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Original Article

Phytochemical Screening, Antioxidant and Gastro-Protective Activity Studies on the Fruit Peels of Selected Varieties of Banana

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Abstract

Background and Aim: Gastric ulcer is a chronic health condition of the gastrointestinal tract with increasing incidence and prevalence affecting both male and female population globally. There are a variety of drugs used in the treatment of this disease, but they are costly and exhibit limited efficacy, and cause adverse reactions. Hence, the present study aimed to screen the phytochemicals, antioxidant and anti-ulcer activities of the ethanolic fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita.
Materials and Methods: The determination of total phenolics and flavonoids were performed using conventional methods. The free radical scavenging activity of the extracts was investigated using the DPPH (1, 1-Diphenyl-2 -picrylhydrazyl). Moreover, the anti-ulcer activity was examined using three ulcer models in rats.
Results: The total phenolic contents of the peel extracts ranged from 12.3 to 40.3 mg gallic acid equivalents (GAE)/g dry weight (dw), whereas the flavonoid content ranged from 2.5 to 16.6 mg GAE/g dw. The results indicated that the peel extracts exhibited free radical scavenging capacity (DPPH) that ranged from 51.52 to 72.00% at the concentration of 100 µg/mL. Moreover, the peel extracts showed gastroprotective activities against alcohol, drug, and stress-induced ulcers in rats. The maximum percentage of ulcer inhibition of the peel extracts against ethanol-induced ulcer was 83.33, whereas it was 100% against both aspirin and cold restraint stress-induced ulcers.
Conclusion: The obtained results suggest that the fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita have antioxidant capacities. They also exhibited anti-ulcer activities, and contained active compounds that are potentially responsible for its biological and pharmacological properties. Likewise, further explorations of the peel extracts are required, for the plant examined in this research is a promising plant potentially applicable in nutraceutical and pharmaceutical industries.
Keywords: Gastroprotective, Anti-ulcer, Antioxidant, Phytochemicals, Banana peels.

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Introduction

Gastric ulcer is one of the most widespread diseases of the gastrointestinal tract whose incidence and prevalence is progressing worldwide (1). It affects more than 10% of the global population, and is responsible for an estimated 15,000 deaths annually (2, 3). This disease affects both men and women with an estimated prevalence ranging from 8–11% and 11–14% in females and males, respectively. Gastric ulcer is caused by the disruption of the balance between aggressive and protective factors in the stomach (3). Some of these protective factors are problem associated with the mucosal barrier, mucus secretion and cell regeneration; whereas aggressive factors might include the gastric mucosa (such as acid-pepsin secretion) associated with the digestion process and other determinants, including the extreme consumption of alcohol, excessive use of non-steroidal anti-inflammatory drugs (NSAIDs), exposure to stress, and Helicobacter pylori infection (5).

On the other hand, there have been a variety of drugs included in the conventional treatment management of gastric ulcer that primarily aimed at therapeutically controlling the acid secretion. These drugs include, though are not limited to, antacids, proton pump inhibitors, and antihistamines. However, Laloo *et al.* reported that most of these currently available drugs are costly, exhibit limited efficacy, and are associated with certain health problems that result in abnormal adverse reactions in the human body. Consequently, Saheed *et al.* reported that gastrointestinal toxicity and other inherent adverse effects of conventional drug therapy for gastric ulcer remain a significant interference to their application in clinical practice. Hence, it is essential to discover other alternative remedies that might be potentially cheaper and safer antiulcer agents. Saheed *et al.* argued that these alternatives should be investigated in medicinal plants which might be sources of antiulcerogenic drugs. Moreover, several medicinal plants have been the focus of various studies because of their inherent phytoconstituents that play a significant role in exhibiting biological and pharmacological activities, such as being anti-ulcer agents. However, a few studies explored the potential use of other plant materials or parts which have been regarded as waste, particularly in fruits.

As a fruit growing in tropical regions, banana belongs to the Musaceae family. This fruit is grown in several countries worldwide (6, 7) such as the Philippines. The annual production of banana reaches the figure of 102 million. Meanwhile, banana peel comprises roughly 35% of the whole fruit weight. Hence, the quantity of banana peel produced annually is no less than 36 million tons. This fact is a potential issue to be further explored. However, the bulk of the by-product (peel) is usually disposed of the landfill or regarded as general waste (8). Nonetheless, it was reported that all parts of banana have medicinal applications (9). Shadma *et al.* stated that the fruit peel is one of these parts. Similarly, Kapadia *et al.* reported that banana peels exhibited medicinal properties.

Moreover, even the waste materials obtained from peels, seeds, and stones during the processing of fruits and vegetables could be utilized as sources of phytochemicals and antioxidants. Thus, this study examined the potential biological activity of the fruit peels of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita which is locally cultivated in the Province of Albay, Philippines. Hence, the ethanolic fruit peel extracts of these varities of banana was evaluated to determine their gastric ulcer inhibition capacity against various ulcer-induction models in animals. Furthermore, the present study also explores the essential phytochemicals of the fruit peel extracts that might potentially generate biological and pharmacological activities in the treatment and prevention of common human diseases such as a gastric ulcer.

Materials and Methods

Collection of Banana and Taxonomic Identification

Unripe banana fruit samples (Saba, Latundan and Señorita) were purchased in local markets of Tabaco City, Bacacay, Malinao and Ligao City, Province of Albay, the Philippines. Other samples were secured from the local farmers of Ligao City and Malinao. The researcher ensures that the banana fruits are locally

cultivated in the Province of Albay. Unripe banana fruits were the preferred samples to ensure that they are not chemically treated to induce ripening. Moreover, following collecting banana fruits, some of its samples were sent to the Botany Department of the National Museum, the Philippines, that provides scientific names.

Banana Peel Preparation and Extraction

The ripeness of banana fruits has already been described by certain researchers (10). Banana peels were manually separated from the common edible part of the fruit and cleaned under running tap water. Subsequently, they were dried thoroughly with clean cloth. The fruit peels were then air-dried in room temperature for about four to six weeks, and were later cut into small pieces and ground using a mechanical blender until fine powder was produced. Extraction of fruit materials was carried out using the Soxhlet method (11, 12) with some modifications. The powdered peel (1.0 kg) of every variety of bananas was extracted exhaustively with 95% ethanol (analytical grade). The extraction of every variety of bananas lasted for about six hours. The ratio of plant material to solvent in every set up of extraction was 30g in 250ml, respectively. The extract was filtered using Whatman filter paper no.1, and the filtrates were then evaporated using a rotary vacuum evaporator. The samples were stored at 4°C until use.

