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Alanine Aminotransferase and Aspertate Aminotransaminase Activities in Wistar Rats Fed with *Musa paradisiaca* (Plantain) Stem Pulp in Aluminium Chloride Induced Hepatic Oxidative Stress

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ABSTRACT: In this study, the effect of *Musa paradisiaca* (plantain) stem pulp on aluminium chloride ($AlCl_3$) induced hepatotoxicity was studied. Fifteen (15) healthy female wistar rats after acclimatization for two weeks were randomly distributed to three (3) groups, with five (5) rats in each group. Group 1 served as control and received as control pelletized growers feed and distilled water throughout the experiment (14 days). Group 2 received 100mg/kg/body weight (b.w.) of aluminium chloride and was fed with pelletized growers feed and distilled water for 14 days and group 3 received 100mg/kgb.w of aluminium chloride and 2mL/kg of the juice gotten from *M. paradisiaca* and were also allowed free access to feed and water *ad libitum* for 14 days. Blood samples were collected via cardiac puncture and analyzed for AST, ALT, MDA and SOD. Results revealed that there was a significant increase in AST and ALT levels respectively from 67.83±1.39 to 173.40±0.81 and 43.73±1.00 to 128.24±0.68 after treatment with $AlCl_3$ compared to control while administration of *M. paradisiaca* extract ameliorated the adverse effects of $AlCl_3$ when compared to $AlCl_3$ treated groups from 173.40±0.81 to 72.40±1.71 and 128.24±0.68 to 45.83±1.22 respectively. There was a significant decrease ($P<0.05$) in SOD level from 6.04± 0.49 to 2.56±0.86 of $AlCl_3$ compared to control and a significant increase ($P<0.05$) from 2.56±0.86 to 6.00±1. 56 in SOD level was observed in *M. paradisiaca* treated groups when compared to $AlCl_3$ treated group. It was also observed that there was a significant ($P<0.05$) from 401.09±0.10 to 1207.98±1.39 in MDA level after treatment with $AlCl_3$ compared to control while there was a significant decrease ($P<0.05$) from 1207.98±1.39 to 388.83±31.15 in MDA level of *M. paradisiaca* treated groups when compared to the $AlCl_3$ treated groups. It was observed that *M. paradisiaca* showed a mitigating effect on aluminium chloride-induced hepatotoxicity and thus justifying the hepatoprotective property of *M. paradisiaca*.

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Liver diseases contribute markedly to the global burden of diseases and are major causes of illness and death worldwide (Lucky *et al.*, 2017). Liver diseases remain a public health challenge, for which the development of new pharmaceutical treatments is required. The evaluation of the hepato-protective benefits of medicinal plants using laboratory animals is a useful initial step in determining drugs of new biomolecules. Natural products from ethnomedicine provide safe and effective alternative treatments for hepatotoxicity. Many previous reports have associated these hepatoprotective effects with endogenous phytoextracts or Phyto-compounds that are rich in natural antioxidants (Lucky *et al.*, 2017). Hence an increasing number of bioactive compounds and plant extracts have been evaluated for hepato-protective and antioxidant effects against hepatotoxin-induced liver damage (El-Hadary and Ramadan, 2015). The phenolic compounds commonly found in both edible and traditional medicinal plants are incriminated with multiple biological activities, including free radical scavenging activity. It has been suggested that natural antioxidants in food, such as phenolic compounds or flavonoids, might play an essential role in the prevention of oxidative stress-related disorders and diseases, and the reduction of premature mortality

