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# Effects of Turmeric Rhizome Powder Supplemented Diet on Indomethacin-induced Toxicity in Wistar Rats

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Author AGO designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors OBA, OAO and SFA supervised the execution of the design and editing of the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

Turmeric (*Curcuma longa*) *L* rhizome powder (TRP) was commonly reported to have antiulcerogenic and non-toxicity effects. However, the scientific evidence showing the effectiveness of turmeric in the treatment of gastric ulcer and its non-toxicity effect are controversial. The aim of the study was to investigate the effects of different percentages of turmeric rhizome powder supplemented diet on toxicity induced by indomethacin in Wistar rats. This study investigated the effects of TRP formulated diet on the activities of blood enzymes in indomethacin-induced gastric ulcerated Wistar rats. This investigation was carried out through a 28-day experiment using corn-starch flour meal-based diet containing four levels of TRP (1%, 2%, 5% and 10%) as treatments with five replicates in a completely randomized design. The remaining three groups were fed with basal diet, one group received standard drug, another received no treatment but induced while the last group received no treatment and not induced. 35 male Wistar rats weighing 150-200 g were housed in seven cages

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and received feed and water *ad-libitum*. At the end of the experiment, all the animals were sacrificed, blood and some organs were collected and evaluated for hepatoxicity and nephrotoxicity induced by indomethacin (60mg/kg bw). Measurements of serum, kidney and liver alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were performed. Statistical evaluation of the results at a $p < 0.05$ showed significantly elevated values ($P \leq 0.05$) of these enzymes in the kidney of rats in groups B, C, E and G when compared with group F. Increase in kidney ALT and AST activities of animals in groups A, C and D was detected in comparison with group F. Furthermore, there was increase in hepatic ALT and ALP activities of animals in groups A, B, C, D and E compared with animals in group F but a significant increase ($P \leq 0.05$) in group G in comparison with group F. Likewise, there was significant increase ($P \leq 0.05$) in liver AST activities of rats in groups A, B, C, E and G compared with group F, however, insignificant increase ($P \leq 0.05$) was observed in animals in group D in comparison with rats in group F. Indomethacin induced rats (group F) showed a significant increase in serum levels of ALT, AST and ALP compared with rats in groups E and G in all the groups but those fed on 1%, 2%, 5% and 10% turmeric supplemented diet showed decrease in comparison with group F. The increased levels of these enzymes in the serum of animals in ulcerogenic group and some in group D (10%TRP group) could be a sign of tissue injury due to relative toxicity of indomethacin induction in animal model and deleterious effect of turmeric rhizome powder at large concentration. However, decrease levels of these enzymes in pretreated groups could indicate the attenuating potential of turmeric at moderate dose against toxicity effect of indomethacin induction. Therefore, turmeric rhizome powder should be consumed with caution and its percentage in the whole recipe should not be up to 10% (100g/kg).

*Keywords: Curcuma longa; Indomethacin; toxicity ALP; AST ALT; ulcer; damage.*

## 1. INTRODUCTION

*Curcuma longa L.* (Zingiberaceae) is widely cultivated in tropical areas of Asia and in Africa especially in Southwest. Turmeric rhizome powder also called *curcuma longa* is commonly used as spice and herbal medicine. It has been reported to be effective in the treatment of peptic ulcer, flatulence, diarrhea, inflammation and itching [1]. It was even reported in [2] that turmeric was one of the recommended herbal medicines for primary health care system in Thailand. It is also commonly consumed in diverse form in Nigeria because of the awareness of its medicinal value. Inclusion of medicinal plant in our daily meal or their use in modern medicine would be accepted if it is supported by scientific verification of their safety and efficacy. However, the scientific data showing the effectiveness of turmeric in the treatment of gastric ulcer is still controversial [3,4]. It was reported in [5] that ethanolic extract of *curcuma longa* has protective effect against hypothermic-restraint stress, pyloric ligation, indomethacin and reserpine-induced ulcer in rats. Contrarily, no protective action of curcumin against histamine-induced gastric ulceration in guinea pig was found as reported in [6,7]. Furthermore, it was reveals in [8] that higher concentration of curcumin is not safe for the body system and many research studies revealed that high dose of curcumin was ulcerogenic and hepato-toxic [9,10]. Liver which is an important and largest organ in human body is the site for essential biochemical reactions and excretion. Some medicinal agents may injure the organ when consumed in overdoses and sometimes even when consumed within therapeutic range [11].

Since there are contradicting reports on the safety of consuming turmeric powder in large quantity and the exact concentration of turmeric rhizome powder in diet that could have deleterious effect has not been popularly documented, it is very important therefore to elucidate those contradicting reports [12]. It is also essential to obtain additional scientific proof to justify that the consumption of TRP could enhance gastric mucosa, hepatic and renal preservation. Thus, this study investigated the anti-hepatoxicity and anti-nephrotoxicity effects of diet containing different percentages of TRP against indomethacin-induced gastric ulcer in Wistar rats using some biomarker enzymes. Biomarker enzymes employed in the investigation are Alkaline phosphatase (ALP), Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST). ALP is a pervasive membrane-bound glycoprotein that catalyzes the hydrolysis of phosphate monoesters at alkaline pH values and it can be found in intestine, germ cell, liver/bone/kidney (L/B/K) which can also be tissue non-specific [13]. AST is a cytoplasmic

and mitochondrial enzyme most commonly found in the heart, liver, erythrocytes, skeletal muscles, pancreas, kidney, brain tissue and lungs [14]. AST serve as a biomarker to diagonize the diseased state of the aforementioned tissues or damage to them [15]. It is liable for aspartate metabolism (transamination). The quantity of aspartate aminotransferase available in the blood stream is equivalent to the quantity of cells affected by the injury or disease, however, the elevation level is dependent on the duration for which the blood is tested following the injury [14]. ALT is a cytoplasmic enzyme primarily found in the liver and to a lesser extent in kidney, heart and skeletal muscles [14,16,17]. ALT is responsible for metabolism or transamination of alanine.

