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# Protective Antiulcer Property of *Ricinodendron heudelotii (Euphorbiaceae*) Seed Oil and Its GC/MS Profile

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## ABSTRACT

**Background and Purpose:** Peptic ulcer has remained a disease of public health concern. Current therapies are not ideal, necessitating the search for better alternatives. This study evaluated the antiulcer property of *Ricinodendron heudelotii* in rats.

**Methods:** Seed oil from *R. heudelotii* was extracted and subjected to qualitative phytochemical screening. Gas chromatography/ mass spectrometry (GC/MS) was performed to determine its phytoconstituents. Oral acute toxicity and antiulcer property were evaluated in male Sprague-Dawley rats. The animals were pretreated with doses of 20 and 40 mL/kg of the seed oil on ethanol and aspirin-induced gastric ulcer models with ulcer index, percentage ulcer protection, gastric volume, and gastric pH as the parameters, and cimetidine as the standard drug.

**Results:** Qualitative analysis of the oil showed the presence of alkaloids, flavonoids, tannins, phenols, saponins, glycosides, steroids, and fixed oil. GC/MS characterization of the oil revealed 21 distinct constituents with phthalates as the most abundant. There were no noticeable toxicological signs at the dose of 5000 mL/kg. Pretreatment with 20 mL/kg and 40 mL/kg of the seed oil, and 400 mg/kg of cimetidine protected by 65.45%, 56.70% and 65.74% respectively against ethanol-induced gastric ulcers. Similarly, in aspirin-induced ulcers, protection was 70.26%, 71.35%, and 64.23% following pretreatment with cimetidine (400 mg/kg), seed oil (20 mL/kg) and seed oil (40 mL/kg) respectively. Gastric volume and gastric pH were significantly reduced in rats pretreated with the seed oil or cimetidine in comparison with control.

**Conclusion:** The seed oil extract from *R. heudelotii* appears safe and has a protective effect against animal models of gastric ulcers. Therefore, the oil has potential for use in the treatment of peptic ulcer disease.

## INTRODUCTION

Peptic ulcer disease (PUD) is associated with a disparity between factors that are protective and those that are offensive. The disease involves hyperacidity, damage to the mucus barrier, increase in reactive oxygen species, and peroxidation with attendant inflammatory mediators (Rozza *et al*., 2015). It has been estimated that the prevalence of gastric ulcers in the world may range from 20% to 30% with a high relapse rate of approximately 60% (Ren *et al*., 2022). *Helicobacter pylori* infection contributes to development of PUD, with symptoms such as nausea, epigastric pain, fullness, and bloating (Zulfiqar *et al*., 2024). PUD can be aggravated by stress, smoking, alcohol, poor nutrition, and non-steroidal anti-inflammatory drugs (NSAIDs) (Andreo *et al*., 2006). The pro ulcer factors (physical, psychological, chemical) are naturally countered by protective factors like mucin, bicarbonate, prostaglandins $I_2/E_2$, blood flow, antioxidants, sulfhydryl compounds, nitric oxide, and cell regeneration/growth factors (Almasaudi *et al*., 2017). Clinically, ulcer management involves the promotion of protective factors while minimizing mucosal disruption by pro factors. Antiulcer drugs include proton pump inhibitors, $H_2$-receptor antagonists, antacids, antibiotics, prostaglandin analogs, and mucosal protective agents (Beserra *et al*., 2011; Almasaudi *et al*., 2017). The aforementioned agents, though effective, have drawbacks like toxicity, poor symptom control, relapse, tolerance, and are often not affordable by an average family in sub-Saharan Africa (Rozza *et al*., 2015). These drawbacks have increased the use of herbal alternatives. Herbs are known to be richly endowed with secondary metabolites that have antioxidant, anti-inflammatory, inhibition of gastric acidity, and muco-protective properties (Bi *et al*., 2014; Abdelzaher *et al*., 2017).

*Ricinodendron heudelotii*, also known as "njangsa" by the Bangangté tribe of Cameroon and "ọrùnmọdò" by the Yoruba tribe of Nigeria, is a tree that bears oily seeds and is known for its medicinal values (Odinga *et al*., 2016). It is native to many African countries especially those in east and west Africa. It is a multipurpose tree that provides food and many valuable products to the local population (Oti *et al*., 2024). In Cameroonian folk medicine, parts of the plant are used for the treatment of poison, stomach pains, malaria, rheumatism, menstrual pains, among others. The seed is rich in phenolics, flavonoids, alkaloids, tannins, saponins, and carotenoids (Odinga *et al*., 2016), a light-yellow sweet tasting oil that is approximately 47% w/w of the seed, and some compounds believed to be toxic (Tachie *et al*., 2024).

