucosal ulcerations in an acetic acid-induced ulcer in a dose-dependent manner.[25]

Antibacterial Activity

The *Urtica simensis* leaf extract and various solvent fractions exhibited significant antibacterial activity against eight different gram-negative and gram-positive bacterial strains. The investigator evaluated the antibacterial effect using the agar well diffusion antibacterial activity assay and the micro-dilution method using eight different gram-negative and gram-positive bacterial strains, namely, *Streptococcus pyogenes, Streptococcus pneumoniae, Shigella flexneri, Pseudomonas aeruginosa, Escherichia coli, Salmonella typhi, Staphylococcus aureus*, and *Klebsiella pneumoniae*. The extract and each solvent fraction of *Urtica simensis* shown considerable antibacterial activity against the test bacteria when tested at the doses of 200, 400, and 800 mg/kg using the agar-well diffusion method. The zone of inhibition achieved from each quantity of the extract and solvent fractions varied from the test bacterial strains, according to the investigator. Accordingly, *S. pneumonia* had the highest average zone of inhibition at 800 mg/mL concentration among gram-positive bacteria species, followed by *S. aureus and S. pyogenes* with zones of inhibition of 20.00 mm and 19.33 mm, respectively. In other words, the maximum average inhibition at similar concentrations in gram-negative bacteria species was 19.00 mm (*K. pneumonia*), followed by 18.67 mm (*S. flexneri*) and 18.33 (*P. aeruginosa*). In contrast, no zone of inhibition was observed against *S. typhi* in 200 mg/mL of an 80% methanol extract. The investigator also stated that the zone of inhibition of each solvent fraction varies depending on the bacterium, with some solvent fractions showing no zone of inhibition on some test bacterial strains.[21]

Additionally, the researchers established the extracts' minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) against each solvent fraction's tested bacterial species. The MIC value of *Urtica simensis* extract and various solvent fractions have demonstrated a zone of inhibition in an agar well diffusion test higher than or equal to 7 mm in diameter for all test bacterium species, according to the investigator's findings. This result validates the plant's historical uses and confirms its antibacterial abilities.[21]

Likewise, the MBC values of the extracts against test organisms ranged from 5.21 mg/mL (ethyl acetate fraction against *E. coli* and n-butanol fraction against *S. pneumonia* and *S. aureus*) to 16.67 mg/mL (chloroform fraction against *E. coli* and 80% methanol fraction against *K. pneumonia*). In addition, 6.25 mg/mL (*S. pneumoniae*) and 5.21 mg/mL (*S. aureus*) were recorded as the minimum values for 80% methanol extract and n-butanol fractions, respectively. On the other hand, the maximum MBC value in the ethyl acetate fraction was 10.42 (*S. Typhi*). For chloroform fraction, the MBC value ranges from 6.25 mg/mL (*P. aeruginosa*) to 16.67 mg/mL in *E. coli*. The MIC and MFC were also determined by the investigator and it was found that the values ranged between the concentrations of 3.13–16.67 mg/mL (MIC) and 6.25–20.83 mg/mL (MFC) against fungal species.[21]

The crude extract and each solvent fraction shown activities with varying degrees of efficiency against each bacterium, despite the investigator's report revealing the antibacterial activities of the extract and each solvent fraction against tested bacterial strains. The different concentrations of active secondary metabolites present in the extract and each solvent fraction, as well as the various activities of these active phytoconstituents against different bacterial species, can be used to explain why the extract and each solvent fraction have different efficacies against gram-positive and gram-negative bacterial strains. These secondary metabolites are anticipated to influence the extract's and each solvent fraction's antibacterial activity via several suggested mechanisms.[21]

Antifungal Activity

As compared to the standard treatment, the tested fungal strains (*Trichophyton mentagrophytes* and *Aspergillus niger*) were significantly less susceptible to the antifungal effects of *Urtica simensis* leaf extract and its solvent fractions at the observed test doses (200, 400, and 800 mg/kg). When compared to the standard drug, the concentration of the extract and each concentration of the solvent fractions revealed noticeably different zones of inhibition from one another.[21]

Conclusion

The objective of this review is to show the recent advances in the exploration of the plant *Urtica simensis*. The information presented in this review on the ethnobotanical, phytochemical, ethnopharmacological, and toxicological properties of the plant will provide detailed evidence for the use of this plant for various ailments, including gastritis, heart disease, diabetes, gonorrhea, and malaria. The plant is reported to contain mainly terpenoids, saponins, tannins, flavonoids, steroids, alkaloids, polyphenols, sterols, oxalate, and ascorbic acid (vitamin C), which have demonstrated a wide range of pharmacological activities, including antioxidant, antiproliferative, antidiabetic, cardioprotective, anti-ulcer, antibacterial, and antifungal effects. Until now, no study has been conducted that has resulted in pure active components for a specific disease; thus, there is room for research that will lead to commercial utilization of *Urtica simensis* soon.

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

The current work was significantly contributed to by all authors, who also took part in its conception, design, execution, data collection, analysis, and interpretation, article drafting, revision, or critical review, final approval of the version to be published, agreement on the journal to which the article has been submitted, and commitment to full responsibility for the work. The concept and proposal were both created by TYT. The final draft for publishing was written by MMZ, SBD, and GTA who also gave it a critical assessment. The final document was read by all authors, who all gave their approval.

Disclosure

The authors report no conflicts of interest in this work.

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