

## Comparative Effect of *Curcuma longa* and *Piper nigrum* Extract and their Mixture on some Haematological Indices of Indomethacin-Induced Gastric Ulceration in Albino Rats

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### ABSTRACT

Peptic ulcer disease (PUD) which includes gastric and duodenal ulcer is one of the unresolved medical problems facing numerous patients in a wide range of age of both sexes worldwide. Many medicinal plants are known to exhibit antiulcer activity and some have been confirmed scientifically to possess gastro protective and antiulcer property and also found to be useful in its treatment. Among these medicinal plants turmeric (*Curcuma longa*) and black pepper (*Piper nigrum*) have been reported to possess gastroprotective potentials. However, the effect of the combination of turmeric and black pepper on the haematological indices of ulcerated rats hasn't been considered. As a result, this study was designed to evaluate the effect of aqueous extract of *Curcuma longa* and *Piper nigrum* on some haematological parameters of indomethacin-induced gastric ulceration in albino rats. Total of sixty (60) albino rats was used for this study. After acclimatization for 14 days, the animals were randomly allocated into six groups (n=10). Group A (normal control): rats was fed on pellet and allowed free access to water, rats in Group B (Ulcerated control) were given only indomethacin at a dose of 50mg/Kg body weight. Animals in group C (Standard control) was given indomethacin after pre-treatment with omeprazole (20mg/kg) body weight. Group D, E, and F comprised ulcerated rats pre-treated with turmeric (200mg/kg body weight), black pepper (100mg/kg body weight), turmeric and black pepper (200mg/Kg + 100mg/kg respectively) body weight. Treatments with the reference drug and extracts lasted for 21 days prior to ulcer induction on the twenty-third day. 4 h post ulcer induction, the animals were humanely sacrificed under chloroform anaesthesia and blood samples were collected for further haematological studies. The result obtained from this study showed that there were no significant ( $p > 0.05$ ) differences in PCV, HbC, TWBC, NEUT, MON, EOS, BAS, RBC and PLT levels across all groups, with LYM being significantly ( $p < 0.05$ ) different in group E compared with Group F. The study found that *Curcuma longa* and *Piper nigrum* extracts, either alone or in combination, do not significantly alter haematological indices in albino rats with gastric ulcers caused by indomethacin, suggesting they may be beneficial without negative systemic impact. However, lymphocyte levels significantly decreased in the group treated with a mixture of *Curcuma longa* and *Piper nigrum*, suggesting a potential mild immunomodulatory effect.

**Keywords:** Haematological Indices, Indomethacin, Ulcer, *Curcuma longa* and *Piper nigrum*

### INTRODUCTION

Peptic Ulcer Disease (PUD) is clinically described as a disruption of the continuity of the gastrointestinal mucosal lining which appears as sores of at least 0.5cm in diameter in endoscopic studies [1]. It is one of the commonest ailments of the alimentary system [2], and affect about 4 million of the world's population annually, with incidence of complications in approximately 10–20% [3]; [1]. It is largely classified as gastric ulcers (GU) or duodenal ulcers (DU) based on the affected section of the gastrointestinal tract (GIT). Typically, patient with acid peptic diseases presents with mucosal disruption which is considered to be as a result of hyper secretive acidic environment, which leads to epigastric pain which may subside when food or alkali is consumed. [1].

PUD is predominantly caused by the activities of *Helicobacter Pylori* (*H. Pylori*) and/or Non-Steroidal Anti-inflammatory Drugs (NSAIDs). While the activities of *H. Pylori* creates imbalance in acid production and regulation through inflammation-induced increased gastric secretion and decreased somatostatin secretion, NSAIDs, which offer many benefits such as reduction of pain, fever, and inflammation, are being taken regularly by some people which makes them to be five (5) times more likely to develop PUD than people who do not take them [5]. Cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) are enzymes that produce prostaglandins, which promote pain, inflammation, and fever. NSAIDs work by inhibiting these two enzymes [6]. These medications often cause Peptic Ulcer Disease because COX-1 produces an additional type of prostaglandin that protects the stomach lining from stomach acid [7]. By inhibiting COX-1, NSAIDs increase the risk of ulcers and GI bleeding by making the mucosal cells more vulnerable to hydrochloric acid and pepsin damage [6].

Apart from the activities of *H. pylori* and NSAIDs, studies have identified risk factors of PUD which are mostly modifiable. The modifiable risk factors include the use of corticosteroids, anticoagulants, coffee, alcohol, smoking, stress, spicy foods, use of unclean water sources and fasting; while non-modifiable risk factors include genetics, age, gender and past history of PUD. [5]; [8]; [9]; [10]. Since PUD impacts negatively on the health-related quality of life of the affected individuals hence, there have been a rapid change in the concept of gastric ulcer management, ranging from conventional vagotomy, prostaglandin analogs, H<sub>2</sub> receptor antagonists and antacids to proton pump inhibitors, such as cimetidine, ranitidine, misoprostol, omeprazole and esomeprazole but then gastrointestinal toxicity remains an impediment to their application in clinical practice [11]; [12]; [13]. However, there have been needs to search for non toxic, easily assessable and affordable anti ulcer medication.

Phytotherapy of some therapeutic plant extracts that are highly valued and widely used in traditional system of medicine such as *curcuma longa* and *piper nigrum* are being investigated to ascertain if they could provide efficient formulation for better management, as such discovering effective and safe drugs that also have gastro-protective activity.