Determination of Total Phenolic Content

The total phenolic content in the banana fruit peel extracts was determined spectrophotometrically (UH5300) using the Folin-Ciocalteu method (13). Gallic acid was utilized as the standard. An aliquot of the crude extract and standard was added to Folin Ciocalteau reagent and 7.5% sodium carbonate. Absorbance was read at 765nm. The content of phenolic compounds was identified from the standard curve, and was exhibited as gallic acid equivalent (GAE) in mg per gram dry weight (mg/g dw of the extracted compound). All the tests were analyzed in triplicates.

Determination of Total Flavonoid Content

The flavonoid content in the banana fruit peel extracts was determined using aluminum chloride colorimetric assay (14, 15). Quercetin was used as the standard. An aliquot of the crude extracts and standard was added to distilled water, sodium nitrite, and aluminum chloride. The mixtures were incubated, added to NaOH, and were then mixed. The mixtures were allowed cooled, and the absorbance was measured at 510 nm. The total flavonoid content was evaluated from the calibration curve and was exhibited as mg quercetin equivalent per g of dry weight. All the samples were analyzed in triplicates.

Determination of Antioxidant Activity by DPPH-Scavenging Assay

The free radical scavenging activity of the peel extracts of three varieties of banana and standard solution (ascorbic acid) were studied using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging method (15). The assay mixture encompassed 2 ml of 1.0 mmol/L DPPH radical solution developed in methanol and 1 ml of standard or extract solution of distinct concentrations (5-100mcg/mL). The solution was quickly blended and incubated in the dark at 37 °C for 30 minutes. The absorbance of every solution was assessed at 517 nm against a blank using spectrophotometer (UH5300). Ascorbic acid was used as the reference standard, and the reaction without the samples was used as the control. All the determinations were carried out in triplicates. The following formula calculated the percentage of radical scavenging (5%):

$$\% \text{ Free radical scavenging activity} = \frac{A_c - A_8}{A_c} \times 100$$

Where A_c = Absorbance of control at 517 nm; A_8 = Absorbance of plant sample/extract.

The concentration of the sample needed to scavenge 50% of the DPPH free radical (IC50) was assessed from the curve of percent inhibitions plotted against the respective concentration.

Ethical Approval for Animal Use

Before conducting the acute toxicity and gastric ulcer studies, the researcher sent an application to the Bicol University Animal Care and Use Committee (BUACUC) that reviewed the research protocol. After a thorough examination, the committee issued the endorsement with the approval certificate number

PRF-2017-09-017 to proceed with the in vivo studies.

Experimental Animals Used for Toxicity Study

Female Sprague-Dawley rats that were used is 6-8 weeks old and weighed 110-140 g were obtained from the Food and Drug Administration (FDA) in Alabang, Muntinlupa City, the Philippines. The animals were kept in a sanitized polycarbonate cages that contained sterile rice haul as beddings. The animal colony was kept under controlled circumstances of temperature (23±2 ◦C), humidity (50±5%) and a 12 h light–dark cycle. Prior to conducting the toxicity study, the animals were given commercially formulated rat food and water *ad libitum* until they aged 8-12 weeks old and weighted 180 – 250 g. Moreover, the toxicity study was conducted in line with the guidelines of the Bicol University Animal Care and Use Committee (BUACUC) and the Philippine Association for Laboratory Animal Science (PALAS).

Experimental Animals Used for Anti-Ulcer Studies

Male Sprague-Dawley rats weighing 150-200 g were obtained from the Food and Drug Administration (FDA) in Alabang, Muntinlupa City, the Philippines. The animals were kept in sanitized polycarbonate cages that contained sterile rice haul as beddings. The animal colony was kept under controlled circumstances. That is to say, the temperature was 23±2 ◦C, and humidity was 50±5%. There was a 12 h light–dark cycle. The rats were acclimatized for seven days. They were fed with commercially formulated rat feed and water *ad libitum*. Similarly, all the anti-ulcer studies were carried out in compliance with the guidelines of the Bicol University Animal Care and Use Committee (BUACUC) and the Philippine Association for Laboratory Animal Science (PALAS).

Acute Toxicity Determination

The acute toxicity examination of the fruit peel extracts of the three kinds of banana was initially performed to determine the non-toxic dose to be used in the gastric ulcer studies. The acute toxicity investigation was conducted in compliance with the 'Guidelines for Testing Chemicals-Acute Oral Toxicity-Up-and-Down-Procedure (UDP)' outlined by the Organization for Economic Co-operation and Development (OECD) Test Guideline (TG) No. 425. A single dose of 2,000mg/kg of the crude extract of each plant material was administered to the three test groups, and distilled water was given to the control group with five rats in each group by oral gavage. Following the overnight fasting period, the fasted body weight of the rats was measured, and the dose was assessed based on the fasted body weight of every animal. Following the administration of water in the control group and fruit peel extracts in the test groups, food was withheld for a further 3-4 hours. The occurrence of toxic symptoms was observed and recorded systematically at 1, 2, 4, and 6 hours after the treatment period daily for 14 days. Alterations occurring in the physical appearance such as in the skin and fur, eyes, and mucous membranes of the rats were monitored. Moreover, abnormal changes in the behavioral pattern, and manifestations of injury or enduring signs of severe distress among the rats, including irritability, tremors, lethargy, sleep, coma, convulsions, salivation, and diarrhea (OECD, TG No. 425) were closely observed daily during the period of toxicity study.

Histopathological Analysis

After completing the 14-day experimental period of the toxicity study, all the female Sprague-Dawley rats were sacrificed by cervical dislocation. Vital organs such as the brain, heart, kidneys, liver, lungs, and spleen were isolated and examined for any lesions macroscopically. After that, all the vital organs isolated from every rat were fixed in 10% buffered formalin. They were regularly processed and embedded in paraffin wax. Paraffin sections (5 μm) were cut on glass slides and stained with hematoxylin and eosin. The slides were investigated by Dr. Joseph S. Masangkay, a veterinary pathologist from the University of the Philippines, Los Baños, Laguna. A light microscope was used, and the magnified images of the structure of the tissues were captured for further research.