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(Lucky *et al.,* 2017). Flavonoids are certainly ubiquitous in the epidermal cells of plant parts such as the flowers, leaves, stems, roots, seeds, and fruits, and exist in glycosidic and non-glucosidic forms (Agati *et al.*, 2012). *Musa paradisiaca* is a popular medicinal plant belonging to the Musaceae family. This plant commonly known as plantain is a highly nutritious food eaten all over the world. (Mahmood, *et al.,* 2018). A wide range of phytochemical constituents has been isolated from this plant. It has long been used in traditional Ayurvedic medicine for various diseases (Ketiku, 2017). The plant has been shown to have the following pharmacological activities namely analgesic, antidepressant, adaptogenic, anticonvulsant, CNS depressant, antidiarrhoeal, antiurolithiatic, anti-ulcerative, antimicrobial, antidiabetic, (Lewis, *et al.,* 2016) antioxidant, antilipidemic, antihypertensive, antiatherosclerotic, cytotoxic, Thrombolytic, Antimalarial, Anti snake venom, Mutagenic, hepatoprotective, Hair growth-promoting, wound healing, bio-absorptive, and tablet disintegrant and many other activities (Mondal, *et al.,* 2014; Panigrahi, *et al.,* 2017). Aluminium (Al) is the most abundant metal in the environment, and it constitutes 8.13% of the earth's crust. Oral aluminium exposure is primarily due to its presence in food (cooking utensils, food additives), drinking water, cosmetics, and therapeutic preparations. Aluminium is absorbed through the skin, gastrointestinal tract, lungs, and nasal mucosa. Subsequently, most of the absorbed aluminium is transported in serum by transferrin and accumulates in different tissues such as the liver, kidneys, brain, and heart (Reiter et al., 2007). However, studies have implicated aluminium as a factor in nephrotoxicity (Kutlubay *et al.,* 2007), hepatotoxicity (Bhasin *et al.,* 2014), hematotoxicity (Turgut *et al.,* 2007), and neurotoxicity (Stevanovic *et al.,* 2009). Moreso, aluminium compounds may bind to DNA and RNA and cause inhibition in such enzymes as acid and alkaline phosphatases, hexokinase, phosphodiesterase, and phosphooxidase (Ochmanski & Barabasz, 2000). In addition, aluminium may induce alteration in biochemical parameters, lipid peroxidation, and reduction of the antioxidant enzymes activities in plasma and different tissues of male rats and rabbits (Newairy *et al.,* 2009; Turkez *et al.,* 2011).

Therefore, the present study was aimed to investigate the protective effect of *M. paradisiaca* stem pulp against $AlCl_3$ toxicity using AST, ALT, SOD, and MDA as biomarkers.

MATERIALS AND METHODS

Experimental Animals: Fifteen (15) healthy adult female Wistar albino rats weighing 100-150g were used for this study. They were obtained from the animal house of the Department of Pharmacology, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria and were maintained under standard housing conditions (photoperiod: 12h natural light and 12h dark). The animals were acclimatized for two weeks and were fed pelletized growers feed and were exposed to clean tap water throughout the period of the study. All animal experimental protocols were approved by the Committee of Scientific Ethics at Niger Delta University, Wilberforce Island, and were carried out by its guidelines for animal use.

Chemicals/Reagents: Aluminium chloride was obtained from Merck-Schuhardt, Germany, assay kits for AST, ALT, SOD, and MDA were obtained from Teco diagnostics Ltd. USA., and Randox Laboratories Ltd., United Kingdom. All other reagents/chemicals were obtained from standard suppliers and were of analytical grade.

Source of M. paradisiaca: The stem of *M. paradisiaca* (plantain) were obtained from a farm in Amassoma, Wilberforce Island and was identified and confirmed at the Herbarium of the Department of Plant Science and Biotechnology, Niger Delta University, Wilberforce Island.

Preparation of Extracts: The fresh stem of *M. paradisiaca* was rinsed in clean water. The outer green part of the stem was peeled off. The white inner portion of the stem of *M. paradisiaca* (plantain) was cut into small pieces and 100g was weighed. 100ml of distilled water was added with the weighed 100g of the stem and was mechanically crushed with the aid of a homogenizer (Saisho, Model S – 742). The resulting mixture was filtered with the aid of sterile cheesecloth and the juice was stored in an airtight container and stored 4℃ in a refrigerator.

Experimental Design: The healthy female Wistar albino rats, after acclimatization for a period of two weeks, were randomly distributed to three (3) groups, with four (5) rats in each group.

Group 1: Served as control and received as control and feed on pelleted grower's feed and distilled water throughout the experiment (14days).

Group 2: Received 100mg/kg b.w. of aluminium chloride and fed with pelleted grower's feed and distilled water for 14days.

Group 3: Received 100mg/kg b.w. of aluminium chloride and after the period of one hour the juice gotten from the stem of *M. paradisiaca* (plantain) was

given to the rats and fed with pelleted grower's feed and distilled water for 14days.

Sample Collection: At the end of the experimental period, the animals were anaesthetized in a chloroform chamber and blood samples collected via cardiac puncture into sample bottles, the blood samples were allowed to clot for 10 min at room temperature and subsequently centrifuged to obtain the serum used for biochemical analysis.

*Biochemical Parameters***:** Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined as described by Reitman & Frankel, (1957). Superoxide dismutase (SOD) activity was by the methods of Misra and Fridovich (1972). The assay method of Hunter *et al*. (1963) as modified by Gutteridge and Wilkins (1980) was adopted for the assay of Malondialdehyde (MDA) concentration.

