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Gastro-protective effect of palm kernel (*Eleasis guinensis*) oil enriched diet on indomethacin induced gastric ulcer in rats

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Palm kernel oil (PKO) resembles coconut oil in preparations and both are the only sources of lauric oil available on the world market. It has been shown to be used to control diseases such as cancer, obesity, and immune disorders, as an anti-aging and antioxidant agent. The present study investigated the gastric protective property of PKO against indomethacin-induced gastric ulceration in rats. 20 male Wistar rats were divided into 4 groups of 5 each. All mice in groups 2, 3 and 4, except group 1, served as controls, were fed a daily diet of 5, 10 and 25% PKO, respectively. Rats were fed a PKO-supplemented diet for 21 days prior to ulceration with a single oral dose of indomethacin (40 mg/kg body weight) on day 22. Gastric volume, gastric acid concentration, gastric pH, bicarbonate, mean ulcer index and percentage ulcer inhibition were determined. The results showed a significant decrease ($P < 0.05$) in gastric juice volume, gastric acid concentration and mean ulcer index in mice of groups 3 and 4 compared with mice of group 1 (control group), ants. However, a significant increase ($p<0.05$) was observed in gastric pH, bicarbonate, and percentage ulcer index in groups 3 and 4 rats compared to group 1 rats. These findings are indicative of the gastro-protective potentials of PKO to be capable of ameliorating indomethacin-induced gastric ulceration in rats. The probable mechanisms of action of PKO need further investigation.

Key words: Gastro-protective, NSAIDS, palm kernel oil, rats.

INTRODUCTION

Oil palm (*Elaeis guineensis*) is mainly grown in tropical regions such as Africa, Latin America, South Pacific and Southeast Asia (Atasie and Akinhanmi, 2009). Oil palm produces two different oils namely palm oil produced

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from the fibrous middle coat of the fruit and palm kernel oil extracted from the white flesh of the seeds (Norizzah et al., 2014).

Palm kernel oil is referred to as lauric oil because of its high lauric acid composition (C12, 48%), a medium-chain fat comparable to that in breast milk and with similar nutritional effects (Kabara, 1990; Pantazaris and Ahmad, 2004). It has been used to control diseases such as immune disorders, cancer, obesity, and also as an anti-aging agent, antioxidant, and in mainstream medical practice as an antidote for toxicity and wound healing (Asagba et al., 2008; Ekpa, 1995).

A gastric ulcer is a benign lesion of the mucosal epithelium during gastric exposure to excess acid and active pepsin. Positive peptic ulcers, in which the gastric mucosa is damaged and perforated, leading to bleeding, are common worldwide and affect up to 10% of the world's population (Zapata-Colindres et al., 2006).

The pathophysiology of this disease is a multifactorial process caused by an imbalance of gastric mucosa (pepsin) and gastric mucosal destructive factors (acidity) and by endogenous and exogenous causes include infection, *Helicobacter pylori*, acids, smoking, stress, pepsin, stress, and harmful agents such as excessive alcohol intake and prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs) (Syam et al., 2009).

NSAIDs such as indomethacin are an example of the major known causative factors responsible for the development of peptic ulcers. These drugs are widely prescribed mainly for pain and inflammation (Brooks et al., 1999). Long-term NSAID use has been shown to cause gastric mucosal injury mainly by decreasing prostaglandin (PG) synthesis through inhibition of the enzyme cyclooxygenase (COX) and partly through a COX-independent mechanism (Wallace, 2009).

The scientific community is increasingly interested in the production of anti-cancer drugs of plant origin that are effective, non-toxic, and inexpensive, have no side effects and are easily accessible to the public, especially in developing country. Therefore, the present study investigated the possible gastroprotective effect of a diet rich in palm kernel oil (without guinensis) on indomethacin-induced gastric ulceration in rats.

EXPERIMENTAL DESIGN

Twenty (20) male Wistar rats were used for this study. The mice were 8 to 10 weeks old and weighed between 170 and 200 g. They were randomly divided into four groups of 5 mice each. Rats from each group were housed in separate cages at the Animal House, Madonna University, Nigeria, following a natural day and night cycle. Rats were fed a standard diet and given water liberally. They were given two weeks of acclimatization and then treated as follows: Group 1: control group; the rats in this group received only mouse chow. Group 2: Rats in this group were fed a 5% PKO-enriched diet. Group 3: Rats in this group received a 10% PKO-rich diet. Group 4: Rats in this group received a diet rich in 25% PKO. All animals were housed and handled according to research protocols established by the National Research Center Animal Care Committee, following the recommendations of the National Institutes of Health Guidelines on the Care of Animals and the Use of Laboratory Animals (Publication No. 85-23, revised 1985).

