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Prophylactic Efficacy of Aqueous Extract of *Curcuma longa* against Indomethacin-Induced Ulcer in Male Wistar Rats

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Abstract

Evaluation of the anti-ulcerogenic and prophylactic efficacy of aqueous extract of Curcuma longa on indomethacin-induced ulcer in albino rats was the aim of this study. Thirty adult male rats of body weight between 150 and 200g were used and were divided into six groups of five rats each. Group I was treated with 0.8mg/ml of Omeprazole for seven days. Group II was treated with a solution of 0.8 g/ml Curcuma longa for seven days, while group III received distilled water for seven days. This group served as the control group. Groups IV, V and VI were treated similarly as groups I, II and III respectively but were treated for fourteen days. Gastric ulceration was induced in the rats by the administration of 50 mg/kg indomethacin after pre-treatment with distilled water, omeprazole and Curcuma longa for 7 and 14 days respectively. Significant ulcer inhibition was produced in the groups treated with Curcuma longa and Omeprazole when compared with control groups at $p<0.05$, but omeprazole-treated group showed greater ulcer inhibition (72.60 % and 74.29 %) when compared with the Curcuma longa -treated groups (46.53% and 43.84%) after 7 and 14 days respectively. This study showed that Curcuma longa possesses anti-ulcerogenic properties and can be used as herbal remedy for the prevention of gastro-intestinal ulcers.

Keywords:

Curcuma longa, curcumin, Ulcer inhibition, anti-ulcerogenic properties, gastro-intestinal ulcer

1. Introduction

Peptic ulcer diseases comprise of heterogeneous disorders, which manifest as a break in the lining of the gastrointestinal mucosa bathed by acid and pepsin. It is the most predominant of the gastrointestinal diseases [1, 2] with a worldwide prevalence of about 40% in the developed countries and 80% in the developing countries. It is generally recognized that peptic ulcer is caused by a lack of equilibrium between the gastric aggressive factors and the mucosal defensive factors [3]. Although several orthodox pharmaceutical drugs have been employed in the management of peptic ulcers e.g. antacids, anti-cholinergic drugs, histamine H_2-receptor antagonists, antihistaminics and more recently, proton-pump inhibitors. Most of these drugs, however, produce several adverse reactions, like arrhythmias, impotence, gynecomastia and hematopoeitic changes [4]. In recent years, there has been growing interest in alternative therapies especially from plant sources due to their perceived lower side effects, ease of accessibility and affordability [5].

Curcuma longa commonly referred to as turmeric is a rhizomatous herbaceous perennial plant of the ginger family, Zingiberaceae [6]. *Curcuma longa* has been used in traditional remedy for a wide range of ailments, including wound healing, urinary and gastrointestinal tract infections, and liver ailments [7]. Curcumin has been defined as the most active component in *Curcuma longa* and has been shown to have considerable gastroprotective, anti-ulcerogenic and

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therapeutic effect in gastric ulcer disease [7]. It has been reported to heal peptic ulcer [8]. This study is to investigate its ability to prevent peptic ulcer.

2. Methodology

2.1. Plant Preparation

Tumric root extract in the form of a powder, was purchased from Foodco, Bodija, Ibadan. It was weighed accordingly and administered in aqueous solution.

2.2. Chemicals

Omeprazole (Cipla) and indomethacin (Sun) were of analytical grade.

2.3. Experimental Design

Thirty (30) healthy male albino rats with body weights between 150 and 200 g were used for this study. They were bought from 'Imrat animal house' of the University College Hospital, Ibadan and were housed in Educational Advancement Centre animal house.

They were allowed 14 days to acclimatize before the commencement of treatment. The animals were maintained on a standard pellet diet throughout the acclimatization and treatment period. They were divided into six groups of five rats each. Group I was exposed to omeprazole for seven days, group II was exposed to *Curcuma longa* solution for seven days and group III was exposed to distilled water for seven days. This group served as the control group. Groups IV, V and VI were treated similarly as groups I, II and III respectively but were treated for fourteen days.