Gastric Ulcer Induction

Ethanol-Induced Ulcer (EtOH)

The test was carried out according to the method explicated by other researchers (16) with certain modifications. After 12 hours of fasting except for the water that was provided *ad libitum*, the male Sprague-Dawley rats were randomly divided into five groups of

three animals. Forty-five minutes before the ulcer induction with absolute ethanol, the first group received 2 ml/kg of distilled water (control), and the second group was treated with omeprazole at 40 mg/kg (reference drug, but part of the test group). The remaining groups was given 500 mg/kg of ethanolic fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita, respectively. All the treatments were given orally by gavage using a gavage needle. Forty-five minutes after the treatment, all the animals received absolute ethanol at 1 mL/200 g to induce gastric ulcers. After one hour, the rats were sacrificed via conducting cervical dislocation, and the stomachs were removed and opened along the greater curvature. Subsequently, the stomachs were gently rinsed with distilled water in order to remove the gastric materials before the macroscopic examination. Examination of gastric ulcers was analyzed using the method described by Alphin and Ward (1967) as indicated in Table 1. Furthermore, images of the rats' stomachs were taken for further analysis.

Non-Steroidal Anti-Inflammatory Drugs (aspirin)-Induced Ulcer

The experiment was conducted according to the method as described by other researchers (17) with certain modifications. After 12 hours of fasting except for the water that was provided *ad libitum*, the male Sprague-Dawley rats were randomly divided into five groups of three animals. Forty-five minutes before the ulcer induction with aspirin (ASP), the first group received 2 ml/kg of distilled water (control), and the second group was treated with omeprazole at 40 mg/kg (reference drug, but part of the test group). The remaining groups received 500 mg/kg of ethanolic fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita, respectively. All the treatments were given orally by gavage using a gavage needle. Forty-five minutes after the treatment, all the animals were given ASP at 200 mg/kg to induce gastric ulcers. After four hours, the animals were sacrificed via conducting cervical dislocation, and the stomachs were removed and opened along the greater curvature. Subsequently, the ulcers were investigated as described in EtOH-induced ulcer models.

Cold-Restrain Stress-Induced Ulcer (CRS)

The experiment was carried out based on the method described by previous researchers (18) with some modifications. The random assignment of the groups and the number of animals per group were the same as the ASP and EtOH-induced ulcer models. Moreover, the pre-treatment dosages of the control, and test substances (omeprazole and banana fruit peel extracts) were the same as those described in the previously mentioned ulcer models. CRS was induced in the 12-hour fasted experimental male Sprague-Dawley rats by strapping the fore and hind limbs on a wooden plank and kept for 2 hours at a temperature of 4–6 °C. Subsequently, the rats were humanely killed by cervical dislocation, and ulcers were examined as described in ASP-induced and EtOH-induced ulcer models.

Statistical Analysis of Data

The data required for anti-ulcer cases was replicated three times in all groups, and the results were exhibited as mean ± S.E.M. The statistical distinction between the mean ulcer index (UI), percent ulcer inhibition (% Inhibition) of the groups treated with the ethanolic fruit peel extract of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita and Omeprazole (test groups), including the group treated with distilled water (control group), was calculated using analysis of variance (ANOVA) method. The mean ulcer score in every group of male Sprague-Dawley rats was multiplied by the number of animals in a group divided by 100% that was expressed as the mean UI. On the other hand, the UI of the control group was subtracted by the UI of each test group and divided by the UI of the control group that gives the % ulcer inhibition of every test group.

Results and Discussion

Total Phenolic Content

Phenolic compounds or polyphenols are plant metabolites (19, 20) that form as one of the most plentiful and widely found groups of substances in plants with several known phenol groups (21, 22). The number of the total phenolics of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita,' measured by a slightly modified Folin–Ciocalteu method, varied in plant materials' extract

Table 1: Ulcer scoring (Alphin and Ward, 1967).

ULCER SCORE	CRITERIA
0	Normal Stomach/No Ulcer
0.5	Punctuate or pinpoint ulcers
1.0	Two or more small hemorrhagic ulcers
2.0	Ulcers greater than 3mm in diameter

Table 2: Effects of the fruit peel extracts of the three varieties of banana on ethanol-induced ulcer in rats.

Treatment	**Ulcer Index**	**Percent ulcer inhibition**
Distilled water, 2 ml/kg	$2.00^{a} \pm 0.00$	-
Omeprazole, 40mg/kg	$2.00^{a} \pm 0.00$	00.00
M. acuminata Colla, 500mg/kg	$0.33^{a} \pm 0.19$	83.33
M. paradisiaca L., 500mg/kg	$1.00^{a} \pm 0.33$	50.00
M. acuminata Colla cv. Señorita, 500mg/kg	$0.67^{a} \pm 0.38$	66.67

Results are presented as means ± standard errors of means, n = 3
Means with same superscrips are not significantly different at 5% level of significance.

Table 3: Effects of the fruit peel extracts of three varieties of banana on aspirin-induced ulcer in rats.

Treatment	**Ulcer Index**	**Percent ulcer inhibition**
Distilled water, 2 ml/kg	$2.00^{a} \pm 0.00$	-
Omeprazole, 40mg/kg	$0.00^{b} \pm 0.00$	100.00
M. acuminata Colla, 500mg/kg	$0.33^{b} \pm 0.19$	83.33
M. paradisiaca L., 500mg/kg	$0.00^{b} \pm 0.00$	100.00
M. acuminata Colla cv. Señorita, 500mg/kg	$0.33^{b} \pm 0.19$	83.33

Results are presented as means ± standard errors of means, n = 3
Means with same superscripts are not significantly different at 5% level of significance.

Table 4: Effects of the peel extracts of three varieties of banana on cold restraint stress-induced ulcer in rats.

Treatment	**Ulcer Index**	**Percent ulcer inhibition**
Distilled water, 2 ml/kg	$2.00^{a} \pm 0.00$	-
Omeprazole, 40mg/kg	$0.00^{b} \pm 0.00$	100.00
M. acuminata Colla, 500mg/kg	$1.00^{ab} \pm 0.33$	50.00
M. paradisiaca L., 500mg/kg	$0.00^{b} \pm 0.00$	100.00
M. acuminata Colla cv. Señorita, 500mg/kg	$0.67^{b} \pm 0.38$	66.67

Results are presented as means ± standard errors of means, n = 3
Means with same superscrips are not significantly different at 5% level of significance.

and ranged from 12.3 to 40.3mg gallic acid equivalents (GAE)/g dry weight (dw) as indicated in Figure 1. The highest level of phenolics was found in *M. acuminata* Colla cv. 'Señorita' (40.3mg GAE/gm), while the *M. paradisiaca* L. contains 25.2mg GAE/gm, and the phenolics found in *M. acuminata* Colla were quite low (12.3 mg GAE/gm). Similarly, other have dealt with the presence of phenolic compounds in the banana fruit peel. As a rich source of phenolic compounds (23), banana peel ranks second regarding phenolic content compared with other fruits' peel, including avocado, pineapple, papaya, passion fruit, watermelon, and melon (24).