The rest of the paper is organized as follows. Section 2 presented the materials and method used for the research while results and discussion are presented in section 3. Finally the conclusion is drawn in section 4.

## 2. MATERIALS AND METHODS

The experimental study was conducted in the Department of Biochemistry, Faculty of Science, Ekiti-State University, Ado- Ekiti, Ekiti State, Nigeria in the year 2020.

### 2.1 Sample Collection and Preparation

The rhizome part of turmeric was purchased locally from Mojere market, Ado Ekiti, Ekiti State, Nigeria. Identification of the rhizome was carried out in the Herbarium Unit of the Department of Plant Science and Biotechnology, Ekiti State University Ado-Ekiti, Nigeria by Mr Omotayo, the chief Technologist with Herbarium No: UHAE/2021144. The clean sample was steamed for about 10 to 15 minutes and allowed to cool down. It was allowed to dry at room temperature and thereafter ground into powdery form using a mixer grinder and stored in an airtight polythene bag prior to analysis.

All chemicals used were of analytical grade, while distilled water was used in the analysis. Indomethacin and omeprazole used were obtained from Aromokeye pharmaceutical shop along Iworoko road, Ado- Ekiti, Ekiti state, Nigeria.

### 2.2 Reagents

Standard Randox kits were used to determine Alkaline Phosphatase (ALP), Aspartate Transaminase (AST) and Alkaline Transaminase (ALT).

### 2.3 Rats and experimental diets

The rats were purchased from Animal house of College of the Medicine, Ekiti State University, Ado-Ekiti, Nigeria and were kept and fed in plastic cages. The experiment went on for 28 consecutive days. The rats were divided into Group A (1% TRP diet+ 60mg/kg bw indomethacin (IND) group]; Group B (2% TRP diet + 60mg/kg bw IND group); Group C (5% diet TRP + 60mg/kg bw IND group); Group D (10% TRP diet + 60mg/kg bw IND group); Group E (basal diet + 20mg/kg bw Omeprazole + 60mg/kg bw (IND group); Group F (btasal diet + 60mg/kg bw IND group) and Group G (Control group). Each group consisted of 5 rats. Initial body weight of all the rats was measured on 1st day of the experiment. At the 28th days, their final body weights were taken, foods withdrawn from them for 24 hours but they were made to have free access to water and after this fasting they were all induced with indomethacin orally except rats in group G. They were left for 6 hours after which all the rats were anaesthetized by approximately 90% chloroform and sacrificed.

*Curcuma longa* rhizome supplemented diets were formulated using a modified method of Oluwafemi et al. [18] as shown in Table 1.

### 2.4 Induction of Ulcer Using Indomethacin

Ulcer induction was accomplished by a single oral dose of indomethacin (60mg/kg) using intubation according to the modified methods of Shahin et al. [19], Gaw et al. [20] and Akpamu et al. [21]. The animals were anaesthetized and sacrificed through cardiac puncture, after sixth hours of induction [19].

### 2.5 Blood Sample Collection and Tissue Preparation

Rats in all the groups were anaesthetized and sacrificed at the end of the feeding experiment. Through cardiac puncture, blood was collected into plain tubes and centrifuged at 3000 x g for 15 minutes. A Pasteur's pipette was used to collect the supernatant into the plain bottle and the supernatant serum obtained was appropriately labeled and kept in the freezer at -20$^0$C for biochemical analysis.

**Table 1. Diet composition for control and test rats (g/kg)**

| Ingredients | Group A (1%) | Group B (2%) | Group C (5%) | Group D (10%) | Group E(STD) | Group F(NC) | Group G(CTL) |
|---|---|---|---|---|---|---|---|
| Corn Starch | 560 | 550 | 520 | 470 | 570 | 570 | 570 |
| Protein | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| Sucrose | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Vitamin-Mineral mix | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Cellulose | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Vegetable oil | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Turmeric powder | 10 | 20 | 50 | 100 | - | - | - |

*Protein source: Dano slim milk; Cellulose: Rice husk; STD: Standard drug (Omeprazole); NC: Negative control (ulcerogenic group); CTL: Control*

*NB: The weight of the corn starch used is not uniform in order to compensate for the weight of the added Turmeric powder in groups A-D*

## 2.6 Isolation and Homogenization of Tissues

The isolated tissues were blotted with filter paper, weighed and immediately stored in ice cold of 7.4M Phosphate buffer solution. The liver and kidney were cut with a clean scalpel and were homogenized using Teflon homogenizer in ice-cold 7.4M phosphate buffer solution. The homogenates were stored in the freezer (-20$^0$C) for biochemical analysis.

## 2.7 Hepatoxicity and Nephrotoxicity Biomarkers

Blood serum associated liver and kidney biomarker enzymes: Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) were determined based on the method of Rietman and Frankel [22] using commercially available kits (Randox Laboratories, UK). On the other hand, Alkaline Phosphatase (ALP) activity was estimated using an assay kit obtained from Randox Laboratories (UK) which was based on the method of Schlebusch et al. [23].

