



Research Article

Comparative effect of ginger (an anti-inflammatory medicinal herb) and aspirin (a non-steroidal anti-inflammatory drug) on liver enzymes in male albino Wistar rats

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ABSTRACT

Background: Herbal therapies mediate similar functions with those of some well-known drugs. Ginger and aspirin are herbal and drug therapies respectively which are used for the treatment of anti-inflammatory conditions. Non-steroidal medicinal drugs especially aspirin and acetaminophen are usually linked to drug-induced liver injury. Therefore, this research seeks to compare the effect of these two therapies on liver function using aspartate aminotransferase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) as the biomarkers. The aim of the study was to establish if ginger will offer a better hepatocellular protection considering that the use of aspirin in treating inflammatory disorders is already linked to liver injury.

Methods: AST, ALT, ALP, Total, conjugated and unconjugated bilirubin were assessed in this study using 18 Wistar rats. The animals were divided into three groups (control, ginger and aspirin), six (6) rats per group. The three groups of animals were allowed access to food and water daily throughout the experimental period. Ginger group animals were administered 150 mg/kg dose of aqueous ginger extract while aspirin group of animals also received 150 mg/kg dose of aspirin for four weeks. Control group received normal saline of equal volume with the test groups. **Results:** AST, ALT, total and conjugated bilirubin was significantly lower in ginger group compared to aspirin and the control group ($P < 0.05$). However, ALP was significantly higher in ginger group compared to aspirin and the control group ($P < 0.05$). Unconjugated bilirubin showed no significant difference among experimental groups. **Conclusion:** Result showed that ginger offered a better hepatocellular protection compared to aspirin group following decrease AST and ALT concentration in the ginger group.

Keywords:

ginger; anti-inflammatory; aspirin; liver

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1. Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin and acetaminophen have been an important intervention in patient management and treatment of painful inflammatory conditions as well as fever (Ghlichloo & Gerriets, 2022). However, they have the tendency to cause liver damage (LiverTox, 2020).

Considering the high index of liver damage due to NSAIDs such as aspirin (LiverTox, 2017), it becomes necessary to look for herbal alternative which will be useful in reducing inflammation without possible liver damage. Consequently, folk medicine has attempted the use of herbs such as ginger, scientifically called *Zingiber officinale* in treating complications that results from inflammation. However, little is known concerning the efficacy of the herb in reducing complications that results from inflammation such as liver damage. Using human and other animal models such as mice, ginger shows a broad and positive anti-inflammatory activity, hence it is suitable for the treatment of inflammation, fever and headache (Ozkur *et al.*, 2022).

Ginger is a plant native to Asia. Its root which is commonly available and used as spice for several dishes is suitable for the treatment of arthritis, inflammation and various types of infection (Fletcher, 2020; Bodagh *et al.* 2018).

Following the high hepatocellular induced injury associated with aspirin. It will be worthwhile to assessed if ginger, an herbal anti-inflammatory therapy will offer a better protective function on the liver as against a conventional orthodox medicine (aspirin) used for anti-inflammatory purpose using rats as the experimental animals.

2. Methods

2.1 Collection, preparation and storage of ginger aqueous extract

Ginger was procured from a trader in Jos, Nigeria. It was peeled and dried in an oven. Dried ginger was ground to dust, weighed and soaked in 150 ml of water.

The supernatant was filtered using Whatman's filter paper (large) to remove all forms of debris. The filtered solution of ginger was introduced into an oven at a temperature of 60°C for a period of 3 days to get the dried extract of ginger.

The dried extract of ginger was a thick brown gummy paste. The extract was scrubbed and collected into a sample bottle. The weight of the extract was 90 g. It was refrigerated to be used at a standard concentration for the ginger group administration.