*Curcumin*, the natural phenolic active ingredient of turmeric (*Curcuma longa*) rhizome, has been used in Asia as a herbal remedy for a variety of diseases [14] phytochemicals such as Terpenes, phytosterols several bioactive essential oils, were revealed, other bioactive compounds were also isolated from methanol extract of *curcuma longa* rhizome. [15]; [16]. The phytochemicals analysis carried out by [12] revealed the percentages of total phenolic, alkaloid and saponin ( $4.91 \pm 1.0$ ,  $6.64 \pm 1.0$  and  $2.30 \pm 0.0$ ) respectively and flavonoids  $6.15 \pm 0.03$ , the presence of these also confirmed the medicinal properties of turmeric rhizomes. [17]. Similar to chili, turmeric is commonly used in Asian cuisine to add a yellow color, both as a flavor and as a preservative [18]. In addition to the use of curcumin as an anti-inflammatory in ancient times, it has also been used to treat gastrointestinal (GI) diseases such as indigestion, flatulence, diarrhea, and even gastric and duodenal ulcers [19]. Great attention has been paid to the medical applications of *Curcumin* in the treatment of human diseases associated with oxidative stress and inflammation, including different cancers [19]. *Curcumin* treatment has also led to the improvement of metabolic parameters involving aging-associated diseases such as atherosclerosis, diabetes, cardiovascular disease, and chronic kidney diseases [20]; [21]. Interestingly, some promising effects of curcumin have been observed in the alleviation by this turmeric derivative of the chronic inflammatory conditions such as arthritis, uveitis, and inflammatory bowel disease [22]. In some instances, *Curcumin* has been found to aid in the prevention and treatment of various cancers [23]. Recently, the anticarcinogenic activity of *Curcumin* has been documented in the GI tract because this compound has proven to exert a therapeutic effect on different human GI cancers such as esophageal, gastric, and small and large intestinal cancer [24]; [25].

*Piper nigrum* (Black pepper) is one of the most commonly used spices and considered as "The King of Spices" due to its trade in the international market [26]; [27]. Black pepper is used as medicinal agent, a preservative, and in perfumery [28]. The genus *Piper* has more than 1000 species but the most well known species are *Piper nigrum*, *Piper longum* and *Piper betli* [29]. Black pepper can be used for many different purposes such as human dietaries, as medicine, as biocontrol agents [27]; [3]; [30]. Black Pepper is used worldwide in different types of sauces and dishes like meat dishes, as rubs, salad dressings. It contains major pungent alkaloid piperine (1-piperoyl piperidine) which is known to possess many interesting pharmacological actions [31], as well as other beneficial compounds such as tannins, saponins, terpenes, steroids, flavones, flavonoids [32]. A study conducted by [33] revealed that black pepper fruits are endowed with essential oils (1.0–2.5%) and alkaloids (5–9%) also a study showed that it contains Tannins (0.81–2.25) Saponins (1.73), and Flavonoids 1.28. [34]; [35].

[36] reported that this plant and its active components piperine can stimulate the digestive enzymes of pancreas and intestine and also increases biliary bile acid secretion when orally administered. Black pepper is important for its medicinal values [37]. Medicinally black pepper can be used digestive disorder like large intestine toxins, different gastric problems, diarrhoea and indigestion and also can be used against respiratory disorder including cold, fever and asthma [38]; [39]; [40]. Piperine exhibits diverse pharmacological activities like antihypertensive

and anti-platelet [41], antioxidant, antitumor [42] antipyretic, analgesic, anti-inflammatory, anti-diarrheal, anti-spasmodic, hepato-protective [5], antibacterial, antifungal, anti-thyroids, anti-apoptotic, anti-spermatogenic, insecticidal and larvicidal activities. Piperine has been found to enhance the therapeutic efficacy of many drugs, vaccines and nutrients by increasing oral bioavailability [43]. Research supports that combining the piperine in black pepper with the curcumin in turmeric enhances curcumin absorption by up to 2,000%, [44]; [45], thus in one study Shoba and colleagues reported that adding 20 mg of piperine to 2 grams of curcumin increased its absorption significantly by slowing down the breakdown of curcumin by the liver, thereby increasing its blood levels [45]

## MATERIALS AND METHODS

### Materials

#### Equipment and Instruments

The equipment and instruments used was of good analytical grade.

#### Chemicals and Reagents

Indomethacin and esomeprazole was respectively procured from Kapit Pharmaceutical Limited, Nigeria and Ranbaxy Laboratories, India. Trichloroacetic acid (TCA), dimethylaminobenzaldehyde, epinephrine, acetyl acetone, bovine serum albumin (BSA), gallic acid, aluminum chloride, quercetin and thiobarbituric acid (TBA) were products of Sigma Chemical Co. (St. Louis, MO, USA). Assay kits from Randox Laboratories limited, United Kingdom was used. Other chemicals used was of analytical grade from reputable companies in the world.

#### Plant collection and authentication

*Curcuma longa* rhizomes and piper nigrum peppercorns were collected locally and were botanically identified by a Botanist in the department of Botany, Ebonyi state university, Nigeria.

#### Preparation of extracts

*Curcuma longa* rhizomes and black pepper was air-dried at room temperature for 10 days to constant weight. The dried samples were then be pulverized with an electric blender (model: Bajaj Stormix: 410501), weighed and kept airtight prior to extraction. Powdered samples of turmeric (180g) and black pepper (250g) was separately extracted in 1.8 litres and 2.5 litres of 70% alcohol respectively. For 120 hours using a rotary evaporator kept at a temperature of 40°C. The solutions obtained was filtered with Whatman No. 1 filter paper and yielded 25.56% and 17.60% for turmeric and black pepper respectively.

## METHODS

### Experimental animals

Wister albino rats was purchased from Animal Unit of Faculty of Veterinary Medicine, University of Nigeria, Nsukka, Enugu, Nigeria. All animals received humane care in accordance with the National Institute of Health guidelines for the care and use of laboratory animals. The animals were left to acclimatize for one week before the start of the experiment and housed in standard clean cages under a controlled room temperature of 21–25 °C and a 12 h light/dark cycle. The animals were given free access to clean water and standard chow diet *ad libitum*.

### Ulcer Induction

After a 24 hour fasting period, gastric ulceration was induced in the animals according to the procedure described by [46]. Briefly the rats was administered orally at a dose of (50mg/kg body weight) of indomethacin; this dosage used was based on previous findings that rats administered 50mg/kg body weight of indomethacin presented a very high degree of weakness, behavioral changes, reduced physical activity and very high ulcer index. [47].

