Research Article

Antiulcerogenic activities of *Heterotis rotundifolia* (Sm.) Jacq. Fel extract and fractions and their phytochemical constituents

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Abstract

Objective: *Heterotis rotundifolia* (Sm.) Jacq. Fel used traditionally by the Ibibio people of Southern Nigeria for the treatment of pain, stomach ulcer, malaria and other inflammatory diseases was evaluated for antiulcer activity. **Materials and Methods:** In this study, the effects of the extract (300-900 mg/kg) and different fractions [n-hexane (HEX), ethyl acetate (EAC), methanol (MET) and aqueous (AQU), 600 mg/kg) on experimentally induced ulcer were studied in rats using ethanol, indomethacin and histamine –induced ulcer models. **Results**: The extract (300-900 mg/kg) inhibited ethanol, indomethacin and histamine –induced ulcer models in a dose dependent fashion. The various degrees of inhibitions were statistically significant ($p<0.05$, 0.01, 0.001). The effect of the extract and the different fractions were comparable to that of the standard drugs used, the MET fraction having the highest activity. GC-MS analysis of the MET extract revealed the presence of polyunsaturated fatty acids such as tridecanoic acid-12-methyl ester, *cis*-5,8,11,14,17-Eicosapentaenoic acid, octadecanoic acid methyl ester, tetracosanoic acid, 9,12-Octadecadienoic acid (Z,Z)-, and hexadecanoic acid ethyl ester. **Conclusion**: Thus, *H. rotundifolia* demonstrated a good antiulcer activity which supports the use of this plant among the Ibibio people of Southern Nigeria ethnopharmacology for ulcer treatment.

Keywords: Antiulcer, *Heterotis rotundifolia*, phytochemistry, gastroprotective, polyunsaturated

Introduction

Peptic ulceration is a gastrointestinal disease affecting people globally, with about 10% of the world's population under the siege as a result of distortion of normal equilibrium between mucosal protective factors and aggressive factors (Narayanan *et al*., 2018; Smolic *et. al.*, 2019). Research revealed that dietary lifestyle, continuous consumption of non-steroidal anti-inflammatory drugs (NSAIDs), infections caused by Helicobacter pylori and Zollinger–Ellison syndrome are the main causes of peptic ulcer (Le *et al*., 2022; Lokman *et al*., 2022). These causative factors activate neutrophils in the gastric tissue resulting in the production of excessive amounts of reactive oxygen species (ROS) and nitrogen reactive species (RNS) leading to the depletion of endogenous antioxidant system and the development of mucosal oxidative damage (Al-Quraishy *et al*., 2017; Lanas & Chan, 2017). Common symptoms of peptic ulcers include, bleeding, burning pain in the upper abdomen, belching, nausea, vomiting and loss of appetite. Treatment for peptic ulcer includes antibiotics such as bismuth, tetracycline and metronidazole, the use of antacids, H2 blockers and proton pump inhibitors PPIs such as magnesium sulphate and lansoprazole (Waller *et al*., 2005; Katzung, 2004). Prostaglandins analogue such as

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misoprostol can advocate for prophylaxis of inflammatory-induced mucosal injury, increases mucosal resistance and inhibit acid effect. However, significant side effect such as continuous case of diarrhoea is observed, moreover, the medication is also expensive (Waller *et al.*, 2005). Currently, combination therapy of PPIs and antibiotics such as amoxicillin and clarithromycin are main therapeutic agents for peptic ulcer. These drugs have also been reported to cause adverse effects such as arrhythmias, gynaecomastia, hyperplasia**,** hematopoiesis, constipation, allergies and diarrhoea (Sandhaya *et al*., 2013). In some instances, poor absorptivity is observed (Hoogerwerf and Pasricha, 2001). Current research interest is on the utilization of herbal medicines to provide effective treatment and control strategy for diseases. This, hopefully would serve as a better alternative because of current advantages and health benefits derived (Amani *et al*., 2013; Enin *et al*., 2021a). Plant-derived-medicines are also cheaper, with lesser side effects and have a wider cultural acceptance (Dhuley, 1999; Goel and Sairam, 2002). *H. rotundifolia* (Sm.) Jac-Fel has a good profile of phytochemical constituents (Abere, 2009). Ethnopharmacologically, the plant has been used for the treatment of gastrointestinal disorders, stomach aches, venereal diseases, rheumatism, pneumonia, conjunctivitis (Gill, 1992; Yeboah, 2017). In Ibibio traditional medicine, the leaf decoction is taken for the treatment of diarrhoea, cough, bacterial infection, painful swelling, dysentery and venereal diseases (Alonge, 2006; Yeboah, 2017). It is reported to be useful in preventing miscarriages (Abere *et al*., 2009), gonorrhoea and headache (Olufemi *et al.*, 2014), conjunctivitis and infertility (Nondo *et al*., 2015). Biological activities including antidiarrhea, anti-plasmodial, antibacterial, antifertility and antioxidant activities have also been reported (Amri and Kisangau, 2012). Phytochemical studies carried out on the plant have revealed the presence of terpenes, flavonoids, tannins, alkaloid, glycosides and secondary metabolites such as vitexin (8-β-D-glucopyranosyl apigenin), isovitexin (6-β-D-glucopyranosyl apigenin), orientin (8-β-D-glycopyranosyl luteolin), isorientin (6-β-D-glycopyranosyl luteolin) and pheophytin A (Rath 1995; Pham-Huy 2008; Chisom Friday *et al*., 2021). In this study, we report the gastroprotective effects of extract and fractions of *H. rotundifolia* in ulcer-induced rats.

