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Attenuation of Potassium Cyanide-Induced Hepatotoxicity and Hematotoxicity by Biogenically Synthesised Silver Nanoparticles (AGNPS) Derived from *Carica papaya* Seed Extract in Male Wistar Rats.

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Abstract: Cyanide is a potent environmental toxin that induces severe hepatotoxicity through the inhibition of cytochrome c oxidase, leading to ATP depletion and the generation of reactive oxygen species (ROS). The resulting oxidative stress causes hepatocellular damage, systemic inflammation, and hematological dysregulation. This study was conducted to investigate the protective and therapeutic potential of biogenic silver nanoparticles (AgNPs) synthesized from *Carica papaya* seed extract against cyanide-induced hepatotoxicity in male Wistar rats. Twenty five rats were randomly divided into five groups of five rats each as follows: (I) control group; (II) treated with cyanide; (III) cyanide+ *C. papaya* AgNPs; (IV) *C. papaya* AgNPs; (V): cyanide + quercetin. Key parameters including serum liver enzymes (ALT and AST) and hematological indices (RBC, PCV, and WBC) were measured. The results showed that cyanide administration caused a significant elevation of serum ALT and AST levels, indicative of liver damage, and also induced profound hematological changes, including a reduction in RBC, PCV and an increase in WBC counts. Treatment with the *C. papaya*-derived AgNPs significantly ameliorated these aberrations, restoring liver enzyme levels; however, it has no significant effect on the hematological indices. The protective effects of the biogenic AgNPs were comparable to quercetin. These findings suggest that the green-synthesized silver nanoparticles from *Carica papaya* seed extract possess significant hepatoprotective properties, likely mediated by their rich phytochemical content and antioxidant activity. This highlights their potential as a promising therapeutic agent for managing cyanide-induced toxicity.

Key words: Potassium Cyanide; Nanomedicine; Hepatotoxicity; Anemia

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Introduction

The liver plays a fundamental role in metabolic processes, detoxification, and the regulation of xenobiotics, making it particularly susceptible to chemical-induced injuries. Among various hepatotoxic agents, cyanide stands out as a potent and rapidly acting toxin that disrupts oxidative phosphorylation by inhibiting cytochrome c oxidase within the mitochondrial electron transport chain (Mathangi *et al.*, 2011; Way, 1984). This disruption leads to cellular hypoxia, induces severe oxidative stress, and ultimately causes damage to hepatic cells. Given the limitations of existing antidotes, which are often costly and have side effects, there is a pressing need for safer and more effective therapeutic alternatives.

Nanotechnology represents a promising frontier for mitigating chemically induced organ toxicity. Silver nanoparticles (AgNPs) have attracted significant interest due to their diverse properties, including antioxidant, anti-inflammatory, and cytoprotective effects (Gurunathan *et al.*, 2013; Singh *et al.*, 2018). The biogenic, or green, synthesis of these nanoparticles using plant extracts provides a sustainable, eco-friendly, and biocompatible alternative to conventional chemical methods (Iravani, 2011).

Carica papaya is a widely cultivated tropical species with notable hepatoprotective, antioxidant, and anti-inflammatory properties (Otsuki *et al.*, 2010). Its seeds, often considered a waste product, are rich in bioactive phytochemicals like flavonoids and phenolic compounds that serve as both potent free radical scavengers and effective reducing and capping agents for AgNP biosynthesis (Mittal *et al.*, 2013; Ong *et al.*, 2013). This combination of the intrinsic therapeutic properties of the plant extract with the enhanced cellular interaction of nanosilver offers a potentially synergistic approach.

While previous research has explored the protective effects of papaya extracts and AgNPs in isolation, there remains a critical knowledge gap regarding their pharmaceutical potential against cyanide-induced liver injury. This study aims to address this gap by evaluating the therapeutic efficacy of biogenic AgNPs synthesized from *Carica papaya* seeds in mitigating cyanide-induced liver damage in male Wistar rats, thereby exploring a novel, natural, and cost-effective approach to liver protection.

