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Research Paper

Gastroprotective Effects of *Dendropthoe pentandra* Leaf Ethanol Extract on Peptic Ulcer Animal Models

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Abstract
Dendrophthoe pentandra (Loranthaceae) is a semi-parasitic plant with several diverse metabolites and biological activities and is widely used in traditional medicine. This study aims to evaluate the gastroprotective effectiveness of the ethanol extract of *D. pentandra* leaves in animals induced by an acute peptic ulcer with absolute ethanol. The gastroprotective effect of the extract (100, 250 and 500 mg/kg doses) was evaluated through ulcer index parameters, physicochemical properties of gastric fluid, and histopathological analysis. The study results of the study showed that the ethanol extract of *D. pentandra* leaves at a dose of 500 mg/kg could provide a protective effect equivalent to omeprazole. Histopathological analysis proved the improvement of the mucous membrane structure in the animals pre-treated with the extract. Based on these findings, it can be concluded that the ethanol extract of *D. pentandra* leaves is effective as an anti-ulcer drug, so it is feasible to be developed as a gastroprotective from herbal.

Keywords
Dendrophthoe pentandra, Gastroprotektive, Ethanol Extract, Peptic Ulcer

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1. INTRODUCTION

A peptic ulcer is a lesion of the gastric mucosa caused by increasing levels of gastric acid and pepsin (Jincy and Sunil, 2020). The incidence of peptic ulcers and their complications affects 10% of the world's population and has steadily increased over the past decades (Zhou et al., 2020). Peptic ulcers are caused by aggressive factors in the gastric that are more dominant than defensive factors. Aggressive factors can come from NSAID drugs, *Helicobacter pylori* infection, alcohol, smoking, and stressful conditions (Raish et al., 2021). Currently, more researchers in the medical world are interested in finding drugs to prevent or treat peptic ulcers. This is because existing synthetic drugs have risk factors for side effects and interactions which are another problem in the therapy (Park et al., 2019). The search for gastroprotective agents from natural products attract researchers because they are believed to be safer, more effective, and easier to accept because they are easier to obtain and cheaper (Bansal and Goel, 2012). Natural products have been reported to be effective in preventing gastric ulcers *Parkia speciosa* (Fitrya et al., 2022a), *Grewia optiva* (Aslam et al., 2020), *Helicantes elasticus* (Jincy and Sunil, 2020) and *Moringa oleifera* (Ijioma et al., 2018).

Dendrophthoe pentandra (Loranthaceae) is a semi-parasitic plant. Even though this plant is parasitic to its host, this plant is endowed with a large number of metabolites and a diverse bioactivity Sahakitpichan et al. (2017) so it is widely used in traditional medicine (Kong et al., 2023; Mu'nisa et al., 2019). This parasitic plant is known by the local name Benalu (Indonesia), reported to contain secondary metabolites in the form of flavonoids and phenolics, including quercetin (Hardiyanti et al., 2019), quercitrin, rutin, quercetagetin and kaemferol (Kong et al., 2023). In addition, *D. Petandara* also contains catechins and procyanidins (Sahakitpichan et al., 2017).

In Indonesia, people use the Benalu leaves to treat cancer. Moreover, it is also used to treat ulcers, asthma, paralysis, menstrual disorders, pulmonary tuberculosis, and so on (Kong et al., 2023). Pharmacological studies of the parasite plant that have been reported include antioxidants (Hardiyanti et al., 2019), antidiabetic and hepatoprotective (Hasan et al., 2018), anticancer (Endharti and Permana, 2017; Karunaratne and Uduwela, 2020), antidiabetic (Alharits et al., 2020; Hasan et al., 2018), antihypercholesterol (Mu'nisa et al., 2019), and anti-inflammatory (Endharti et al., 2016). There are no reports regarding the activity of Benalu leaves as an antiulcer. This study evaluate Benalu leaf extract's antiulcer effect in animal models-induced peptic ulcers with absolute ethanol.