### Experimental designs

Total of sixty (60) albino rats was randomly allocated into six groups (n=10). Doses of (200mg/kg body weight) turmeric was administered, selecting this dose of curcumin, was informed by previous findings that at dose of 200mg/kg an effective protection against hyperacidity was observed [48]. Doses of (100mg/kg body weight) black pepper was administered; a study showed that *Piper nigrum* offered a prophylactic treatment at a dose of 100 and 200/kg body weight [49]. Group A (normal control): rats was fed on pellet and allowed free access to water, rats Group B (Ulcerated control) were given only indomethacin at a dose of 50mg/Kg body weight. Animals in group C (Standard control) will be given indomethacin after pre-treatment with omperazole (20mg/kg) body weight; it was selected as a standard treatment and dose based on a present study carried out by [50]. Group D,E, and F comprised ulcerated rats pre-treated with turmeric (200mg/kg body weight), black pepper (100mg/kg body weight), turmeric and black pepper (200mg/Kg + 100mg/kg respectively) body weight. Treatments with the reference drug and extracts lasted for 21 days prior to indomethacin administration. These were orally administered once daily using oral intubator with *ad libitum* provision of food and water throughout the experimental period. On the twenty-second day prior to ulcer induction, the animals were fasted for 24 hours and animals in groups B – F were thereafter indomethacin at a dose of 50mg/Kg body weight.

### Blood sample collection

Blood samples were collected from the abdominal aorta into Ethylenediamine tetraacetic acid (EDTA) and Lithium heparin sample bottles and kept in the refrigerator for further haematological studies.

### Determination of Haematological Parameters (PCV, HB, RBC, Platelets and WBC)

Haematological parameters (packed cell volume, haemoglobin concentration, red blood cell count, red cell indices, total white blood cell count and differential and platelets were determined using Mindray automated haematology analyser (BC-2800VET, Indiamart Inter MESH Ltd, Uttar Pradesh, India).

### Statistical Analysis

The data was analysed using the statistical package for social science (SPSS Inc., Chicago, IL, USA) version 21.0. One-way analysis of variance (One-way ANOVA) was used to determine significant difference among group. Results were expressed as mean  $\pm$  standard error of mean (SEM). The results were considered statistically significant different at  $p$  values less than 0.05

## RESULTS

### Comparative Effect of Turmeric, Black Pepper and their Mixture on Haematological Parameters of Indomethacin-Induced Ulceration in Rats

The result obtained from this study as presented in table 1 showed that there was no significant ( $P > 0.05$ ) in PCV, HbC, TWBC, NEUT, MON, EOS, BAS, RBC, and PLT across the groups. LYM was significantly ( $P < 0.05$ ) decreased in group E when compared with group F.

**Table 1:** Comparative effect of turmeric, black pepper and their mixture on haematological parameters of indomethacin-induced ulceration in rats.

| Parameters             | Experimental Groups |                    |                    |                    |                               |                               |
|------------------------|---------------------|--------------------|--------------------|--------------------|-------------------------------|-------------------------------|
|                        | A                   | B                  | C                  | D                  | E                             | F                             |
| PCV (%)                | 45.02 $\pm$ 0.95    | 44.32 $\pm$ 1.08   | 45.00 $\pm$ 1.48   | 41.66 $\pm$ 0.83   | 42.34 $\pm$ 0.83              | 42.93 $\pm$ 2.00              |
| HbC (g/dL)             | 14.68 $\pm$ 0.37    | 15.00 $\pm$ 0.26   | 15.20 $\pm$ 0.36   | 14.32 $\pm$ 0.38   | 14.74 $\pm$ 0.16              | 14.08 $\pm$ 0.69              |
| TWBC<br>( $10^9/L$ )   | 13.99 $\pm$ 1.66    | 14.12 $\pm$ 1.36   | 16.82 $\pm$ 2.60   | 14.83 $\pm$ 1.36   | 12.90 $\pm$ 0.49              | 15.86 $\pm$ 4.15              |
| NEUT (%)               | 10.62 $\pm$ 2.96    | 14.93 $\pm$ 2.56   | 14.60 $\pm$ 4.83   | 13.54 $\pm$ 2.78   | 20.94 $\pm$ 2.00              | 7.65 $\pm$ 1.24               |
| LYM (%)                | 81.94 $\pm$ 5.32    | 78.28 $\pm$ 4.43   | 78.88 $\pm$ 4.51   | 79.96 $\pm$ 4.66   | 66.32 $\pm$ 2.19 <sup>e</sup> | 90.05 $\pm$ 1.01 <sup>d</sup> |
| MON (%)                | 7.40 $\pm$ 2.40     | 6.77 $\pm$ 2.08    | 6.48 $\pm$ 2.36    | 6.28 $\pm$ 2.76    | 10.82 $\pm$ 2.36              | 2.00 $\pm$ 0.46               |
| EOS (%)                | 0.04 $\pm$ 0.02     | 0.02 $\pm$ 0.02    | 0.04 $\pm$ 0.02    | 0.04 $\pm$ 0.02    | 0.12 $\pm$ 0.10               | 0.15 $\pm$ 0.09               |
| BAS (%)                | 0.00 $\pm$ 0.00     | 0.00 $\pm$ 0.00    | 0.00 $\pm$ 0.00    | 0.00 $\pm$ 0.00    | 0.00 $\pm$ 0.00               | 0.00 $\pm$ 0.00               |
| RBC<br>( $10^{12}/L$ ) | 7.92 $\pm$ 0.26     | 8.27 $\pm$ 0.15    | 8.01 $\pm$ 0.16    | 7.52 $\pm$ 0.15    | 8.02 $\pm$ 0.13               | 7.56 $\pm$ 0.50               |
| PLT<br>( $10^9/L$ )    | 865.20 $\pm$ 58.79  | 846.33 $\pm$ 65.75 | 891.00 $\pm$ 86.47 | 812.60 $\pm$ 83.81 | 869.40 $\pm$ 53.97            | 869.25 $\pm$ 223.95           |

Values are expressed as mean  $\pm$  SEM, n = 10. Values with different superscripts are statistically significant ( $p < 0.05$ ). PCV: Packed cell volume; LYM: Lymphocytes; PLT: Platelets; NEUT: Neutrophils; MON: Monocytes; EOS: Eosinophils; BAS: Basophils.