This study aimed to establish the gastroprotective property of the seed and a GC/MS characterization of the constituents.

## MATERIALS AND METHODS

### Drugs and Chemicals

Ethanol was purchased from Sigma-Aldrich via a local representative in Nigeria. Cimetidine (Tagamet®, GlaxoSmithKline) was purchased from a representative and used as a reference drug while aspirin (Bayer Pharm Co.) was also obtained from a representative. Cimetidine was prepared in water while aspirin was suspended in 1% carboxymethylcellulose. All other chemicals used in this study were of analytical grade.

### Plant Material and Oil Extraction

Dried seeds of *R. heudelotii* were obtained from a forest at the outskirts of Port Harcourt, Rivers State, Nigeria which lies within latitudes 4°20' and 5°50'N and longitudes 6°20' and 7°35'. The dried seeds were identified by a taxonomist at the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Enugu State University of Science and Technology, Enugu, Nigeria where a voucher specimen was deposited with reference FPS/Pharm/15/214.

The seeds were air dried until constant weight and ground with a mechanical grinder to obtain a coarse powder. The ground powder was extracted with n-hexane (1500 mL) and allowed to stand for 72 h with intermittent shaking in the morning and evening. The extract was concentrated in a rotary evaporator at 35ºC. The floating oil was recovered from the seed by decantation and stored in an airtight container until used (Nwachukwu, 2019).

### Qualitative Phytochemical Analysis of the Seed Oil

The qualitative phytochemical analysis of the oil extracted from *R. heudelotii* seeds was performed following standard methods (Mumtaz *et al*., 2014).

### Gas chromatography-mass spectrometry (GC/MS) analysis

GC/MS analysis was performed via a combined 7890A gas chromatography system (Agilent 19091-433HP, USA) and mass spectrophotometer, attached with an HP-5 MS fused silica column (5% phenyl methyl siloxane 30.0 m × 250 µm, film thickness 0.25 µm), and interfaced with 5675C Inert MSD with Triple-Axis detector. Helium gas was the carrier gas and a column velocity flow of 1.0 ml/min was used. GC-MS conditions are ion-source temperature, 250 °C; interface temperature, 300°C; pressure, 16.2 psi; out time, 1.8 mm; and 1 µL injector in split mode with split ratio 1:50 with injection temperature of 300°C. The relative percentage amount of each component was calculated by comparing its average peak area to total area. Identification of components was performed using their retention indices and interpretation of mass spectrum was conducted based on the database of the

National Institute of Standards and Technology (NSIT) (Okolo and Orisakwe, 2021).

**Experimental Animals**

Apparently healthy male Sprague-Dawley rats (150 – 170 g) were purchased from the animal house of the Department of Pharmacology, Enugu State University of Science and Technology, Nigeria. They were housed in cages with raised floors to prevent coprophagy (Chen *et al*., 2015; Almasaudi *et al*., 2017). All animal experiments were carried out according to the guidelines and protocols approved by Enugu State University of Science and Technology Research Ethics Committee, with the reference number ESUT/REC/2023/056.

**Oral Acute Toxicity Test**

The rats were housed in steel cages and allowed to acclimatize for two weeks with food and water *ad libitum*. The rats were given the oil at doses ranging from 5 mL/kg to 50 mL/kg using an orogastric tube. The animals were examined for toxicological symptoms such as changes in behavior, feeding, defecation, and death (Okolo *et al*., 2020).

**Ulcer Induction**

The animals were allowed access to food and water 24 h before induction of ulcer but water was withdrawn 2 h before the experiment. Gastric ulcer was induced by administering absolute ethanol (5 mL/kg) by gavage. Aspirin, suspended in 1% carboxymethylcellulose was administered *per os* at a dose of 500 mg/kg (Shah and Patel, 2012; Al Batran *et al*., 2013). One-hour post-induction, the animals were given 20 or 40 mL/kg of the oil. Six hours post-induction, the animals were sacrificed, and stomachs were removed and opened along the greater curvature for determination of ulcer index (UI) using the formula:

$$UI = \frac{10}{X}$$

$$\text{Where } X = \frac{\text{Total Mucosal area}}{\text{Total ulcerated area}}$$

The acid secretory parameters like pH, titratable acid, and volume of gastric secretion were also measured (Cairns *et al*., 2002; Shah and Patel, 2012).