Phenolic compounds display expansive physiological

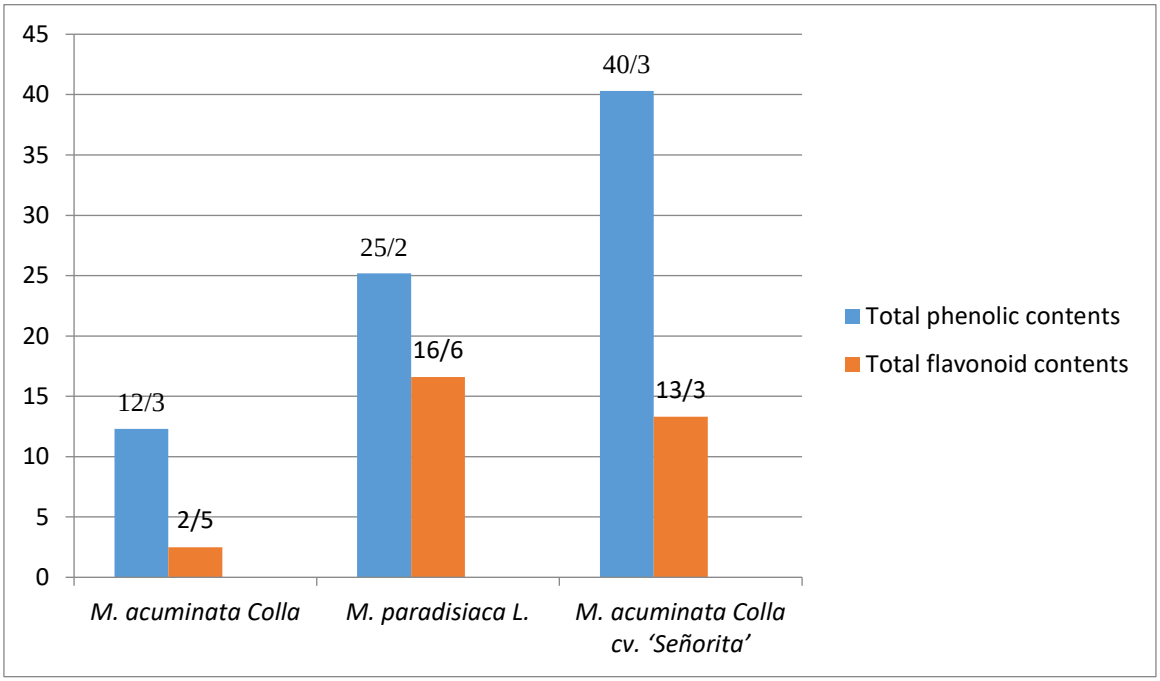

Figure 1. The total phenolic and flavonoid contents (mg GAE/gm) of the ethanolic peel extracts of the three varieties of banana.

properties, including anti-allergenic, anti-atherogenic, anti-inflammatory, anti-microbial, antioxidant, anti-thrombotic, cardioprotective, and vasodilatory properties (25, 26, 27, 28). These beneficial effects were brought about by the phenolic compounds that have been attributed to their antioxidant capacity (29). Similarly, the presence of these compounds in the fruit peel extracts of different kinds of banana under investigation means the existence of a new potential source of essential phytochemicals that will offer biological and pharmacological properties in the preservation of human health and prevention of the risk of many maladies.

Total Flavonoid Content

Flavonoids comprise the largest group of plant phenols that comprise more than half of the eight thousand polyphenols that occur naturally (30). They are subclassified as flavones, flavonols, flavanones and flavanonols, and flavanols, chalcones, isoflavonoids, anthocyanins (anthocyanidins), and bioflavonoids (dimer of flavones, flavonols, and flavanones) (31, 32, 33). Flavonoids are ubiquitously present in fruits, vegetables, nuts, seeds, stems, flowers, tea, wine, propolis, and honey (34).

Similarly, flavonoid compounds were seen in the fruit peel extracts of the three varieties of banana under investigation. As shown in Figure 1, the number of total flavonoids of banana fruit peels, measured by slightly modified aluminum chloride colorimetric assay, varied in plant materials' extract and ranged from 2.5 to 16.6 mg gallic acid equivalents (GAE)/g dry weight (dw). The greatest level of flavonoids was found in *M. paradisiaca* L. (16.6mg GAE/gm), while the total flavonoid was detected to be quite low in *M. acuminata* Colla fruit peel extract. On the other hand, the *M. acuminata* Colla cv. 'Señorita' has a relatively high flavonoid content (13.3mg GAE/gm). Since flavonoids comprise the largest group of plant phenolics, they are the most abundantly and widely distributed group of phenolic compounds existing almost entirely in all plant parts, particularly the photosynthesizing plant cells (35). Hence, fruits and vegetables are the primary dietary sources of these flavonoids. Consumption of flavonoid-rich foods might be beneficial due to their remarkable biological characteristics that improve stability in human health and help reduce the risk of ailments. Dietary flavonoids might contribute to the protection of the body against free radicals by supplementing the body's antioxidant defenses (36). They are considered to be 'nutraceutical' substances (37). Likewise, the