Statistical Parameters: Data are expressed as Mean ± Standard deviation. The statistical significance was evaluated by one-way Analysis of Variance (ANOVA) using SPSS (Statistical Package for Social Sciences) Version 16.0 and the individual mean compared by post hoc LSD and Turkey method. Values were considered statistically significant when ($p<0.05$).

RESULTS AND DISCUSSION

The results of the effect of administration of *M. Paradisiaca* extract on the ALT and AST level of female albino Wistar rat as presented in Table 1, showed a significant increase in AST and ALT levels from 67.83 ± 1.39 to 173.40 ± 0.81 and 43.73 ± 1.00 to 128.24±0.68 respectively after treatment with $AlCl_3$ compared to control while administration of *M. paradisiaca* extract ameliorated the adverse effects of the $AlCl_3$ when compared to $AlCl_3$ treated groups from 173.40 ± 0.81 to 72.40±1.71 and 128.24±0.68 to 45.83 ± 1.22 respectively. Table 2 showed that there was a significant increase ($p<0.05$) from 401.09±0.10 to 1207.98±1.39 in MDA levels after treatment with $AlCl_3$ compared to control while there was a significant decrease ($p<0.05$) from 1207.98±1.39 to 388.83±1.15 in MDA levels of *M. paradisiaca* treated groups when compared to the $AlCl_3$ treated group. While the results in Table 3 showed a significant decrease ($p<0.05$) in SOD level from 6.04±0.49 to 2.56±0.86 of $AlCl_3$ compared to control and a significant increase ($p<0.05$) from 2.56±0.86 to 6.00±1.54 in SOD level was observed in M. paradisiaca treated groups when compared to the $AlCl_3$ treated group. The present study was carried out with a view of ascertaining the hepatoxicity of aluminium chloride using plasma enzymes (AST, and ALT) as hepatic health markers and oxidative stress induction capability of aluminium chloride using MDA and SOD as biomarkers and evaluating the ameliorating potentials of *M. paradisiaca* pulp against such toxicities. The oral administration of $AlCl_3$ caused a significant increase ($p < 0.05$) in the plasma level of enzymes, ALT, AST. These results are, however, in accordance with Al-Qayim & Saadoon, (2013), Bhasin *et al.,* (2014) and Okail *et al.,* (2020). The significant increase in plasma levels of AST and ALT arising from $AlCl_3$ administration may be due to free radical generation and oxidative stress causing cellular degeneration and alteration of functional integrity of tissue cell membrane permeability (Fu *et al.,* 2014; Zhang *et al.,* 2016; Sun *et al.,* 2018; Gomes *et al.,* 2019; Okail *et al.,* 2020), which therefore result in the leakage of these enzymes from the injured cells to the plasma (Imam *et al.,* 2016; Kpomah & Kpomah, 2018). However, the oral administration of the *M. paradisiaca* pulp after 14 days at 2mls per Kg/b.w was able to cause significant reduction ($p < 0.05$) in the elevated AST and ALT levels due to due the $AlCl_3$ induced toxicity, an indication that *M. paradisiaca* pulp tends to repair/prevent damage and the restriction of enzymes leakage through cellular membranes repair. These results are, however, in agreement with the finding of Issa *et al.,* (2018) who concluded that *M. paradisiaca* pulp mostly reversed the action of CCl_4 on the function and structure of the liver. Moreover, the hepatoprotective effect of *M. paradisiaca* may be directly linked to the stabilization of redox state in the cells (El-Guendouz *et al.,* 2017; Ibrahim *et al.,* 2019).

Table 1: The effect of administration of *M. Paradisiaca* extract on the ALT and AST level of female albino Wistar rat

Treatment	AST (IU/L)	ALT (IU/L)
Control	67.83 ± 1.39 [a]	43.73 ± 1.00 [a]
$AlCl_3$(100mg/kg b.w)	173.40 ± 0.81 [b]	128.24 ± 0.68 [b]
Plantain Stem Juice (2ml/kg b.w) + $AlCl_3$ (100mg/kg b.w) for 14 days	72.40 ± 1.71 [c]	45.83±1.22 [c]

Data are Mean ± SD (n=5). Mean in the same column with a different superscript letter(s) are significantly different (p<0.05).

Table 2: The effect of administration of *M. Paradisiaca* on Malondialdehyde level of Wistar rats

Treatment	MDA (nmol/mg protein)
Control	401.09 ± 0.10 [a]
$AlCl_3$ (100mg/kg b.w)	1207.98 ± 1.39 [b]
Plantain Stem Juice (2ml/kg b.w) + $AlCl_3$ (100mg/kg b.w) for 14 days	388.83 ± 1.15 [a]

Data are Mean ± SD (n = 5). Mean in the same column with a different superscript letter(s) are significantly different (p<0.05).

