Alanine Aminotransferase and Aspartate 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 (AlCl3) 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/kg/b.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±1.71 and 43.73±1.00 to 128.24±0.68 after treatment with AlCl3 compared to control while administration of M. paradisiaca extract ameliorated the adverse effects of AlCl3 when compared to AlCl3 treated groups when compared to control. 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 AlCl3 compared to control while there was a significant decrease (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 AlCl3 treated group. It was 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 AlCl3 compared to control while there was a significant decrease (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 AlCl3 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 hepatoprotective 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.
(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-glycosidic 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, antidiarrheal, antiurolithiatic, anti-inflammatory, antimicrobial, antidiabetic, (Lewis, et al., 2016) antioxidant, antihypertensive, antiatherosclerotic, and phosphooxidase, 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., 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 AlCl₃ 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 pelleted 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-Schuhhardt, 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°C 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 14 days.

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 AlCl3 compared to control while administration of M. paradisiaca extract ameliorated the adverse effects of the AlCl3 when compared to AlCl3 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 AlCl3 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 AlCl3 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 AlCl3 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 AlCl3 treated group. The present study was carried out with a view of ascertaining the hepatic toxicity 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 AlCl3 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 AlCl3 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 (Ibrahim 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 AlCl3 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 CCl4 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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ALT (IU/L)</th>
<th>AST (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>43.73 ± 1.00</td>
<td>67.83 ± 1.39</td>
</tr>
<tr>
<td>AlCl3 (100mg/kg b.w)</td>
<td>128.24 ± 0.68</td>
<td>173.40 ± 0.81</td>
</tr>
<tr>
<td>Plantain Stem Juice (2ml/kg b.w) + AlCl3 (100mg/kg b.w) for 14 days</td>
<td>45.83 ± 1.22</td>
<td>72.40 ± 1.71</td>
</tr>
</tbody>
</table>

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 rat

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MDA (nmol/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.01 ± 0.10</td>
</tr>
<tr>
<td>AlCl3 (100mg/kg b.w)</td>
<td>1207.98 ± 1.39</td>
</tr>
<tr>
<td>Plantain Stem Juice (2ml/kg b.w) + AlCl3 (100mg/kg b.w) for 14 days</td>
<td>388.83 ± 1.15</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SOD (Unit/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.04 ± 0.49</td>
</tr>
<tr>
<td>AlCl$_3$ (100mg/kg b.w)</td>
<td>2.56 ± 0.86</td>
</tr>
<tr>
<td>Plantain Stem Juice (2ml/kg b.w)</td>
<td>6.00 ± 1.54</td>
</tr>
<tr>
<td>14 days</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SOD (Unit/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{AlCl}_3$(100mg/kg b.w)</td>
<td>2.56 ± 0.86</td>
</tr>
<tr>
<td>$\text{AlCl}_3$(100mg/kg b.w)</td>
<td>6.00 ± 1.54</td>
</tr>
</tbody>
</table>

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 oxygen 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 hepatotoxicity. 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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