**Statistical Analysis**

All the values represent the mean ± standard error of mean. The differences between different groups were analyzed using one-way analysis of variance (one-way ANOVA) followed by Tukey's post hoc test (GraphPad Prism Statistical Software version 9.0., San Diego, California, USA). A p-value of less than 0.05 was considered statistically significant.

## RESULTS

**Qualitative Phytochemical Screening of the Seed Oil**

Table 1 shows the classes of phytoconstituents of *R. heudelotii* oil seed. Alkaloids, flavonoids, tannins, phenols, saponins, glycosides, steroids, and fixed oils were present.

**GC/MS Identified Phytoconstituents of the Seed Oil**

Table 2 shows the phytoconstituents of *R. heudelottii* as detected by gas chromatography/mass spectrometry analysis. The phytochemicals detected are phthalate esters (74.05%), fatty acids (12.34%), amides (7.67%), hydrocarbons (4.79%), and alcohols (1.15%). The chromatogram showing retention time and peak sizes of the compounds are shown in Figure 1 while the structures of some are shown in Figure 2.

**Effect of Pretreatment with the Seed oil on Ulcer Index in Ethanol-induced Gastric Ulcers**

Table 3 shows the effect of pretreatment with *R. heudelotii* seed oil on ethanol-induced gastric ulcers in rats. Administration of ethanol significantly ($P$<0.001) increased the ulcer index but pretreatment with the oil significantly reduced the ulcer index and protected the gastric mucosa from ethanol induced damage.

**Effect of Pretreatment with the Seed Oil on Ulcer Index in Aspirin-induced Gastric Ulcers**

The effect of pretreatment with *R. heudelotii* seed oil on aspirin-induced gastric ulcers in rats is shown in Table 4. Administration of aspirin significantly ($P$<0.001) increased the ulcer index, but pretreatment with the seed oil significantly reduced the ulcer index and protected the gastric mucosa from aspirin-induced damage.

**Effect of Pretreatment with the Seed Oil on pH and Gastric Volume in Ethanol-induced Gastric Ulcers**

Table 5 shows the effect of pretreatment with the seed oil of *R. heudelotii* on pH, and gastric volume in ethanol-induced gastric ulcer in rats. Administration of ethanol significantly ($P$<0.001) increased gastric volume while decreasing pH. Pretreatment with the oil significantly attenuated increased gastric volume while significantly ($P$< 0.001) increasing the pH. While ethanol reduced the pH to 1.64 ± 0.38 in ethanol only group, *R. heudelotti* seed oil dose-dependently increased the pH as seen in the groups that received 20 mL/kg and 40 mL/kg of oil to be 5.58±0.42 and 5.44±0.48 respectively. Ethanol significantly increased gastric volume to 3.36±0.41 mL when compared to normal rats that had the value of 0.88±0.26 mL. Pretreatment with the seed oil significantly and dose-dependently reduced the volume to 1.22±0.44 mL and 0.88 ± 0.25 mL respectively at the doses of 20 mL/kg and 40 mL/kg.

**Effect of Pretreatment with the *Seed* Oil on pH and Gastric Volume in Aspirin-induced Gastric Ulcers**

The effect of *R. heudelotti* seed oil on aspirin induced gastric volume and pH is as presented in Table 6. Administration of aspirin significantly ($P$<0.001) decreased the pH of the gastric fluid (1.43±0.38) when compared to normal control. However, treatment with cimetidine and oil from *R. heudelotti* seed ameliorated this phenomenon dose-dependently as seen in the values of groups that received either cimetidine or 20 mL/kg or 40 mL/kg of oil (5.48±0.42, 5.55±0.55, and 5.18±0.73) respectively. Furthermore, aspirin significantly increased the gastric volume (3.40±0.45 mL) as against the control (0.88±0.26 mL). Treatment with cimetidine or oil from *R. heudelotti* seed oil improved this pathological distortion as seen in the values of gastric volume of the groups treated with cimetidine, 200 mg or 400 mg (1.34±0.63 mL, 1.25±0.35 mL, and 1.50±0.72 mL) respectively. The dose of 20 mL/kg of *R. heudelotti* seed oil group seemed to have a better effect than the dose of 40 mL/kg.