## 2.8 Statistical Analysis

All data were analyzed by one-way analysis of variance (ANOVA) followed by Tukey's post hoc test and the results were expressed as the mean (n=5) ± standard error of the mean (SEM). Graph Pad Prism version 7.0 was used for the constructions of graphs and the significant level was set at $P < 0.05$ (95% confidence level). * = degree of significant; * =significant difference at $P \leq 0.05$, ** = significant difference at $P \leq 0.01$ and *** = significant difference at $P \leq 0.001$.

## 3. RESULTS AND DISCUSSION

Fig. 1-3 shows the effects of different percentages of TRP supplemented diet and STD on marker enzymes of some selected organs (kidney, liver and serum) of indomethacin-induced ulcerated rats. There was decrease ($P \leq 0.05$) in serum ALT, AST and ALP activities of indomethacin-induced ulcerated animals pretreated with 1%, 5%, 10% TRP supplemented diet compared with group F but there was significant reduction ($P \leq 0.05$) in serum activities of all these enzymes in groups CTL and STD groups in comparison with rats in group F (Fig. 1, 4 and 9). But kidney ALT activity of indomethacin-induced ulcerated animals pretreated with 1%, 5%, 10% TRP supplemented diet increase when compared with group F with significant elevation in STD and CTL groups in comparison with group F (Fig. 2). In addition, insignificant upsurge in kidney AST activity was observed in all TRP pretreated groups but that of 2%, STD and CTL (group G) groups showed significant elevation of kidney AST activities compared with group F (Fig. 5). However, a significant increase ($P \leq 0.05$) in kidney ALP activities was observed in all prophylactic treated groups except 10% group which showed insignificant upsurge ($P \leq 0.05$) and CTL group in comparison with group F. It is noteworthy that there was significant increase ($P \leq 0.05$) in kidney ALP activities of all animals pretreated with TRP, omeprazole and in CTL in comparison with 10% group (Fig. 8). Moreover, increased hepatic ALT and ALP activities of animals in groups A, B, C, D and E compared with group F was observed in this study but significant elevation ($P \leq 0.05$) in group G was observed compared with group F (Fig. 3 and Fig. 9). Additionally, there was significant upsurge ($P \leq 0.05$) in hepatic AST activities of all animals in groups A, B, C, E and G when compared with group F, nonetheless, insignificant elevation ($P \leq 0.05$) was observed in group D animals in comparison with group F animals (Fig. 6).

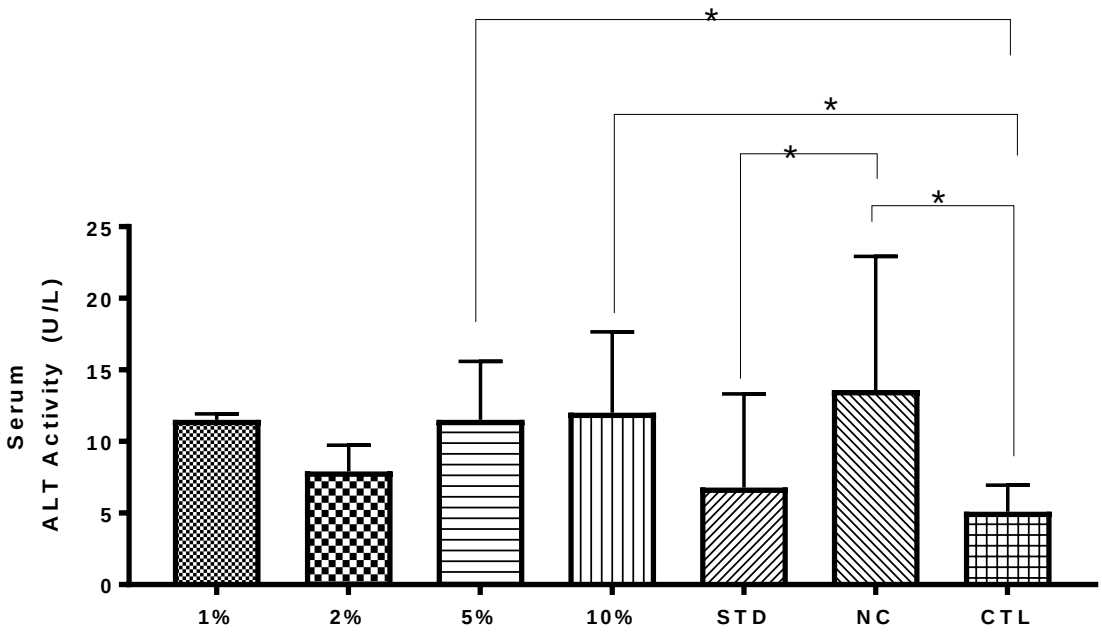


**Fig. 1. The effects of turmeric rhizome powder (TRP) supplemented diet at different percentages and standard drug on ALT activity in the serum of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n = 5; * = degree of significant; * = significant difference at P ≤ 0.05*