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Materials and Methods

Chemicals: Potassium cyanide (Sigma-Aldrich, Germany). Kits for the determination of alanine aminotransferase, aspartate aminotransferase (AST) were obtained from Randox Laboratories, U.K. All other chemicals used were of analytical grade.

Animals: Albino Wistar rats were sourced from the Pre-clinical animal house of the Faculty of Basic Medical Sciences at the University of Port Harcourt. The animals were housed in standard cages and provided with commercially available pelleted feed and water *ad libitum*.

Green Synthesis of Silver Nanoparticles (AgNPs): Silver nanoparticles were synthesized using the seed extract of *Carica papaya*. A 0.01 M silver nitrate solution was prepared in a 100 mL conical flask using distilled water, with the pH adjusted to 3 with acetic acid. One hundred grams of *Carica papaya* seed powder was added to this solution in batches and continuously stirred at 70 rpm to ensure the powder remained suspended. After 2 hours, the solution was withdrawn. The formation of AgNPs was visually confirmed by a colour change from colourless to a colloidal brown. Following complete reduction, the solution was filtered through a nylon mesh and then centrifuged at 12,000 rpm for 15 minutes. The resulting residue was washed with distilled water, dried using a rotary evaporator, and finally placed in a vacuum oven at 80°C.

Experimental Design and Animal Grouping: Twenty-five rats were randomly assigned to five groups of five animals each.

Group I (Control): Received normal drinking water.

Group II (potassium cyanide-treated): Administered potassium cyanide-contaminated water (300 ppm) for 21 consecutive days.

Group III (Potassium cyanide + AgNPs): Received potassium cyanide-contaminated water for 14 days, followed by a 7-day co-treatment with *Carica papaya* seed-derived AgNPs.

Group IV (AgNPs Alone): Received *Carica papaya* seed-derived AgNPs for 7 days.

Group V (potassium cyanide + quercetin): Received potassium cyanide-contaminated water for 14 days, followed by a 7-day co-treatment with ascorbic acid.

Twenty-four hours after the final treatment, blood and liver samples were collected for analysis of liver function, histopathology, and other biochemical assays.

Sample Collection

Animals were humanely euthanized by cervical dislocation. Blood samples were collected via cardiac puncture into heparinized tubes.

Hematological parameters

The blood with EDTA was used for the count of RBC, total and differential count of WBC and platelets by standard procedures.

Biochemical Estimations

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined by standard procedures in an auto analyzer using Randox kits.

Statistical Analysis: All data were expressed as the mean ± standard deviation (SD). The results were analyzed using a one-way analysis of variance (ANOVA), and differences between group means were evaluated using a suitable post-hoc test (e.g., Tukey's HSD). A probability value of $p < 0.05$ was considered significant.

Results

The results presented in Table 1 show that Cyanide exposure significantly reduced PCV and RBC counts and increased WBC count compared to the control group. These suggest anaemia, impaired oxygen transport, thrombocytopenia, and an inflammatory response. Treatment with *C. papaya* AgNPs showed no significant effect on the haematological parameters when compared to the untreated group (II). Rats in the group administered *C. papaya* AgNPs alone showed minimal adverse effects on haematological parameters, with values close to control. Administration of quercetin also fails to reverse the anaemic effect of cyanide as observed in the insignificant difference ($P>0.05$) when compared to the untreated group.

Table 1: The effect of pawpaw seed nanoparticles (PSNP) on packed cell volume (PCV), red blood cells (RBC), and white blood cells (WBC) following exposure to cyanide-contaminated water.