A 0.8g/ml solution of *Curcuma longa* was prepared daily and the animals in groups II and V were allowed to drink *ad libitum*. This was done because people feed on tumeric without attention to dosage. A 0.8mg/ml solution of omeprazole was prepared daily and the animals in groups I and IV were allowed to drink *ad libitum* while groups III and VI drank distilled water throughout the period of administration. All the animal treatments were carried out in accordance with the principles of laboratory animal care of the National Institute of Nutrition (NIN) guide for Laboratory Animal Welfare.

At the end of the administration, the animals were deprived of food for 18 hours and 50 mg/kg of indomethacin was administered orally (p.o) to the rats. After 8 hours of indomethacin administration, the animals were sacrificed by chloroform anesthesia and the stomach removed and opened along the greater curvature, rinsed with copious volume of normal saline and pinned on a board.

2.4. Parameters Measured

2.4.1. Ulcer Index

Ulcer index was measured. The ulcers scores were given based on their intensity as follows

Normal stomach…….	0.0
Red coloration……	0.5
Spot ulcer……	1.0
Hemorrhagic streak…….....	1.5
Ulcers……..	2.0
Perforation……...	3.0

Measurement of gastric ulcerations was done by first dissecting the stomachs along their greater curvature and fixing on a board [9]. Examination was carried out macroscopically with a hand lens (x 2). The ulcer indices (UI) of the control and treated groups were calculated using the method of Ezike *et al.*, [10].

$$\text{Ulcer index (mm)} = \frac{\textbf{Number of ulcers (A) x Size of ulcers (B)}}{\textbf{Magnification power of the lens used (x 2)}}$$

2.4.2 Percentage Ulcer Inhibition

Percentage ulcer inhibition was calculated relative to control as follows:

$$\% \text{ Ulcer Inhibition (\% U.I)} = \left(1 - \frac{U_t}{U_c}\right) \text{ x } 100$$

Where U_t and U_c represent the ulcer index of the treated and control groups respectively.

2.5. Statistical Analysis

Data were subjected to analysis using the Statistical Package for Social Sciences (SPSS), version 21.0. Results were presented as Mean $\pm$ Standard deviations. Student's t-test was used for comparison of the mean. Difference between means were considered to be significant at $p<0.05$.

3. Result

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Indomethacin induced gastric ulcer in 24 out of 30 (80 %) rats used in this study.

Table 1: Effect of Different Treatments on Ulcer Index in Indomethacin-Induced Ulcer in 7 days

Treatments	Ulcer Index (mm)	% Ulcer Inhibition (%UI)
Control	60.83 ± 6.29[a]	0.00[a]
Omeprazole	16.67 ± 2.89[b]	72.60[b]
Curcuma longa	34.00 ± 3.61[c]	43.84[c]

Results are presented as mean ± standard deviation where n=5. Values with different superscript along the same column is said to be significant at $p<0.05$

Table 2: Effect of Different Treatments on Gastric Ulcer index in Indomethacin-Induced Ulcer in 14 days

Treatments	Ulcer Index (mm)	% Ulcer Inhibition (%UI)
Control	64.83 ± 4.19[a]	0.00[a]
Omeprazole	16.67 ± 2.08[b]	74.29[b]
Curcuma longa	34.67 ± 5.03[c]	46.53[c]

Results are presented as mean ± standard deviation where n=5. Values with different superscript along the same column is said to be significant at $p<0.05$

4. Discussion

Indomethacin is a non-steroidal anti-inflammatory drug (NSAID) that was reported to induce gastric ulcer through multi-mechanisms [11]. The ulcer formation can occur either by direct mucosal injury which involves the breaking of the mucosal barrier and exposure of the underlying tissue to the corrosive action of excess acid and pepsin or by a decrease in endogenous gastric prostaglandin production and release through COX-1 and COX-2 inhibition. Indomethacin also suppresses gastroduodenal bicarbonate secretion, reduces endogenous prostaglandin biosynthesis and disrupts the mucosal barrier as well as mucosal blood flow [12]. It is well known that inhibition of prostaglandin synthesis which is essential for mucosal integrity and regeneration will trigger the mucosal lining damage.