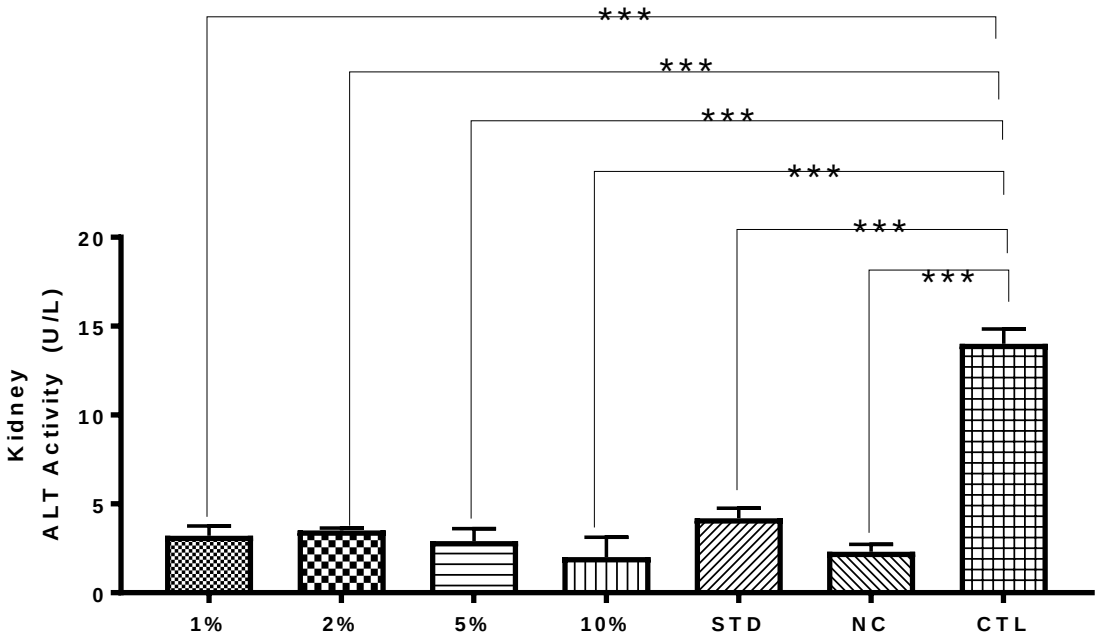


**Fig. 2. The effects of turmeric rhizome powder supplemented diet at different percentages and standard drug on ALT activity in the kidney of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n = 5; * = degree of significant; * =significant difference at P ≤ 0.05, ** = significant difference at P ≤ 0.01 and *** = significant difference at P ≤ 0.001*

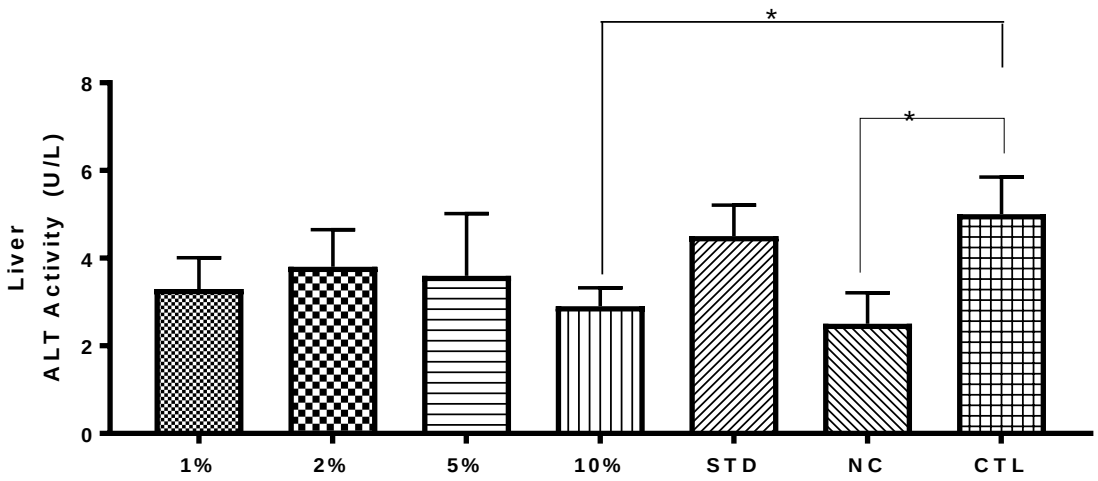


**Fig. 3. The effects of turmeric rhizome powder (TRP) supplemented diet at different percentages and standard drug on ALT activity in the liver of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n = 5; * = degree of significant; * = significant difference at P ≤ 0.05*

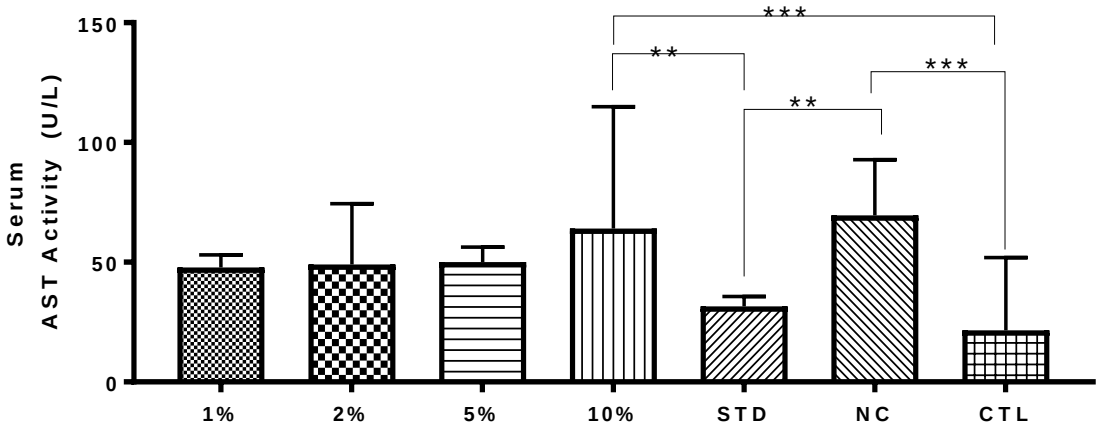


**Fig. 4. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on AST activity in the serum of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n=5. * = degree of significant; * =significant difference at P ≤ 0.05, ** = significant difference at P ≤ 0.01 and *** = significant difference at P ≤ 0.001*

## 3. DISCUSSION

### 3.1 Aminotransferases (ALT/ AST)

The measurement of the diagnostic or marker enzymes activities in serum and tissues plays a well-known and significant role in disease investigation, diagnosis, assessment of drug or plant extract and the use of plant supplement for safety and or toxicity risk [24].

