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Research Article

Gastroprotective Activities of *Canarium schweinfurthii* Fruit and Oil Diets: Role of H^+/K^+ ATPase Activity

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Abstract
Canarium schweinfurthii fruit and fruit-pulp oil is used in folk medicine for the treatment of peptic ulcer although there is limited scientific information this activity. This study aims to investigate the gastro-protective potential and mechanism of the fruit and fruit-pulp oil of *C. schweinfurthii* in indomethacin-induced gastric ulcer. One hundred and forty (140) Wistar rats (120-150g; n=20) were divided into seven groups namely: Groups 1, 2 and 3 were control, untreated, and cimetidine treated (30 mg/kg b.w) while groups 4 and 5 received in their feed 30% and 60% of *C. schweinfurthii* fruit while groups 6 and 7 received 1mL/kg and 2mL/kg of *C. schweinfurthii* oil. They were pre-treated for 14 or 28 days prior to ulcer induction using 40 mg/kg indomethacin for 4 hours. Basal and stimulated gastric acid secretion, ulcer scores and stomach biochemical variables were estimated and processed for histological evaluation by days 14 and 28 of gastric ulceration. *Canarium schweinfurthii* fruit and fruit pulp oil significantly decreased gastric ulceration, histamine stimulated gastric acid secretions and lipid peroxidation compared with untreated group. Pre-treatment with high doses of *C. schweinfurthii* fruit and fruit pulp oil significantly increased gastric mucin, mucous cell count and nitric oxide levels as well as catalase activity compared to untreated group. There were no visible lesions in the *C. schweinfurthii* diet fed groups. *Canarium schweinfurthii* fruit and fruit pulp oil inhibit histamine induced gastric acid secretion, H^+K^+ATPase pump activities, increase antioxidant enzymes, nitric oxide level, gastric mucin and mucous cell counts.

Key Words: *Canarium schweinfurthii*, H^+K^+ATPase pump, nitric oxide, mucus cell count

*INTRODUCTION

The stomach is traditionally regarded as a hollow muscular sac that initiates the second phase of digestion. The unique biological function of gastric acid secretion not only initiates the digestive process but also acts as a first line of defense against food-borne microbes (Hunt *et al*., 2015; Martinsen *et al*., 2019). Gastric ulcers are breach or deep lesions penetrating through the stomach or gastric mucosa and muscularis mucosa layers. It is believed that gastric ulcers develop due to an imbalance of aggressive factors (increased reactive oxygen species, Helicobacter pylori, NSAIDs, lipid metabolites, neuropeptides, and gastric acid) and protective factors (mucin, bicarbonate and prostaglandins), causing an interruption to and within the gastric mucosal integrity (Hiraishi *et al*., 1999; Bandyopadhyay *et al*., 2002; Amandep *et al*., 2012; Shin *et al*., 2013, Omeonu *et al*., 2022). Recent studies show prevalence rates for both duodenal and gastric ulcers in both southern and northern Nigeria (Mustapha *et al*., 2008; Ndububa and Adeyemi, 2008; Eniojukan *et al*., 2017). However, over 80% of Nigerians depend on medicinal plants (also known as phytotherapy) in managing various acute and chronic diseases (Hassan *et al*., 2012) as they are cheaper with little or no side effects (Igoli *et al*., 2002; Akinwumi *et al*., 2022). Plant extracts and their crude are the most significant sources of new drugs and have been shown to cause promising results in the treatment of gastric ulcer (Falcao *et al*., 2008; Palle *et al*., 2018). *Canarium schweinfurthii* has been used traditionally for treating ulcer (Noumi *et al*., 2000). *Canarium schweinfurthii* is indigenous to tropical Africa belonging to the Burseraceae family (Orwa *et al*., 2009). It is grown widely in the equatorial forest regions of East, West and Central Africa (Dawang *et al*., 2016). It is common in rocky and flatlands in Plateau (Nyam *et al*., 2018), Bauchi, Southern Kaduna, Niger, Oyo States of Nigeria (Dawang *et al*., 2016). It is called African elemi, purple canary tree or bush candle tree in English. In Nigeria, it is also known by quite a number of local names which include; Berom in Plateau state (Pwat), Atile or Atilis in Hausa, Ube agba in Igbo and Origbo, Elemi or Agbabubu in Yoruba (Gbile *et al*., 1984; Burkill, 1985; Dawang *et al*., 2016). It has also been described as one of the lesser-known seeds with respect to underutilized wild fruits and oil seeds (Maduelosi and Angaye, 2015). *Canarium schweinfurthii* root, bark, fruit, seed, leaf, oil, flower, gum and resin are extensively used in traditional medicine by people of rural areas to manage health problems or as source of their food (Tcheghebe *et al*., 2016). The stem bark decoction of *Canarium schweinfurthii* is used as a remedy for ulcer, roundworms, colic, stomach pains, pain after childbirth, dysentery and gonorrhea (Burkill *et al*., 1985; Johnson and Olsen 1997; Orwa *et al*., 2009; Tcheghebe *et al*., 2016). The oil is used in treatment of ulcer, hot water and fire burns (Tcheghebe *et al*., 2016; Nyam *et al*., 2018). Its decoction is used to cure anemia, eyes diseases, helminthes infection, diarrhea, goiter hypertension, gastro-intestinal disorder, toothache, cardiovascular, condition, yellow fever or to ward

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off evil spirits (Koudou *et al*., 2005; Kouambou *et al*., 2007; Ngbede *et al*., 2008; Okullo *et al*., 2014).

The phytochemical screening of *Canarium schweinfurthii* revealed the presence of active chemical compounds in all its parts. From leaves showed saponins, tannins, cardiac glycoside, steroids and flavonoid (Ngbede *et al*., 2008); from fruit oil: Phenolic compounds (Atawodi *et al*., 2010); From bark: triterpenes, steroids, saponins, lipids and glycosides (Kouambou *et al*., 2007); from resin: Triterpenoic acids (Yousuf *et al*., 2011); from seed: Tannins, balsams, cardiac glycosides, phenols and flavonoids (Uzama *et al*., 2012), canarene (Tamboue *et al*., 2000). The analyses of the fruit mesocarp oil of *Canarium schweinfurthii* by HPLC-UV, HPLC-MS and GC-MS techniques revealed the presence of phenolic compounds such as catechol, p-hydroxybenzaldehyde, dihydroxyphenylacetic acid, tyrosol, p-hydroxybenzoic acid, dihydroxybenzoic acid, vanillic acid, phloretic acid, pinoresinol, secoisolariciresinol (Atawodi, 2010). *Canarium schweinfurthii* fruit and fruit pulp oil contains active chemical compounds like flavonoids. This study was designed to evaluate the anti-ulcer mechanisms of *Canarium schweinfurthii* fruit and fruit pulp oil during indomethancin-induced gastric ulceration in male Wistar rats.