\* = significantly different from group A at  $p < 0.05$ ; a = significantly different from group B at  $p < 0.05$ ; b = significantly different from group C at  $p < 0.05$ ; c = significantly different from group D at  $p < 0.05$ ; d = significantly different from group E at  $p < 0.05$ ; e = significantly different from group F at  $p < 0.05$ .

### DISCUSSION

Peptic ulcer disease (PUD) which includes gastric and duodenal ulcer is one of the unresolved medical problems facing numerous patients in a wide range of age of both sexes worldwide [51], with a global prevalence of 5-10% [52], Nigeria ranked #31 in the world with PUD total deaths of 0.39% according to the World Health Organisation and an unexpected rise in gastric ulcer has also been reported in the South-East [53]; [54]. Many medicinal plants are known to exhibit antiulcer activity [55] and some have been confirmed scientifically to possess gastro protective and antiulcer property and also found to be useful in its treatment [56]; [57]. Some

studies have been conducted on the use of turmeric and black pepper respectively and also its combination to achieve therapeutic effects on various diseases including gastro intestinal diseases. [58] [59]; [60]. However, the effect of the combination of turmeric and black pepper on the haematological indices of ulcerated rats hasn't been considered. As a result, this study was designed to evaluate the effect of ethanolic extract of *Curcuma longa* and *Piper nigrum* on some haematological parameters of indomethacin induced gastric ulceration in albino rats. Haematological parameters are those parameters that are related to the blood and blood-forming organs [61]. These parameters change in relation to the physiological status of an animal. Thus, haematological examination is one of the methods employed in the detection of some changes in health and physiological status, which may not be apparent during physical examination but which affect the fitness of the animal [61]. Blood serves as a pathological indicator of the health of animals that have been exposed to toxicants and other circumstances [62]. The existence of various metabolites and other constituents in the body of the organism can be clinically investigated using a blood examination. During normal clinical evaluation, haematological markers are useful diagnostic tools. It is important for an organism's physiological, nutritional, and pathological condition. It also provides useful information about the animal's immunological condition [62]. The majority of blood illnesses reduce or impair the number of cells, proteins, platelets, or nutrients in the blood. Red and white blood cells, as well as haemoglobin concentration, are the most common clinical indications of illness condition. In healthy people, these indicators are under control [63]. A number of research studies have documented a correlation between PUD and haematologic disorders, such as thrombocytopenia [64]. A good recovery from PUD has been associated with an increase in platelet counts [65]. Additionally, the relationship between red blood cell parameters and digestive diseases has been assessed. It has been demonstrated that PUD brought on by *H pylori* lowers haematocrit (Hct), haemoglobin (Hgb), and erythrocyte count values [66]. In a number of diseases, including gastritis, novel inflammatory biomarkers, including as NLR, MLR, and PLR, have been employed as non-invasive indicators of systemic inflammation [67]. The role of PLR has only been documented in adults, and those characteristics have only been evaluated in relation to gastritis thus far. Consequently, a rise in thrombocyte count and a decrease in lymphocyte count have been linked to a greater PLR [67]. In the present study, there was no significant ( $P > 0.05$ ) difference in PCV, HbC, TWBC, NEUT, MON, EOS, BAS, RBC, and PLT across the groups. LYM was significantly ( $P < 0.05$ ) decreased in group E when compared with group F. In an observational study exploring the impact of uncomplicated peptic ulcer disease (PUD) on haematological parameters, Ahmed et al. (2024) reported that the mean values of Hgb, RBC, Hct, MCV, MCH, MCHC were observed to be significantly lower in uncomplicated PUD when compared to control group. However, the mean values of neutrophil count, monocyte count, neutrophil-to-lymphocyte ratio (NLR) and monocyto-lymphocyte ratio (MLR) were significantly higher in uncomplicated PUD patients than that of the control group. On the other hand, mean values of platelet count and (platelet-to-lymphocyte ratio) PLR were lower in uncomplicated PUD patients in comparison to control group which were statistically non-significant. In contrast to the report of [64] and consistent with the result obtained in this study, [68] reported that there was no significant change in PCV and Hb in PUD patients when compared with the non-peptic ulcer patients. Omeprazole, a proton pump inhibitor, is not a new drug in medical and pharmaceutical circles. Its use for the management of gastric ulcer and gastroesophageal reflux disease (GERD) since its discovery and launch in the 1980's is well documented [69]; [70]. Today, omeprazole (OME) has become one of the most frequently prescribed and widely used medications [71]; [72]. It may also have become a form of standard especially in terms of cost-efficient and clinically effective therapy for gastric ulcer and GERD [73]; [74]. Furthermore, OME (and other proton pump inhibitors) is considered a mainstay in the control of disease manifestations and improvement of quality of life of patients with GERD [75]. This is because it is very effective in suppressing acid secretion (its basic mechanism of action) and has a wide margin of safety [76]; [77]. The safety profile of OME has been well established and documented through several clinical trials and over 30 years of post-market exposure and surveillance [75]. Despite the indications of omeprazole in the management of peptic ulcer disease, it is not devoid of side effects particularly when it regards haematological parameters. On this note, [78] reported that long-term use of omeprazole resulted in a significant ( $p < 0.001$ ) reduction in RBCs and its indices comprising of HGB, MCV, MCH and MCHC with no significant effect on other blood parameters evaluated when compared with the control. Their findings was in contrast with the result obtained from this study which showed no significant ( $p > 0.005$ ) difference in all haematological parameters evaluated in the omeprazole administered group when compared with the control and other groups. This discrepancy in this results maybe due to the difference in the duration of administration. Turmeric and black pepper are two culinary spices that have gained popularity due to their therapeutic potential. Piperine obtained from black pepper has been employed to increase the bioavailability of curcumin gotten from the rhizomes of the turmeric plant. In this study, LYM was significantly ( $P < 0.05$ ) decreased in the group pre-treated with black pepper extract (group E) when compared with the group pre-treated with a combination of turmeric and black pepper extracts (group F), while there was no significant change in the levels of other haematological