Materials and Methods

Plants collection

H. rotundifolia (Sm.) Jacq-Fel. was harvested in August 2021 from a farmland in Uyo, Akwa Ibom State, Nigeria and was identified and authenticated in the Department of Botany and Ecological Studies of University of Uyo, Uyo, Nigeria. Herbarium specimen (UUlt4153) was deposited at Department of Botany, Faculty of Science Herbarium.

Extraction

The plant (stem) was washed, and air-dried for two weeks and reduced to powder using laboratory mill. The powdered material (350 g) was successively macerated with 1000 mL of n-hexane (HEX), ethyl acetate (EAC) and methanol (MET). The liquid filtrate was concentrated and evaporated to dryness *in vacuo* and stored in air tight bottles at 4 °C until use. Another 120 g was soaked in 50% ethanol to obtain the ethanol crude extract. The extract and fractions were stored in a refrigerator at 4˚C until use. Extraction yields of fractions and extract are reported (Table 1).

Phytochemical analyses

Preliminary phytochemical analysis was conducted according to methods described by Yadav and Agrawala (2011) and Patle *et al*. (2020) for the determination of saponins, tannins, phlobatanins, flavonoids, alkaloids, steroids, cardiac glycosides, carbohydrates and terpenes.

Animals

Swiss albino male rats (145 – 170g) used for these experiments were obtained from Animal house of Department of Pharmacology and Toxicology, University of Uyo. The animals were housed in standard cages and were maintained on a standard pelleted feed (Guinea Feed) and water *ad libitum*. Permission and approval for animal studies (UU/CS/AE/14/63) were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo, Uyo.

Determination of median lethal dose (LD_{50})

The median lethal dose (LD_{50}) of the extract was estimated using albino mice by intraperitoneal (i.p) route using a standard method (Lorke, 1983). This involved intraperitoneal administration of different doses of the fractions (100-1000 mg/kg) to groups of three mice each. The animals were observed for manifestation of physical signs of toxicity such as writhing, decreased motor activity, decreased body/limb tone, decreased respiration and death. The number of deaths in each group within 24 hours was recorded. The median
lethal dose (LD_{50}) was determined as;

$$LD_{50} = \sqrt{AB}$$

Where A = maximum dose producing 0% mortality

B = minimum dose producing 100% mortality

Indomethacin-induced ulcer

Male adult albino rats used for the experiment were randomly divided into 9 groups of six rats each. The animals were deprived of food 24 h and water 2 h prior to

the experiment (Alphin and Ward, 1967). Group 1 (control) received only indomethacin (Sigma, 60 mg/kg p.o. dissolved in 5% Na_2CO_3); groups 2 - 4 were pre-treated with the stembark extract 300, 600 and 900 mg/kg respectively, while groups 5-8 were pretreated with different fractions (n-hexane, ethyl acetate, methanol and aqueous, 600 mg/kg) of the plant dissolved in distilled water and administered as aqueous suspension. Dosage in all cases was 600 mg/kg. Group 9 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80). One-hour post administration of the extract, groups 2-9 were administered with indomethacin. Four hours after indomethacin administration, animals were sacrifice by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al*., 1996). Ulcer index (UI) and preventive ratio (PR) of each of the groups pre-treated with fractions were calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al*., 2000). Ulcer index represents the degree of lesion or ulceration caused by the ulcerogen, while preventive ratio is the protective potential of the extract/drug.