Chemicals and drugs

Indomethacin was purchased from Kapit Pharmaceutical Limited, Nigeria Diet formulation.

Formulation of diet

The test diet was formulated by mixing 5, 10 and 25 ml of palm kernel oil with 100 g of rat food.

Induction of gastric ulceration

Causing gastric ulcers After 21 days of treatment, rats were fasted for 24 h before inducing gastric ulcers by taking a single dose of indomethacin 40 mg/kg body weight.

General determination of stomach injury

Rats' stomachs were opened along the greater curve, rinsed with saline and stapled for gross examination. After immobilizing the tissues by immersing them in 10% formalin for 24 h, it was rinsed under running water and examined for ulcers. Ulcers were counted with a magnifying glass (X magnification).

The gastric mucosa was carefully examined for the presence of ulcers and their number was counted using an illuminated magnifying glass (10x) (Zaghlool et al., 2015), ulcer index (UI) scores were calculated based on an arbitrary scale according to Zhou et al. (2020).

Determination of pH of gastric juice

The pH of gastric juice is determined by a pH meter. The acidity of the gastric juices of each rat was assessed individually by immersing the pH indicator strip (PHS-25 pH meter; Microfield, UK) into the gastric juice immediately after gastric bypass. The results are expressed as the pH value.

Determination of gastric juice volume

This was performed as previously described by Heeba et al. (2009). 4 h after gastric ulcer induction, rats were anesthetized, laparotomy for gastrectomy and gastric juice extraction to determine gastric juice volume. 5 ml of distilled water was added to the gastric juice and the resulting solution was centrifuged at 3000 rpm for 10 min.

Determination of bicarbonate in gastric juice

HCO_3^- secretion was measured in the gastric cavity as previously described by Takeuchi et al. (1992).

Determination of gastric acid secretion

Gastric acid in mEq/L was determined in the supernatant (2 ml) by titration with 0.0025 N NaOH using Topfer reagent and phenolphthalein as indicators (Adefisayo et al., 2018). A burette was installed in the laboratory and 0.01 N NaOH was prepared and

Table 1. Effect of palm kernel oil enriched diet on gastric juice volume, gastric acid concentration, gastric pH, bicarbonate and mean ulcer score.

Group	Gastric juice volume (ml/4 h)	Gastric acid concentration (mEq/L)	Gastric pH	Bicarbonate (mmol/L)	Mean ulcer score
Group 1: Control	3.80 ± 0.09	0.93±0.11	2.0 ± 0.02	14.94 ± 0.94	2.75 ± 0.25
Group 2: 5% PKO diet	2.50 ± 0.02	0.73±0.31	4.5 ± 0.04*	21.34 ± 1.34	2.13 ± 0.32
Group 3: 10% PKO diet	2.10 ±0.02*	0.70±0.08*	5.5 ± 0.03*	25.24 ± 1.05*	1.63 ± 0.24*
Group 4: 25% PKO diet	1.40 ±0.03*	0.5±0.02*	6.13± 0.01*	38.19 ±2.45*	0.25 ± 0.14*

Values expressed as Mean ± SEM; of 5 rats per group. One-way ANOVA and LSD revealed significant differences between the control and the treated groups with PKO. *P<0.05.
Source: Author

poured into the burette. 50 ml of distilled water was added to the gastric juice (liquid fraction) inside the single bottles. 25 ml of gastric juice was pipetted into a beaker and 3 drops of Topfer reagent added to compensate for free acidity. The NaOH inside the burette is titrated with the acidic solution in the beaker and observed until a yellow color is obtained. The volume of alkali used, corresponding to the free acidity, was recorded. The aforementioned procedure was repeated with phenolphthalein as indicator. In this experiment, the color change was from colorless to red. The total volume of alkalis added was recorded for the total acidity and was used to determine gastric acidity as shown subsequently. The following formulas are used to determine the concentration of acids:

$CA \times VA = NA$

$CB \times VB = NB$

where CA = concentration of acid used, VA = volume of acid used, CB = concentration of base used, VB = volume of base used, NA = molar ratio of acid used, and NB = molar ratio of base used. Molar units/dL converted to MEq/L.