parameters evaluated when the groups were compared with each other. The reason for this is not fully understood but previous studies have evaluated the effect of turmeric and black pepper alone on the haematological indices of ulcerated animal models but none have evaluated the effect of their combination on haematological parameters of ulcerated animal models. [79], reported that oral administration of curcumin to piroxicam-induced ulcerated rats significantly increased RBCs count, Hb concentration and PCV value and significantly decreased platelets, WBCs, neutrophils, eosinophils, monocytes counts in comparison with the piroxicam treated group. Also, [80], evaluated the effect of aqueous extract of piper nigrum on some physiological parameters and histopathology in female rabbits induced gastric ulceration by aspirin and reported that treatment of rabbits for 30 days with 400mg/kg B.W. of aspirin caused significant decrease in RBC, WBC, PCV, Hb, DWBC relative to the control. And treatment with piper nigrum extract resulted in significant increase in RBC, WBC, PCV and Hb.

### CONCLUSION

This study looked at how *Curcuma longa*, *Piper nigrum*, and their combination affected several haematological indicators in albino rats that had stomach ulcers caused by indomethacin. Analysing these haematological markers sheds light on the possible medical advantages of the plant extracts as well as the systemic consequences of stomach ulcers brought on by indomethacin. The majority of the haematological parameters examined, such as packed cell volume (PCV), haemoglobin concentration (HbC), total white blood cell count (TWBC), neutrophils (NEUT), monocytes (MON), eosinophils (EOS), basophils (BAS), red blood cell count (RBC), and platelet count (PLT), did not show significant differences ( $P > 0.05$ ) between the experimental groups, according to the results. This indicates that these particular haematological indicators were not significantly affected by either the indomethacin-induced stomach ulcer or the *Curcuma longa*, *Piper nigrum*, and their combination therapies. The fact that these parameters did not significantly alter suggests that, when used to treat gastric ulcers, the extracts might not have any harmful effects on the haematological system or cause systemic toxicity. However, compared to group F (combination therapy), lymphocyte (LYM) levels in group E (black pepper alone) shown a substantial drop ( $P < 0.05$ ). Given the combined extracts' potential to impact the immune response in the context of stomach ulceration, the drop in lymphocyte count observed in group E may indicate a minor immunomodulatory effect. This finding suggests that the dosage and combination of these extracts may be involved in immune system modulation; however, more research is needed to determine the therapeutic significance of this alteration. With the exception of lymphocyte count, which demonstrated a significant decrease in one of the treatment groups, the study's findings suggest that *Curcuma longa* and *Piper nigrum* extracts, either alone or in combination, do not significantly alter most haematological indices in albino rats with gastric ulcers caused by indomethacin. According to the findings, the extracts may be beneficial in treating stomach ulcers without having a negative systemic impact and are generally safe in terms of haematological markers. The underlying processes and possible therapeutic uses of these extracts should be investigated further, especially in light of their immunomodulatory properties.

### REFERENCES

1. Habeeb, A., Tiwari ,S.K., Bardia A., Khan, S., Vishwakarma ,S.K. and Habeeb S. (2020). Peptic Ulcer Disease: Descriptive Epidemiology, Risk Factors, Management and Prevention. In Khan AA, editor. Peptic Ulcer Disease, 1<sup>st</sup> ed. India: SMGroup; pp: 1-13.
2. Venkatesan, K., Ravi, P., Alli, P., Valgurunathan, K., Asayas ,B.C.K. and Senchivelan, M. (2017). A study of association between dietary habits and peptic ulcer in M.B.B.S Students in A private Medical College, Puducherry. *Journal of Dental and Medical sciences*. **16** (8): 82-85.
3. Lee, F.Y., Leung , K.L., Lai, B.S., Ng, S.S., Dexter ,S. and Lau ,W.Y. (2001). Predicting mortality and morbidity of patients operated on for perforated peptic ulcers. *Archives of Surgery*. **136** (1): 90-94
4. Eniojukan, J.F., Okonkwo, O.C. and Adje, D. (2017). Risk Factors, management and other correlates of peptic ulcer disease in a university community in south-south Nigeria. *Journal of Pharmaceutical and Biosciences*. **5** (6): 07-15
5. Huang, J., Sridhar, S., Hunt, R., (2002). Role of Helicobacter pylori infection and non-steroidal anti inflammatory drugs in peptic ulcer disease: a meta-analysis. *The Lancet*. **359**:14–22.
6. Russell, R.I. (2001). Non-steroidal anti-inflammatory drugs and gastrointestinal damage-problems and solutions. *Postgraduate Medical Journal*. **77**: 82-88
7. Rafi, A.H. S. (2014). Peptic Ulcer Disease among the Patients with Abdominal Pain Attending the Department Of Medicine in Dhaka Medical College Hospital, Bangladesh. *Journal of Dental and Medical Sciences* **13** (1): 05-20
8. Bashinskaya, B., Nahed, B.V., Redjal, N., Kahle, K.T., Walcott, B.P. (2011). Trends in Peptic Ulcer Disease and the Identification of Helicobacter Pylori as a Causative Organism: Population-based Estimates from the US Nationwide Inpatient Sample. *Journal of Global Infectious Diseases*. **3** (4), 366–370.