Ethanol-induced gastric ulceration

The procedure was similar to that used in indomethacin induced ulceration. The rats were randomly assigned into nine groups of six rats each based on their body weight. Food was withdrawn 24 hours and water 2h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only ethanol (2.5 mL/kg p.o), groups 2 - 4 were pre-treated with the stembark extract 300, 600 and 900 mg/kg respectively, while groups 5-8 were pre-treated with different fractions (n-hexane, ethyl acetate, methanol and aqueous, 600 mg/kg) of the plant dissolved in distilled water and administered as aqueous suspension. Group 9 received propranolol (40 mg/kg p.o. dissolved in distilled water). One hour later, groups 2- 9 were administered with ethanol. Four hours after ethanol administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al*., 2000).

Histamine-induced gastric ulceration in rats

Adult male albino rats weighing 140- 170 g were used for the experiment. They were randomized into 9 groups of six rats each. Food was withdrawn 24 hours and water 2 h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only histamine acid phosphate (Sigma, 100 mg/kg i.p. dissolved in distilled water) (Maity *et al*.,1995); groups 2 - 4 were pre-treated with the stembark extract 300, 600 and 900 mg/kg respectively, while groups 5-8 were pre-treated with different fractions (n-hexane, ethyl acetate, methanol and aqueous, 600 mg/kg) of the plant dissolved in distilled water and administered as aqueous suspension; group 9 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80), 1 hour prior to histamine administration. One hour later, groups 2- 9 were administered with histamine acid phosphate (100 mg/kg, i.p). 18 hours after histamine administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al*., 1996). Ulcer indexes (UI) and preventive ratio (PR) of each of the groups pretreated with the extract were calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al*., 2000).

Gas Chromatography-Mass Spectrometer Analysis

H. rotundifolia methanol extract was subjected to a GCMS analysis. The methanol extract (500 µL) was transferred to a GC vial and injected onto a GCMS-QP2010SE SHIMADZU, Japan on a spitless injector. Column flow was set to 1.0 mL/min using helium as the carrier gas. The temperature program started with a temperature of 60 ^{0}C held for 1 min; a ramp of 5 ^{0}C/min to 180 ^{0}C, followed by a ramp of 20 ^{0}C/min to 250 ^{0}C. Data were acquired by means of GC solution software.

Statistical Analysis

Data are reported as mean ± standard error of the mean (SEM) and were analyzed statistically using One-way ANOVA followed by Turkey-Kramer multiple comparison. test and values of $p < 0.01$ were considered significant.

Results

Percentage Weight of sample

The percentage weights of the fractions were 3.7, 3.3, 2.5 and 4.6%, while the ethanol extract afforded 10.27% (Table 1).

Table 1. Extracts yield of *H. rotundifolia*

S/N	Fractions	Weight (g)	Yield (%)
1.	HEX	13.13	3.75
2.	EAC	11.56	3.30
3.	MET	8.90	2.54
4.	AQU	16.32	4.66
5.	ETH	12.32	10.27

Acute Toxicity Test Result

Extract exhibited an LD_{50} value above 5000 mg/kg having shown no mortality at all the doses tested. Based on Lorke's rule (Lorke,1983), the extract is assumed to be safe with negligible toxicity. Invariably, the experimental doses used were relatively safe.

Phytochemical screening

The phytochemical screening of extract and fractions revealed the presence of alkaloids, cardiac glycosides, tannins, saponins, terpenes and flavonoids (Table 2).

Effect of fractions on indomethacin –induced ulcer

The extract (300-900 mg/kg) and fractions pretreatment (p.o.) on indomethacin-induced gastric ulceration showed dose-dependent and significant (p<0.05-0.001) reductions in ulcer indices in pretreated groups relative to control. Methanol fraction was found to exert the highest reductive effect (66.66%) followed by aqueous fraction (61.16%) and the highest dose (900 mg/kg) had preventive ratio of 91.66% Ulcerations observed in the stomachs of the extract/fractions-pretreated groups were pinpoint wounds and no severe wound compared to that present in the stomach of the animals in the control group. The standard drug, cimetidine, was the most effective with preventive ration of 94.50 % (Table 3).