MATERIALS AND METHODS

Experimental animals: One hundred and forty (140) Male Wistar rats weighing between 100-120g (n = 20) were procured from the Central Animal House, College of Medicine, University of Ibadan. They were housed in clean, well-ventilated poly-propylene cages and provided standard rat chow and clean tap water ad libitum. They were acclimatized for two weeks before any experimental work was done and maintained under standard condition of 12 hours of alternating light and dark cycle. All experiments were conducted adhering to the Guidelines of University of Ibadan. Animal Care and Use Research Ethics Committee, (UI-ACUREC/061-0819/28).

Plant collection and authentication: The plant and fruit of *C. schweinfurthii* were purchased from a local market in Jos, Plateau State. They were identified and authenticated at the Forest Reserve Institute of Nigeria, (FHI No: 112972).

Feed preparation: The basal diet was standard rat chow containing 25.5% protein, 4.0% lipids, 53.5% carbohydrate, 4.0% fiber, 7.0% ash and 6.0% water. *Canarium schweinfurthii* fruits diet was prepared following the method by Salami *et al*., 2018. The fruits and fruit pulp oil were purchased. The fruits were washed in warm water (26^{o}C) for 15 minutes. The seeds were removed, and the fruit pulps were air dried for about 7 days at room temperature. The dried fruit pulp was milled into fine powder. The blended fruit pulp was then mixed with standard rat chow in the proportion of 30% and 60% while the fruit pulp oil was then mixed with standard rat chow in the proportion of 1mL/kg and 2mLs/kg.

Experimental design: Animals were divided according to the following experimental groups in a two phase study for gastric ulceration (N=70, n=10) and gastric acid secretion (N=70, n=10) on both days 14 and 28 pretreatment.

Group I: Normal Control (CO) fed basal diet without ulcer induction.

Group II: Ulcer Untreated (UU) fed basal diet with ulcer induction without treatment.

Group III: Cimetidine treated group (CM) fed basal diet with ulcer induction treated with 30mg/kg b.w cimetidine.

Group IV: Test group 1 on low dose (LF) fed basal diet supplemented with 30% *Canarium schweinfurthii* fruits.

Group V: Test group 2 on high dose (HF) fed basal diet supplemented with 60% *Canarium schweinfurthii* fruits.

Group VI: Test group 3 on low oil quantity (LO) fed basal diet supplemented + 1mL/kg b.w of *Canarium schweinfurthii* fruit pulp oil.

Group VII: Test group 4 on high oil quantity (HO) fed basal diet supplemented + 2mLs/kg b.w of *Canarium schweinfurthii* fruit pulp oil.

Gastric acid secretion experimental procedure: Prior to experiment, animals were fasted overnight with free access to water. They were anesthetized intraperitoneally with a cocktail of Xylazine (5mg/kg) and Ketamine (60mg/kg) anaesthesia as previously reported by Shaefer *et al*., 2005; Salami *et al*., 2021. They were then affixed on the dissecting board and laparatomy was performed. A midline incision was made through the skin of the neck and blunt dissection was done to expose the trachea. A small cut was made in the upper part of the trachea. Fluid was removed from the airway using a moist cotton wool. The technique is known as the continuous perfusion technique designed by Ghosh and Schid (1955) modified by Amure and Ginsburg, 1964.

Basal and stimulated gastric acid secretion: Effluent was collected for a period of 30 minutes to ascertain basal secretion after which histamine (1mL/kg) was administered. Gastric effluent was collected every 10 minutes and the acidity assayed by titration as described below.

Titration technique: The effluent (10 mLs) from the rat was titrated against 0.0025 N NaOH using 2 drops of phenolphthalein as indicator. The conical flask was well shaken during the titration until a pink color was observed, which signifies the end point of titration.

Calculations:

Titrable acidity in each sample was calculated as

CA= (CB X VB) / VA … Equation 1

Where CA= Acid concentration of gastric secretion, CB= Concentration of NaOH, VA= Volume of gastric effluent, VB= Volume of NaOH used to titrate.

Concentration (MEq/L) = Concentration (mmol/L) x Valency

Induction of gastric ulcer using indomethacin: Indomethacin (40 mg/kg) was administered orally to overnight fasted animals, after receiving their respective pre-treatment (days14 or 28). Four hours after, the animals were sacrificed by cervical dislocation thereafter laparotomy was done with the stomach excised, opened by cutting along the greater curvature, rinsed in cold phosphate buffer and pinned on a filter paper. The degree of ulceration was evaluated and

counted with the aid of a magnifying lens using the method of Alpin and Ward, 1967 as modified by Elegbe and Bamgbose, 1976.

The following criteria in table 1 were used for the scoring

Table 1:
Ulcer Score Grades

Ulcer	Criteria
0	Normal stomach (No ulcer)
0.5	Punctuated haemorrhage / Pin Point
1.0	Two or more small haemorrhage ulcer
2.0	Ulcer greater than 2mm in diameter

Determination and Estimation of Mean Ulcer Score (MUS) Index of Ulceration:

The ulcers index (UI) is expressed as: (M x N) / 100 … Equation 2
Where M = mean number of ulcers per rat in the group, N=number of rats with ulcer in the group.

Percentage Inhibition (% Inhibition) = (UI control – UI treated / UI control) X 100 … Equation 3

Gastric biochemical variable estimation: The excised, cleaned stomachs were then homogenized with a tissue homogenizer, centrifuged at 4ºC at 5000 rpm for 10 minutes using a cold centrifuge. The supernatants from each sample were kept in the freezer at -20ºC pending biochemical assays. Gastric protein concentration was estimated according to the method of Gornal *et al*., 1949, with slight modification. Potassium iodide was added to the Biuret reagent to prevent precipitation of CU2+ as Cuprous Oxide. The degree of Lipid peroxidation was determined according to the method of Varshney and Kale, 1990. The SOD activity in gastric tissue homogenates was determined as described by Misra and Fridovich, 1972. Catalase activity of the gastric tissue homogenate was determined according to the method of Sinha, 1972. The amount of Nitric Oxide was measured in the gastric mucosa according to the method of Moshage *et al*.,1995. Gastric mucin level was determined according to the method of Winzle, 1955. Gastric H^+/K^+ATPase pump assay was carried out by the method of Bewaji *et al*. 1985 and Salami *et al*., 2018.

Histological processing and histomorphometry: Histology: A portion of the stomach sample were cut, fixed in 10% formalin and later embedded in paraffin and sectioned at 5µm in an automated microtome. Staining was done with the Haematoxylin and Eosin (H&E) and Periodic Acid Schiff (PAS) technique after which the stained sections were evaluated morphologically for inflammation, granulation, regeneration and vascular integrity (Salami *et al*., 2018; 2021). A microphotograph was taken to show microscopic changes or pathology.

Statistical analysis: Data was expressed as Mean ± SEM. Statistical difference between the groups was calculated using two way ANOVA. $p \leq 0.05$ was considered significant.

RESULTS

Effect of *C. schweinfurthii* fruit and fruit pulp oil diet on percentage body weight change: *C. schweinfurthii* fruit significantly reduced the percentage body weight in the low fruit compared with all other groups by the second week till the end of the experiment, (Figure 1).