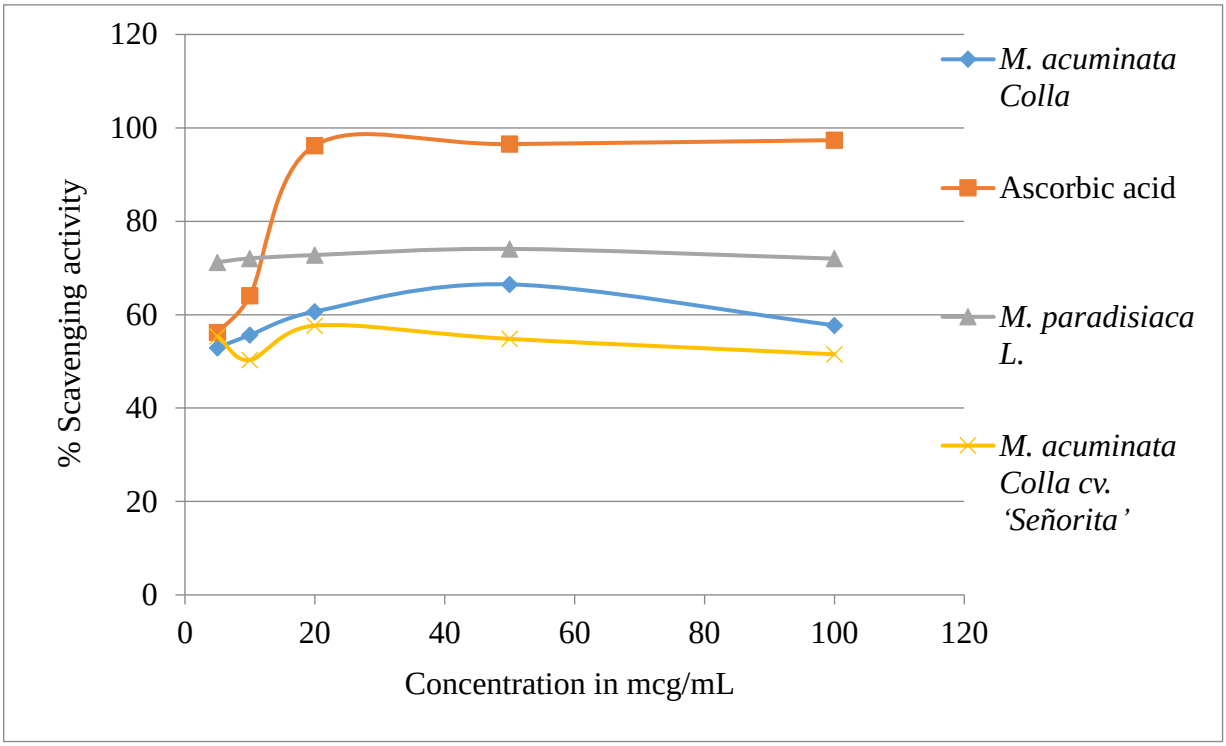

Figure 2. Percent scavenging activity of the peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., *M. acuminata* Colla cv. 'Señorita' and Ascorbic acid.

fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita that contain a considerable amount of flavonoids might be further investigated to establish their fruit peels as a potential source of this vital plant compound, and later for its possible inclusion as one of the nutraceuticals.

DPPH (2, 2-diphenyl1-1-picryl-hydrazyl) Free Radical Scavenging Activity

An antioxidant is a potent substance that contributes to the prevention of the gathering of excessive amounts of free radicals in biological systems (38). Hence, antioxidants decrease the risk of developing certain human diseases. Free radicals and other reactive oxygen species (ROS) are constantly generated during normal physiological processes, especially in pathological conditions (39). However, there are certain defense mechanisms that might be able to scavenge free radicals and protect the body against their harmful effects. Therefore, the fruit peel extracts of three varieties of banana were investigated for their potential free radical scavenging effects or antioxidant activities. In this research, the scavenging effects of the fruit peel extracts of *M. paradisiaca* L., *M. acuminata* Colla, and *M. acuminata* Colla cv. 'Señorita' on the DPPH free radicals were compared with standard anti-oxidant ascorbic acid. The radical form of DPPH is absorbed in 517nm, but when it is reduced by antioxidants, its absorption diminishes because of the creation of DPPH-H, its non-radical state (40). In this investigation, hydrogen-donating antioxidants exhibited free radical scavenging activities exhibited as a percentage of inhibition.

This research indicated that the DPPH free radical scavenging activity of three varieties of banana varied from 51.52 to 72.00% at the concentration of 100 µg/mL. As depicted in Figure 2, the results revealed that the peel extract of *M. paradisiaca* L. could exhibit the highest radical scavenging activity with 72.00%, followed by *M. acuminata* Colla and *M. acuminata* Colla cv. 'Señorita' with 57.73% and 51.52%, respectively, whereas ascorbic acid as the reference control showed a 97.37% radical scavenging activity at the same concentration. In *M. acuminata* Colla, the radical scavenging activity increased as the

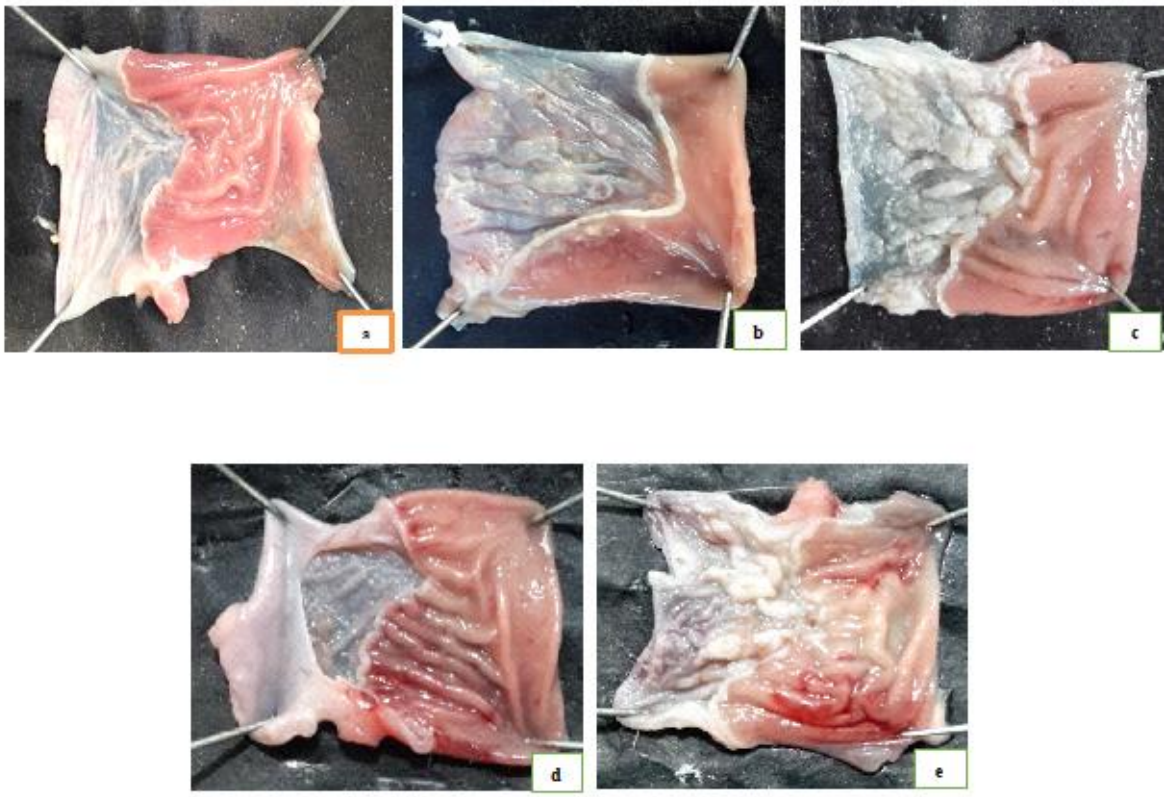

Figure 3. Photographic views of the rats' stomach: (a) Ethanol-induced ulcer treated with *M. acuminata* Colla, (b) Ethanol-induced ulcer treated with *M. paradisiaca* L., (c) Ethanol-induced ulcer treated with *M. acuminata* Colla cv. Señorita, (d) Ethanol-induced ulcer treated with Omeprazole, (e) Ethanol-induced ulcer treated with Distilled water.

concentration of its fruit peel extract rose. Hence, the decrease in the concentration of DPPH might be rooted in the scavenging capacity of the fruit peel extract of *M. acuminata* Colla.