2. EXPERIMENTAL SECTION

2.1 Materials and Methods

2.1.1 Chemicals and Plant Material

The Benalu leaf was collected in August 2020 in Rasuan Darat village, East Ogan Komering Ulu District, South Sumatra. Determination of *D. pentandra* was done at LIPI BKT Purwodadi Botanical Garden with No. B-282/IPH.6/KS.02/VII/2020 and specimen vouchers are stored in the laboratory. The chemicals used were: Ethanol 70% (Brataco), Omeprazole (Dexa Medica®), ethanol absolute (Merck®), and Alcian Blue Stain (Sigma®).

2.1.2 Extract Preparation

One kg of dry Benalu leaf powder was extracted by maceration method using 3 L of 70% ethanol three times. After filtering, the total filtrate was evaporated with a rotavapor (Yamato® RE301) to obtain an ethanol extract of Benalu leaves (EDP) (Fitrya et al., 2019).

2.1.3 Determination of Flavonoid Content

As much as 20 mg of EDP extract was dissolved in 10 mL of ethanol and then centrifuged to obtain a concentration of 2000 ppm. The test solution (0.5 mL) was added with 0.1 mL of 10% AlCl3, 0.1 mL of 1 M Na acetate, and 2.8 mL of distilled water and then incubated for 30 minutes. The absorbance was measured using a UV-Vis spectrophotometer (Biobase®) at 438 nm. Total flavonoids were calculated using the linear regression equation of the quercetin standard curve. The total flavonoid content is expressed as grams of quercetin equivalent per gram of extract (Fitrya et al., 2022b).

2.1.4 Gastroprotective Effect Test

The gastroprotective effect test of EDP refers to the previous (Ijioma et al., 2018; Jincy and Sunil, 2020; Hussaini et al., 2012). The experimental animal was the male Wistar rat (2-3 months, 190-210 g). A total of 30 rats were acclimatized in a cage for one week (temperature 22^{o}C; 12 hours dark/light; humidity 55.5%). After the adaptation period, the rats were divided into six groups: three control and three test groups. The control group consisted of normal, negative, and positive controls, each was given 0.5% Na CMC, 1 mL/200 g absolute ethanol, and 20 mg/kg omeprazole. The test group had three extract dose levels: 125, 250, and 500 mg/kg. Each group consists of 5 animals. All animals were treated according to their group for 14 days. On the 15^{th} day, the animals were fasted for 24 hours. After fasting, the animals induced peptic ulcers with absolute ethanol orally. Two hours after induction, the animals were sacrificed under petroleum ether anesthesia. Animals were dissected, and gastric organs were opened for index ulcer, macroscopic and microscopic analysis. Gastric fluid was separated for volume, pH, and acidity of gastric fluid. The lesion profile in the gastric was observed and photographed with a camera (Canon® Mirroless M10). Lesion area was determined using Software Image J. Ulcer index (UI) was calculated using the equation: UI = (mean ulcer per rat + mean severity score + percentage of mice with ulcers) $\times 10^{-1}$ (Yoo et al., 2020). The titration method determined gastric juice's acidity (Jincy and Sunil, 2020). All animal treatments have received approval from the Health Research Ethics Committee, Palembang Ministry of Health Health Polytechnic No 541/KEPK//Adm2/XII/2020.

2.1.5 Data analysis

All values are reported as mean ± SD and analyzed using SPSS 26 software. The normality of data was analyzed using the Shapiro-Wilk method. The data that is normally distributed ($p > 0.05$) was continued with testing using the one-way ANOVA. Tukey's posthoc test was carried out to determine the differences between groups. Differences were considered statistically significant ($p < 0.05$).

3. RESULTS AND DISCUSSION

3.1 Total Flavonoid Content

Based on the measurement, the total flavonoid content of Benalu leaves was 97.249 mg QE/g ethanol extract (9.725%). The content of these flavonoids is higher than that reported by Mustarichie et al. (2015), namely 68 mg QE/g extract. This difference may be caused by differences in hosts where the parasite in this study grows on Rambutan (*Nephelium lappaceum*) trees while the parasite reported by the Official 2015 grows on *Camellia sinensis* trees.