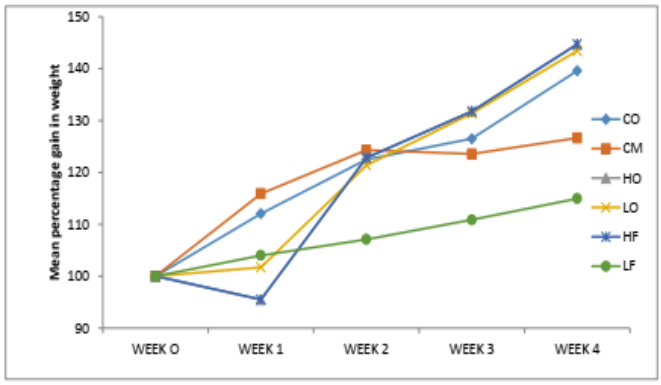


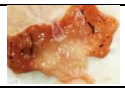
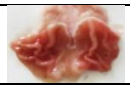
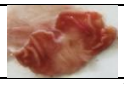
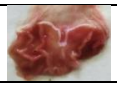
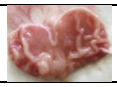
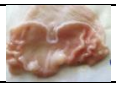
Figure 1:
Effect of *Canarium schweinfurtii* fruit and oil on percentage body weight change by weeks 2 and 4 of diet pre-treatment.

Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

Effect of *C. schweinfurthii* fruit and fruit pulp oil diet on mean ulcer score and mucus cell counts: After two weeks pre-treatment, there was a significant decrease in mean ulcer score in High Fruit (HF), Low Fruit (LF), High Oil (HO), Low Oil (LO), and Cimetidine (CM) groups compared with Ulcer Untreated (UU) group, (Table 2). After four weeks pretreatment, there was a significant decrease in mean ulcer score in High Fruit (HF), Low Fruit (LF), High Oil (HO), Low Oil (LO), and Cimetidine (CM) groups compared with Ulcer Untreated (UU) group, (Table 2). *C. schweinfurthii* fruit and fruit pulp oil significantly increased the mucus cell counts at both weeks 2 and 4 compared with the control groups, (Table 2; Plates 1 and 2).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on hematological variables and blood inflammatory markers: *Canarium schweinfurthii* fruit pulp oil significantly reduced packed cell volume, and hemoglobin content by 2 and 4 weeks of experiment compared with other groups, (Table 3). The platelet count of the control group significantly increased compared with all other experimental groups by 2 weeks while the lymphocyte counts decreased by 2 and 4 weeks, (Table 4). The neutrophil/lymphocyte count significantly increased in the control group by week 4 of experiment, (Table 5). *C. schweinfurthii* fruit and fruit pulp oil diets significantly reduced the NO/MDA level compared with the control and cimetidine groups by weeks 2 and 4 of experiment, (Table 5).

Table 2:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on mean ulcer score, percentage inhibition and mucous cell count

Groups	Macroscopic Mean Ulcer Score		Percentage Inhibition (%)		Microscopic Mucous Cell Count	
	Week 2	Week 4	Week 2	Week 4	Week 2	Week 4
UU	 24.88 ±3.00	 15.50 ± 0.29	0	0	275.33 ± 10.83	198.33 ± 34.95^{bcde}
HF	 9.25 ± 2.66^{acdef}	 4.75 ± 2.65^{adef}	62.81^{cdef}	80.90	446.00 ± 29.00^{acdef}	479.00± 62.0^{acdef}
LF	 2.50 ± 1.50^{abf}	 5.37 ± 2.20^{adef}	89.94	78.39^{bdef}	368.33 ± 35.62	592.33 ± 29.55^{af}
HO	 1.00 ± 0.41^{a}	 0.00 ± 0.00 ^{abcef}	96.49	100.00	299.33 ± 25.16^{bcef}	549.33 ± 61.33^{af}
LO	 2.50 ± 1.28^{abf}	 0.50 ± 0.30^{abc}	89.99	97.98	357.67 ± 14.09	444.67± 24.33^{af}
CM	 0.50 ± 0.20^{a}	 0.30 ± 0.14 ^{abc}	97.98	99.89	355.00 ± 23.15	297.66 ±33.73^{abcde}

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: ^{a}– control (CO), ^{b}– high fruit (HF), ^{c}– low fruit (LF), ^{d}– high oil (HO), ^{e}– low oil (LO), ^{f}– cimetidine (CM). where HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

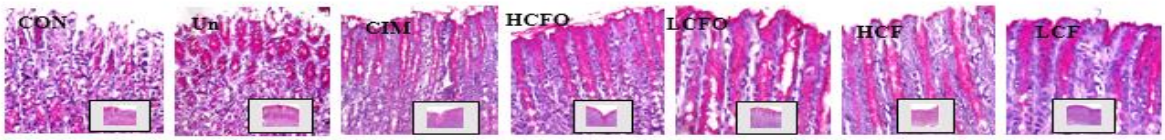


PLATE 1: Photomicrographs of PAS stain gastric tissue by 2 weeks pre-treatment MAGX400 (XI00 inserted) CON: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **Un**: **CIM**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **HCFO**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **LCFO**: abundant surface epithelia mucin production (thin arrow), moderately stained foveolar and mucus neck cells. **HCF**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **LCF**: abundant surface epithelia mucin production (thin arrow), moderately stained foveolar and weakly stained mucus neck cells.

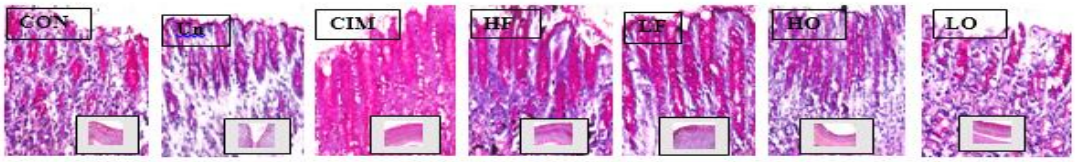


PLATE 2: Photomicrographs of PAS stain gastric tissue by 4 weeks pretreatment MAGX400 (X100 inserted) CON:abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **Un**: surface epithelia mucin production (thin arrow) **CIM**: surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **HF**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **LF**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. **HO**: surface epithelial mucin production (thin arrow) and focal areas of weakly stained mucus cells (black arrow). **LO**: abundant surface epithelia mucin production (thin arrow), weakly stained foveolar and mucus neck cells. There are focal areas of weakly stained mucus cells (black arrow).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on Liver and Kidney (Creatinine) function tests and Lipid profiles: *Canarium schweinfurthii* high fruit diet significantly increased the AST and creatinine levels compared with other experimental groups by the fourth week of treatment. The ALP levels significantly increased in the cimetidine treated groups alone compared with other groups by week 2 of treatment, (Table 6). The total cholesterol level and High-density lipoprotein (HDL) significantly decreased in the *Canarium schweinfurthii* fruit pulp oil compared with control by week 4 while *Canarium schweinfurthii* low fruit pulp oil diet significantly increased High density Lipoprotein by the week 2 of experiment, (Table 7).

Table 3:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on hematological indices.