Similarly, Morais *et al.* reported that banana peel has a greater radical scavenging activity and compared to other fruit peels. Moreover, some other researchers have indicated the positive relationship between free radical scavenging capacity and the total phenolic content, in which the radical scavenging activity increased when the increase of phenolic compound content rose (41). Hence, a great correlation between DPPH radical scavenging potential and total phenolic content was indicated (42). Furthermore, other studies found that ripe banana peel also contained other compounds, including the anthocyanins delphinidin and cyanidin (43), catecholamines, dopamine, and L-dopa (44) that might be responsible for exhibiting the biological activities.

On the other hand, the findings of the present study revealed that the extracts characterized by a relatively high level of total phenolic contents exhibited a remarkable radical scavenging activity, which could be associated with the intrinsic nature of phenolic compounds. Potentially, it contributes to their electron transfer or hydrogen donating ability (45). Furthermore, González-Montelongo *et al.* stated that the antioxidant capacity of fruit peel extracts could also be influenced by alterations that occur in the quality and quantity of phenolic compounds and other bioactive compounds that are found in the extracts. They include, though are not limited to, catecholamines and anthocyanins that have been examined in the study conducted on the peel extract of *M. acuminata* Colla AAA. Moreover, the *M. paradisiaca* L. was indicated to be nearly as potent as

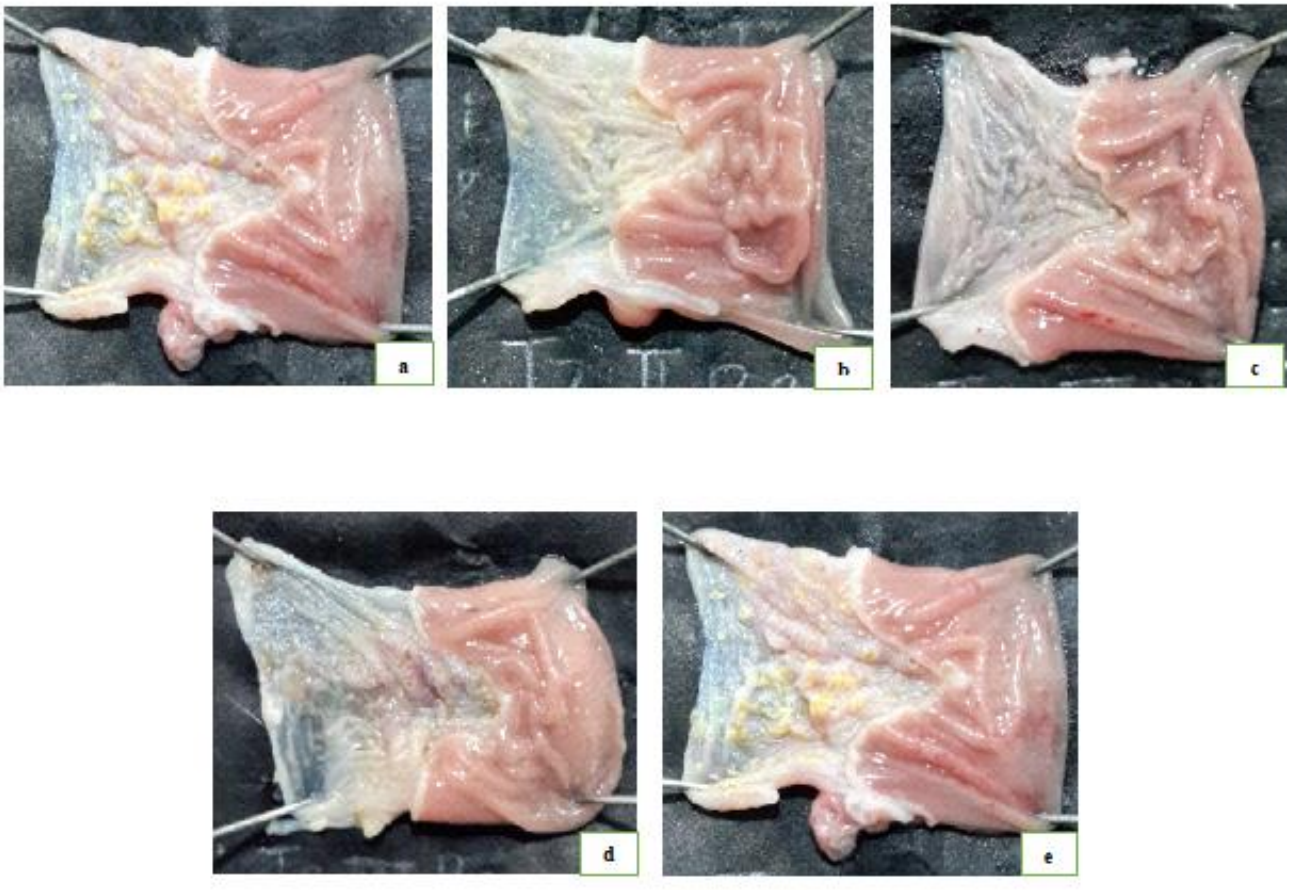

Figure 4. Photographic views of rats' stomach: (a) Aspirin-induced ulcer treated with *M. acuminata* Colla, (b) Aspirin-induced ulcer treated with *M. paradisiaca* L., (c) Aspirin-induced ulcer treated with *M. acuminata* Colla cv. Señorita, (d) Aspirin-induced ulcer treated with Omeprazole, (e) Aspirin-induced ulcer treated with Distilled water.

the ascorbic acid with a maximum inhibition of 72.00% at the concentration of 100 µg/mL which is comparable to 97.37% for ascorbic acid at the same concentration. Thus, the results also indicate that the peel extract of *M. paradisiaca* L. might assist in the prevention of degenerative diseases, and might potentially prevent the development of complications of an existing chronic disease caused by oxidative stress by increasing circulating scavengers or antioxidants.