3.2 Ulcer Index and Macroscopic Profile of Gastric

A peptic ulcer is a mucosal lesion caused by an imbalance between defensive and aggressive factors (Aslam et al., 2020; Zhou et al., 2020). Absolute ethanol is a chemical that can cause ulceration, characterized by bleeding and erosion of the gastric mucosa. Macroscopic observation showed that the gastric condition of the normal group did not find any ulcer spots or homeragic stress (bleeding). The macroscopic profile of the positive group almost resembled the normal group, with no ulcers but hemorrhagic stress. In contrast, the negative control group's gastric appeared reddish. There were lesions, and bleeding in the gastric mucosa. While the test group showed a dose-dependent ulceration rate, in the 125 mg dose group the gastric appeared reddish and there were ulcers, and the 250 mg dose group had a reddish color but no ulcers. Gastric macroscopy of the 500 mg dose group resembled the normal group; there was no bleeding or lesions, and only spot ulcers were present. The macroscopic observations of the rat gastric are shown in Figure 1.

Absolute ethanol diffusion into the gastric mucosa will trigger oxidative stress and inflammatory signaling pathways that damage gastric tissue. Absolute ethanol can stimulate neutrophil infiltration and subsequently regenerate ROS molecules (Aslam et al., 2020). An increase in ROS and neutrophils to the injured area accelerates ulceration because neutrophil aggregation induces retention of tissue disruptive substances such as proteases and leukotrienes. As a result, the integrity of the

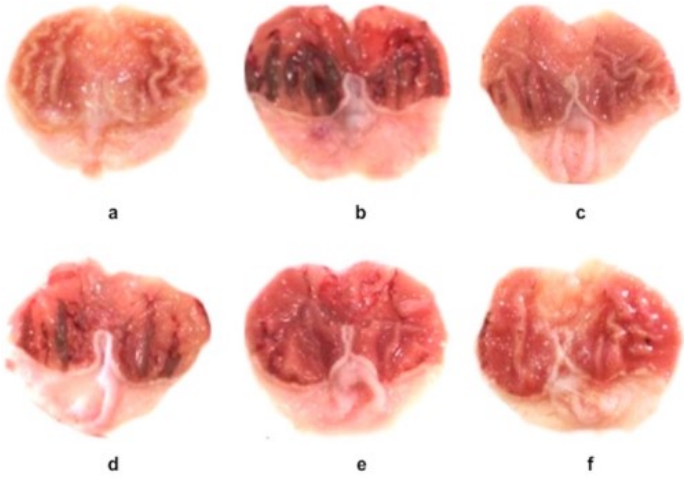

Figure 1. Effect of EDP on Gastric Macroscopic of Rats Induced with Ethanol (a) Normal; (b) Negative Control; (c) Positive Control; (d-f) Tes Groups: Doses of 125, 250 dan 500 mg/kg

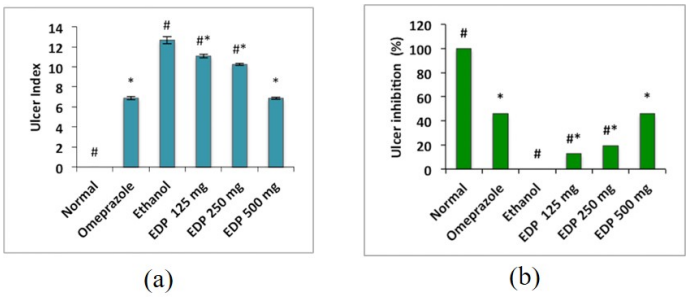

Figure 2. The Ulcer Index (a) and Ulcer Inhibition Percentage (b) of Animals Treated with Ethanol Extract of Benalu Leaves. Data are Expressed as Mean ± SD (n=5), ♯P<0.05 is Significantly Different from the Positive Control, and ∗P<0.05 is Significantly Different from the Negative Control

mucous membranes is damaged and bleeding occurs (de Souza et al., 2019; Guzmán-Gómez et al., 2018; Rozza et al., 2014).

From the LSD post hoc test on the ulcer index, it was found that the negative control was significantly different ($p<0.05$) from the normal control and the positive control. This proves that ethanol can induce ulcers in rats. There was no significant difference in the positive control and 500 mg test groups ($p>0.05$). The 500 mg dose group had a protective index (45.842%), equal to the positive control (45.750%), while the 125 mg and 250 mg dose groups did not provide maximum protection (Figure 2).

