PRINT ISSN 1119-8362
Electronic ISSN 2659-1502

Full-text Available Online at
https://www.ajol.info/index.php/jasem
http://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 27 (3) 615-617 March 2023

Effect of Nutmeg on Transaminase Activities in Liver and Serum of Adult Wistar rats

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ABSTRACT: This study examines the activities of alanine aminotransaminase (ALT) and aspartate aminotransferase (AST) in the liver of 30 adult Wistar rats exposed to nutmeg for 30 days. 1 g of nutmeg was administered to group A (n=10), 2 g of nutmeg to group B (n=10) and group C (n=10) was used as the control. Enzyme activities were assayed in both serum and liver (tissue homogenate) spectrophotometrically. Results obtained showed a significant increase ($p < 0.05$) in level of AST in serum of rats in group A and B (20.2±7.29 and 23.2 ± 3.27 U/L) when compared to the control group (14.8± 1.78 U/L) while serum ALT level was significantly reduced (5.2± 1.78 and 4.2 ± 0.04 U/L) compared to the control group (7.0 ± 2.6 U/L) but the differences based on dosage was statistically insignificant ($p \geq 0.05$). The enzyme activities in liver tissue homogenate showed a significant increase ($p < 0.05$) in AST levels (13.8 ± 1.14, 14.6 ± 1.78 and 12.8 ± 0.08 U/L) among test groups and between controls but ALT levels though lower in treated groups than control, was statistically insignificant ($p \geq 0.05$) among test and between control group (4.6 ± 1.34, 4.0 ± 0.08 and 5.8 ± 0.03 U/L). Differences in enzyme activities due to nutmeg administration may lead to hepatocellular injury as well as myocardial infarction. The results suggests that dosage and long-term consumption of nutmeg could have severe health implication as it affects liver function as well as other associated organ of the body.

DOI: **https://dx.doi.org/10.4314/jasem.v27i3.28**

Cite this paper as: AWHIN, P. E; AJOH, A. I; ERUTERE, B. (2023). Effect of nutmeg on transaminase activities in liver and serum of adult Wistar rats. *J. Appl. Sci. Environ. Manage.* 27 (3) 615-617

Dates: Received: 07 February 2023; Revised: 18 March 2023; Accepted: 28 March 2023
Published: 31 March 2023

Keywords: nutmeg; liver; aspartate aminotransferase; alanine aminotransferase

Nutmeg is the ripe seed of the tropical dioeciously evergreen tree *Myristica fragrams* Houlth of the family myristacaceae (Milton, 2004). It is frequently used as spice with a wide array of pharmacological activities and widely used in traditional as well as modern medicine. Nutmeg (*M. fragrans*) has been used for several years in herbal medicine for treating digestive problems including diarrhea and flatulence (Kuete, 2017). It is also used for the treatment of external skin infections (Abourashed and El-Alfy, 2016). Studies have revealed its various important biological activities, including anticancer activity (Le *et al.*, 2017) as well as antioxidant activity, anti-inflammatory activity, antibacterial activity (Matulyte *et al.*, 2020), analgesics activity (Mishra *et al.*, 2018), and antidiabetic activity (Lestari *et al.*, 2019). Indirect evidence suggested that hot spices may interact with epithelia cells of the gastrointestinal tract (GIT) to modulate their transport properties (Demetriades *et al.*, 2005; De Milto and Frey, 2005). Nutmeg is an important source of various types of compounds with diverse chemical structures and pharmacological activities. Nutmeg extract has been found to have bacteriostatic effect against *Helicobacter pylori*. Reduction of gastric acidity and gastric secretion have been demonstrated in rabbits given nutmeg extract (Jan *et al.*, 2005). Irrespective of the numerous uses of nutmeg, it has also been classified as risky and toxic because an overdose can be harmful and sometimes deadly (Forrester, 2005). Well known as natural flavor

source, nutmeg has been found to have constituents of toxicological concern called "Active Principle" which are chemically defined substances that occur in certain flavouring source materials (Beckman and Armberg-muller, 2005). Nutmeg has been proven to cause fatty liver in cat that later died from the nutmeg oil, but in cases of human this is not clear (UKM, 1991). Myristician a chemical constituent of nutmeg has been proven as an inducer of rat liver P450 enzyme and that the induction involves increase in mRNA levels except in the case of p450 2EL (Beckman and Amberg-muller, 2005). Nutmeg a common household spice, sometimes abused for its hallucinogenic properties has been well reported in medical researches but the medical perspective is lacking. The importance of this report is the presentation of the biochemical perspective of nutmeg toxicity, how it affects one of the most vital body internal organs (the liver) whose function is also the detoxification of substances. Therefore, the objective of this paper is to evaluate the effect of nutmeg on transaminase activities in liver and serum of adult Wistar rats.