2.2 Experimental animals

Eighteen male albino Wistar rats weighing 80 – 120g were the animals of choice in this study. The animals were made to acclimatize for two weeks. Thereafter, they were separated into three groups (control, ginger and aspirin), each rat in a separate cage. Six (6) rats were randomly assigned to each group. They were maintained in an animal house at a temperature of $28 \pm 2^\circ\text{C}$ and light-dark cycle daily.

2.3 Determination of the LD₅₀

The LD₅₀ of ginger (*Zingiber officinale*) was determined using the method of Lorke (Lorke, 1983). One hundred (100) albino Wistar rats were divided into 5 different groups, n = 20. Different doses (100, 400, 800 and 1200 mg/kg) of the ginger extract were administered intraperitoneally to rats in their respective groups except for the control group that received normal saline. All animals had free access to feed and water.

The animals were left untouched for 48 hours and allowed free access to food and water. After 48 hours, the numbers of death animals in each group was recorded.

2.4 Drug administration

After one week of acclimatization, 150mg/kg doses of prepared solution of aspirin was administered to the aspirin group orally while 150 mg/kg doses of prepared solutions of ginger was administered to the ginger group orally, once daily for four weeks with the aid of an orogastric cannula. The aspirin dose was chosen based on the standard prescription (150mg) of the drug for an adult of 70 kg whereas that of ginger extract was chosen based on the toxicity study (LD₅₀) carried out on the extract. The lethal dose of ginger was

300mg/kg. Following the lethal dose, the test dose used for administering the animals was 150mg/kg.

2.5 Measurement of Alkaline phosphatase

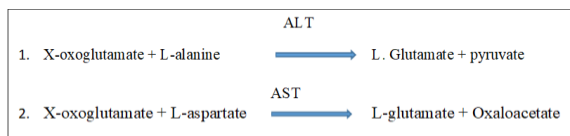
This was done by the optimized standard method recommended by the Deutsche Geseiischage for Klinische Chemic GSCC and used by Kelechi and co workers (Kelechi *et al*, 2019).

2.6 Measurement of Alanine transaminase, Aspartate aminotransferase and Bilirubin

The measurement of AST and ALT activities in the serum was done using endpoint colorimetric-diagnostic kit (Randox : Laboratories UK) based on Reitman and Frankel (1957) method as used by Kelechi *et al* (2019).

Principle:

The pyruvate produced by transamination reaction between L-alanine and Ketoglutarate reacts with 2,4, dinitrophenyl hydrazine to give a coloured hydrazine which was used to measure alanine aminotransferase activity. The oxaloacetate hydrazine formed with 2.4 dinitrophenyl hydrazine was used to measure aspartate aminotransferase (AST). Both AST and ALT were read at 540nm wavelength.



Serum bilirubin concentration was measured using the method described by Sherlock (1951)

2.7 Statistical Analysis

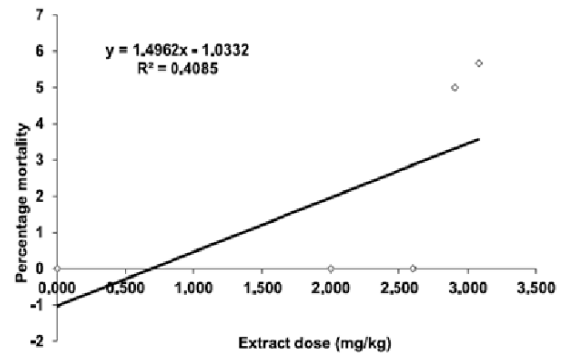
The data were computed and analyzed using Microsoft Excel (Microsoft office version 2013). The One-way Analysis of Variance (ANOVA) was used to analyze the data. Values were considered significant at $p < 0.05$.

3. Results

3.1 Lethality study of aqueous ginger root extract and effective dose of administration

The lethality study to determine LD₅₀ of ginger at doses of 100, 400, 800 and 1200 mg/kg body weight gave a result of 496.17 mg/kg graphically (Fig. 1). The LD₅₀ of ginger extract was determined from the graph of percentage mortality of the animals in probit plotted against

the Log₁₀ of the dose of the extract that was administered on the animals as shown in Figure 1. The percentage mortality was determined from the number of deaths recorded in each of the groups of animals used for the LD₅₀ study. The effective doses are doses below the LD₅₀ as these doses are considered safe for the animals in carrying out the research. Exactly 150 mg/kg was the effective dose chosen for administration in this research work.