The decrease in the ulcer index and the increase in the percentage of inhibition in the group that received the extract pre-treatment proved that EDP could protect the gastric from damage caused by absolute ethanol. Based on the ulcer inhibition value shown by EDP 500 mg, it can be stated that the extract's effectiveness is as great as omeprazole, namely 100%. The smaller the ulcer index value indicates the better the protective effect provided (Sattar et al., 2019). Omeprazole shows the lowest ulcer index value because this drug can prevent ulcers by inhibiting the proton pump so that it inactivates H+K+ATPase which which increases gastric acid secretion (Jincy and Sunil, 2020).

3.3 Effect of the Extract on Gastric Fluid Parameters

Analysis of gastric fluid parameters including volume, pH, total acidity of gastric juice, and mucin levels. LSD post hoc analysis showed that the gastric fluid volume of the positive control, the 250 and 500 mg group was significantly different from the negative control ($p<0.05$). In contrast, the 125 mg dose and the negative control were insignificantly different ($p>0.05$). At the same time, the pH value showed no significant difference between all groups ($p>0.05$). For the total acidity of gastric juice, the negative control had a significant difference ($p<0.05$) from the normal and positive controls. In contrast the total acidity of the positive control did not differ significantly from the normal control ($p>0.05$). The 250 mg and 500 mg dose groups were insignificantly different from the positive control ($p>0.05$). As for mucin levels, the 125 mg group did not differ significantly from the negative group ($p>0.05$), and the 250 and 500 mg groups did not differ from the positive group ($p>0.05$) (Figure 3).

In line with the decrease in ulcer index, analysis of gastric juice parameters showed that EDP can reduce total gastric fluid volume and acidity, significantly increasing mucin levels compared to the untreated group. The main function of this gastric fluid was to kill microorganisms entering the gastric, thus preventing infectious agents from reaching the intestine (Martinsen et al., 2019). The ethanol could increase gastric acid secretion by stimulating the release of histamine (Fitrya et al., 2022a). The EDP could reduce acidity and gastric fluid volume because it contained flavonoids inhibiting the histidine decarboxylase enzyme. The histidine decarboxylase inhibited the release of histamine in the gastric mucosa, inhibiting the formation of gastric acid (Zakaria et al., 2015). The EDP had high antioxidant activity derived from the flavonoids it contains (IC_{50} 6.8 μg/mL) (Fitrilia et al., 2015). With their antioxidant activity, flavonoids worked to activate antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxide (GPx) which neutralize free radicals. Therefore reducing oxidative stress causes damage to the gastric mucosal tissue (Wu et al., 2018). According to Endharti et al. (2016), the flavonoids in Benalu leaf extract have anti-inflammatory activity. Through anti-inflammatory mechanisms, flavonoids reduce inflammation by reducing the myeloperosidase (MPO) enzyme levels (Zhang et al., 2020).

Apart from inhibiting gastric acid secretion, increasing the quality and quantity of mucus is the main target of the antiulcer therapy (Akomas et al., 2014; Ijioma et al., 2018), because mucus is a physical barrier that prevents rediffusion of hydrogen ions and increases the buffering of gastric juice so that it can re-