**Table 1:** Classes of phytochemicals in the oil from *R. heudelottii* seed extract.

| Constituents | Results |
|---|---|
| **Alkaloids** | + |
| **Flavonoids** | + |
| **Tannins** | + |
| **Phenols** | + |
| **Saponins** | + |
| **Glycosides** | + |
| **Steroids** | + |
| **Fixed oil** | + |

+ represents present.

**Table 2:** Phytocompounds compounds detected by GC/MS.

| Peak | Retention Time | % Area | Molecular formula | Molecular weight (g/mol) | Compound name/ Synonyms |
|---|---|---|---|---|---|
| 1 | 16.894 | 0.67 | $C_{18}H_{36}$ | 252.5 | Cetene<br>1-Octadecene<br>**Octadec-1-ene** |
| 2 | 17.785 | 0.56 | $C_{12}H_{20}O_7$ | 276.28 | Triethyl citrate<br>Ethyl citrate<br>**Triethyl 2-hydroxypropane-1,2,3-tricarboxylate** |
| 3 | 19.299 | 1.35 | $C_{19}H_{38}$ | 266.5 | 1-Nonadecene<br>Nonadecene<br>**Nonadec-1-ene** |
| 4 | 19.832 | 0.76 | $C_{15}H_{24}O$ | 220.35 | 1-Formyl-2,2-dimethyl-3-trans-(3-methyl-but-2-enyl)-6-methylidene-cyclohexane<br>2,2-Dimethyl-3-(3-methyl-2-butenyl)-6-methylenecyclohexanecarbaldehyde<br>**1*S*,3*R*)-2,2-dimethyl-3-(3-methylbut-2-enyl)-6-methylidenecyclohexane-1-carbaldehyde** |
| 5 | 20.264 | 14.57 | $C_{20}H_{30}O_4$ | 334.4 | Phthalic acid, isobutyl octyl ester<br>**2-*O*-(2-methylpropyl) 1-*O*-octyl benzene-1,2-dicarboxylate** |
| 6 | 20.609 | 1.15 | $C_{15}H_{26}O_2$ | 238.3657 | (3S,3aS,6R,7R,9aS)-1,1,7-Trimethyldecahydro-3a,7-methanocyclopenta [8] annulene-3,6-diol<br>4,4,8-Trimethyltricyclo [6.3.1.0(1,5)] dodecane-2,9-diol<br>**2-[(2*R*,4*aR*,8*aR*)-4*a*,8-dimethyl-2,3,4,5,6,8*a*-hexahydro-1*H*-naphthalen-2-yl] prop-2-en-1-ol** |

**Table 2:** Phytocompounds compounds detected by GC/MS **(CONT'D)**

| | | | | | |
|---|---|---|---|---|---|
| 7 | 20.770 | 0.61 | $C_{30}H_{50}O_4$ | 474.7 | Phthalic acid, isobutyl octadecyl ester<br>isobutyl octadecyl phthalate<br>**2-*O*-(2-methylpropyl) 1-*O*-octadecyl benzene-1,2-dicarboxylate** |
| 8 | 21.469 | 1.08 | $C_{19}H_{38}$ | 266.5 | 1-Nonadecene<br>Nonadecene<br>**Nonadec-1-ene** |
| 9 | 22.421 | 58.31 | $C_{24}H_{38}O_4$ | 390.6 | Bis(2-ethylhexyl) phthalate<br>Di(2-ethylhexyl) phthalate<br>**Bis(2-ethylhexyl) benzene-1,2-dicarboxylate** |
| 10 | 23.443 | 0.93 | $C_{22}H_{44}$ | 308.6 | 1-Docosene<br>Docosene<br>**Docos-1-ene** |
| 11 | 24.312 | 7.67 | $C_{18}H_{19}NO_2S$ | 313.4 | 1,2,3,4-Tetrahydroquinoline trans-2-phenyl-1-cyclopropanesulfonamide<br>Quinoline, 1,2,3,4-tetrahydro-1-((2-phenylcyclopropyl)sulfonyl)-, trans-<br>**1-[(1*S*,2*R*)-2-phenylcyclopropyl]sulfonyl-3,4-dihydro-2*H*-quinoline** |
| 12 | 24.889 | 12.34 | $C_{22}H_{46}O_2Si$ | 370.7 | (Trimethylsilyl)methyl stearate<br>**Trimethylsilylmethyl octadecanoate** |