Effect of fractions on ethanol –induced ulcer

Pretreatment of rats with extract and fractions of H. rotundifolia offered considerable protection to the animals from ethanol–induced ulcer (Table 4). This protection was dose-dependent and significant (p<0.05-0.01) as shown in the reduction of ulcer indices relative to control. The highest dose of the extract (900mg/kg) and *n*-hexane fraction had the highest effect with preventive ratio of 86.80% which was similar to that of the standard drug, propranolol-treated group. Ethyl acetate fraction had a preventive ratio of 73.80%. The standard drug, propranolol, gave a preventive ratio of 86.80% (Table 4).

Effect of fractions on histamine –induced ulcer

Administration of the extract and fractions of *H. rotundifolia* exerted a dose dependent and significant (p<0.01-0.001) reductions in histamine-induced gastric ulceration at all doses and fractions-treated groups when compared to control (Table 3). The highest dose of the extract (900 mg/kg), ethyl acetate and methanol fractions

Table 2.Preliminary phytochemical screening of *H. rotundifolia*

TEST	HEX	EAC	MET	AQU	ETH
Saponins	+++	++	++	+	+
Tannins	-	-	+++	++	+++
Phlobatanins	-	-	++	+	NC
Flavonoids	-	-	++	+	++
Alkaloid	-	-	+	+	+
Terpenoid	-	-	+	-	++
Steroid	+++	+	+	+	++
Cardiac glycoside	+++	+	++	+	++
Carbohydrate	-	+	++	+	+++
Anthraquinones	-	-	-	-	-

Where +++ shows strong presence, ++ shows partially strong, + shows weak and − shows absence of phytochemical contents, NC means not confirmed.

Table 3. Effect of fractions on indomethacin-induced ulcer

Treatment	DOSE (mg/kg)	Ulcer indices	Preventive ratio
Control normal	60	12.00 ±0.57	-
Indomethacin			
Cimetidine	100	0.66 ±0.66^{c}	94.50
Extract	300	6.00±1.72^{a}	50.00
	600	2.66±0.33^{c}	77.83
	900	1.00±0.50^{c}	91.66
n-Hexane fraction	600	5.33±1.33^{a}	55.58
Ethyl acetate fraction	600	5.33 ± 1.33^{a}	55.58
Methanol fraction	600	4.00 ± 0.00^{b}	66.66
Aqueous fraction	600	4.66 ± 1.70^{b}	61.16

Data are expressed as MEAN ± SEM, Significant at $^{a}p < 0.05$, $^{b}p<0.01$, $^{c}p<0.001$, when compared to control. (n=6).

Table 4. Effect of fractions on ethanol-induced ulcer

Treatment	DOSE (mg/kg)	Ulcer indices	Preventive ratio
Control normal	60	5.00 ±0.33	-
Propranolol	40	0.66 ±0.33^{c}	86.80
Extract	300	3.66±0.33^{a}	26.80
	600	2.00±0.57^{b}	60.00
	900	0.66±0.33^{c}	86.80
n-hexane fraction	600	0.66±0.33^{c}	86.80
Ethyl acetate fraction	600	1.33± 0.33^{c}	73.40
Methanol fraction	600	1.00 ± 0.00^{c}	80.00
Aqueous fraction	600	2.66 ± 0.33^{c}	46.80

Data are expressed as MEAN ± SEM, Significant at $^{a}p < 0.05$, when compared to control. (n=6).

Table 5. Effect of fractions on histamine-induced ulcer

Treatment	DOSE (mg/kg)	Ulcer indices	Preventive ratio
Control normal	-	4.00 ±0.16	-
Cimetidine	100	0.00 ±0.00^{c}	100
Extract	300	1.33±0.33^{b}	66.75
	600	0.50±0.28^{c}	87.50
	900	0.66 ±0.23^{c}	83.50
n-Hexane fraction	600	1.33±0.33^{b}	66.75
Ethyl acetate fraction	600	0.66± 0.16^{c}	83.50
Methanol fraction	600	0.66 ± 0.16^{c}	83.50
Aqueous fraction	600	1.33 ± 0.33^{b}	66.75

Data are expressed as MEAN ± SEM, Significant at $^{a}p < 0.05$, $^{b}p<0.01$, $^{c}p<0.001$, when compared to control. (n=6).