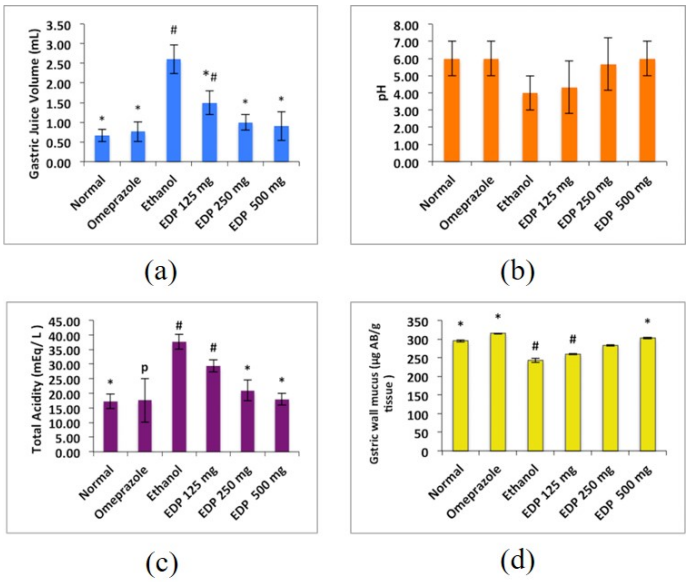

Figure 3. Effect of *D. pentandra* Extract on Gastric Fluid Volume (a), pH (b), Total Acidity (c), and Levels of Mucin (d) Data is Normally Distributed (n=5); ♯p<0.05 Compared to the Positive Control, ∗p<0.05 Compared to the Negative Control

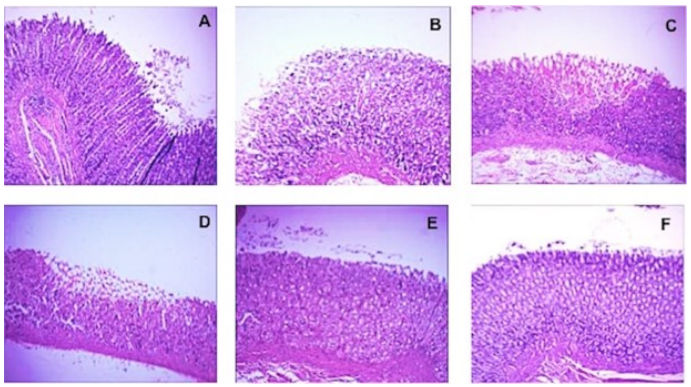

Figure 4. Photomicrograph Effect of *Dendrophthoe pentandra* Extract on the Gastric Mucosa of Rats (H&E stain 100x) (A) Normal, (B) Negative, (C) Positive, (D-F) 125, 250, and 500 mg/kg Dose Groups

sist ulcer formation (de Souza et al., 2019; Halim et al., 2017). The cytoprotective effect of a drug is determined by its ability to increase gastric mucus secretion (De Olinda et al., 2008). This study shows that EDP can bind Alcian Blue, especially at 250 and 500 mg doses. This capacity indicates that EDP can increase mucus secretion and provide a cytoprotective effect. Pre-treatment with EDP markedly inhibited ulceration, especially at a dose of 500 mg, the effect was no different compared to omeprazole.

3.4 Effect of Extract on Gastric Histology

The microscopic observations reveal no erosion and necrosis in the normal group. Epithelial cells appeared neatly arranged, very different from the negative control, which showed erosion and necrosis in the epithelial layer. In contrast, the mucosal epithelial cells of the positive control group showed mild necrosis. The test group showed reduced epithelial damage with increasing doses. In the 125 mg group there were erosion and necrosis, the 250 mg dose had less necrosis; at the 500 mg dose, no erosion and necrosis were found (Figure 4).

Histopathological analysis proved that EDP at doses of 250 mg and 500 mg could protect the gastric mucosa from cell damage caused by ethanol. This protective effect is believed to come from the flavonoids and phenolics in the EDP. The EDP was reported to contain quercetin, quercitrin, rutin and kaemferol, which are effective as antioxidants and anti-inflammatory (Kong et al., 2023). Quercetin can reduce ROS such as superoxide anions, peroxyl and hydroxyl radicals (Yasin et al., 2020). The antioxidant activity also works to stimulate wound contraction and the formation of new capillaries and fibroblasts (Fitrya et al., 2022a; Jincy and Sunil, 2020). Anti-inflammatory activity inhibits COX enzymes and stimulates the generation of prostaglandins (Najini et al., 2018). In addition, there were gallic acid and epicatechin (Kong et al., 2023), which are tannin compounds that can protect the outermost layer of the mucosa and make the mucous layer less permeable, so it is more resistant to mechanical damage and irritation. Tannins form protective polycles or cytoprotective effects by increasing protein deposition in ulcers so as not to exacerbate ulcers. Therefore, these findings prove that EDP has anti-ulcer activity worthy of further development.