ALT which is one of the marker enzymes has been recognized as a cytoplasmic enzyme that is found majorly in the liver and to a lesser extent in heart, skeletal muscles and kidney [14]. In human body, liver is the site for essential biochemical reactions and excretion, an important and largest organ. There is a grave consequence therefore, when damage is done to the liver. Liver plays a significant role in excretion and detoxification of many exogenous and

endogenous compounds. Therefore, any impairment of its functions or injury to it may lead to many health implications [25]. Furthermore, the liver plays a vital function in clearing and transforming chemicals thus, it is vulnerable to the toxicity from these agents. Some medicinal agents may injure the organ when consumed in overdoses and sometimes even consumed within therapeutic range. Hepatotoxins are chemicals that cause liver injury [26].

In this study, serum ALT activity was decreased in all animals prophylactically treated with 1% to 10% TRP supplemented diet (group A, B, C and D) and reduced significantly in STD and CTL groups (group E and G) compared with group F (NC). A non-significant increase in kidney ALT activities of rats pretreated with 1%, 2%, 5% ,STD (group A,B, C, E) and significant increase in group G (CTL/normal) when compared with group F and 10% groups (F and D). There was reduction in hepatic ALT activity of rats in group D and F when compared with group G, though, the reduction in hepatic ALT activities of rats in group D did not commensurate with that of animals in group F. Increase in the serum ALT level in group D and F is in line with the result reported in [8,27].

Increased ALT activity in the blood is an indication of conditions in which cells are damaged or apoptosis [28]. Thus, there can be cellular leakage and degradation of the functional integrity of cell membrane in the liver [28-29]. Hence, increased serum levels of ALT in groups F and D revealed the damage done by the indomethacin into the organs and the impotency of TRP at 10% to mitigate its deleterious effect on them. It has been reported that membrane damage or necrosis discharges the enzyme into circulation; thus, it can be measured in the serum [26]. Elevated serum levels of ALT and AST have been used as signals for some forms of hepatic diseases. The substantial decrease ($P \leq 0.05$) in the kidney and hepatic ALT of the rats in groups F and D is indicative of injury to the plasma membrane of these tissues at the cellular level, causing an increased efflux of these enzymes into the extracellular fluid [30-31]. Furthermore, this reduction could limit the catalytic activity of this enzyme and thereby reduce the conversion of alanine to pyruvate which is an intermediate in gluconeogenesis.

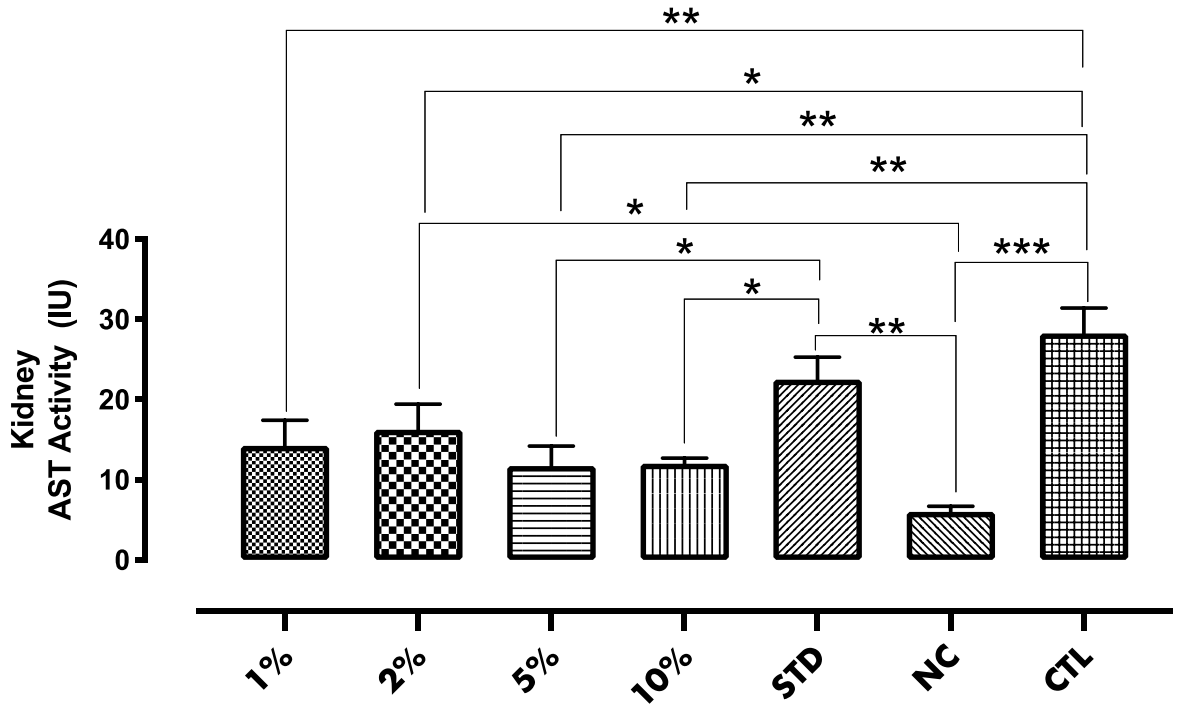


**Fig. 5. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on AST activity in the kidney of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n=5; * = degree of significant; * = significant difference at P ≤ 0.05, ** = significant difference at P ≤ 0.01 and *** = significant difference at P ≤ 0.001*