Peptic ulcer is a common illness in internal medicine which affects a considerable number of people worldwide [13]. Although, many products are available for the treatment of gastric ulcers (e.g., antacids and antihistaminics), most of these drugs produce several adverse effects, such as arrhythmias, impotence, gynecomastia, and hematopoeitic changes [4]. The extracts of many herbal plants have been shown to produce promising results for the treatment of gastric ulcers with fewer or negligible side effects [14].

Curcuma longa has been used in traditional remedy for a wide range of ailments, including wound healing, urinary and gastrointestinal tract infections, and liver ailments [7]. Curcumin has been defined as the most active component in *Curcuma longa* and has been shown to have considerable gastroprotective, anti-ulcerogenic and therapeutic effect in gastric ulcer disease [7]. It has been reported to heal peptic ulcer [8]. This study is to investigate its ability to prevent peptic ulcer.

In this study, there was a significant decrease in the measured gastric ulcer index in the stomach of omeprazole-treated animals when compared with the control and *Curcuma longa* treated animals. The aqueous extract of turmeric (*Curcuma longa*) exhibited anti-ulcerogenic effect against indomethacin-induced gastric ulcer as there was a percentage ulcer inhibition of 43.84% and 46.53% in the rats pre-treated for 7 and 14 days respectively when compared with the control groups (Tables 1 and 2). The gastroprotective effect exhibited by *Curcuma longa* powder may be attributed to the presence of flavonoids and polypheolic compounds which include curcumin and other curcuminoids [15]. This result is in agreement with the study of Airaodion *et al.* [16] who reported that *Moringa olefera* leaf was able to prevent peptic ulcer due to the presence of flavonoid.

Many studies have examined the anti-ulcerogenic activities of plants containing flavonoids [16, 17, 18]. Plants containing flavonoids were found to be effective in preventing this kind of lesion mainly because of their anti-inflammatory activity and anti-oxidant properties. They protect the gastric mucosa against a variety of ulcerogenic agents and oxidation processes which are involved in the mechanisms of several gastric disorders, including ulcerogenesis in different mammalian species [16, 18]. *Curcuma longa* extract has also been reported to exert its anti-ulcer activity by increasing the synthesis of endogenous prostaglandins, which in turn promote mucus secretion and enhance the mucosal barrier against the actions of various damaging agents [7].

In this study, a significant decrease was observed in the percentage ulcer inhibition of animals treated with aqueous extract of *Curcuma longa* (46.53% and 43.84%) when compared with those of omeprazole-treated animals (74.29% and 72.60%) after 7 and 14 days respectively. This might be attributed to poor solubility of curcumin in water as well as its poor bioavailability, whereas omeprazole is a standard ulcer drug in which its active ingredient is well extracted. Study by Ravindranath and Chandrasekhra (1981) revealed that only a trace amount of curcumin was present in the stomach and intestine of the rats. In view of poor availability of curcumin, it is unlikely that substantial concentration of curcumin occur in the body after ingestion.

When seven and fourteen days' *Curcuma longa*-treated animals were compared at $p<0.05$, there was no significant difference in protection against gastric ulceration caused by indomethacin induction. Similarly, when seven and fourteen days' omeprazole-treated animals were compared at $p< 0.05$, no significant difference in protection against gastric ulceration caused by indomethacin induction was observed. Therefore, further treatment with *Curcuma longa* and omeprazole does not guarantee greater protection as far as the treatment is ongoing before ulcer induction.

5. Conclusion

The significant increase in the percentage ulcer inhibition observed in *Curcuma longa*–treated groups (46.53% and 43.84%) when compared with the control groups after 7 and 14 days respectively showed that aqueous extract of *Curcuma longa* has prophylactic efficacy against indomethacin-induced ulcer. Further studies on the anti-ulcerative and prophylactic effect of *Curcuma longa* on peptic ulcer should be carried out with ethanoic or methanoic extracts of *Curcuma longa*.

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