(LD₅₀= 496.17mg/kg and the effective dose used for administration = 150mg/kg)

Fig 1: Lethality study of ginger extract

3.2 Comparison of serum aspartate aminotransferase (AST) concentrations between experimental groups

The mean \pm SEM serum AST concentration of the control, aspirin and ginger group were 179 ± 2.17 , 177.67 ± 3.14 and 146.83 ± 1.01 IU/L, respectively. The result showed a significant decrease in the serum AST concentration of rats in the ginger group when compared to that of rats in the aspirin and control group ($P < 0.05$). There was no significant decrease of serum AST in aspirin group compared to the control group (Fig 2).

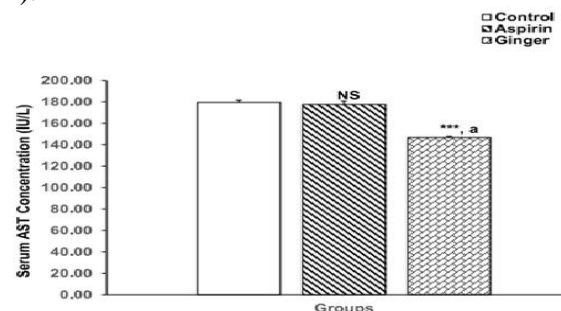


Fig 2: Serum AST concentration between experimental animals

3.3 Comparison of serum alanine transaminase (ALT) concentration between experimental groups

The mean \pm SEM serum ALT concentration of the control, aspirin and ginger group were 53.00 ± 1.15 , 66.83 ± 2.06 and 64.67 ± 0.88 IU/L respectively. The result showed that the ALT serum concentrations of rats in aspirin and ginger group were significantly higher than those of the rats in the control group ($P < 0.05$). However, ALT concentrations between aspirin and ginger group showed no significant differences (Fig 3).

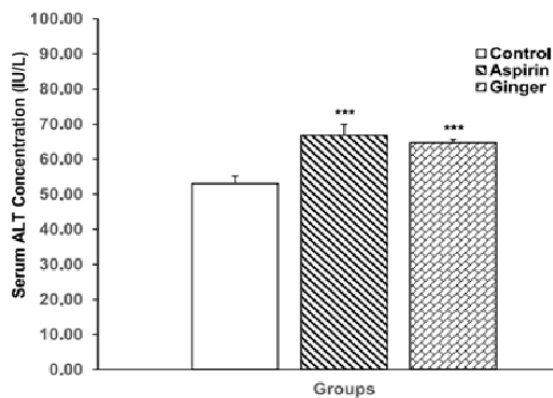


Fig 3: Serum ALT concentrations between experimental groups

3.4 Comparison of serum alkaline phosphatase (ALP) concentration between experimental groups

The mean \pm SEM serum ALP concentration of the control, aspirin and ginger group were 453.33 ± 2.16 , 294.17 ± 435 and 584.17 ± 7.73 IU/L, respectively. The result showed that there was a significant increase in the serum ALP concentration of rats in ginger group when compared to that of the rats in the aspirin and control group ($P < 0.05$). (Fig 4)

