The Protective Effects of Turmeric on Liver Enzymes of Metronidazole-Treated Adult Male Wistar Rats

Chukwu Victoria O.¹, Akudike Chijioke J.*,¹, Ezejindu Damian N.¹ and Ihim Augustine C.²

¹Department of Anatomy, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State Nigeria
²Department of Medical Laboratory Science, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State Nigeria

*Correspondence Info:
Akudike Chijioke J.
Department of Anatomy,
College of Health Sciences,
Nnamdi Azikiwe University,
Nnewi Campus, Anambra State Nigeria.
E-mail: akudikechijiokej@gmail.com

Abstract
Over the years, research works on the different liver enzymes has proven to be very helpful to man. This study evaluates the protective effects of turmeric on the liver enzymes of metronidazole-treated adult male wistar rats. With previous researches, metronidazole has been found to exert some negative effects on some organs of the body like the testis, kidney etc but the turmeric on its own part, has been found to have no side effects with a host of beneficial functions such as its anti-oxidant and antimicrobial effect amongst a host of other functions. In this study, twenty wistar rats with weight range of between 165-180g were assigned into four groups A, B, C and D of 5 each. The experimental groups A, B and C were orally administered 200mg of metronidazole, 400mg of metronidazole and 400mg of metronidazole as well as 400mg of turmeric respectively for duration of twenty-eight days while the group D served as control and were orally administered water and feed only. Twenty four hours after the last administration, the animals were anaesthetized under chloroform inhalation and dissected for organ collection. Blood for serum preparation was collected into sterile plain tubes and stored in the refrigerator for analysis. Serum samples from the bloods were analyzed for liver enzymes activities using randox kit method. The study revealed that turmeric helped reduced the effects of metronidazole on the serum activities of ALT, AST and ALP on the liver. This present study suggests that metronidazole could have negative effects on the liver and so advises that turmeric be added when on metronidazole administration.

Keywords: Liver enzymes, Protective, Metronidazole, Turmeric, Serum

1. Introduction
The liver contains thousands of enzymes and some of these enzymes are also present in serum in very low concentration. These enzymes have no known function in serum other than to provide very useful information about hepatic state and disorders. They are distributed in plasma and interstitial fluid and have characteristic half-lives which are usually measured in days. The elevation of a given enzymes activity in serum reflects its increase rate of entrance into serum from damaged liver cells, some of these enzymes include AST, ALT, ALP etc. Specific isoenzymes of AST are present in the liver cells mitochondria & cytoplasm while ALT is confirmed to the cytoplasm [1]. Their serum levels can be altered especially in hepatocellular diseases such as acute disease and they are often referred to as hepatocellular enzymes. These abnormal liver enzyme levels may signal liver damage [2].

Turmeric is a perennial spice that comes from the root Curcuma longa, a member of the ginger family, Zingiberaceae [3]. This plant is characterized by its tall, reed-like stems and underground rhizome systems. The main and active principle of this plant turmeric is a polyphenol compound called curcumin. It can be used for culinary purposes which include using it in pickling soups, pepper soups, vegetables, egg dishes and meats [4].

www.ssjournals.com
The most important feature of turmeric is that it has no side effects despite being a therapeutic agent with multiple beneficial functions [5]. It is considered to be an effective antioxidant against oxidative tissue damage. It can significantly inhibit the generation of reactive oxygen species, both in vitro and in vivo [6].

In addition, turmeric is also considered to be a potent cancer chemopreventive agent [7][8] and could have a range of pharmacological actions which includes hepatoprotective effects, anti inflammatory activity, anticarcinogenic effect, anti-oxidant effect, gastrointestinal effect, antimicrobial effect and cardiovascular effects.

Metronidazole is a nitroimidazole anti-infective agent which has specific activity against a number of obligate anaerobic organisms and protozoa. It is a common antibiotic drug widely used in veterinary and human medicine for the treatment of trichomoniasis, giardiasis, amebiasis and anaerobic bacterial infections [9].