	PCV (%)		HB (g/dl)		RBC x 10^6µl		Platelet (millions/cu mm)		ESR (mm/hr)	
	WEEK 2	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**
CO	43.00.± 1.54	40.80 ± 2.72	14.20 ± 0.41	13.38 ± 0.95	7.20 ± 0.31	6.90 ± 0.46	126600.00 ± 12959.94	12080.00 ± 5379.59	0.80± 0.055	0.90± 0.05
HF	46.00 ± 2.30	43.00 ± 2.77	15.02± 0.66	13.94 ± 0.96	7.42 ± 0.36	7.10 ± 0.57	15560.00 ± 25366.51[a]	11840.00 ± 4523.27	0.90± 0.13	1.04± 0.11
LF	48.60 ± 0.81	45.20 ± 1.15	15.88 ± 0.16	14.80 ± 0.37	8.08 ± 0.19	7.70 ± 0.19	15000.00 ± 15877.66[a]	12600.00 ± 4159.32	0.92± 0.04	0.80± 0.00
HO	44.20 ± 3.87	41.60 ± 2.31	14.40 ± 1.34	13.48 ± 0.79	7.37 ± 0.79	6.90 ± 0.39	14600.00 ± 10114.35[ae]	11480.00 ± 3455.43[cf]	1.02± 0.12[ae]	0.82± 0.02
LO	41.00 ± 3.00[bcf]	37.60 ± 3.28[bcf]	13.30 ± 1.03[bcf]	12.20 ± 1.14	6.73 ± 0.63[c]	6.14 ± 0.53	11580.00 ± 4103.66[abcdf]	11440.00 ± 5564.17 [ae]	0.76± 0.02	0.96± 0.13
CM	47.80 ± 0.58	50.20 ± 0.49 [ade]	15.70 ± 0.08	17.10 ± 0.31[abde]	7.80 ± 0.18	8.40 ± 0.07 [a]	14940.00 ± 13840.52 [ae]	10920.00 ± 11774.55[ac]	0.84± 0.04	0.92± 0.037

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: [a]– control (CO), [b]– high fruit (HF), [c]– low fruit (LF), [d]– high oil (HO), [e]– low oil (LO), [f]– cimetidine (CM). where HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

Table 4:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on white blood cell indices.

Group	WBC (x10^3/µL)		Lymphocyte (%)		Neutrophil (%)		Eosinophil (%)		Monocyte (%)	
	WEEK 2	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**	**WEEK 2**	**WEEK 4**
CO	3490.00 ± 120.83	4420.00 ± 270	70.60 ± 1.33	73.40 ± 1.17	25.40 ± 1.03	23.40 ± 1.69	2.00 ± 0.44	1.00 ± 0.31	2.00 ± 0.31	2.20 ± 0.37
HF	3940.00 ± 601.33	4290.00 ± 283.90	72.60 ± 1.44	71.80 ± 2.04	25.00 ± 1.64	25.60 ± 2.54	1.80 ± 0.37	1.40 ± 0.51	1.80 ± 0.20	1.20 ± 0.37 [a]
LF	3320.00 ± 492.08	3860.00 ± 224.94	73.20 ± 0.74	73.60 ± 0.81	24.40 ± 0.92	23.00 ± 1.04	1.20 ± 0.58	2.00 ± 0.63	1.20 ± 0.37	1.40 ± 0.24[a]
HO	3370.00 ± 605.72	3480.00 ± 303.97[ab]	70.20 ± 2.04	73.00 ± 1.30	26.40 ± 1.63	23.20 ± 1.56	1.60 ± 0.51	2.00 ± 0.55	1.80 ± 0.37	1.80 ± 0.20
LO	3640.00 ± 988.10	3470.00 ± 433.76[ab]	68.60 ± 1.21[bcf]	67.00 ± 0.71 [acdf]	27.40 ± 0.74	29.80 ± 0.86	1.80 ± 0.37	1.40 ± 0.51	1.60 ± 0.24	1.80 ± 0.20
CM	4070.00 ± 552.17[cd]	3850.00 ± 344.60[ab]	73.40 ± 0.75	78.60 ± 1.20[b,e]	24.00 ± 0.83	17.60 ± 1.46 [b,e]	1.40 ± 0.24	1.80 ± 0.20	1.20 ± 0.20	1.80 ± 0.37

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: [a]– control (CO), [b]– high fruit (HF), [c]– low fruit (LF), [d]– high oil (HO), [e]– low oil (LO), [f]– cimetidine (CM). where HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

Table 5:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on blood inflammatory markers

Groups	Neutrophil/lymphocyte (N/L)		Monocyte/lymphocyte (M/L)		Platelet/Nitric oxide (P/NO) (millions/mm^3/µmol/tissue)		Nitric oxide/Malonaldehyde (NO/MDA) (µmg/tissue/µmol/mg protein)	
	WEEK 2	WEEK 4	WEEK 2	WEEK 4	WEEK 2	WEEK 4	WEEK 2	WEEK 4
CO	0.29 ± 0.02	0.29 ± 0.02	0.02 ± 0.00	0.02 ± 0.01	6620.35 ± 1063.08	2296.54 ± 322.07	6107588.00 ± 1028467.00	5996228.00± 263125.50
HF	0.34 ± 0.03	0.28 ± 0.04	0.02 ± 0.00	0.01 ± 0.01	7564.01 ± 637.26	3105.08 ± 200.15	280205.00 ± 203790.00^{af}	488717.00 ± 186562.40^{acf}
LF	0.35 ± 0.028	0.34 ± 0.01	0.00 ± 0.01	0.02 ± 0.00	5808.37 ± 1075.88^{b}	6930.76 ± 3660.49^{be}	115611.00 ± 115296.90 ^{abdef}	386404.00 ± 5354450^{abf}
HO	0.36 ± 0.02	0.27 ± 0.01	0.03 ± 0.00	0.02 ± 0.00	4928.10 ± 535.47^{ab}	6791.75 ± 392.17^{be}	152246.00 ± 283079.30^{af}	449151.00 ± 217979.40^{acf}
LO	0.37 ± 0.02	0.42 ± 0.00^{abcdf}	0.03 ± 0.00	0.02 ± 0.00	8553.90 ± 93.79^{acd}	4669.00 ± 297.56	158343.00 ± 95971.08^{af}	339406.00 ± 67399.51^{abdf}
CM	0.35 ± 0.00	0.19 ± 0.02^{abcde}	0.01 ± 0.00	0.03 ± 0.00^{d,e}	3979.03 ± 410.86^{abce}	5529.06 ± 307.16^{b}	2412778.00 ± 259609.90	2057956.00 ± 144850.30^{abcde}

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: ^{a}– control (CO), ^{b}– high fruit (HF), ^{c}– low fruit (LF), ^{d}– high oil (HO), ^{e}– low oil (LO), ^{f}– cimetidine (CM). where HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w).