9. Jemikajah, D.J., Okogun, G.R., (2014). Health point prevalence of *Helicobacter pylori* in central hospital, Warri, Nigeria. *African Journal of Cellular Pathology*. **3**: 57-60.
10. Etukudo, O.M, Ikpeme, E.E. and Ekanem, E.E. (2012). Seroprevalence of *Helicobacter pylori* infection among children seen in a tertiary hospital in Uyo, Southern Nigeria. *Pan African Medical Journal*. 12-39.
11. HE, J.X., Akao, T., Nishino, T. and Tani, T. (2002). The influence of commonly prescribed synthetic drugs for peptic ulcer on the pharmacokinetic fate of glycyrrhizin from shao-yao-Gancao-tang. *Biological and Pharmaceutical Bulletin*. **24**(12):1395-1399.
12. Chanda, S., Baravalia, Y., Kaneria, M. (2011). Protective effect of *Polyalthia longifolia* var. *Pendula* leaves on ethanol and ethanol/HCL induced ulcer in rats and its antimicrobial potency. *Asian Pacific Journal Tropical Medicine*. **4**:673-679.
13. Palle, S., Kanakalatha, A. and Kavitha, C.N. (2018). Gastroprotective and antiulcer effects of *Celastrus paniculatus* seed oil against several gastric ulcer models in rats. *Journal of Dietary Supplements*. **15**:373-385.
14. Hatcher, H., Planalp, R., Cho, J., Torti, F.M. and Torti, S.V. (2008). Curcumin: From ancient medicine to current clinical trials. *Cellular and Molecular Life Sciences*. **65**:1631-1652.
15. Akter J., Islam, M.Z., Takara, K., Hossain, M.A. and Sano, A. (2019). Isolation and structural elucidation of antifungal compounds from Ryudai gold (*Curcuma longa*) against *Fusarium solani* sensu lato isolated from American manatee. *Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology*, **219**: 87-94.
16. Jaiswal, D. and Agrawal, S. (2011). Ultraviolet-B induced changes in physiology, phenylpropanoid pathway, and essential oil composition in two *Curcuma* species (*C. caesia* Roxb. and *C. longa* L.). *Ecotoxicology and Environmental Safety* **208**: 111739.
17. Ifebajo, A. Y. and Folahan, O.O. (2020). nutrients and phytochemicals composition of methanolic extract of four edible spices commonly used in the preparation of soups in south-west Nigeria. *Journal of Dietitians Association of Nigeria*, **11**: 2.
18. Goel, A., Kunnumakkara, A.B. and Aggarwal, B.B. (2008). Curcumin as “Curcumin”: From kitchen to clinic. *Biochemical Pharmacology*. **75**:787-809.
19. Menon, V.P. and Sudheer, A.R. (2007). Antioxidant and anti-inflammatory properties of curcumin. *Advances in Experimental Medicine and Biology*. **595**:105-125.
20. Kunnumakkara, A.B., Anad, P. and Aggarwal, B.B. (2008). Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signalling proteins. *Cancer Letters*. **269**:199-225
21. Anand, P., Sundaram, C., Jhurani, S., Kunnumakkara, A.B. and Aggarwal, B.B. (2008). Curcumin and cancer: An “old-age” disease with an “age-old” solution. *Cancer Letters*. **267**:133-164.
22. Lang, A., Salomon, N., Wu, J.C., Kopylov, U., Lahat, A., Har-Noy, O., Ching, J.Y., Cheong, P.K., Avidan, B. and Gamus, D. (2015). Curcumin in combination with mesalazine induces remission in patients with mild-to-moderate ulcerative colitis in a randomized controlled trial. *Clinical Gastroenterology and Hepatology*. **13**: 1444-1449.
23. Adiwidjaja, J., McLachlan, A.J. and Boddy, A.V. (2017). Curcumin as a clinically-promising anti-cancer agent: Pharmacokinetics and drug interactions. *Expert Opinion Drug on Metabolism Toxicology*. **13**:953-972.
24. Sundar Dhilip Kumar, S., Houreld, N.N., and Abrahamse, H. (2018). Therapeutic potential and recent advances of curcumin in the treatment of aging-associated diseases. *Molecules*. **23**(4): 835.
25. Morris, J., Fang, Y., De Mukhopdhyay, K. and Wargovich, M.J. (2016). Natural agents used in chemoprevention of aerodigestive and GI cancers. *Current Pharmacology Reports*. **2**:11-20.
26. Mathew, P.J, Mathew, P.M. and Kumar, V. (2001). Graph clustering of *Piper nigrum* L. (black pepper). *Euphytica*. **18**: 257-264.
27. Srinivasan. (2007). Black pepper and its pungent principle piperine: a review of diverse physiological effects. *Critical Reviews in Food Science and Nutrition*. **47**(8): 735-748.
28. Singh, D. (2008). Anti-trichomonas activity of *Sapindus* saponins, a candidate for development as microbicidal contraceptive. *Journal of Antimicrobial Chemotherapy*. **62**: 526-534.
29. Vasavirama, K. and Upender, M. (2014). Piperine: a valuable alkaloid from piper species. *International Journal of Pharmacy and Pharmaceutical Sciences*. **6**(4): 34-38.
30. Hussain, A., Naz, S., Nazir, H. and Shinwari, Z.K. (2011). Tissue culture of black pepper (*Piper nigrum* L.) in Pakistan. *Pakistan Journal of Botany*. **43**: 1069-1078.