4. CONCLUSION

Based on the study's results, it was concluded that the ethanol extract of Benalu leaves (*Dendropthoe pentandra*) was proven to have a gastroprotective effect on the gastric of rats induced by peptic ulcer. The effectiveness of the extract is as great as omeprazole. Gastroprotective activity is believed to come from flavonoid compounds that work through antioxidant and anti-inflammatory pathways. This study did not cover the toxicity effect of the extract; therefore, the toxicity study is to be carried out in the future.

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REFERENCES

Akomas, S., G. Ezeifeka, and S. Ijioma (2014). Justification for the Use of Musa Paradisiaca Green Fruit Extract for GIT Mucosa Protection and Ulcer Treatment. *Continental J. Animal and Veterinary Research*, **6**; 29–35

Alharits, L., N. M. Hemelda, and W. Handayani (2020). Allelopathic Activity of Dendrophthoe Pentandra as a Poten-

tial Bioherbicide to Inhibit Seed Germination and Seedling Growth of Eleusine Indica. *Nusantara Bioscience*, **12**(1); 33–39

Aslam, S., M. A. Tahir, and M. S. Abbasi (2020). Gastro-Protective Effect of Grewia optiva (Dhamna) Leaf Extract on Ethanol Induced Gastric Ulcer in Rats. *Asian Journal of Research and Reports in Gastroenterology*, **4**(1); 19–25

Bansal, V. K. and R. K. Goel (2012). Gastroprotective Effect of Acacia Nilotica Young Seedless Pod Extract: Role of Polyphenolic Constituents. *Asian Pacific Journal of Tropical Medicine*, **5**(7); 523–528

De Olinda, T., T. Lemos, L. Machado, V. Rao, and F. Santos (2008). Quebrachitol-induced Gastroprotection Against Acute Gastric Lesions: Role of Prostaglandins, Nitric Oxide and K+ ATP Channels. *Phytomedicine*, **15**(5); 327–333

de Souza, M. C., A. J. Vieira, F. P. Beserra, C. H. Pellizzon, R. H. Nóbrega, and A. L. Rozza (2019). Gastroprotective Effect of Limonene In Rats: Influence on Oxidative Stress, Inflammation and Gene Expression. *Phytomedicine*, **53**; 37–42

Endharti, A. T. and S. Permana (2017). Extract from Mango Mistletoes Dendrophthoe Pentandra Ameliorates TNBS-induced Colitis by Regulating CD4+ T Cells in Mesenteric Lymph Nodes. *BMC Complementary and Alternative Medicine*, **17**(1); 1–8

Endharti, A. T., A. Wulandari, A. Listyana, E. Norahmawati, and S. Permana (2016). Dendrophthoe Pentandra (L.) Miq Extract Effectively Inhibits Inflammation, Proliferation and Induces p53 Expression on Colitis-associated Colon Cancer. *Bmc Complementary and Alternative Medicine*, **16**(1); 1–8

Fitrilia, T., M. Bintang, and M. Safithri (2015). Phytochemical Screening and Antioxidant Activity of Clove Mistletoe Leaf Extract (Dendrophthoe pentandra (l.) Miq.). *IOSR Journal of Pharmacy*, **5**(8); 13–18

Fitrya, F., A. Amriani, R. P. Novita, A. Ahmadi, and R. Nabilah (2022a). Efektivitas Ekstrak Etanol Polong Petai [Parkia speciosa Hassk.] Sebagai Anti Ulcer Pada Tikus Wistar yang Diinduksi Etanol Absolut. *Jurnal Sains Farmasi & Klinis*, **9**(1); 64–70 (In Indonesia)

Fitrya, F., A. Amriani, R. P. Novita, A. Salsabila, S. M. Siregar, and Y. Anafisya (2022b). Evaluation of Ethanol Extracts from Three Species of Artocarpus as Natural Gastroprotective Agents: in Vivo and Histopathological Studies. *Journal of Complementary and Integrative Medicine*, **19**(4); 967–974

Fitrya, F., A. Annisa, S. Nikita, and C. Ranna (2019). Alpha Glukosidase Inhibitory Test and Total Phenolic Content of Ethanol Extract of Parkia Speciosa Plant. *Science and Technology Indonesia*, **4**(1); 1–4