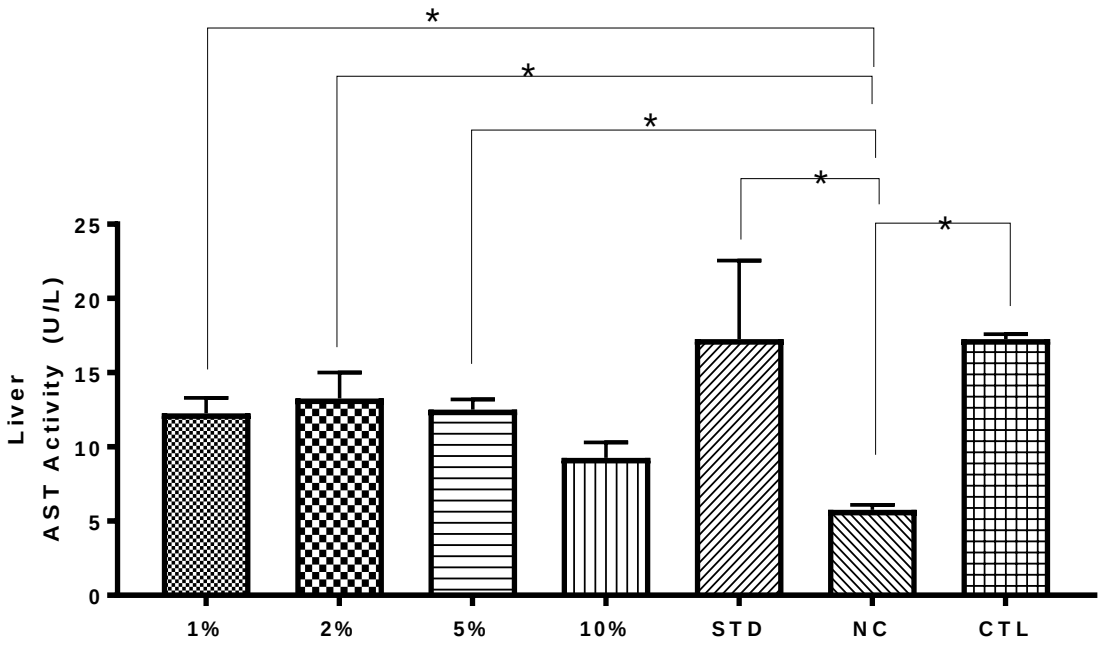


**Fig. 6. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on AST activity in the liver of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n=5; * = degree of significant; * = significant difference at P ≤ 0.05*

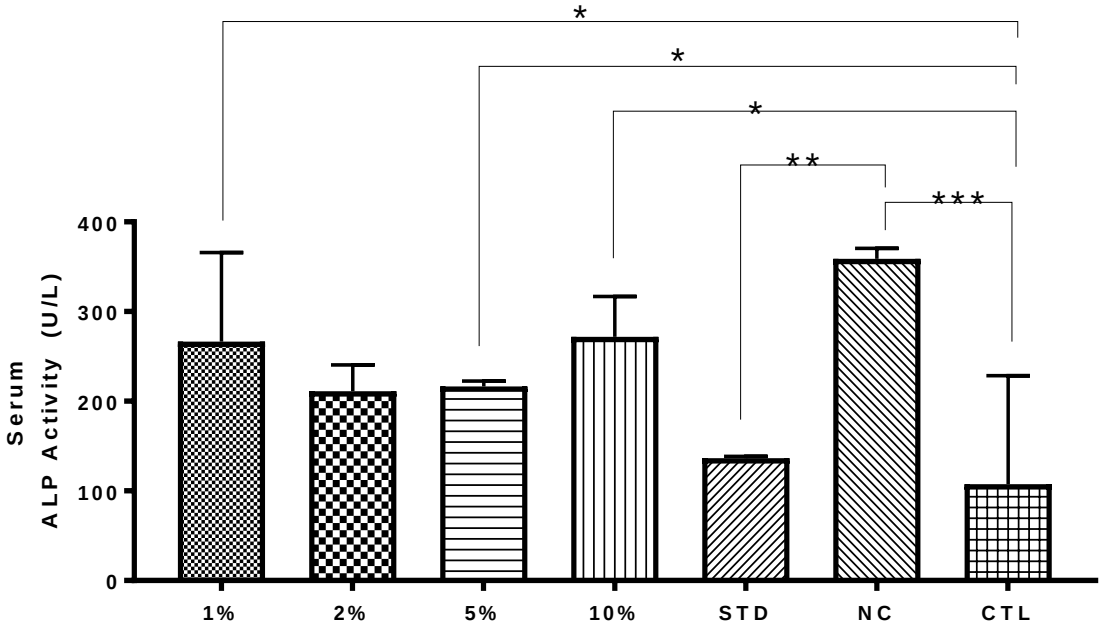


**Fig. 7. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on ALP activity in the serum of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n = 5; * = degree of significant; * = significant difference at P ≤ 0.05, ** = significant difference at P ≤ 0.01 and *** = significant difference at P ≤ 0.001*