Hence, the increase in free radical scavenging capacity of *M. paradisiaca* L. could be due to the existence of greater phenolic contents and the essential nature of phenolic compounds, and potentially because of the presence of other bioactive compounds in its peel extract. On the other hand, *M. acuminata* Colla and *M. acuminata* Colla cv. 'Señorita' appeared to have moderate scavenging activity against DPPH. This phenomenon is either because of low concentration of the antioxidants in their extracts or due to the antagonistic behavior of the active compounds that ultimately hinders antioxidant effects (46, 47). Also, both the solvent and distinct antioxidant compounds are influential on the efficacy of the extraction and the activity of the obtained extracts. Thus, the findings of this study might also further suggest the necessity of conducting comparative studies for every plant by-product to determine the extraction circumstances that create maximum antioxidant activity. Furthermore, the present study also agrees with the suggestion by González-Montelongo *et al.* to conduct the isolation and characterization of individual phenolic compounds. In this case, it will also be performed in the by-product (peels) extracts of the *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv,

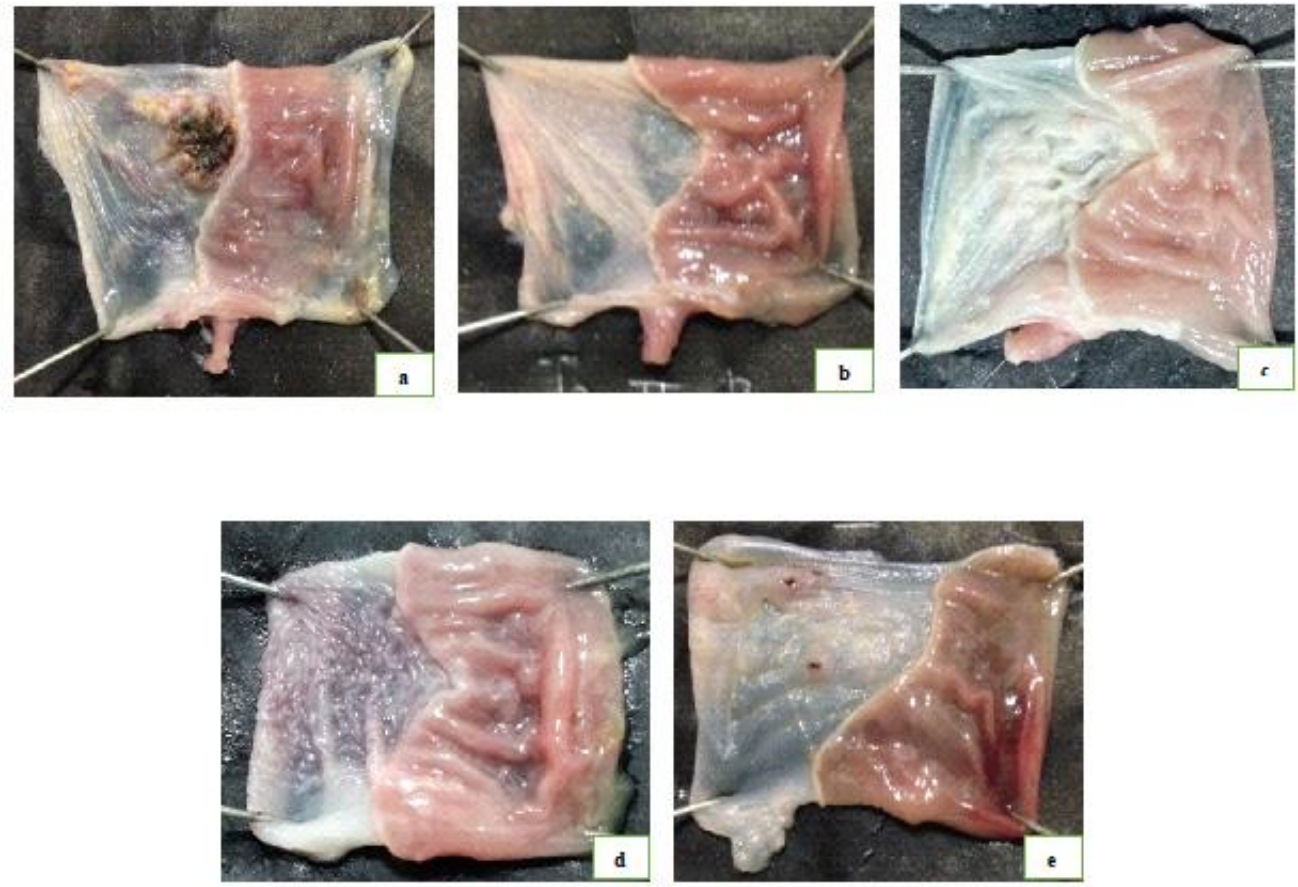

Figure 5. Photographic views of rats' stomach: (a) Cold-restraint stress-ulcer induced treated with *M. acuminata* Colla, (b) Cold-restraint stress-ulcer induced with *M. paradisiaca* L., (c) Cold-restraint stress-ulcer induced treated with *M. acuminata* Colla cv. Señorita, (d) Cold-restraint stress-ulcer induced treated with Omeprazole, (e) Cold-restraint stress-ulcer induced treated with Distilled water.

Señorita to determine the mechanisms involved in the antioxidant activity.

Acute Toxicity Study

The toxicity study of the peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita' at 2000mg/kg showed no mortality. Moreover, during the 14-day experimental period of observation, the rats did not exhibit any change in the physical appearance such as in the skin and fur, eyes, and mucous membranes. Furthermore, there were no signs of abnormal changes in the behavioral pattern, injury, or enduring signs of severe distress among the rats, including irritability, tremors, lethargy, sleep, coma, convulsions, salivation, and diarrhea, respectively. Moreover, the histological examination of the liver, kidneys, and spleen did not show any differences between the control and test groups. With this, the peel extracts were found to be safe and higher than 2000 mg/kg, p.o. in rats, thus 500 mg/kg, p.o. was selected for gastric ulcer studies.

Gastric Ulcer Studies

A peptic ulcer developed during the disruption of the equilibrium between the driving determinants (gastric acid, pepsin, etc.) and the gastrointestinal components that maintain the integrity of gastrointestinal mucosal membrane (48, 49). Hence, an agent that exhibits a capacity to restore the balance by developing the activity of the cytoprotective agents or minimizing the secretion of gastric acid could have the role of an anti-ulcerative agent (49). Hence, the present study investigated the potential anti-ulcer capacity of the fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita' using various ulcer induction models in rats that cause a gastric ulcer in different mechanisms such as

alcohol-induced (ethanol), aspirin-induced (NSAIDs), and cold-restraint stress (CRS) induced ulcers.