Ulcer quantification

The degree of ulceration in animals was quantified using the procedure described by Szabo and Hollander (1985) with some modifications.

After gastric juice is removed from the stomach, the stomach is pinned on a soft board. Scoring of the ulcer was then performed as follows: 1 = the ulcer was 1 mm or less in diameter; 2 = erosion with a diameter of 1 to 2 mm; 3 = erosion with a diameter greater than 2 mm. The overall score was divided by a factor of 10 and the results obtained were indicated as the mean ulcer index. The ulcer inhibition percentage was also calculated as follows:

Percent ulcer inhibition = Mean ulcer control index - Mean controlled ulcer index × 100 / Witness mean ulcer control

RESULTS

Table 1 shows the effect of a PKO-rich diet on gastric fluid volume, gastric acid concentration, gastric pH, and bicarbonate and mean ulcer score.

There was a significant decrease ($p<0.05$) in gastric juice volume (ml/4 h) in groups 3 and 4 rats (2.10± 0.02) and (1.40±0.03), respectively when compared with the control group (3.80 ± 0.09).

Also, a significant decrease ($p<0.05$) was observed in gastric acid concentration (mEq/L) in groups 3 and 4 rats (0.70 ± 0.08) and (0.5±0.02), respectively when compared with the control group (0.93 ± 0.11).

Gastric pH showed a significant increase ($p<0.05$) in groups 2, 3 and 4 rats (4.5±0.04), (5.5±0.03) and (6.13±0.01), respectively when compared with the control group (2.0±0.02).

Furthermore, bicarbonate concentration (mmol/L) increased significantly ($p<0.05$) in groups 2, 3 and 4 rats (21.34±1.34), (25.24±1.05), and (38.19±2.45), respectively when compared with the control group (14.94±0. 94).

The mean ulcer score index decreased significantly ($p<0.05$) in groups 3 and 4 rats (1.63±0.24) b and (0.25±0.14), respectively when compared with the control group (2.75± 0.25).

As shown in Figure 1, the percentage ulcer inhibition increased significantly ($p<0.05$) in a dose-dependent manner in groups 2, 3, and 4 rats, respectively.

DISCUSSION

The present study determined the gastroprotective effect of a diet rich in palm kernel oil on indomethacin-induced gastric ulceration in rats. The significant increase in ulcer index, as well as gastric acid volume, following oral administration of indomethacin in untreated, ulcerated rats, can be attributed to the generation of free radicals or inhibition of synthesis prostaglandins, as reported in the work of Ajani et al. (2014), Hong et al. (2014), Inas et al. (2011), and Lichtenberger (2005). Decreased prostaglandin levels are thought to be due to decreased gastroprotection as well as increased gastric secretion, which are important events in the etiology of mucosal ulcers (Bech et al., 2000; Biplab et al., 2011). Untreated ulceration in this study is consistent with an earlier study by Vijender et al. (2012). Stomach acid is an important factor in ulcer formation in rats. However, gastric acid secretion is increased and the acid can further digest the gastric wall, leading to the formation of gastric ulcers (Goel and Bhattacharya, 1991).

The significant reduction observed in PKO-treated rats may be due to the presence of flavonoids (such as