Table 6. GC-MS analysis of *H. rotundifolia* methanol fraction.

No	Compound	Retention time (RT)	Sum of Area (%)
1.	Benzene, 1,2,3-trimethyl-	5.677	0.14
2.	Undecane	5.837	0.09
3.	Dodecanoic acid, methyl ester	11.758	0.12
4.	Dodecanoic acid	12.306	0.97
5.	1-Hexadecanol	1 2.560	0.18
6.	Cyclohexane, decyl-	13.206	0.03
7.	Tridecanoic acid, 12-methyl-, methyl ester	13.696	0.19
8.	Tetradecanoic acid	14.163	1.45
9.	1-Nonadecene	14.427	0.25
10.	Nonadecane	14.510	0.13
11.	2-Pentadecanone, 6,10,14-trimethyl-	14.800	0.21
12.	3-Eicosyne	14.843	0.51
13.	Pentadecanoic acid	14.974	0..23
14.	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	15.040	0.40
15.	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	15.202	0.28
16.	7-Hexadecenoic acid, methyl ester, (Z)-	15.265	0.15
17.	2-methylhexacosane	15.365	0.14
18.	Hexadecanoic acid, methyl ester	15.466	1.19
19.	Dibutyl phthalate	15.596	0.20
20.	1-Decanol, 2-hexyl-	15.667	0.27
21.	Cyclohexanol, 5-methyl-2-(1-methylethyl)-,	15.718	0.23
22.	n-Hexadecanoic acid	16.124	13.80
23.	Eicosane	16.200	0.59
24.	Heptadecanoic acid, methyl ester	16.292	0.33
25.	n-Hexadecanoic acid	16.711	0.75
26.	Methyl 10-trans,12-cis-octadecadienoate	16.931	7.88
27.	9-Octadecenoic acid, methyl ester, (E)-	17.013	4.41
28.	Tetratetracontane	17.093	0.18
29.	Methyl stearate	17.201	0.85
30.	9,12-Octadecadienoic acid (Z,Z)-	17.777	39.51
31.	Octadecanoic acid	17.992	8.68
32.	9,12-Octadecadienoic acid (Z,Z)-	18.283	0.65
33.	5,8,11,14-Eicosatetraenoic acid, methyl ester,	18.492	0.56
34.	6,9,12-Octadecatrien-1-ol	18.703	0.56
35.	8,11,14-Eicosatrienoic acid, (Z,Z,Z)-	18.833	0.63
36.	*cis*-5,8,11,14,17-Eicosapentaenoic acid	19.067	1.38
37.	Palmitoleic acid	19.386	1.27
38.	Eicosanoic acid	19.658	1.73
39.	Octacosanol	19.961	0.34
40.	Pentadecanal-	20.167	0.11
41.	*cis*-5,8,11,14,17-Eicosapentaenoic acid	20.734	0.45
42.	*Bis*(2-ethylhexyl) phthalate	21.043	0.75
43.	(R)-(-)-14-Methyl-8-hexadecyn-1-ol	21.183	0.13
44.	Docosanoic acid	21.362	0.48
45.	1-Heneicosanol	21.671	0.22
46.	1,3-Benzenedicarboxylic acid, bis(2-ethylhexyl	22.689	0.26
47.	Cyclohexane, 1-(1-tetradecylpentadecyl)-	23.164	0.27
48.	Heptadecafluorononanoic acid, undecyl ester	23.498	0.49
49.	Tetracosanoic acid	23.967	0.56
50.	Stigmasta-5,22-dien-3-ol, acetate, (3 beta.)-	24.096	0.46
51.	Pregnane-3,17,20-triol, cyclic 17,20-[(1,1-dime	24.482	1.39
52.	δ-D-Mannofuranoside, 2,3:5,6-DI-O-ethyl	24.892	0.92

were found to exert the highest effect with preventive ratio of 83.50%. However, the standard drug, cimetidine produced a preventive ratio of 100% (Table 5).