Table 6:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on liver and kidney function tests

	AST (µl)		ALP (µl)		ALT (µl)		Bilirubin (mg/dl)		Creatinine (mg/dl)	
	WEEK 2	WEEK4	WEEK 2	WEEK4	WEEK 2	WEEK4	WEEK 2	WEEK4	WEEK 2	WEEK4
CO	42.40 ± 1.16	41.80 ± 1.32	101.00 ± 4.62	102.40 ± 3.96	31.40 ± 0.74	31.40 ± 0.92	0.26 ± 0.02	0.28 ± 0.02	0.74 ± 0.04	0.78± 0.02
HF	38.00 ± 0.89^{a}	44.80 ± 1.77^{acd}	80.50 ± 2.61^{a}	117.40 ± 4.17^{c}	26.80 ± 0.73^{a}	34.20 ± 1.15	0.24 ± 0.02	0.28 ± 0.03	0.60 ± 0.03	0.96 ± 0.08^{acd}
LF	37.40 ± 0.24^{a}	40.40 ± 1.20	76.00 ± 1.06^{a}	98.80 ± 5.53	27.40 ± 0.67	30.00 ± 1.64	0.22 ± 0.02	0.22 ± 0.02	0.62 ± 0.03	0.70 ± 0.00^{b}
HO	39.00 ± 1.14	40.20 ± 0.73	84.50 ± 3.07^{a}	103.00 ± 6.18	27.60 ± 1.24	27.80 ± 1.11^{b}	0.26 ± 0.02	0.22 ± 0.02	0.64 ± 0.04	0.70 ± 0.02^{b}
LO	39.60 ± 0.51	43.00 ± 1.58	82.00 ± 2.02^{a}	109.40 ± 4.29	28.80 ± 0.58	31.20 ± 1.31	0.30 ± 0.00	0.30 ± 0.03^{cd}	0.68 ± 0.02	0.82 ± 0.09
CM	37.40 ± 0.92^{a}	46.00 ± 0.63^{acd}	77.50 ± 2.22 ^{a}	123.40 ± 2.71^{a,c,d}	27.00 ± 0.77	34.60 ± 0.74	0.20 ± 0.00	0.28 ± 0.02	0.60 ± 0.03	0.80 ± 0.03

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: ^{a}– control (CO), ^{b}– high fruit (HF), ^{c}– low fruit (LF), ^{d}– high oil (HO), ^{e}– low oil (LO), ^{f}– cimetidine (CM). **Where** HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on basal and stimulated gastric acid secretion:
Canarium schweinfurthii low and high fruit pulp oil diets significantly increased while the fruit (low and high) diet significantly increased basal gastric acid secretion compared with other groups by 2 weeks of treatment. On stimulation with histamine, the *Canarium schweinfurthii* fruit and fruit pulp oil diet groups significantly reduced gastric acid secretion compared with control, (Figures 2a). However, cimetidine significantly reduced gastric acid secretion compared with other experimental groups. By 4 weeks of diet treatment, *Canarium schweinfurthii* fruit and fruit pulp oil diets significantly reduced basal and stimulated gastric acid secretion compared with control (Figure 2b). However, cimetidine treatment significantly reduced stimulated gastric acid secretion compared with all other experimental groups (Figure 2b).

Table 7:
Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on lipid profile

Group	Total Cholesterol (mg/dl)		Triglyceride (mg/dl)		High Density Lipoprotein (HDL) (mg/dl)		Low Density Lipoprotein (LDL) (mg/dl)	
	2 WEEKS	4 WEEKS	2 WEEKS	4 WEEKS	2 WEEKS	4 WEEKS	2 WEEKS	4 WEEKS
CO	66.20 ±1.96	74.20 ± 2.06	43.40 ± 1.54	54.60 ± 1.78	35.60 ± 1.81	38.20 ± 0.58	39.28 ± 1.29	46.92 ± 2.25
HF	71.40 ± 3.49	71.20 ± 1.74	45.40 ± 1.94	52.00 ± 2.21	33.60 ± 4.57	37.60 ± 2.23	46.88 ± 5.79[a]	44.00 ± 0.49
LF	73.00 ± 2.05	73.60 ± 1.21	45.20 ± 1.32	52.80 ± 0.66	40.60 ± 1.03	40.20 ± 0.97	41.44 ± 1.26	43.96 ± 1.94
HO	73.80 ± 3.53	69.60 ±0.81[aef]	46.00 ± 2.39	47.60 ± 1.78[a]	41.60 ± 2.06	35.40 ± 1.50[cef]	41.40 ± 2.11	43.72 ± 1.53
LO	77.20 ± 1.85[a]	75.00 ± 0.89	49.60 ± 2.56	55.00 ± 1.00	44.40 ± 1.50[abf]	40.20 ± 1.88	42.72 ± 1.43	45.80 ± 1.48
CM	71.00 ± 2.95	76.20 ± 0.49	45.40 ± 1.72	50.00 ± 1.92	37.80 ± 2.84	40.00 ± 1.52	42.28 ± 1.04	44.40 ± 1.46

Values are expressed as Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance** compared with: [a]– control (CO), [b]– high fruit (HF), [c]– low fruit (LF), [d]– high oil (HO), [e]– low oil (LO), [f]– cimetidine (CM). where HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w).

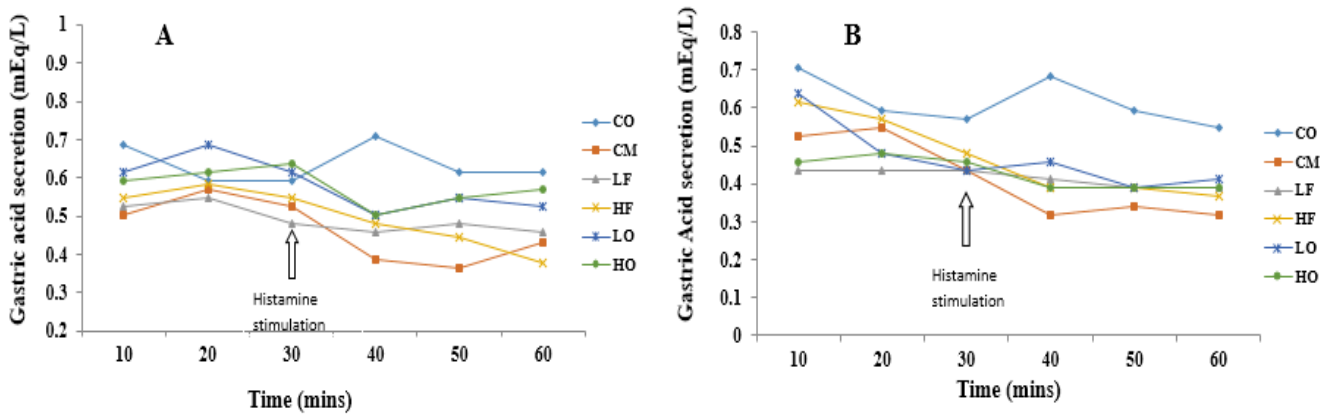


Figure 2: Effect of *Canarium schweinfurtii* fruit and oil on gastric acid secretion by weeks 2 (A) and 4 (B) of diet pre-treatment.

Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mLs/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric lipid peroxidation: malondialdehyde (MDA) level: Gastric MDA level in the UU group significantly increased compared with CO group at both weeks 2 and 4. By week 2, the HF and HO groups significant decreased in MDA level compared with UU group. Gastric tissue MDA level was significantly increased in LF group compared with CO group, Figure 3. MDA level was significantly reduced in HO, LO, HF and LF when compared with UU group. Also, there was a statistically significant decrease in MDA level in HO group compared with LF group, Figure 3.