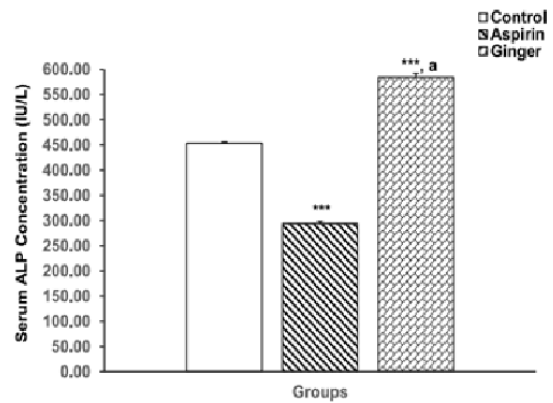


Fig 4: Serum ALP concentrations between experimental groups

3.5 Comparison of serum total bilirubin concentration between experimental groups

The mean \pm SEM serum total bilirubin concentration of the control, aspirin and ginger groups were 9.23 ± 0.12 , 11.78 ± 0.40 and 12.93 ± 0.19 mmol/L respectively. The result showed a significant increase in the serum total bilirubin concentration of rats in the aspirin and ginger group when compare to that of the rats in the control group ($P < 0.05$). There was a significant increase in the serum total bilirubin concentration of the rats in the ginger group compared to the aspirin group (Fig 5).

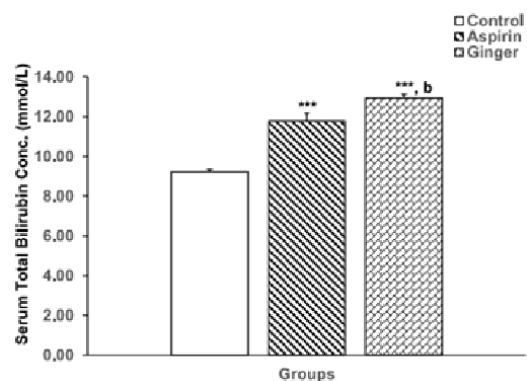


Fig 5: Serum total bilirubin concentration between experimental groups

3.6 Serum conjugated and unconjugated bilirubin concentration

The mean \pm SEM serum conjugated bilirubin concentration of the control, aspirin and ginger

groups were 3.82 ± 0.11 , 5.95 ± 0.53 and 7.58 ± 0.16 mmol/L, respectively. The result showed that there was a significant increase in the serum conjugated bilirubin concentrations of rats in the aspirin and ginger group when compared to that of the rats in the control group ($P < 0.05$). There was also a significantly lower serum conjugated bilirubin concentration of rats in the aspirin group when compared to those of the ginger group ($P < 0.05$).

The mean \pm SEM serum unconjugated bilirubin concentration of the control, aspirin and ginger group were 5.37 ± 0.13 , 5.90 ± 0.25 and 5.35 ± 0.20 mmol/L respectively. The results showed that the comparison of the serum unconjugated bilirubin concentration between the rats of the ginger and aspirin group to that of the control group was not significant (Fig 6).

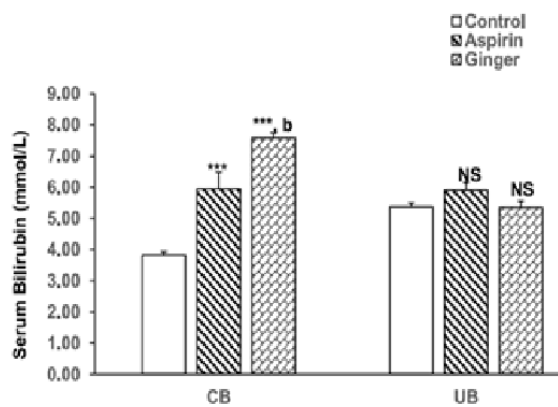


Fig 6: Serum conjugated and unconjugated bilirubin concentration between experimental groups

4. Discussion

Specific serum enzymes are used to assess the hepatocellular or liver functions in the laboratory. Among all of the enzymes, aminotransferases (AST and ALT) are markers of hepatocellular injury (Lala, Goyal & Minter, 2022). AST is present in cytosolic and mitochondrial isoenzyme and is found in the liver, cardiac muscles, skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes and red blood cells. It is not as sensitive or specific for the liver compared to ALT. Therefore, in many cases, elevation in AST may be seen as secondary to non-hepatic causes as well. ALT is a cytosolic enzyme that is found in high concentration in the liver. Hence, in liver injury, ALT is a more precise marker (Ruhl &

Everhart, 2010). This research showed increase ALT in groups of rats administered with ginger and aspirin. However, the ginger group ALT concentration were lower than those of the aspirin group. AST concentration in ginger group was significantly lower than that of aspirin and control group. The result goes further to ascertain the fact that ginger offers a better hepatocellular protective function compared to aspirin which is often used as an orthodox anti-inflammatory agent.