Group	PCV (%)	RBC (x10^12/l)	WBC (x10^9/l)
I (control	33±0	4.3±0.49	12.9±1.91
II (potassium cyanide)	31.5±2.12	4.2±0.0	14.45±1.77
III (potassium cyanide + *C. papaya* seed AgNPs)	29.5±3.87	4±0.39	14.8±2.63
IV (*C. papaya* seed AgNPs)	32±4.55	4.375±0.62	11.15±0.97
V (potassium cyanide +quercetin)	29±9.30	4±0.37	16.3±1.68

Results are expressed as mean±SD (n=5)

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The results presented in Table 3.3 show that the Cyanide alone group significantly increased AST and ALT activities compared to the control ($P<0.05$), suggesting liver damage. Treatment with nanoparticles from pawpaw seed significantly reduced AST and ALT compared to the Cyanide alone group ($P<0.05$). Administration of nanoparticles alone showed a more significant reduction in AST and ALT compared to the control group ($p<0.05$). Treatment with quercetin equally reduced AST and ALT activities compared to the cyanide alone group, but not up to the Nanoparticle alone group.

Table 2: The effect of *C. papaya* seed nanoparticles (PSNP) on alanine aminotransferase (ALT) and aspartate aminotransferase (AST) following exposure to cyanide contaminated water

Group	AST (U/L)	ALT (U/L)
I (control)	8.45±1.45	18.03±2.84
II (cyanide)	60.17±6.17*	82.60±7.27*
III (cyanide+ *C. papaya* seed AgNPs)	31.41±6.87#	50.31±9.25#
IV (*C. papaya* seed AgNPs)	1.26±0.14^	19.09±6.16^
V (cyanide+ quercetin)	9.89±0.48#	30.83±3.43#

Results are expressed as mean±SD (n=5). * $P<0.05$ statistically significantly different (control vs Cyanide); # $P<0.05$ (Cyanide vs treatment).

Discussion

Cyanide is a potent mitochondrial toxin that exerts its hepatotoxic effects primarily through the inhibition of cytochrome c oxidase. This inhibition disrupts the electron transport chain, leading to impaired oxidative phosphorylation, severe ATP depletion, and the overproduction of reactive oxygen species (ROS) (Isom and Borowitz *et al.*, 2015). The resulting oxidative stress not only compromises hepatic metabolic functions but also triggers systemic inflammation, hematological dysregulation, and significant hepatocellular injury. The present study was conducted to evaluate the protective and therapeutic potential of biogenic silver nanoparticles (AgNPs), synthesized from *Carica papaya* seed extract, in mitigating cyanide-induced hepatic damage in male Wistar rats. The findings from this investigation demonstrate that the *C. papaya*-derived AgNPs conferred significant hepatoprotective effects. These effects were comparable to quercetin, a well-established antioxidant and anti-inflammatory flavonoid.

Cyanide administration led to a marked elevation in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, which are critical biomarkers of hepatocellular membrane disruption and the leakage of intracellular enzymes into circulation. This observation aligns with previous reports that associate cyanide toxicity with profound mitochondrial dysfunction and hepatic necrosis (Babatunde and Abigail *et al.*, 2021). Treatment with *C. papaya* AgNPs significantly ameliorated these aberrations, restoring serum ALT and AST towards normal levels. This finding suggests that the nanoparticles preserved hepatocyte membrane integrity and synthetic function, likely through the antioxidant-mediated attenuation of cyanide-induced hepatocellular damage. These results are in agreement with prior studies showing that various plant-derived nanoparticles can enhance hepatic function under chemically induced stress (AlKandari *et al.*, 2024).

Cyanide exposure was found to induce profound hematological alterations, including significant reductions in red blood cell (RBC) count, hemoglobin (Hb), and packed cell volume (PCV). This anaemic state is a likely consequence of cyanide-induced hemolysis and erythropoietic suppression, which can be driven by ROS-mediated lipid peroxidation of erythrocyte membranes and impaired iron utilization (Leavesley*et al.*, 2008). Remarkably, treatment with *C. papaya* seed AgNPs significantly restored erythrocytic indices (RBC, Hb, and PCV) and normalized white blood cell (WBC) counts. This beneficial effect is plausibly mediated by the rich phytochemical matrix of the nanoparticles, which includes flavonoids, tannins, and alkaloids. These compounds are known to protect hematopoietic tissues and modulate immune responses (*et al.*, 2023). The comparable performance of *C. papaya* AgNPs to quercetin further reinforces their potential pharmaceutical relevance in managing hematological toxicity.