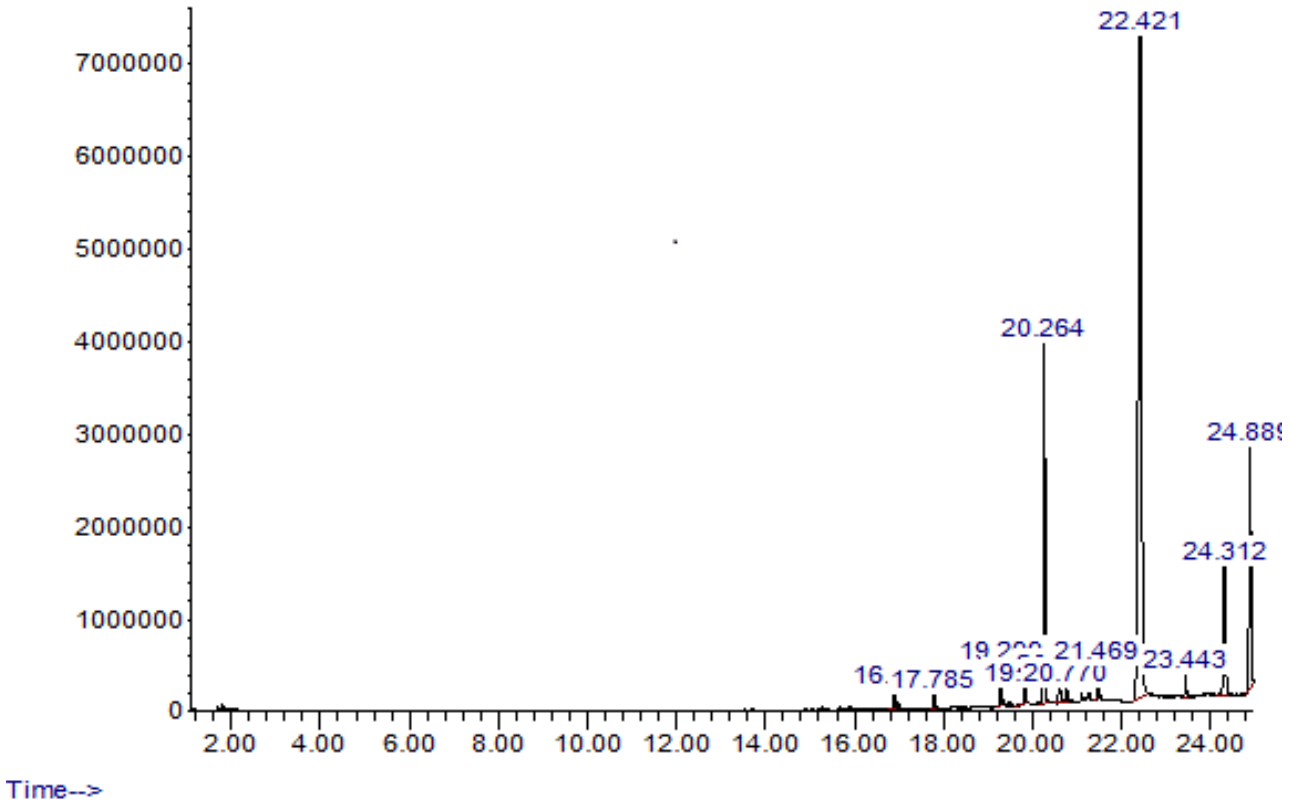


**Figure 1:** The chromatogram of gas chromatography/mass spectrometry analysis of *R. heudelotii* seed oil.

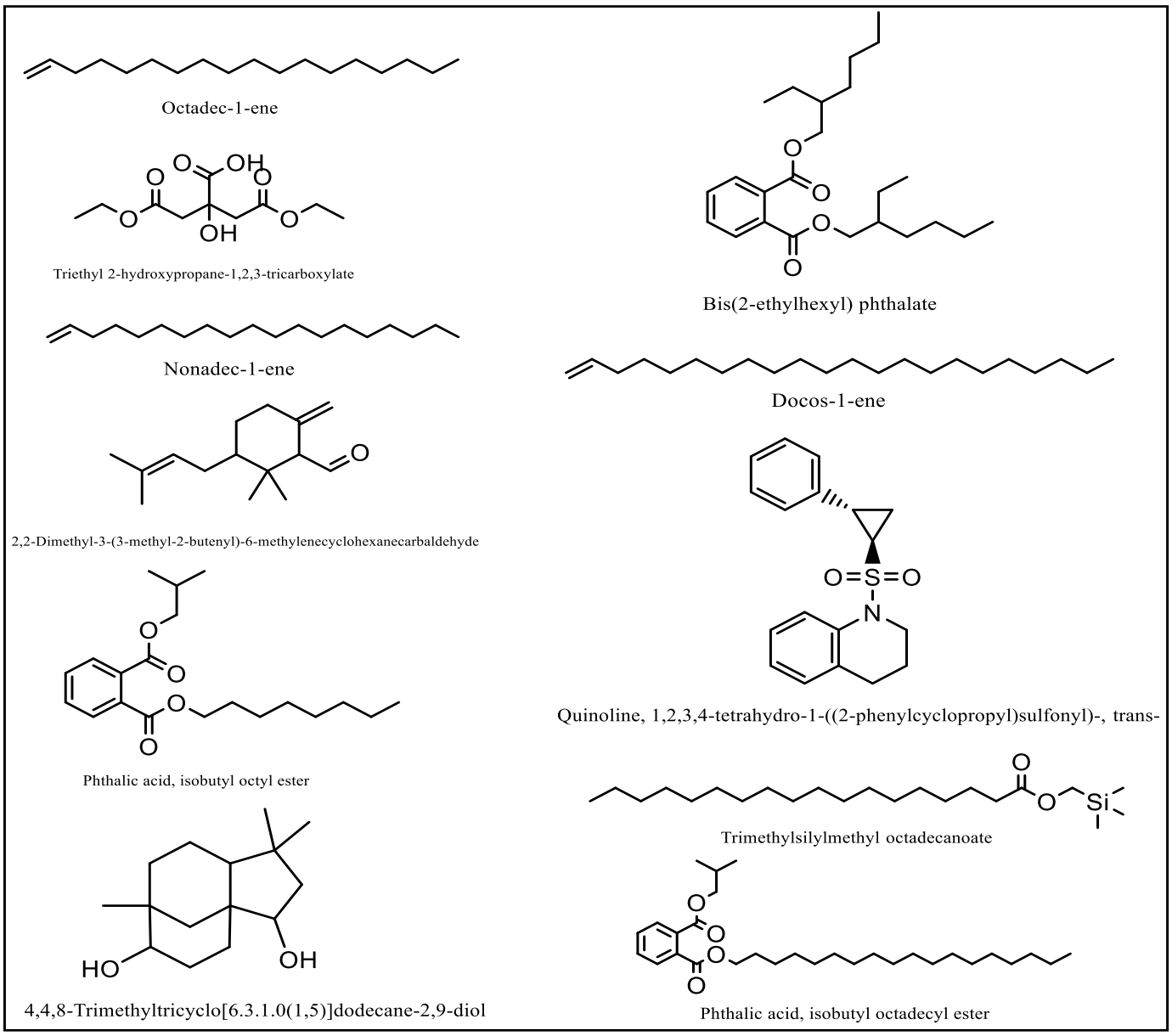


**Figure 2:** The chemical structures of some of the compounds identified in GC/MS analysis of *R. heudelotii* seed oil.

**Table 3:** Effect of pretreatment with *R. heudelotii* seed oil on ulcer index in ethanol-induced gastric ulcers.

| Groups | Treatment | Ulcer Index | Ulcer Protection (%) |
|---|---|---|---|
| I | Control | 0.00 ±0.00 | - |
| II | Ethanol Only | 4.11±1.68*** | - |
| III | Ethanol + Cimetidine (400 mg/kg) | 1.49±0.93# | 63.74 |
| IV | Ethanol + EERh (200 mg/kg) | 1.42±0.59# | 65.45 |
| V | Ethanol + EERh (400 mg/kg) | 1.78±1.20# | 56.70 |

***$P$<0.001 compared with control; #$P$<0.05 compared with ethanol-only group, n= 5.

**Table 4:** Effect of pretreatment with *R. heudelotii* seed oil extract on aspirin-induced gastric ulcers in rats.

| Groups | Treatment | Ulcer Index | Ulcer protection (%) |
|---|---|---|---|
| I | Control | 0.00 ± 0.00 | - |
| II | Aspirin Only | 5.48 ± 0.88$^{***}$ | - |
| III | Aspirin + Cimetidine (400 mg/kg) | 1.63 ± 0.93$^{*\#\#\#}$ | 70.26 |
| IV | Aspirin + EERh (200 mg/Kg) | 1.57 ± 0.84$^{\#\#\#}$ | 71.35 |
| V | Aspirin + EERh (400 mg/Kg) | 1.96 ± 0.31$^{*}$ | 64.23 |

$^{***}P$<0.001 compared with the control group, $^{*}P$<0.05 compared with the control group, $^{\#\#\#}P$<0.001 versus aspirin-only group, n=5.