Guzmán-Gómez, O., R. V. García-Rodríguez, L. Quevedo-Corona, R. Pérez-Pastén-Borja, N. L. Rivero-Ramírez, E. Ríos-Castro, S. Pérez-Gutiérrez, J. Pérez-Ramos, and G. A. Chamorro-Cevallos (2018). Amelioration of Ethanol-induced Gastric Ulcers in Rats Pretreated with Phycobiliproteins of Arthrospira (spirulina) Maxima. *Nutrients*, **10**(6); 763

Halim, S. Z., Z. A. Zakaria, M. H. Omar, N. Mohtarrudin, I. R. A. Wahab, and M. N. H. Abdullah (2017). Synergistic Gastroprotective Activity of Methanolic Extract of a Mixture Of Melastoma Malabathricum and Muntingia Calabura Leaves in Rats. *Bmc Complementary and Alternative Medicine*, **17**; 1–16

Hardiyanti, R., L. Marpaung, I. K. Adnyana, and P. Simanjuntak (2019). Isolation of Quercitrin From Dendrophthoe Pentandra (L.) Miq Leaves and It's Antioxidant and Antibacterial Activities. *Rasayan Journal of Chemistry*, **12**(3); 1822–1827

Hasan, M., M. T. Ali, R. Khan, P. Palit, A. Islam, V. Seidel, R. Akter, and L. Nahar (2018). Hepatoprotective, Antihyperglycemic and Antidiabetic Effects of Dendrophthoe Pentandra Leaf Extract in Rats. *Clinical Phytoscience*, **4**(1); 1–7

Hussaini, J., N. A. Othman, M. A. Abdulla, N. A. Majid, H. M. Faroq, and S. Ismail (2012). Gastroprotective Effects of Dicranopteris Linearis Leaf Extract Against Ethanol-induced Gastric Mucosal Injury in Rats. *Scientific Research and Essays*, **7**(18); 1761–1767

Ijioma, S., E. Nwaogazi, A. Nwankwo, H. Oshilonya, C. Ekeleme, and L. Oshilonya (2018). Histological Exhibition of the Gastroprotective Effect of Moringa Oleifera Leaf Extract. *Comparative Clinical Pathology*, **27**; 327–332

Jincy, J. and C. Sunil (2020). Exploring Antiulcer and Anti-inflammatory Activities of Methanolic Leaves Extract of an Indian Mistletoe Helicantes Elasticus (Desv.) Danser. *South African Journal of Botany*, **133**; 10–16

Karunaratne, R. and D. Uduwela (2020). A Comparison of the Bioactivity of Dendrophthoe Falcata on the Hosts; Limonia Acidissima and Mangifera Indica. *Ceylon Journal of Science*, **49**(2); 159–164

Kong, D., L. Wang, Y. Niu, L. Cheng, B. Sang, D. Wang, J. Tian, W. Zhao, X. Liu, and Y. Chen (2023). Dendrophthoe Falcata (Lf) Ettingsh. and Dendrophthoe Pentandra (L.) Miq.: A Review of Traditional Medical Uses, Phytochemistry, Pharmacology, Toxicity, and Applications. *Frontiers in Pharmacology*, **14**; 1–18

Martinsen, T. C., R. Fossmark, and H. L. Waldum (2019). The Phylogeny and Biological Function of Gastric Juice—microbiological Consequences of Removing Gastric Acid. *International Journal of Molecular Sciences*, **20**(23); 6031

Mu'nisa, A., Y. Hala, A. M. Taiyeb, and D. K. Sari (2019). Effect of Boiled Water Parasite Kapok (Dendrophthoe pentandra) Leaves on Total Cholesterol Levels and Histopathology of Hepar of Hypercholesterolemic Mice. *Materials Science Forum*, **967**; 51–55

Mustarichie, R., S. Warya, N. M. Saptarini, and D. Ramdhani (2015). Total Flavonoid Content and Antiinflammatory Properties of Indonesian Mistletoes (Dendrophtoe pentandra (l.) Miq.) Ethanol Extract. *World Journal of Pharmaceutical Research*, **4**(4); 287–302