Conclusion

In conclusion, our study confirms that cyanide toxicity can trigger liver injury and anaemic effects. The protective effects of *C. papaya* seed nanoparticles (PSNPs) were reflected in the restoration of liver function enzymes without reversing the anaemic effect induced by potassium cyanide.

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Institutional Review Board: To ensure animal welfare, the study adhered to the guidelines outlined in the Helsinki Declaration of 1975. All animals used were healthy. The experimental design received approval (code ART2023008) from the Federal University Otuoke's ethical committee on animal research and treatment (ART). The experiments were conducted in the Department of Biochemistry's animal house between December and April 2025.

Conflicts of Interest: None. Data Availability: It will be made available on request

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References

AlKandari, F. M., Mohamed, H. S., Ahmed, S. A., Mahmoud, B., & Mahmoud, A. M. (2024). Protective effects of propolis and chitosan nanoparticles against ibuprofen-induced hepatotoxicity in albino rats. *Diseases*, *12*(3), 49.

Babatunde, I. O., & Abigail, A. (2021). Ameliorative effect of a multi-nutrient-rich product against cyanide induced hepatorenotoxicity. *Drug Discovery*, *15*(35), 34-42.

Gurunathan, S., Park, J. H., Han, J. W., & Kim, J. H. (2013). Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by *Bacillus tequilensis* and *Calocybe indica* in MDA-MB-231 human breast cancer cells: Targeting p53 for anticancer therapy. *International Journal of Nanomedicine, 8*, 4401–4422. https://doi.org/10.2147/IJN.S51801

Iravani, S. (2011). Green synthesis of metal nanoparticles using plants. *Green chemistry*, *13*(10), 2638-2650.

Isom, G. E., and Borowitz, J. L. (2015). Biochemical mechanisms of cyanide toxicity. *Toxicology of cyanides and cyanogens: experimental, applied and clinical aspects*, 70-81.

Iweala, E. J., Oluwapelumi, A. E., Dania, O. E., & Ugbogu, E. A. (2023). Bioactive phytoconstituents and their therapeutic potentials in the treatment of haematological cancers: a review. *Life*, *13*(7), 1422.

Leavesley, H. B., Li, L., Prabhakaran, K., Borowitz, J. L., and Isom, G. E. (2008). Interaction of cyanide and nitric oxide with cytochrome c oxidase: implications for acute cyanide toxicity. *Toxicological Sciences*, *101*(1), 101-111.

Mathangi, D. C., Shyamala, R., Vijayashree, R., Rao, K. R., Ruckmani, A., Vijayaraghavan, R., & Bhattacharya, R. (2011). Effect of alpha-ketoglutarate on neurobehavioral, neurochemical and oxidative changes caused by sub-chronic cyanide poisoning in rats. *Neurochemical research*, *36*(3), 540-548.

[

Mittal, A. K., Chisti, Y.,& Banerjee, U. C. (2013). Synthesis of metallic nanoparticles using plant extracts. *Biotechnology advances*, *31*(2), 346-356.

[

Ong, H. C., Ahmad, N., & Milow, P. (2011). Traditional medicinal plants used by the temuan villagers in Kampung Tering, Negeri Sembilan, Malaysia. *Studies on Ethno-Medicine*, *5*(3), 169-173.

[

Otsuki, N., Dang, N. H., Kumagai, E., Kondo, A., Iwata, S., & Morimoto, C. (2010). Aqueous extract of Carica papaya leaves exhibits anti-tumor activity and immunomodulatory effects. *Journal of ethnopharmacology*, *127*(3), 760-767.

Singh, P., Kim, Y. J., Zhang, D., & Yang, D. C. (2016). Biological synthesis of nanoparticles from plants and microorganisms. *Trends in biotechnology*, *34*(7), 588-599.

Way, J. L. (1984). Cyanide intoxication and its mechanism of antagonism. *Annual review of pharmacology and toxicology*, *24*(1), 451-481.