Metronidazole has been shown to have negative effects on sperm analysis and testis structure, reducing the germinal epithelium volume and the number of spermatocytes and spermatids but the ameliorative effects of curcumin found in turmeric after therapeutic treatment with metronidazole showed to protect spermatocytes found within the testis [10].

Effects of metronidazole toxicity on reproduction, spermatogenesis, plasma gonadotrophin and testosterone, has being reported to have suppressive actions [11].

This present study aimed to investigate the protective effects of turmeric on the liver enzymes of metronidazole-treated adult male wistar rats.

2. Materials and Method

2.1 Breeding of Animals

Twenty adult male wistar rats were used for this study and they were obtained from a local farm at Nsukka, Enugu State, of the South-Eastern part of Nigeria. They were kept in the animal house of the Department of Anatomy, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Nigeria.

2.2 Duration of Experiment

The entire study lasted for six weeks during which the animals underwent acclimatization for a period of two weeks and the substances for test were administered for a period of twenty-eight days.

2.3 Materials for Study

The materials used in this study are as follows:

1. Twenty adult male wistar rats.
2. Metronidazole of 400mg and 200mg which were produced by M&B Pharmaceuticals, with expiration date of 2018. They were purchased from God’s will Pharmacy at Nnewi, Anambra State, Nigeria in the month of June, 2014. It was grounded to fine powder before being dissolved in a known quantity of water 10 minutes before administration daily.
3. Turmeric powder produced and packaged in India by TRS Asia’s Finest Foods with expiration date of 2016 was purchased from the main market at Nnewi town. Before administration, the turmeric powder was weighed and prepared into solution form.
4. Growers mash produced by Premier Feed Mills Co. Ltd (subsidiary of Flour Mills Nigeria Plc) in Sapele, Delta State, Nigeria and used as feed for the animals throughout the duration of the study.
5. Standard cages which were four in number.
6. Electronic Weighing Balance with an accuracy range of 100g.
7. Syringes and canula for administering the extracts.
8. Sterile syringes and needles.

2.4 Experimental Protocols

Twenty apparently healthy adult male wistar rats were assigned to four different cages in a group of five each for acclimatization prior to the commencement of the solution administration. Groups A, B and C served as the test groups receiving A-200mg/kg body weight/day of metronidazole, B-400mg/kg body weight/day of metronidazole and C-400mg/kg body weight/day of metronidazole as well as 400mg/kg body weight/day of turmeric while Group D served as the control group receiving the water and feed only.

These solutions were administered for 28 days respectively. 24 hours after the last administration, the weights of the animals were recorded. About 5ml of blood was collected from animals in all the groups by cardiac puncture using sterile syringes with needles. The animals were then sacrificed under the influence of chloroform vapour and dissected. Liver organs were harvested and weighed. The blood is transferred into a dry sterile container without an anti-coagulant and allowed to clot to separate the cells from the serum. Serum samples are store in the refrigerator until the analysis of liver enzymes (AST, ALT, and ALP).

2.5 Biochemical Determination

Biochemical parameters were assayed using standard methods; the activities of serum Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and Alkaline Phosphatase (ALP) were determined using randox kit method.
3. Results and Discussions

3.1 Physical Observations

During the period of administration of the solutions, the adult rats in groups A, B and C appeared less active than those in the group D.

3.2 Morphometric Analysis of Body and Liver Weight Changes

Increase in body and liver weights was noticed in the rats of groups A, B and C than those of group D;

Table 1: Comparative summary of body and liver weights of all groups respectively.

| Group/Parameter | Group A n=4 | Group B n=4 | Group C n=4 | Group D n=4 | F-Value n=4 | P-Value n=4 |
|-----------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Liver weight    | 5.76±0.43   | 5.97±0.58   | 6.56±0.45   | 5.53±0.12   | 4.240       | 0.029       |
| Initial body weight | 185.00±12.91 | 185.00±12.91 | 182.50±9.57 | 165.00±10.00 | 2.841       | 0.083       |
| Final body weight  | 215.00±12.91 | 215.00±12.91 | 210.00±8.17 | 195.00±10.00 | 2.867       | 0.081       |

(Mean ± SEM given for each measurement)

Fig. 1: Bar chart on the liver weights of the animals.