Najini, R., M. S. Bachri, and S. Yuliani (2018). The Gastroprotective Effects of Canna Edulis Ker. Tuber Starch on Peptic

Ulcer and The Histopathological Profile of Rat Stomach. *Pharmaciana*, **8**(1); 43–52

Park, J. U., J. H. Kang, M. A. A. Rahman, A. Hussain, J. S. Cho, and Y. I. Lee (2019). Gastroprotective Effects of Plants Extracts on Gastric Mucosal Injury In Experimental Sprague-dawley Rats. *BioMed Research International*, **2019**; 1–11

Raish, M., M. Shahid, Y. A. Bin Jardan, M. A. Ansari, K. M. Alkharfy, A. Ahad, I. A. Abdelrahman, A. Ahmad, and F. I. Al-Jenoobi (2021). Gastroprotective Effect of Sinapic Acid on Ethanol-induced Gastric Ulcers in Rats: Involvement of Nrf2/HO-1 and Nf-κb Signaling and Antiapoptotic Role. *Frontiers in Pharmacology*, **12**; 622815

Rozza, A. L., F. Meira de Faria, A. R. Souza Brito, and C. H. Pellizzon (2014). The Gastroprotective Effect of Menthol: Involvement of Anti-apoptotic, Antioxidant and Anti-inflammatory Activities. *PloS one*, **9**(1); 1–6

Sahakitpichan, P., W. Disadee, R. Buntawong, N. Chimnoi, S. Ruchirawat, and T. Kanchanapoom (2017). A Furan-2-carbonyl C-glucoside and an Alkyl Glucoside from the Parasitic Plant, Dendrophthoe Pentandra. *Phytochemistry Letters*, **21**; 90–93

Sattar, A., A. Abdo, M. N. Mushtaq, I. Anjum, and A. Anjum (2019). Evaluation of Gastro-protective Activity of Myristica Fragrans on Ethanol-induced Ulcer in Albino Rats. *Anais da Academia Brasileira de Ciências*, **91**(2); 1–8

Wu, X., Q. Huang, N. Xu, J. Cai, D. Luo, Q. Zhang, Z. Su, C. Gao, and Y. Liu (2018). Antioxidative and Anti-inflammatory Effects of Water Extract of Acrostichum Aureum Linn. Against Ethanol-induced Gastric Ulcer in Rats. *Evidence Based Complementary and Alternative Medicine*, **2018**; 1–10

Yasin, H., F. Tariq, A. Sameen, N. Ahmad, M. F. Manzoor, M. Yasin, T. Tariq, M. W. Iqbal, B. Ishfaq, and S. Mahmood (2020). Ethanolic Extract of Okra Has a Potential Gastroprotective Effect on Acute Gastric Lesions in Sprague Dawley Rats. *Food Science & Nutrition*, **8**(12); 6691–6698

Yoo, C. Y., H. U. Son, A. Fanar, H. J. Choi, M. B. Alam, and S. H. Lee (2020). Opuntia Humifusa Aqueous Extract Alleviates Ethanol-induced Gastric Ulcer in a Mouse Model. *Asian Pacific Journal of Tropical Biomedicine*, **10**(9); 403

Zakaria, Z. A., T. Balan, S. S. Mamat, N. Mohtarrudin, T. L. Kek, and M. Z. Salleh (2015). Mechanisms of Gastroprotection of Methanol Extract of Melastoma Malabathricum Leaves. *BMC Complementary and Alternative Medicine*, **15**; 1–15

Zhang, W., Y. Lian, Q. Li, L. Sun, R. Chen, X. Lai, Z. Lai, E. Yuan, and S. Sun (2020). Preventative and Therapeutic Potential of Flavonoids in Peptic Ulcers. *Molecules*, **25**(20); 4626

Zhou, D., Q. Yang, T. Tian, Y. Chang, Y. Li, L. R. Duan, H. Li, and S. W. Wang (2020). Gastroprotective Effect of Gallic Acid Against Ethanol-induced Gastric Ulcer in Rats: Involvement of the Nrf2/HO-1 Signaling and Anti-apoptosis Role. *Biomedicine & Pharmacotherapy*, **126**; 110075