MATERIALS AND METHODS

Animals: 30 adult Wistar rats of both sex with an average weight of 250 g were randomly assigned into three groups (A, B and C) of 10 rats each. Group A and B were test groups treated with 1 and 2 g of nutmeg respectively thoroughly mixed with grower's mash on a daily basis for thirty-one (31) days equivalent to a whole-body dose of 0.1 and 0.2 myristicin mg/kg/day, respectively. Group C (control group) received equal amount of feeds without nutmeg addition for same period.

Sample collection: The rats were sacrificed on the thirty-second day of the experiment by cervical dislocation. Blood specimen was collected into plain sterile bottles for serum ALT and AST estimation. Excised liver tissue was obtained by quick dissection of the abdominal wall which was homogenized with 10 ml normal saline, centrifuged and supernatant obtained for tissue enzyme activities.

Sample analysis: The biochemical investigations in serum and liver samples were carried out with the following using commercially available kits as supplied by TECO Diagnostic, Anahein, USA. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were as determined by the method of Reitman and Frankel (1957).

Statistical analysis: The data obtained was analyzed. Group means were compared using analysis of variance (ANOVA) and Duncan test for post-hoc analysis.

RESULTS AND DISCUSSSION

The results of the ALT and AST estimation based on dosage of nutmeg administered both in serum and liver tissue are presented in Tables 1 and 2. ALT level in serum was significantly reduced and this was more in group 2 rats administered with 2g of nutmeg. The activity of ALT was also more reduced in liver compared to serum although this was not statistically significant ($p \geq 0.05$) within and among groups. AST levels in serum and liver tissue was significantly increased ($P \leq 0.05$) between groups with highest value observed among group B treated with 2 g of nutmeg when compared with group A and C. The activity was also higher in serum compared to liver tissues for all groups and these values are statistically significant.

Table 1. ALT level in rats administered with 1 and 2 g of nutmeg respectively.

Group	Nutmeg dosage (g)	Serum ALT (U/L)	Liver ALT (U/L)
A	1	5.20 ± 1.78^{a}	4.60 ± 1.34^{a}
B	2	4.20 ± 0.04^{a}	4.00 ± 0.08^{a}
C	Nil	7.00 ± 2.60^{b}	5.80 ± 0.03^{a}

Results are expressed as Mean±SD. Values bearing different superscript on a row differ significantly (p<0.05)

Table 2. AST levels in both serum and liver tissue of rats administered with 1 and 2g of nutmeg respectively.

Group	Nutmeg dosage (g)	Serum AST (U/L)	Liver AST (U/L)
A	1	20.20 ± 7.29^{a}	13.80 ± 1.14^{a}
B	2	23.20 ± 3.27^{a}	14.60 ± 1.78^{a}
C	Nil	14.80 ± 1.78^{b}	12.80 ± 0.08^{b}

Results are expressed as Mean±SD. Values bearing different superscript on a row differ significantly (p<0.05)

The result obtained from the study shows statistically significant increase ($P \leq 0.05$) in the activities of Aspartate aminotransferase in serum (20.22 ± 7.29 and 23.2 ± 3.27 U/L) of adult Wistar rats fed with 1 and 2 g of nutmeg when compared with control (14.6 ± 1.78 U/L). This was the same in the AST activities in liver tissue among test groups, A and B (13.8 ± 1.14 and 14.6 ± 1.78) when compared to the control group, C (12.8 ± 0.08 U/L) respectively. The significantly increased AST activity may be as a result of cellular injury. Myristicin isolated from nutmeg seed has been

reported to be an inducer of fatty liver (Beckman *et al.*, 2005).

There was also a higher serum AST activity compared to the activities of the enzyme in liver tissue. This might be as a result of myocardial infarction that is a destruction of an area of heart muscles due to a cut off in the supply of blood as a result of clotting in coronary artery. Previous research has reported that oral administration of nutmeg results in an increase in aspartate aminotransferase (Morita *et al.*, 2003). The higher serum AST level could be as a contributory result of other organ and muscular disease (Deverenx, 2005). Alanine aminotransferase level in serum was significantly reduced in the test groups A and B (5.2 ± 1.78 and 4.2 ± 0.04 U/L) when compared to the control group C (7.0 ± 2.6 U/L). Also, ALT activities in serum were higher when compared to that of liver tissue for all groups, although these observed differences were not statistically significant ($p \geq 0.05$). Reduced ALT level has been attributed to heam dilution (Omo *et al.*, 1995) which may be attributed to the degree of renal function (Fabrizi *et al.*, 2001). Although the effect of nutmeg on renal function is yet to be studied.

Conclusion: The study reveals that high doses and long-term consumption of nutmeg could cause disruption and distortion of enzyme function and as well cause damage to the liver. Therefore, the liver and other associate organs could be adversely affected. It is recommended that caution should be advocated in the intake of nutmeg and this should prompt further studies as nutmeg has become a stable spice in our meals.

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