Again, higher levels of bilirubin in the blood, especially conjugated bilirubin usually signifies liver or biliary disorder, anemia, alcohol, drug reaction and autoimmune disorders (Tripathi & Jiali, 2022; Maldonado, Kyle & Schoenfield, 1974); Kalakonda, Jenkins & John, 2017). In this research, aspirin and ginger group showed significant increase in total serum conjugated bilirubin compared to the control group. Though higher levels of bilirubin concentration in the serum points to liver disorders, this doesn't ascertain liver damage often times as it could be linked to other disorders as stated above. The higher levels of conjugated bilirubin seen in ginger group could probably be linked to blood disorders such as anemia or autoimmune disorders which was not assessed in this research work. Hence, this does not rule out the fact that ginger could be of more benefits to the liver compared to the usage of aspirin in treating inflammatory disorders.

This research is in line with other researchers which claims that ginger has a protective effects against piroxicam-induced liver injury by reducing serum marker enzymes, liver fibrosis and apoptosis (Huang, 2019). Some certain research has further shown that liver can be some sort of alleviating agent in treating certain liver disorders. In a certain research, ginger supplementation has been seen to be an effective agent in reducing lipid contents in non-alcoholic fatty liver (Rahimlou *et al*, 2016). Nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide. The pathogenesis of this disease is closely associated with obesity and insulin resistance. Ginger can have hypolipidemic and antioxidant effects and acts as an insulinsensitizer in this conditions. The research further showed that ginger lowered γ -glutamyl transferase, inflammatory cytokines, as well as the insulin resistance index and hepatic steatosis grade in comparison to the placebo.

However, in contrast to this research, ginger showed no significant effect on aspartate aminotransferase. The contradiction here could be due to the already NAFLD condition that was seen in the latter research by Rahimlou *et al* (2016).

Conclusion

Following the result of the liver enzymes analysis, ginger will likely offer more hepatocellular protection when used to treat inflammation as compared to aspirin. In liver enzymes analysis, ALT and AST are usually the most sensitive indicators of hepatocyte injury with ALT being the enzyme mostly associated with liver damages. In the result obtained, irrespective of the fact that ALT levels in ginger and aspirin group were significantly higher than control group, ALT levels of the ginger was however lower than that of the aspirin group. AST levels was lower in ginger group administered animals, further ascertaining the fact that ginger is more hepatocellular protective than aspirin in inflammation treatment. Though conjugated bilirubin concentration was higher in ginger group animals, these may be a pointer to other disorders of the body and not necessarily liver such as blood and autoimmune disorders. Therefore, the result of bilirubin concentration doesn't rule out the fact that ginger could offer hepatocellular protection when used for treating inflammation.

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Authors Contribution

Conceptualisation: EAU and EEO. Investigation: EAU, VKU, AEE, EEO and JOA. Methodology and Analysis: EAU, AMR, EEO, AEE and JOA. Writing-Original Draft: EAU. Supervision: EAU, EEO and AEE

Competing interests

The authors declare no conflict of interest.

Consent for publication

Not applicable

Funding

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Ethics approval and consent to participate

All experiments were performed in accordance with the guideline for care and use of laboratory animal of faculty animal research ethics committee (FAREC-FBMS), Faculty of basic medical sciences, Arthur Jarvis University.

Availability of data and material

The data generated during this research work are available from the corresponding authors on request

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