Fig. 2: Bar chart on the initial and final body weights of the animals.

3.3 Activities of Serum Levels of Asparate Aminotransferase (AST), Alkaline Aminotransferase (ALT) and Alkaline Phosphate (ALP)

Table 2: Comparative summary of activities of serum levels of AST, ALT & ALP in all groups respectively.

| Group/Parameter | Group A | Group B | Group C | Group D | F-Ratio | Prob. of. sign. |
|-----------------|---------|---------|---------|---------|---------|-----------------|
| AST 64.00±21.71 | 350.00±46.09 | 301.00±66.39 | 255.00±27.65 | 3.016 <0.05 |
| ALT 64.00±21.71 | 350.00±46.09 | 301.00±66.39 | 255.00±27.65 | 3.016 <0.05 |
| ALP 293.50±27.93 | 350.00±46.09 | 301.00±66.39 | 255.00±27.65 | 3.016 <0.05 |

(Mean ± SEM given for each group)
4. Discussion

This present study showed by the morphometric analysis of the initial and final body weights of the different groups of animals that there was no significant increase in their weights when the groups are compared to each other. The mean liver weights of the animals also showed an insignificant increase in weight in the groups administered metronidazole alone, although those of the group administered metronidazole and turmeric had more weight than other groups.

The study on the serum level activities of the AST and ALP enzymes showed that those treated with only metronidazole had increased level of the enzyme while the turmeric can be found to reduce the levels of the AST and ALP enzymes. The study on the serum level activity of the ALT enzyme showed that metronidazole brought the level of the enzyme to a low extent.

This study therefore shows that metronidazole has some hepatotoxicity effects especially on the enzymes which were studied for this experimental research but turmeric helped reduce the effects.

5. Conclusion

This study shows that metronidazole has some negative effects on the liver enzymes and could contribute to the causes of increasing rate of liver diseases in our world today.

So therefore, this study suggests that turmeric, which has protective properties, be included in the diet of individuals receiving therapeutic doses of metronidazole, at least for as long as the medication lasts.

Finally, it can also be recommended that turmeric be added to a part of our daily diet because of its anti-oxidative property protect the tissues of the body against the oxidative tissue damaging materials.

References

[1] Wilkinson HJ, Diagnostic Enzymology, Edward Arnold Publishers Ltd, London, 1976, 775.
[2] Giannini GE, Testa R, Savarino V, MAJ, 2005; 172(3): 367-379.
[3] Pierce A, Guide to Natural Medicines, The American Pharmaceutical Association Practical, New York, 1999.
[4] Keshiro OO and Akinyele IO, Food Chem. 1997; 163-167.
[5] Salama AF and El-Bahr SM, Journal of Medical Research Institute, 2007; 28: 167-173.
[6] Joe B and Lokesh BR, Biochimica et Biophysica Acta, 1994; 1224: 255-263.
[7] Duvoix A, Blasius R and Delhalle S, Lett, 2005; 223:181-90.
[8] Agarwal A and Prabakaran SA, Ind J Exp Biol, 2005; 43: 963-974.
[9] Frey HH and Löscher W, Lehrbuch der Pharmakologie und Toxikologie für die Veterinärmedizin 1996; 1: 502-503.
[10] Noorafshan Ali, Saied Karbalay-Doust, Armita Valizadeh, Elham Aliabadi and Hossein Mirkhani, Society of Toxicologic Pathology, 2010; 38: 366-374.
[11] Sohrabi D, Alipour M and Mellati AA, Iranian Journal of Reproductive Medicine, 2007; 5: 69-72.