Ethanol is considered as a common aggressive determinant in the pathogenesis of peptic ulcer (50). It brings about ulceration following increased generation of reactive oxygen species (ROS) which is stimulated by lipid peroxidation, and harmfully affects the cells and cellular membranes of the mucosal epithelium (51). As described by Ghasi (as indicated in Figure 3, e), the oral administration of ethanol resulted in the creation of severe ulcers and hemorrhagic streaks on the gastric mucosa of the control group. Whereas, pre-treatment of the animals with a 500mg/kg body weight of ethanolic fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita' before ethanol administration protected against ulcerogenesis by 83.33% (UI 0.33a ± 0.19), 50.00% (1.00 a ± 0.33) and 66.67% (0.67 a ± 0.38), respectively. However, the results with regard to the groups and the reference anti-ulcer agent, omeprazole, were not statistically different at 5% level of confidence, which offered 00.00% protection, and its UI is 2.00 a ± 0.00 as depicted in Table 2. With this, the results show that the red coloration seen in the gastric mucosa is caused by the damaging effect of ethanol, which is partially inhibited by the fruit peel extracts of the three varieties of banana. Moreover, it indicates that all the lesions (perforations, ulcers, or hemorrhagic streaks) were developed due to the disruption of the vascular tissues of the gastric mucosal endothelium (52).

On the other hand, non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin have adverse impacts on the gastroduodenal mucosa causing ulcerative lesions on the mucous membrane. This ulcerative lesion might be the outcome of several mechanisms such as the suppression of the synthesis of gastric cytoprotective prostaglandin E2 (via cyclooxygenase enzyme inhibition), decline of blood supply to gastric mucosa, the rise of gastric secretion, and the inactivation of the growth determinants that are affective in mucosal defense and repair (53). In this research, the impact of orally administered ethanolic fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita' on gastric damage induced by aspirin (200mg/kg body weight) in Sprague-Dawley rats after four hours has been shown in Figure 4. The results indicated that the peel extracts of the three varieties of banana could inhibit the development of ulcers in rats. Maximal inhibition (100%) was displayed by *M. paradisiaca* L. (UI of 0.00 b ± 0.00) and the reference drug was omeprazole (UI of 0.00 b ± 0.00), whereas *M. acuminata* Colla (UI of 0.33 b ± 0.19) and *M. acuminata* Colla cv. Señorita (UI of 0.33 b ± 0.19) offered the same ulcer protection of 83.33% against the damaging effect of aspirin. However, the results associated with the treated groups and the reference anti-ulcer agent, omeprazole, were not statistically different at 5% level of confidence (as shown in Table 3). With this, the fruit peel extracts of the three varieties of banana might have acted against the impact of aspirin by reactivating prostaglandin synthesis hindered by aspirin, or the processes that are necessary for the regeneration of gastrointestinal mucosa, as described by Ghasi. On the other hand, Ghasi reported that the reference drug (omeprazole) initiated a mechanism or mechanisms that could be distinguished from the cyclooxygenase pathway that could be blocking the development of gastric ulcers. This inhibition of gastric ulcer is attributed to the antioxidant property of omeprazole, the scavenging of hydroxyl radicals (54).

Another model of ulcer induction used in the study was the cold-restraint stress ulcer in rats. Stress is of high significance in the development of gastroduodenal ulceration. The authors reported that ulcers caused by stress are likely to be mediated by histamine release with enhancement in acid secretion and a decrease in mucus production (55). Other mechanisms that might be involved in the onset of stress-induced ulcers include the rise gastric motility, vagal overactivity (56), mast cell degranulation (57), the decline of gastric mucosal blood flow (58) and reduced prostaglandin synthesis (59).

However, generally, stress-induced ulcers also involve damage by reactive oxygen species (ROS) in addition to acid and pepsin related factors. The level of Lipid Peroxidation (LPO) increases during stress due to an increase in the generation of ROS that results in oxidative damage. Superoxide dismutase (SOD) changes the reactive superoxide radical to H2O2. If it

is not scavenged by Catalase (CAT), it could by itself induce lipid peroxidation through the generation of hydroxyl radicals. Hence, the decrease in the levels of CAT will result in an increase in accumulation of ROS, and ultimately increases lipid peroxidation and tissue damage, as reported by Sairam *et al.* & Eswaran *et al*. Consequently, damage to gastric mucosa leads to the development of an ulcer.

However, as shown in Figure 5, the results of the present study revealed that the pre-treatment of the fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. 'Señorita' displayed gastroprotection against stress-ulcer mechanisms in rats. Primarily, the fruit peel extract of *M. paradisiaca* L. offered 100.00% (UI of 0.00 b ± 0.00) ulcer inhibition which is similar to the effect of reference drug omeprazole which also exhibited 100.00% (UI of 0.00 b ± 0.00) ulcer inhibition. On the other hand, the fruit peel extract of *M. acuminata* Colla and *M. acuminata* Colla cv. Señorita offered 50.00% (UI of 1.00 ab ± 0.33) and 66.67% (UI of 0.67 b ± 0.38) ulcer inhibition against stress-ulcer mechanisms in rats respectively. Hence, the results associated with the treated groups and the reference anti-ulcer agent, omeprazole, were not statistically different at 5% level of confidence (as depicted in Table 4).

The results of ulcer inhibition effects displayed by the three varieties of banana against the damaging effects of aspirin and stress could be linked to the presence of phytochemicals from the fruit peel extracts which possessed the antioxidant capacity. Phenolic compounds have antiulcerogenic impacts pertaining to cytoprotective activity (60). Similarly, Imam & Akter reported that leucocyanidin, a flavonoid which is found in the banana fruit peel, remarkably increases the thickness of the mucous membrane layer of the stomach. Therefore, the fruit peel extracts of these varieties of banana exhibit high capacities to be used for medicinal purposes if they are optimally explored and processed.

Conclusion

The present study indicated that the fruit peel extracts of *M. acuminata* Colla, *M. paradisiaca* L., and *M. acuminata* Colla cv. Señorita could exhibit anti-ulcer properties. It also suggests that fruit peel extracts are potential sources of natural antioxidants that contribute to the maintenance of human health. They might treat diseases, and prevent certain ailments. Furthermore, banana peel extracts contain active compounds that are potentially responsible for its biological and pharmacological activities. On the other hand, the findings also warrant other extraction methods and further phytochemical analysis to isolate the elements responsible for the exhibition of these therapeutic activities. Moreover, the potential medical use of the fruit peels of banana not only treat various human ailments, but also prevent potential environmental harms of this by-product which is regarded as waste.

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Conflict of Interest

The author declares that he has no conflict of interest.

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