**Table 5:** Effect of pretreatment with *R. heudelotii* seed oil on pH and gastric volume in ethanol-induced gastric ulcer

| Groups | Treatment | pH (By Meter) | pH (Titration) | Gastric Volume (mL) |
|---|---|---|---|---|
| I | Control | 3.1±0.29 | 2.77±0.50 | 0.88±0.26 |
| II | Ethanol Only | 1.64±0.38$^{***}$ | 0.90±0.11$^{**}$ | 3.36±0.41$^{***}$ |
| III | Ethanol + Cimetidine (400 mg/Kg) | 5.48±0.35$^{***\#\#\#}$ | 5.51±0.77$^{***\#\#\#}$ | 1.14±0.59$^{\#\#\#}$ |
| IV | Ethanol + EERh (200 mg/Kg) | 5.58±0.42$^{***\#\#\#}$ | 5.30±0.71$^{***\#\#\#}$ | 1.22±0.44$^{\#\#\#}$ |
| V | Ethanol + EERh (400 mg/Kg) | 5.44±0.48$^{***\#\#\#}$ | 5.42±0.65$^{***\#\#\#}$ | 0.88±0.25$^{\#\#\#}$ |

$^{**}P$<0.01, $^{***}P$<0.001 compared with control group, $^{\#\#\#}P$<0.001 compared with ethanol-only group, n= 5.

**Table 6:** Effect of pretreatment with *R. heudelotii* seed oil on pH and gastric volume in aspirin-induced gastric ulcers

| Groups | Treatment | pH (By Meter) | pH (Titration) | Gastric Volume (mL) |
|---|---|---|---|---|
| I | Control | 3.1±0.29 | 2.77±0.50 | 0.88±0.26 |
| II | Aspirin Only | 1.43±0.38 $^{***}$ | 1.22±0.49 $^{***}$ | 3.40±0.45$^{***}$ |
| III | Aspirin + Cimetidine (400 mg/Kg) | 5.48±0.42$^{**\#\#\#}$ | 5.51±0.77$^{***\#\#\#}$ | 1.34±0.63$^{\#\#\#}$ |
| IV | Aspirin + EERh (200 mg/Kg) | 5.55±0.55$^{*\#\#\#}$ | 5.26±0.48$^{**\#\#\#}$ | 1.25±0.35$^{\#\#}$ |
| V | Aspirin + EERh (400 mg/Kg) | 5.18±0.73$^{*\#\#\#}$ | 5.22±0.78$^{**\#\#\#}$ | 1.50±0.72$^{\#\#}$ |

$^{*}P$<0.05, $^{**}P$<0.01 and $^{***}P$<0.001 compared with control group; $^{\#\#}P$<0.01, $^{\#\#\#}P$<0.001 compared with aspirin-only group, n= 5.

## DISCUSSION

This study evaluated the hypothesis that the seed oil extract from *R. heudelotii* protects the stomach of Sprague-Dawley rats from ethanol or aspirin-induced ulcers. It also chemically characterized the oil using gas chromatography and mass spectrometry.

The oil is rich in alkaloids, flavonoids, tannins, phenols, saponins, glycosides, steroids, and fixed oils. These chemical classes especially the polyphenolics with antioxidant properties are known for a variety of biological properties (Kähkönen *et al*., 1999). *R. heudelotii* seed oil contains some carboxylic acids some of which have been linked with antiulcer properties (Manjunatha *et al*., 2024). Yücel *et al*. (2024) suggested that this antiulcer activity could stem from their anti-inflammatory properties. Also, some compounds with the quinoline moiety like 1-[(1S,2R)-2-phenylcyclopropyl]sulfonyl-3,4-dihydro-2H-quinoline have been associated with antiulcer properties (Cheon *et al*., 1998). Rebamipide, an amino acid derivative of 2-(1H)-quinolinone protects the intestinal mucosa in the treatment of ulcer and gastritis. It is therefore possible that part of the antiulcer effect seen in this oil could be attributed to the quinoline skeleton as seen in the GC/MS characterization.