Discussion

H. rotundifolia is used traditionally to treat various gastrointestinal disorders. For this reason, the antiulcer activity of the extract and fractions was evaluated using indomethacin, ethanol and histamine–induced ulcer models. Indomethacin is known to cause ulcer especially in an empty stomach (Bhargava *et al*., 1973) and mostly on the glandular (mucosal) part of the stomach (Evbuonwa and Bolarinwa, 1990; Nwafor *et al*., 1996) by inhibiting prostaglandin synthetase through the cyclooxygenase pathway (Rainsford, 1987). Prostaglandins function to protect the stomach from injury by stimulating the secretion of bicarbonate and mucus, maintaining mucosal blood flow and regulating mucosal turn over and repair (Hayllar and Bjarnason, 1995; Hiruma-Lima *et al*., 2006). Suppression of prostaglandins synthesis by indomethacin results in increase susceptibility of the stomach to mucosal injury and gastroduodenal ulceration. The extract and fractions were observed to significantly reduce mucosal damage in the indomethacin–induced ulcer model, suggesting the possible extracts mobilization and involvement of prostaglandin in the anti-ulcer effect of the extracts (Table 3). Administration of ethanol has been reported to cause disturbances in secretion, damage to the mucosa, alterations in the permeability, gastric mucus depletion and free radical production (Salim, 1990). This is attributed to the release of superoxide anion and hydroperoxy free radicals during metabolism of ethanol as oxygen derived free radicals has been found to be involved in the mechanism of acute and chronic ulceration in the gastric mucosa (Pihan *et al*.,1987). It was observed in this study that the fractions significantly reduced ethanol induced ulcer. This may be due to the cytoprotective and antioxidant effects of the extract. Ethanol is also reported to cause gastric mucosal damage by stimulating the formation of leukotriene C4 (LTC4) (Whittle *et al*., 1985). The extract probably could have caused significant suppression of lipoxygenase activity (Nwafor *et al*., 1996).

Histamine-induced ulceration is known to be mediated by enhanced gastric acid secretion as well as by vasospastic action of histamine (Cho and Pfeiffer, 1981). The fractions were found (Table 5) to have considerable effect suggesting its potential in inhibiting gastric acid secretion and maybe vasospastic activity of histamine.

Phytochemical analysis of *the* extract and fractions revealed the presence of saponins, steroids and cardiac glycosides (Table 2). Alkaloids, terpenoids, saponins, cardiac glycosides, phlobatannins and tannins were found to be present in the MET fraction and ETH extract. However, a negative test was observed for alkaloids, flavonoids, tannins, phlobatannins, and terpenoids in the HEX and EAC, fractions. All the extracts also demonstrated a negative test for anthraquinone. Generally, results obtained from the antiulcer study demonstrate that the methanol extract exhibited a remarkable gastroprotective effect in the various *tested* models. Further analysis of the methanol extract by GC-MS revealed mostly, the presence of polyunsaturated fatty acids, phenols among others (Table 6). Polyunsaturated fatty acids such as p-hydroxycinnamic acid ethyl ester, stigmasterol, docosanoic acid ethyl ester, octadecanoic acid methyl ester, 9-octadecenoic acid (Z)-ethyl ester and hexadecanoic acid ethyl ester have been implicated in antiulcerogenic activity and this activity has been reported to increase with the degree of unsaturation Kumaratilake *et al*., 1992; Thomas *et al*., 1994; Krugliak *et al*., 1995; Suksamrarn *et al*., 2005). Also, alkaloids, flavonoids and triterpenoids have been reported to possess gastroprotective properties (Kirby *et al*., 1989; Philipson & Wright, 1991; Christensen & Kharazmi, 2001). The extract has been reported to be rich in flavonoids and other phenolic compounds (Rath, 1995; Pham-Hug, 2008; Chisom Friday *et al.,* 2021). Flavonoids such as quercetin have been reported to prevent gastric mucosal lesions in various experimental models by increasing the quantity of neutral glycoproteins (Di Carlo *et al*., 1999; Zayachkivska, 2005). Flavonoids protect the gastric mucosa from damage by increasing the mucosal prostaglandin content and by inhibiting histamine secretion. Phenolics and terpenoids have played a substantial role in the development of human medicine as antioxidants, and through their free radical scavenging, and gastroprotective actions (Enin *et al*., 2021b; Jabbar, 2022; Li *et al*., 2022). In this study, we summarized therefore, that these chemical compounds which are found to be present in this extract and fractions may be responsible for the observed antiulcerogenic activities

Conclusion

The results of the present study show that *H. rotundifolia* stem displays gastroprotective activity as demonstrated by inhibition of the formation of ulcers induced through the three different ulcer models. This supports its use in the treatment of gastrointestinal disorders in traditional medicine.

Declaration of competing interest

The authors declare no conflict of interest.

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