31. Ahmad, N., Fazal, H., Abbasi, B. H., Farooq, S., Ali, M. and Khan, M. A. (2015). Biological role of *Piper nigrum* L. (black pepper): a review. *Asian Pacific Journal Tropical Biomedicine*. 1945-1953.
32. Ashokkumar, K., Pandian, A., Murugan, M., Dhanya, M.K., Sathyan, T. and Sivakumar, P. (2020). Profiling bioactive flavonoids and carotenoids in select south Indian spices and nuts. *Natural Produce Research*. **34**:1306-1310.
33. Zheng, J., Zhou, Y., Li, Y., Xu, D.P., Li, S. and Li, H.B. (2016). Spices for prevention and treatment of cancers. *Nutrients*. **8**:495.
34. Nwofia, G.E., Kelechukwu, C. and Nwofia, B.K. (2013). Nutritional composition of some *Piper nigrum* (L.) accessions from Nigeria. *International Journal of Medicinal and Aromatic Plants*. **3**:247-54.
35. Ameh, G.I., Ofordile, E.C. and Nnaemeka, V.E. (2016). Survey for the composition of some common spices cultivated in Nigeria. *Journal of Agricultural and Crop Research*. **4**:66-71.
36. Tiwari, P. and Singh, D. (2008). Anti-trichomonas activity of *Sapindus* saponins, a candidate for development as microbicidal contraceptive. *Journal of Antimicrobial Chemotherapy*. **62**: 526-534.
37. Danduga, R. C. S. R., Kola, P. K. and Matli, B. (2022). Anticancer activity of curcumin alone and in combination with piperine in Dalton lymphoma ascites bearing mice. *Indian Journal of Experimental Biology (IJEb)*. **58**(03): 181-189.
38. Sujatha, R., Luckin, C. B. and Nazeem, P. A. (2003). Histology of organogenesis from callus cultures of black pepper (*Piper nigrum* L.). *Journal of Tropical Agriculture*. **41**: 16-19.
39. Parganiha, R., Verma, S., Chandrakar, S., Pal, S., Sawarkar, H.A. and Kashyap, P. (2011). In vitro anti-asthmatic activity of fruit extract of *Piper nigrum* (Piperaceae). *International Journal of Herbal Drug Research*. **1**: 15-18.
40. Fan, L. S., Muhmad, R., Omar, D. and Rahimani, M. (2011). Insecticidal properties of *Piper nigrum* fruit extracts and essential oils against *Spodoptera litura*. *International Journal of Agriculture and Biology*. **13**: 517-522.
41. Taqvi, S.I., Shah, A. J. and Gilani, A.H. (2008). Blood pressure lowering and effects of piperine. *Journal Cardiovascular Pharmacology*. **52**: 452-458.
42. Moody, J. O. (2015). Antiulcer activities of *Securidaca longepedunculata* Fres. (Polygalaceae) and *Luffa cylindrica* Linn. (Cucurbitaceae) in Wistar rats. *Nigerian Journal of Natural Products and Medicine*. **19**: 85-91.
43. Chitlange, S.S., Payal, B. S., Sanjay D, N. and Dheeraj, N. (2016). Development and validation of RPHPLC method for quantification of piperine from single herb formulation containing *Piper nigrum* extract. *International Journal of Pharmacology Science Reserach*. **6**(2): 16-21.
44. Hewlings, S.J., Kalman, D.S. Curcumin (2017). A Review of Its Effects on Human Health. *Foods*. **6**(10):92
45. Shoba, G., Joy, D., Joseph, T., Majeed, M., Rajendran, R. and Srinivas, P.S. (1998). Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Medica* **64**(4):353-6.
46. Sayanti, B., Susri, R.C., Subrata C. and Sandip K.B. (2007). Healing properties of some Indian medicinal plants against indomethacin-induced gastric ulceration of rats. *Journal of Clinical Biochemistry Nutrition*. **41** (2): 106-114.
47. Akpamu, U., Owoyele, V.B., Ozor, M. and Osifo, V.C. (2013). Indomethacin induced gastric ulcer: model in female Wistar rats. *International Journal Basic Applied Innovative Research*. **2** (4): 78-84.
48. Lobo, R., Kirti, S.P., Annie, S. and Arun, S. (2009). *Curcuma zedoaria* Rosc. (white turmeric): a review of its chemical, pharmacological and ethnomedicinal properties. *Journal of Pharmacy and Pharmacology* Pp 13-21.
49. Hawk, P.B., Oser, B.L. and Summerson, W.H. (1947) 13th ed. Mc Graw-Hill Book Company; New York: 1947. Practical Physiological Chemistry; p. 375.
50. Debnath, P. K., Gode, K. D., Das, D. G. and Sanyal, A. K. (1974). Effects of propranolol on gastric secretion in albino rats. *British Journal of Pharmacology*. **51**:213-6.
51. Abdulla, M. A., Ahmed, K. A. A., Al-Bayat, F. H., Masood, Y. (2010). Gastroprotective effect of *Phyllanthus niruri* leaf extract against ethanol-induced gastric mucosal injury in rats. *African Journal of Pharmacy and Pharmacology*. **4**(5): 226-230.
52. Lanas, A. and Chan, F. K. (2017). Peptic ulcer disease. *The Lancet*. **390**(10094): 613-624.
53. Ibrahim, A., Danbaba, I., Bello, I., Alkali, B. and Zailani, K. (2024). Dynamical Analysis of Peptic Ulcer Disease Model in Nigeria with the Effect of Vaccination and Treatment Program. *African Journal of Advances in Science and Technology Research*. **15**(1): 01-15.
54. Nwokediuko, S. C., Ijoma, U., Obieniu, O. and Picardo, N. (2012). Time trends of upper gastrointestinal diseases in Nigeria. *Annals of Gastroenterology*. **25**(1): 52.