The effect of oil from *R. heudelotii* seed on ulcer index, gastric volume and pH of the gastric fluid is in agreement with previous works (Andreo *et al*., 2006; Akindele *et al*., 2012; Abood *et al*., 2014) who all used the models in the present study and concluded that the antiulcer properties of extracts could be related to their antioxidant potential. Since *R. heudelotii* contains several phenolics as seen from the GC/MS, it is possible that the amelioration in ulcer severity by the seed oil was due to its antioxidant property although this was not investigated. Absolute ethanol has been attributed with necrosis of the ulcer lining which could elicit the release of pro-inflammatory mediators leading to inflammation and increased oxidative stress (El-Feky *et al*., 2024). Treatment with the oil extract reduced these parameters. The results in the present study in aspirin-induced ulcer models agree with other works (Andreo *et al*., 2006; Adefisayo *et al*., 2018; Ahmed *et al*., 2020). Aspirin, as an NSAID, inhibits cyclooxygenase-mediated prostaglandin synthesis and also leads to the generation of oxidative stress which can result in inflammatory processes (Das and Roy, 2012). The antiulcer effect of the oil against aspirin-induced ulcers may be due to presence of derivatives of octadecanoic acid, which has been attributed with a number of activities like anti-inflammatory, hypocholesterolemic, hepatoprotective, anti-histaminic, anti-arthritic, and anti-coronary activities (Oti *et al*., 2024).

Quantitatively, three-quarters of all the compounds identified in the present study are phthalate esters. These esters are compounds of environmental toxicological concern (Khoshmanesh *et al*., 2024). Studies have linked their emergence to the manufacturing sector where they are used as plasticizers to improve durability of manufactured materials (Baloyi *et al*., 2021; Huang *et al*., 2021). They are known to affect different parts of the mammalian system causing different pathologies (Brassea-Pérez *et al*., 2022). Manayi *et al*. (2014) described the presence of phthalate esters in medicinal oil extracted from *Achillea tenuifolia*, a plant known for its medicinal use in managing blood disorders. It has been suggested that phthalate esters could be part of secondary metabolite in plants and bacteria, instead of just a contaminant (Ortiz and Sansinenea, 2018) and they possess some medicinal properties (Tavares and Vine, 1985; El-Sayed, 2013; Fhid *et al*., 2014; Cruz-Ramirez *et al*., 2020). They are known activators of peroxisome proliferator-activated receptors (PPARs), a group of gene-regulating nuclear receptors (Hurst and Waxman, 2003). PPARs are widely expressed in the gastrointestinal tract, especially the gastric region (Fucci *et al*., 2012) where they exert antisecretory properties (Saha, 2015). Administration of bezafibrate, a known agonist of PPARα showed a significant antiulcer property in animal models of ulcer induced by ethanol and NSAIDs (Pathak *et al*., 2007). Also, administration of pioglitazone, a known ligand of $PPAR_{\gamma}$ modulated inflammatory processes by inhibiting tissue necrosis factor alpha (TNFα), nuclear factor kappa-beta (NF-κβ) and other cytokines (Brzozowski *et al*., 2005). Phthalates are known activators of NF-κβ (Kang *et al*., 2016) which in ulcers results in the upregulation of expression of ulcer healing promoting factors (Takahashi *et al*., 2001). Therefore, the presence of large amounts of phthalates may explain the antiulcer property of the seed oil of *R. heudelotti*. Also, prostaglandins (PGs) are known to inhibit gastric secretion, stimulate increase in blood flow and bicarbonate production (Wilson, 1987). Phthalic acid can stimulate prostaglandin production by its effect on prostaglandin $PGE_2$ which promotes ulcer healing and gastric protection.

## CONCLUSION

The seed oil of *R. heudelotii* contains phthalate esters and several other phytoconstituents that may be responsible for its protective effect against ethanol and aspirin induced ulcer models in rats. Being relatively safe, the seed oil has potential in the treatment of peptic ulcer disease.

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Not applicable.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR'S CONTRIBUTION

KOO conceptualized this study. NIA and ROO carried out the experiment. KOO did the data curation. NIA drafted the manuscript while ROO proofread. All authors read the final draft and approved its submission.

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None received for this work.

## AUTHORS' DECLARATION

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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