The ratio of AST to ALT has more clinical utility than assessing individual elevated levels. A coenzyme

pyridoxal-5'-phosphate deficiency may depress serum ALT activity and consequently increase the AST/ALT ratio (Sohocki *et al*., 2017). The ratio increases in progressive liver functional impairment and found 81.3% sensitivity and 55.3% specificity in identifying cirrhotic patients.

Table 2: The effect of administration of *M. paradisiaca* on liver superoxide dismutase.

Treatment	SOD (Unit/mg protein)
Control	6.04 ± 0.49^{a}
$AlCl_3$ (100mg/kg b.w)	2.56 ± 0.86^{b}
Plantain Stem Juice (2ml/kg b.w) + $AlCl_3$ (100mg/kg b.w) for 14 days	6.00 ± 1.54^{a}

Data are Mean ± SD (n = 5). Mean in the same column with different superscript letter(s) are significantly different (p<0.05).

Cells are equipped with an antioxidant defense system to counter the effect of relative oxidative stress. Environmental contaminants are known to induce liver toxicity by perturbing the pro-oxidant and antioxidant balance leading to oxidative stress (Mach *et al.,* 2015). Liver oxidative stress appears to be a common feature in hepatotoxicity which suggest that there may be a benefit to developing better antioxidant therapy for relevant cases (Lindblom *et al.,* 2017). Al may perhaps decrease ferritin synthesis and increase the expression of transferrin receptors, thereby disrupting the normal synthesis of transferrin receptors with ferritin creating increased free iron levels in the cell, resulting in an increase of oxidative damage via the Fenton reaction (Yamanaka *et al.*, 1999). The activity of superoxide dismutase (SOD) is affected by Al exposure because of oxidative stress (Julka and Gill, 1996; Campbell *et al.*, 1999) as evident by a marked decrease in SOD activity from 6.04±0.49 to 2.56±0.86. The reduction in the activity of SOD causes a rise in the level of superoxide anion which inactivates CAT activity. It is considered the first line of defence against the deleterious effect of oxy radicals in the cells by catalyzing the dismutation of superoxide radicals to hydrogen peroxide and molecular oxygen (Krishnamoorthy *et al*., 2016). The oral administration of *M. paradisiaca* however, had a significant increase in the level of SOD activity as evident by the rise from 2.56±0.86 in the Al treated group to 6.00±1.54 in *M paradisiaca* pulp treated group, these findings are, however, consistent with others reported in literature Mokbel and Hashinaga (2005), Vijayakumar *et al.* (2008), the presence of vitamin E and palmitic acid in *M. paradisiaca* (Ahmed *et al*, 2021) which are already known to possess high antioxidant activities, may be related to the greater antioxidant activity (Elagbar *et al.,* 2016; Kaplaner *et al.,* 2017; Ahmed *et al*, 2021). The level of lipid peroxidation increased by the Aluminum chloride administration indicate an imbalance between a pro-oxidant and antioxidant system which could induce oxidative stress. The increase in lipid peroxidation in the liver as observed in the present study could be due to the contaminant increase in the generation of free radicals in the organs of aluminium chloride treated rats. Other studies have reported that ROS induce lipid peroxidation and the toxicity of liver peroxides plays a key role in hepatoxicity. Results also showed a significant increase ($P<0.05$) from 401.09±0.10 to 1207.98±1.39 in MDA levels after treatment with $AlCl_3$ compared to control while there was a significant decrease ($P<0.05$). From 1207.98±1.39 to 388.83±31.15 in MDA levels of *M. Paradisiaca* treated groups when compared to the $AlCl_3$ treated groups and control group. This agrees with Gegia (2017) intro analysis on Wistar rats done with tuberculosis medication isoniazid.

Conclusion: The present findings established that the exposure of animals to aluminium can induce marked detectable alterations in biochemical characteristics and antioxidant activities. Also, our study demonstrated that the *M. Paradisiaca* pulp minimized the toxic effects of $AlCl_3$ by reducing the degenerative changes in the liver as evident by the marked reduction in values of AST and ALT, the ameliorative effect of *M. Paradisiaca* on $AlCl_3$ toxicity was also shown by a marked reduction in the elevated value of MDA and a concomitant increase in the erstwhile decreased value of SOD activity. Consequently, it can be recommended that the exposure to aluminium in our daily life should be reduced, and the oral administration of *M. Paradisiaca* pulp might be a beneficial method in minimizing aluminium toxicity.

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