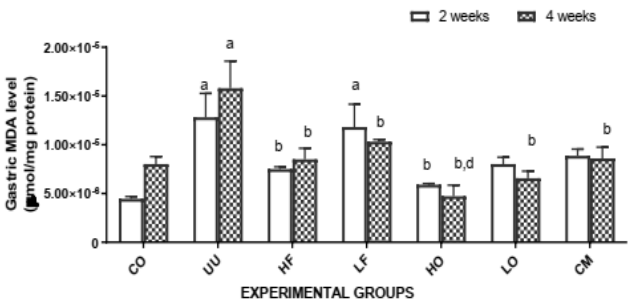


Figure 3:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric MDA level at weeks 2 and 4.

Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w) Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. **Significance**: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU), [d]-compared with low fruit group (LF).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric catalase level: Gastric Catalase activity significantly increase in LF, HO, LO and CM groups compared with CO and UU. Gastric catalase level was significantly increased in LF group compared with HF group by week 2, Figure 4. There was a significant increase in gastric catalase activity in HF, LF, HO, LO and CM groups compared with CO group. Gastric catalase activity was significantly increased in, LF, HO, LO and CM groups compared with UU. There was a significant increase in gastric catalase activity in CM compared with LF by week 4, Figure 4.

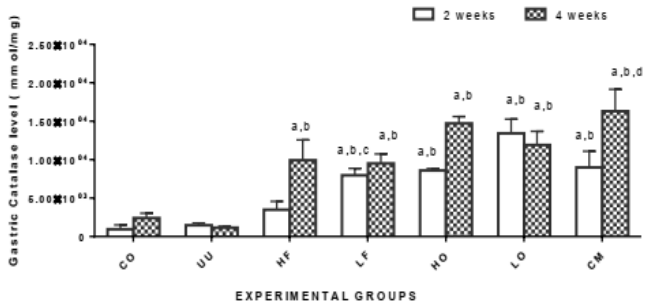


Figure 4:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric Catalase level at weeks 2 and 4.
Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w) Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. Significance: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU) [c]-compared with high fruit group (HF), [d]-compared with low fruit group (LF).

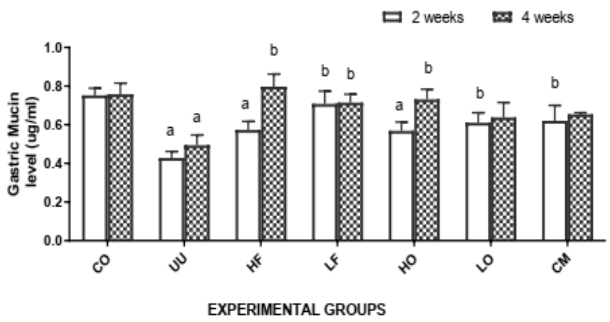


Figure 5:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric mucin level at weeks 2 and 4.
Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mLs/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w) Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. Significance: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric tissue mucin level: By two weeks, there was a significant decrease in gastric tissue mucin level in UU group compared with CO group. Gastric mucin level was significantly increased in LF, LO, and CM groups compared with UU group, Figure 5. By four weeks, gastric mucin level was significantly reduced in UU group compared with CO group. A statistically significant increase in gastric mucin level was recorded in HF, LF, and HO groups when compared with UU group, Figure 5.

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric sulfhydryl tissue level: By two weeks of pre-treatement, sulfhydryl level in LF and HO groups significantly increase compared with CO group. Gastric sulfhydryl level was significantly increased in the LF and HO groups compared with UU group. There was a significant increase in gastric sulfhydryl level in LF and HO groups compared with HF groups. A significant decrease in sulfhydryl level in CM group compared with HO was observed, Figure 6. By four weeks, there was a significant increase in sulfhydryl level in CM group compared with UU group. Gastric sulfhydryl level was significantly increased in CM group compared with LF group, Figure 6.

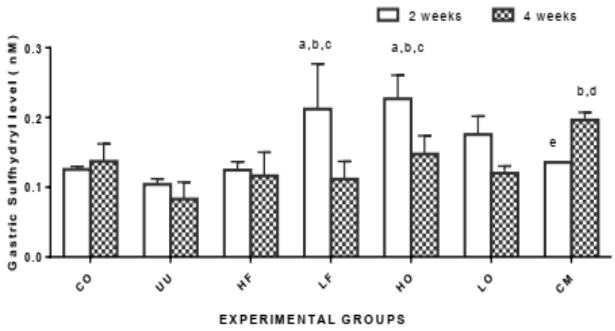


Figure 6:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric sulfhydryl level at weeks 2 and 4.
Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1m/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w) Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. Significance: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU) [c]-compared with high fruit group (HF), [d]-compared with low fruit group (LF), [e]-compared with high oil group (HO).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on Gastric nitric oxide level: After four weeks of pre-treatement with *Canarium schweinfurthii* fruit and fruit pulp oil, HO and HF groups significantly increased gastric tissue nitric oxide level compared with UU groups. Gastric tissue nitric oxide level was significantly reduced in CM group compared with HO and HF groups, Figure 7.

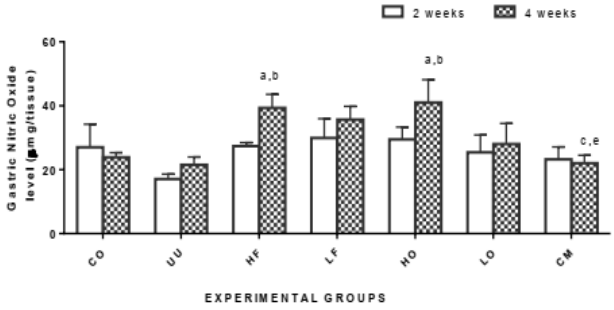


Figure 7:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric nitric oxide level at weeks 2 and 4.
Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)
Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. Significance: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU) [c]-compared with high fruit group (HF), [e]-compared with high oil group (HO).

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric H^+K^+-ATPase activity: By two weeks of pre-treatment, in gastric H^+K^+ ATPase activity significantly increase in UU group compared with CO group but decrease in HF, LF, HO and CM groups compared with UU group. Gastric tissue H^+K^+ ATPase activity was significantly increased in LO group compared with HO group, Figure 8. After four weeks of pre-treatment, H^+K^+ ATPase activity significantly decreased in HF and HO groups compared with UU group but increased in CM group compared with HF, LO and HO groups, Figure 8.