55. Kumar, S., Sharma, S. and Kalra, P. (2011). Antiulcer effect of the methanolic extract of *Tamarindus indica* seeds in different experimental models. *Journal of Pharmacy and Bioallied Sciences*. **3**(2): 236-241.
56. Farombi, E.O. and Owoeye, O.(2011). Antioxidative and chemopreventive properties of *Vernonia amygdalina* and *Garcinia biflavonoid*. *International Journal of Environmental Research and Public Health*. **8**: 2533-2555.
57. Kayode, A.A.A., Sonibare M.A. and Moody, J. O. (2015). Antiulcer activities of *Securidaca longepedunculata* Fres. (Polygalaceae) and *Luffa cylindrica* Linn. (Cucurbitaceae) in Wistar rats. *Nigerian Journal of Natural Products and Medicine*. **19**: 85-91.
58. Lee, H. Y., Kim, S. W., Lee, G. H., Choi, M. K., Jung, H. W., Kim, Y. J., ... and Chae, H. J. (2016). Turmeric extract and its active compound, curcumin, protect against chronic CCl 4-induced liver damage by enhancing antioxidation. *BMC Complementary and Alternative Medicine*. **16**: 1-9.
59. Morsy, M. A., and El-Moselhy, M. A. (2013). Mechanisms of the protective effects of curcumin against indomethacin-induced gastric ulcer in rats. *Pharmacology*. **91**(5-6): 267-274.
60. Dhanya, K., Kizhakkayil, J., Syamkumar, S. and Sasikumar, B. (2007). Isolation and amplification of genomic DNA from recalcitrant dried berries of black pepper (*Piper nigrum* L.). A medicinal spice. *Molecular Biotechnology*. **7**: 165-168.
61. Bamishaiye, E., Muhammad, N. and Bamishaiye, O. (2009). Haematological parameters of albino rats fed on tiger nuts (*Cyperus esculentus*) tuber oil meat-based diet. *The Internet Journal of Nutrition and Wellnes*.**10**(1).
62. Etim, N. N., Enyenihi, G. E., Williams, M. E., Udo, M. D. and Offiong, E. E. (2013). Haematological Parameters: Indicators of the Physiological Status of Farm Animals. *British Journal of Science*.**10**(1): 33-45.
63. Obiandu, C., Owhorji, B. I., Okari, K. and Amechi, C. S. (2022). Actions of *Persea americana* on Some Blood Parameters of Male Wistar Rats. *Scholars International Journal of Anatomy and Physiology*, 105-109.
64. Ahmed, M. N. U., Nabi, Q. M. R. U., Sultana, S., Chowdhury, M. R. A., Ali, M. O. and Rukunuzzaman, M. (2024). Uncomplicated Peptic Ulcer Disease and Its Impact on Hematological Parameters. *Journal of Armed Forces Medical College, Bangladesh*. **20**(1): 22-25.
65. Sheema, K., Ikramdin, U., Arshi, N., Farah, N. and Imran, S. (2017). Role of *Helicobacter pylori* eradication therapy on platelet recovery in chronic immune thrombocytopenic purpura. *Gastroenterology Research and Practice*. **2017**(1): 9529752.
66. Mwafy, S. N. and Afana, W. M. (2018). Hematological parameters, serum iron and vitamin B12 levels in hospitalized Palestinian adult patients infected with *Helicobacter pylori*: a case-control study. *Hematology, Transfusion and Cell Therapy*. **40**(2): 160-165.
67. Farah, R., Hamza, H. and Khamisy-farah, R. (2018). A link between platelet to lymphocyte ratio and *Helicobacter pylori* infection. *Journal of Clinical Laboratory Analysis*. **32**(1): e22222.
68. Ifebajo, A. Y. and Folahan, O.O. (2020).nutrients and phytochemicals composition of methanolic extract of four edible spices commonly used in the preparation of soups in south-west Nigeria. *Journal of Dietitians Association of Nigeria*, **11**: 2.
69. Olbe, L., Carlsson, E. and Lindberg, P. (2003). A proton-pump inhibitor expedition: the case histories of omeprazole and esomeprazole. *Nature Reviews Drug Discovery*. **2**(2): 132-139.
70. Lundell, L. (2015). The physiological background behind and course of development of the first proton pump inhibitor. *Scandinavian Journal of Gastroenterology*. **50**(6): 680-684.
71. Forgacs, I. and Loganayagam, A. (2008). Overprescribing proton pump inhibitors. *BMJ*. **336**(7634): 2-3.
72. Forgerini, M., Mieli, S. and Mastroianni, P. D. C. (2018). Safety assessment of omeprazole use: a review. *Sao Paulo Medical Journal*. **136**: 557-570.
73. Bate, C. M., Riley, S. A., Chapman, R. W., Durnin, A. T. and Taylor, M. D. (1999). Evaluation of omeprazole as a cost-effective diagnostic test for gastro-oesophageal reflux disease. *Alimentary Pharmacology and Therapeutics*. **13**(1): 59-66.
74. Fass, R., Ofman, J. J., Gralnek, I. M., Johnson, C., Camargo, E., Sampliner, R. E., & Fennerty, M. B. (1999). Clinical and economic assessment of the omeprazole test in patients with symptoms suggestive of gastroesophageal reflux disease. *Archives of Internal Medicine*. **159**(18): 2161-2168.
75. Attwood, S. E., Ell, C., Galmiche, J. P., Fiocca, R., Hatlebakk, J. G., Hasselgren, B., ... and Lundell, L. (2015). Long-term safety of proton pump inhibitor therapy assessed under controlled, randomised clinical trial conditions: data from the SOPRAN and LOTUS studies. *Alimentary Pharmacology and Therapeutics*. **41**(11): 1162-1174.
76. Savarino, V., Di Mario, F. and Scarpignato, C. (2009). Proton pump inhibitors in GORD: an overview of their pharmacology, efficacy and safety. *Pharmacological Research*. **59**(3): 135-153.

77. Weersink, R. A., Bouma, M., Burger, D. M., Drenth, J. P., Harkes-Idzinga, S. F., Hunfeld, N. G., ... and Borgsteede, S. D. (2018). Safe use of proton pump inhibitors in patients with cirrhosis. *British Journal of Clinical Pharmacology*. **84**(8): 1806-1820.
78. Al Ali, H. S., Jabbar, A. S., Neamah, N. F. and Ibrahim, N. K. (2023). Long-Term Use of Omeprazole: Effect on Haematological and Biochemical Parameters. *Acta Medica Indonesiana*. **54**(4): 585.
79. Ibrahim, H. A., Metwaly, E. S. K., Galal, A. and Sherif, S. A. (2019). Potential curative effect of curcumin on gastric ulcer induced by piroxicam in male albino rats. *Zagazig Veterinary Journal*. **47**(4): 378-387.
80. AL-Saeed, M. H. (2013). Study The Effect of Aqueous Extract of *Piper nigrum* on Some physiological parameters and Histopathological in Female Rabbit Induced Gastric Ulceration by Aspirin. *Journal of Kerbala University*. **9**(4): 19-32.

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