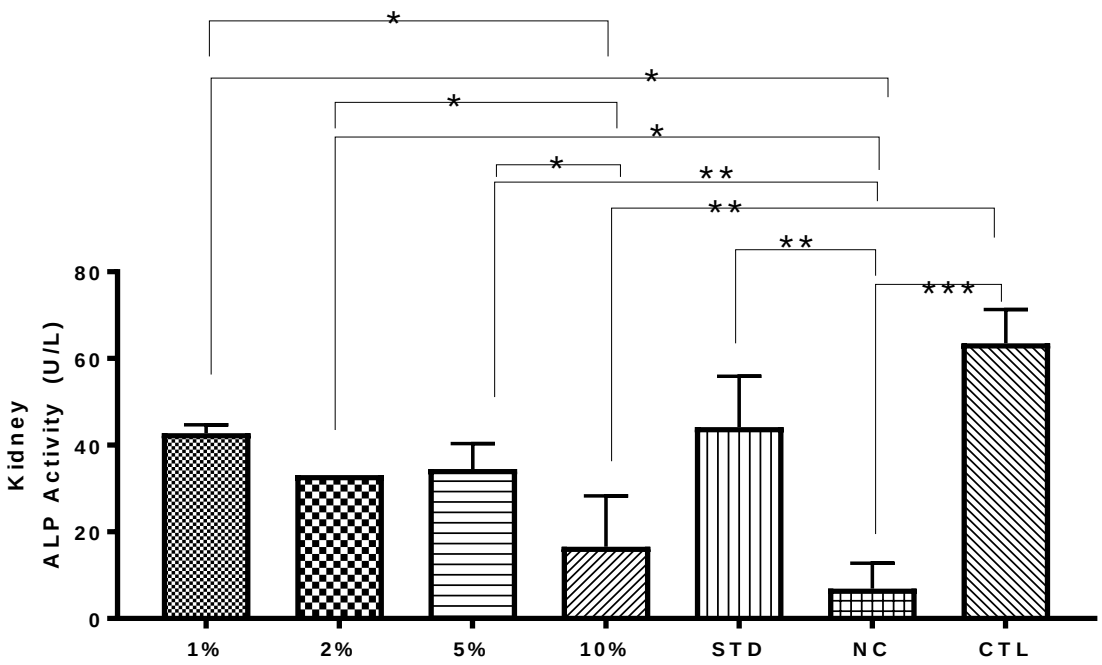


**Fig. 8. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on ALP activity in the kidney of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n=5; * = degree of significant; * = significant difference at P ≤ 0.05 and ** = significant difference at P ≤ 0.01 and *** = significant difference at P ≤ 0.001*

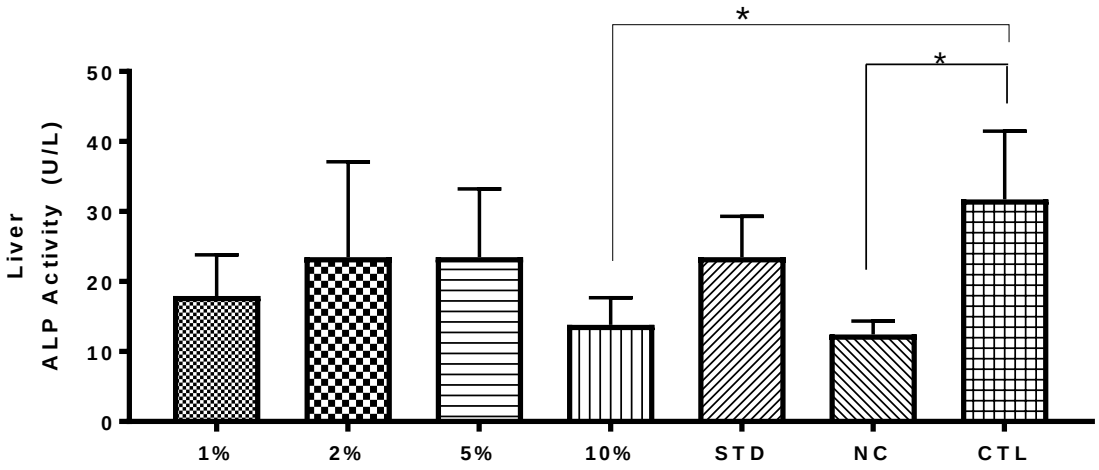


**Fig. 9. The effects of turmeric rhizome powder (TRP) supplemented meal at different percentages and standard drug on ALP activity in the liver of indomethacin-induced ulcerated albino rats**

*All bar charts are displayed as mean ±SEM for n = 5. All bar charts are displayed as mean ±SEM for n = 5; * = degree of significant; * =significant difference at P ≤ 0.05*

The conversion of aspartate and alpha ketoglutarate to oxaloacetate and glutamate is catalyzed by a transaminase enzyme known as aspartate aminotransferase (AST) [32-33]. It was formerly known as serum glutamate oxalate transaminase (SGOT). It is highly present in the

liver and skeletal muscle. AST is typically localized within the cells of the liver, kidney, heart, muscles, gills and other organs but it cannot be found in the bone. It is very vital in monitoring and assessing liver cytolysis. AST presence in the serum could be indicative of organ dysfunction [23]. In addition, elevation in serum AST activity can be due to its leakage into extracellular compartment because of hepatocytes injury. The decrease in the activity of AST in the liver and kidney as observed in this study, with concomitant increase in the serum levels of this enzyme in the ulcerogenic control group (F/NC) rats may suggest hepatic and kidney damage which would have led to the leakage of these enzymes because of the insult imposed by indomethacin induction. This shows the renal toxic and hepatotoxic effects of indomethacin which was mitigated in the groups prophylactically treated with 1-5% TRP supplemented diet and omeprazole which is the standard drug [27]. A significant increase ($P \leq 0.05$) in the liver and kidney AST activities of rats in group E, G and B with moderate increase in groups A, C and D compared with group F was observed in this study. This could be due to the increased synthesis of the enzyme in situ or the pre-treatment enhanced detoxification potential of the liver, since there was no concomitant increase in serum. It shows the liver and kidney appear to be protected from the oxidative stress caused by the induced ulceration.