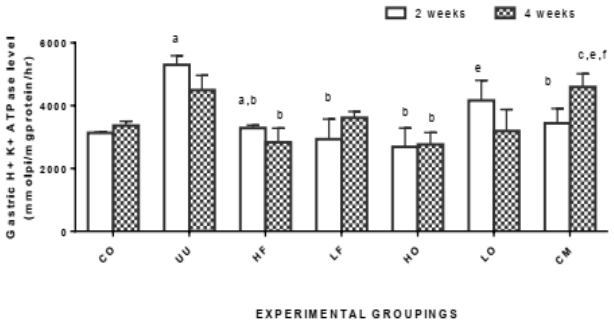


Figure 8:
Effect of *Canarium schweinfurtii* fruit and oil on Gastric H^+K^+ ATPase level at weeks 2 and 4.
Where UU = Ulcer Untreated, HF = High Fruit (60% *C. schweinfurthii* fruits/standard feed mix), LF = Low Fruit (30% *C. schweinfurthii* fruits/standard feed mix), HO = High Oil (2mL/kg b.w *C. schweinfurthii* fruits pulp oil), LO = Low Oil (1mL/kg b.w. *C. schweinfurthii* fruits pulp oil), CM = Cimetidine (30mg/kg b.w)
Vertical bar represent Mean ± SEM. Values are significant when $p \leq 0.05$. Significance: [a]-compared with control group (CO), [b]-compared with ulcer untreated group (UU) [c]-compared with high fruit group (HF), [e]-compared with high oil group (HO).

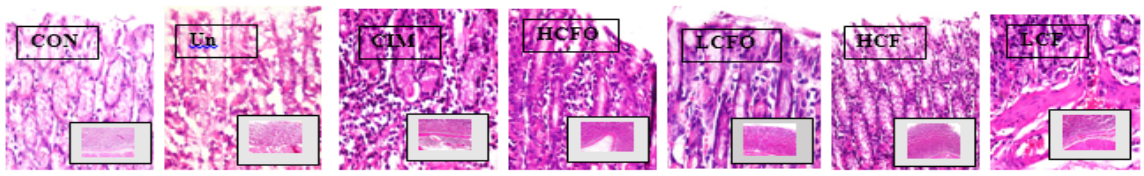


PLATE 3: Photomicrographs of H&E Stain gastric tissue by 2 weeks pretreatment MAGX400 (X100 inserted) C: normal mucosa, submucosa and muscularis. The surface epithelial is well preserved. No significant lesion seen. **Un:** there are few lesion. **CIM:** mild inflammation of the mucosa (slender arrow) and moderate oedema (blue arrow) with severe infiltration of inflammatory cells (dashed arrow). There is mild vascular congestion in the mucosa and submucosa. The surface epithelial is well preserved. **HCFO:** mild inflammation of the mucosa (slender arrow) and mild oedema (black arrow) with mild infiltration of inflammatory cells (dashed arrow). The surface epithelial is well preserved. **LCFO:** very mild papillary infolding (black arrow). The surface epithelial is well preserved. **HCF:** mild vascular congestion (black arrow). The surface epithelial is well preserved. **LCF:** mild vascular congestion (black arrow) and very mild infiltration of inflammatory cells (dashed arrow) to the submucosa.

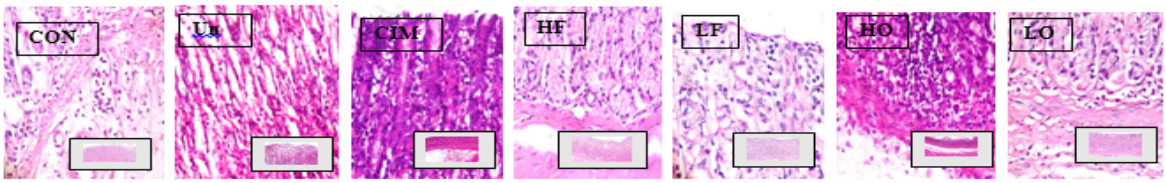


PLATE 4: Photomicrographs of H&E Stained gastric tissue by 4 weeks pre-treatment MAGX400 (X100 inserted) C: mild inflammation of submucosa (thin arrow), very mild oedema (blue arrow) with infiltration of inflammatory cells and mild vascular congestion (black arrow). **Un:** no significant lesion, surface epithelial is poorly preserved. **CIM:** mild inflammation of the mucosa (slender arrow) and moderate oedema (black arrow) with moderate infiltration of inflammatory cells (dashed arrow). The surface epithelial is well preserved. **HF**: normal mucosa, submucosa and muscularis. The surface epithelial is well preserved. No significant lesion seen. **LF:** mild oedema (blue arrow) with infiltration of few inflammatory cells. The surface epithelial is well preserved. **HO**: mild inflammation of the mucosa and moderate oedema (blue arrow) with infiltration of inflammatory cells and adipocytes. There is mild angiogenesis with vascular congestion. The surface epithelial is well preserved. **LO**: mild inflammation of the mucosa and mild oedema (blue arrow) with infiltration of very few inflammatory cells. The surface epithelial is well preserved.

Effect of *Canarium schweinfurthii* fruit and fruit pulp oil diet on gastric tissue histology: *Canarium schweinfurthii* fruit and fruit pulp oil diet presented with well-preserved surface epithelium unlike the ulcerated untreated groups, (Plates 3 and 4) by weeks 2 and 4 of diet pre-treatment.

DISCUSSION

Canarium schweinfurtii fruit and high fruit oil diet treatment increased body weight which might indicated its ability to increase body anabolic activities which might be due to certain inherent phytochemical in *Canarium schweinfurtii* fruits and fruits pulp oil (tannins, flavonoids, and saponins). Few of these phytochemicals (Tannins) prevent irritations and injury to the gastric mucosa by tanning or covering the gastric mucosa

(Asuzu and Onu, 1990; Devaraj and Krishna 2011, Akinwumi *et al*., 2022), thus minimizing the progression or occurrence of gastric ulcer development (John *et al*., 1990; Nwafor *et al*.,

1996; Vidya *et al*., 2013). Saponins however, exert its protective activities in ulceration by the activation of mucous membrane protective factors (Choudhary *et al*., 2013; Vidya *et al*., 2013; Salami and Famurewa 2017); though it has been documented to lyse red blood cells (Bissinger *et al*., 2014). In this study, two- and four-weeks pretreatment with *Canarium schweinfurtii* fruits and fruits pulp oil remarkably decreased the mean ulcer score. *Canarium schweinfurtii* fruit pulp oil diet treatment conferred greater gastroprotection unlike the fruit alone diet in this study. This gastroprotection was comparable with cimetidine. The observed reduced gastric ulcer may be as a result of the inherent phytochemicals in *Canarium schweinfurtii* which conferred protection on the gastric epithelium.