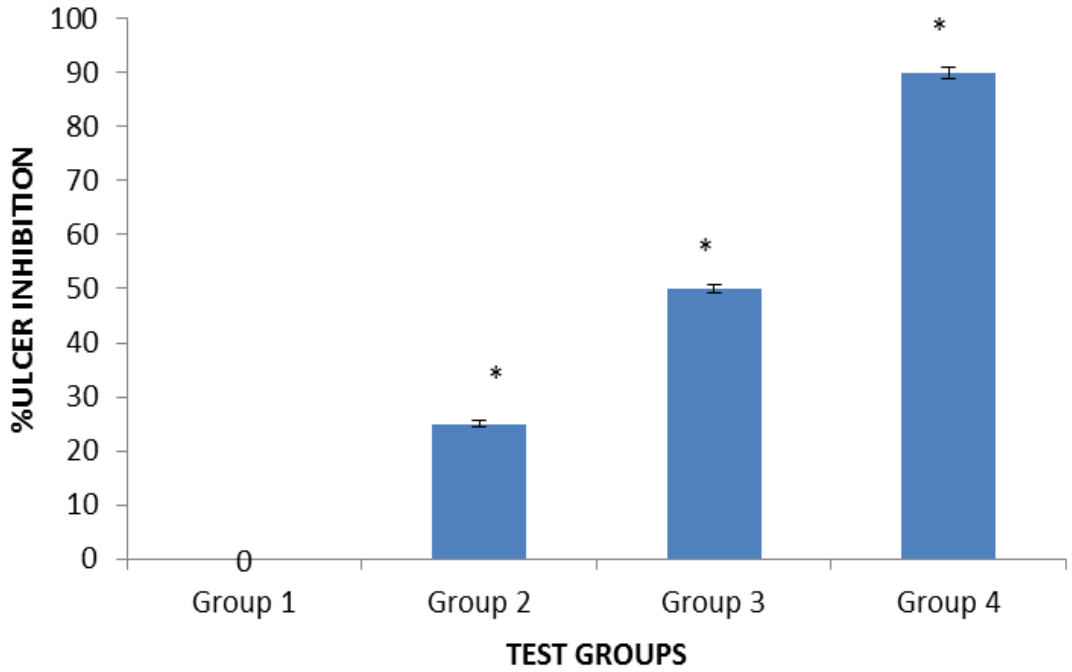

Figure 1. Effect of PKO on % Ulcer Inhibition. Each bar is expressed as mean SEM (n=5). One way ANOVA and LSD revealed significant differences between the control and treated groups. *p<0.05.
Source: Author

quercetin and catechins) that appear to play a very important role in the prevention and treatment of peptic ulcer disease (Middleton et al., 2000). It works by promoting mucus secretion, thus serving as a gastric protective agent. In addition, quercetin has been shown to inhibit the growth of *H. pylori* in *in vitro* studies. In addition, catechins interfere with the formation of histamine in the gastric mucosa and thus exert a protective effect (Middleton et al., 2000).

The results also showed that a diet rich in palm kernels inhibited gastric acid secretion in a dose-dependent manner, with higher concentrations of PKO in the diet inducing lower gastric acid secretion in the rat mucosa. The pH of untreated rats decreased significantly indicating acidity level and volume of gastric secretions. A low pH value is indicative of an increased concentration of hydrogen ions in the gastric juice. This is related to the pathogenesis of gastric ulcers and lesions in laboratory animals (Lu¨llmann et al., 2000). Biochemical analysis of gastric secretions (pH, gastric volume and bicarbonate) and gastric mucosal integrity is commonly used to determine its status following exposure to pharmacological agents (Biplab et al., 2011).

By approaching the cytoprotective properties of any drug or agent, the size of gastric mucosal lesions induced is measured both macroscopically and microscopically (Dabo et al., 2014). Overall observation showed that PKO ameliorated gastric ulcer status by reducing the apparent ulcer index due to slight erosion of the surface epithelium. Furthermore, the decrease in mean ulcer score index in PKO-treated mice may be due to the presence of flavonoids in palm kernel oil which may also play a role in this regard: flavonoids with antioxidant properties. In addition to enhancing systemic mucosal protection by stimulating gastric mucus secretion, flavonoids are potent biological antioxidants (Njoku et al., 2010). Other phytochemicals have been shown to help improve the development of gastric ulcers: tannins are known to "tar" the outermost layer of the stomach lining, making it less permeable and able to greater resist chemical and mechanical damage or irritation (Kolawole and Dapper, 2017; Ibegbulem and Chikezie, 2012).

It is also necessary to clarify other protective mechanisms of the gastric mucosa such as increased mucus secretion, stimulation of prostaglandin release, increased mucosal blood flow, etc., which may also be potentially related to the anti-ulcer effect of palm kernel oil. However, these effects were not studied in this study.

The study results showed that a diet rich in palm kernel oil reduced gastric juice volume, acidity, and mean ulcer index, while increasing gastric pH, gastric bicarbonate, percentile inhibits ulceration in male Wistar rats.

Therefore, we recommend further studies on this issue.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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