There is high level of AST in serum when enzymes leak from the liver cytosol into the blood stream, which is an indication of hepatotoxicity in ulcerated rats. Sustained high levels of AST in serum indicate chronic liver injury [16]. In this study, the increase in serum AST activity in ulcerated rats could indicates liver damage, due to metabolic changes caused by reactive oxygen species imposed by indomethacin induction. The increased serum and concomitant decreased hepatic and kidney AST activities in group D could be indicative of the decreased rate of synthesis of the enzyme or toxicity of *Curcuma longa* at this quantity (10%).

NSAIDs (non-steroidal anti-inflammatory drugs) such as indomethacin has been reported to be toxic to the body organs like liver and kidney. Metabolism and excretion of indomethacin and other toxic compound in the body are carried out in the liver [34-35]. It can be inferred from this study that TRP supplemented diet at 10% could not attenuate the toxic effect of indomethacin on some organs especially kidney and liver but enhanced it. This is in line with the result reported in [27] where it was concluded that turmeric rhizome powder can only be medicinal when it is not consumed in large amount. It was concluded in [36] that turmeric supplement enhance the performance of broilers when used as feed additives in broiler ration at the rate of 0.75% level. In this study also, it can be concluded that turmeric rhizome powder supplemented at concentration lesser than 100g/kg of total recipe could be hepato-, and renal protective especially at 2%.

### 3.1.2 Alkaline Phosphatase (ALP)

It is a marker enzyme for endoplasmic reticulum and plasma membrane of the tissue studied. ALP is an enzyme found in the liver, kidney, intestine and bone and is important for catalyzing the dephosphorylation of proteins. There is tissue nonspecific alkaline phosphatase or liver/ bone/ kidney ALP also [37,27]. It can be used as a diagonisis tool in bone or liver disease or a tumor in these organs, if it is present in serum in large quantity. ALP is mostly used to assess plasma membrane integrity due to its predominant localization in the microvilli of the canaliculi which is found in the plasma membrane [24]. The extent of hepatocellular injury is assessed by the increased level of serum ALP [38]. The significant increase in the serum ALP activity of rats in group F observed in this study as shown in Fig. 7 could be an indication of tissue damage, cytolysis and disruption in the ordered membrane lipid-bilayer structure by induction of indomethacin [39]. Upsurge of serum ALP could constitute a risk to the life of the cells that depend on the different phosphate esters for crucial process because this may result into unselective hydrolysis of phosphate ester metabolite of the liver and thereby reduce ATP synthesis in the body system This is a vital biochemical symptom of cytolysis. Significant reduction was observed in the serum ALP activity of rats in group G, rats in group E and moderate reduction in rats pretreated with TRP supplemented diet. This could imply that omeprazole and TRP have extenuating effect on damage and cytolysis induced by indomethacin.

The animals in CTL group and those that were prophylactically treated with TRP and STD showed significant increased kidney ALP activities compared with animals in groups D and F (10% and ulcerogenic/NC groups) but no concomitant increase in serum. This suggests that *Curcuma longa* rhizome powder could be

renal protective, prevent disruption in the ordered lipid-bilayer of the membrane structure and help the organ to increase their functional activities leading to secretion of this enzyme probably by *de novo* synthesis when consumed in appropriate proportion [39]. The significant decrease in Kidney and hepatic ALP activities of animals fed with 10% TRP supplemented diet and group F could be due to the fact that consumption of turmeric at this percentage could lead to renal-toxicity and hepatotoxicity or otherwise enhanced renal toxic and hepatotoxic effect of indomethacin. The decline in kidney and hepatic ALP activities of animals in group F and prophylactically treated with 10% TRP supplemented diet could be ascribed to the disruption in the ordered membrane lipid-bilayer structure which might be due to lipid peroxidation caused by oxidative stress imposed by indomethacin induction (Fig 8 and 9) resulting into the leakage of ALP out of the cell into the extra cellular fluid [38].

Therefore, adequate transport of required ions or molecules across their cell membrane might be impeded and lead to cells starvation Furthermore, the reduction that was observed in the ALP activity for rats in group F and 10% group might also have adverse effect on other metabolic processes involving the enzyme, such as cleavage of phosphate esters, synthesis of phospholipids, nuclear proteins and nucleic acids Indomethacin has been known to have hepatotoxic effect in both animals and humans [25]. The observation from this study has depicted that *Curcuma longa* could have protective effect against hepatotoxic, renal toxic and ulcerogenic effects of indomethacin, if consumed appropriately, however.

## 4. CONCLUSION

Conclusively, this study reveals the potentials of turmeric rhizome powder diet against hepatotoxicity and renal-toxicity effects of indomethacin induced injuries, accomplished by preventing deleterious effects of the organs thereby inhibiting the leakage of biomarker enzymes into the blood and enhancing their biosynthesis. This is shown by increased activities of the enzymes in the selected tissues (liver and kidney). However, this preventive potential of turmeric rhizome powder is dose-dependent. Since there was increase in the serum activities of these enzymes in animals prophylactically treated 10% turmeric rhizome powder diet with concomitant decrease in the tissues, the consumption of turmeric rhizome powder should not be up to 10% (100g/kg w/w) of the whole recipe or ingredients. Therefore, consumption of turmeric rhizome powder diet at this concentration (100g/kg) might be deleterious to those tissues (liver and kidney) and not be safe for consumption also.

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## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as special national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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