Canarium schweinfurtii fruits and fruits pulp oil diets treated group reduced basal and histamine stimulated gastric acid secretion at 2 and especially 4 weeks unlike the control group, respectively. Regulation of gastric acid secretion by the parietal cells is an important factor in the pathogenesis of peptic ulcer, a key therapeutic target for ulcer diseases (Jain *et al*., 2007, Prabhu and Shivani, 2014, Xie *et al*., 2022). The observed decrease in basal and histamine induced gastric acid secretion may be linked to the flavonoid content of *Canarium schweinfurtii* fruits and fruit pulp oil. Triterpenes and flavonoids (Shaba *et al*., 2013; Katary and Salahuddin 2017) have been documented to exert anti-histaminic activity (De Lira Mota *et al*., 2009; Sakat *et al*., 2012; Salami *et al*., 2020). *Canarium schweinfurtii* fruit and high fruit oil diet treatment promotes increased haematological variables (packed cell volume, haemoglobin, and red blood cell count) except the low oil diet at four weeks pretreatment. *Canarium schweinfurtii* fruit and high fruit oil diet treatment elevated the platelet counts at two weeks pretreatment except the low oil diet pretreated groups. It may be that the *Canarium schweinfurtii* fruit and high fruit oil diet stimulated erythropoietic activities thus prevented anaemia which is a hallmark of gastric ulceration. The *Canarium schweinfurtii* fruit and high fruit oil diet treatment reduced blood inflammatory markers (erythrocyte sedimentation rate, neutrophil/lymphocyte, monocyte/lymphocyte, NO/MDA ratios, indicating its ability to ameliorated inflammatory cells infiltration into gastric tissues and its related stress leading to gastric ulceration. *Canarium schweinfurtii* fruit pulp oil diet at low dose caused anaemia with increased neutrophil/lymphocyte, at four weeks with reduced platelet counts. This observations were absent in the *Canarium schweinfurtii* high fruit pulp oil treated groups. Certain medicinal plants (though beneficial) have been observed to alter liver and kidney function test which in most cases is linked to toxicity at doses administered. Increased ALT, ALP, AST and bilirubin levels above normal threshold are evidence of liver toxicity which are detrimental. (Giannini *et al*., 2005; Ablat *et al*., 2023) *Canarium schweinfurtii* fruit and high fruit oil diet treatment however, did not cause damage to the liver and kidney cells which is evident in the Liver (ALT, ALP, AST, Bilirubin contents) and kidney (Creatinine) function tests. This is also suggestive that the doses and concentration used in this study were not toxic. *Canarium schweinfurtii* fruit and high fruit oil diet treatment also did not cause dyslipidemia at the doses used in this study.

Pre-treatment with *Canarium schweinfurtii* fruits and fruits pulp oil diet led to reduced MDA level and increase catalase level across the groups, indicating a decrease in the indomethacin -induced oxidative stress. The increase in catalase level observed in the high oil treated group is similar to that observed in the cimetidine treated group. These findings are in harmony with earlier reports who noted the antioxidant property *Canarium schweinfurtii* fruits and fruits pulp oil (Obame *et al*., 2007; Dongmo *et al*., 2010; Gazuwa *et al*., 2016). *Canarium schweinfurtii* fruits and fruits pulp oil contains Vitamin C, phenolic and flavonoids compounds with antioxidant properties. These antioxidant activities may be attributed to various mechanisms, like prevention of chain initiation, binding of transition metal ion catalysts, prevention of continued hydrogen abstraction, reductive capacity, radical scavenging activity and decomposition of peroxides (Kumaran and Karunakaran 2006, Yumrutas and Saygideger, 2012).

Gastric mucus plays an important role in the gastric ulcer defense mechanism, it forms a continuous mucus gel-like protective barrier covering the entire gastric mucosa and maintains a pH of 6–7 in the gastric acidic environment (pH 1–2) (Zakaria *et al*., 2014). Mucins are produced by various specialized epithelial cells, especially goblet cells. They play an important protective role by forming a physical, chemical and immunological barrier between the gastric lumen and epithelial surface (Niv and Boltin 2012; Alese *et al*., 2018). Mucin is the primary agent which lends protection against acid and pepsin, thus, any derangement in mucin secretion may be deleterious. Secretion of mucin is mediated by prostaglandin E-2 (PGE 2) and supported by nitric oxide, hydrogen sulfide, growth factors and trefoil peptides (Yakoob *et al*., 2005; Jia *et al*., 2023). The mucin-unstirred layer maintains a stable pH above the mucosa and prevents enzymatic attack by pepsin.

In this study, gastric mucin level was found to be elevated in the *Canarium schweinfurtii* fruits and fruits pulp oil diet treated groups. This is evident in the increase gastric mucous cell counts and gastric mucin level of the *Canarium schweinfurtii* fruits and fruits pulp oil diet treated groups. It may probably be that *Canarium schweinfurtii* fruits and fruits pulp oil diet enhanced the gastric epithelial defense factors especially the mucous cells as well as its secretions evident in the observed reduced basal and stimulated gastric acid secretion. The increase in sulfhydryl level in group treated with low *Canarium schweinfurtii* fruits and high *Canarium schweinfurtii* oil helps in recycling endogenous antioxidant vitamins, thereby preventing lipid peroxidation. They also protect mucus by preventing rupture of disulphide bridges that join the mucus subunits and maintain structural integrity (Adhikary *et al*., 2011). The increase in sulfhydryl level may be due to the presence of flavonoids in *Canarium schweinfurtii* fruit and oils.

Nitric oxide (NO) is a mediator of gastrointestinal mucosal defense, it improves the mucosal blood flow, protects the integrity of epithelial tissue and inhibits activation, adhesion and migration of leucocytes in the inflammatory (Khattab *et al*., 2001, Elena and Arrieta 2019) resulting in increasing mucus synthesis and accelerating ulcer healing (Katary and Salahuddin, 2017). In this study, there was an increase in nitric oxide level in the high *Canarium schweinfurtii* fruits and fruits pulp oil treated groups. Nitric oxide has been documented to enhance mucus synthesis probably through restoration of depleted mucus cells (Kumar *et al*., 2014, Liang *et al*., 2021). This increased nitric oxide might have led to the observed increase mucin level via restoration of the depleted gastric mucus cells counts in this study. In contrast, there was a decrease in nitric oxide level in cimetidine treated group, this is similar to the report of Hunter, 2000. The increase in nitric

oxide level observed in this study may be due to the presence of phenolic acid (vanillic acid) in *Canarium schweinfurtii* fruits and fruits pulp oil since vanilic acid has been reported to increase nitric oxide (Kuma *et al*., 2014; Katary and Salahuddin, 2017).

Anti-ulcer therapy is usually aimed primarily at reducing the amount of secreted acid by inhibiting H^+K^+ATPase activity with proton pump inhibitors (PPIs), or by preventing histamine from reaching its target on the parietal cell basolateral membrane using the competitive H2-blocker (Srebro *et al*., 2022). Administration of *Canarium schweinfurtii* fruits and fruit pulp oil reduced gastric H^+K^+-ATPase activity. It may probably be that *Canarium schweinfurtii* fruits and fruit pulp oil act as a proton pump inhibitor evident from the reduced histamine stimulated gastric acid secretion. Several phytochemical constituents have been found in *Canarium schweinfurtii* fruits and fruit pulp oil which might have conferred gastro-protective activities, few of these include oleic acid, vanilic acid, and flavonoids. Further studies are aimed at isolating these compounds in *Canarium schweinfurtii* fruits and fruit pulp oil to access their gastro-protective principles.

CONCLUSION

Canarium schweinfurtii fruits and fruits pulp oil exerts its anti-ulcer effect basically by acting as a proton pump inhibitor besides its antioxidant activity; increased gastric nitric oxide and mucin secreted probably from the increased gastric mucous cell.

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