



Hepatotoxicity of Sodium Cyanide: A Study on Liver Function Parameters in Rabbits

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ABSTRACT :

Sodium cyanide (NaCN) is a toxic substance that can cause liver damage. This study aimed to investigate the effects of NaCN on liver function parameters in rabbits. Rabbits were administered NaCN orally at a dose of 0.05 mg/kg for 30, 60, and 90 days. Liver function parameters, including AST, ALT, ALP, Total Bilirubin, Conjugated Bilirubin, Total Protein, and Albumin, were assessed. Significant elevations in AST, ALT, and ALP were observed in NaCN-treated groups, indicating liver cell damage and inflammation. Total Bilirubin and Conjugated Bilirubin levels increased, suggesting impaired liver function and bile metabolism. Total Protein and Albumin levels decreased, indicating impaired liver synthetic function. This study demonstrates that NaCN administration causes significant liver damage and dysfunction in rabbits, which worsens with increasing duration of exposure. These findings suggest that NaCN is hepatotoxic and can cause liver damage in animals. Further studies are needed to understand the mechanisms of NaCN-induced liver toxicity and to explore potential therapeutic interventions.

Keywords: Sodium cyanide, Liver Damage, Liver Function Parameters, Hepatotoxicity

1. INTRODUCTION :

Cyanide is a toxic and ubiquitous substance found in various environmental sources and has been implicated in numerous cases of poisoning in humans and animals. Cyanide intoxication mostly results from the ingestion of foods, environmental pollution, chemical warfare, suicide and homicide.

Foods like cassava (*Manihot esculenta*) contain naturally occurring cyanide compounds (linamarin and lotaustralin) that can release cyanide when ingested (Montagnac, Davis and Tanumihardjo, 2009). Fruits like apricots, peaches, and cherries have pits that contain amygdalin, which can release cyanide when ingested (Holzbecher, Moss and Ellenberger, 1984). Industrial activities such as mining, smelting, and electroplating can also release cyanide into the environment, contaminating soil and water sources (Kjeldsen, 1999).

Cyanide is a rapidly acting toxin that inhibits cellular respiration, leading to severe health effects and death (ATSDR, 2020). The toxicity of cyanide is well-documented, and its effects can be devastating. The mechanism of cyanide toxicity involves cyanide ions (CN⁻) binding to cytochrome c oxidase in the mitochondria, preventing the transfer of electrons and inhibiting oxidative phosphorylation (Way, 1984). This halts the production of ATP, the primary energy source for cellular functions. The brain, heart, and liver are particularly vulnerable to cyanide toxicity due to their high energy requirements (Hall and Rumack, 2019).

Routes of entry of cyanide into the body include inhalation, skin absorption and ingestion.

1. **Inhalation:** Breathing cyanide-containing gases, such as hydrogen cyanide or cyanogen chloride (Hall and Rumack 2018) (NIOSH, 2020).
2. **Ingestion:** Consuming cyanide-contaminated food, water, or substances (ATSDR, 2020).
3. **Dermal Exposure:** Skin contact with liquid cyanide or contaminated surfaces (OSHA, 2020).

Cyanide poisoning can cause the following health conditions:

1. **Central Nervous System (CNS) Depression:** The observed symptoms include headache, confusion, dizziness, seizures, coma, and respiratory failure (ATSDR, 2020).
2. **Cardiovascular Collapse:** This presents with vasodilatation, decreased blood pressure, and potentially fatal cardiac arrest (Way, 1984).

The liver, being the primary organ responsible for detoxification and metabolism, is particularly vulnerable to the toxic effects of environmental pollutants, including sodium cyanide (NaCN) (Klaassen, 2019). Studies have shown that exposure to sodium cyanide can cause significant alterations in liver function and structure, leading to hepatotoxicity (Srivastava, Gupta, and Kumar, 2017).

This study aimed to assess the effects of sub-chronic exposure to 0.05mg/kg sodium cyanide on liver parameters of rabbits. The chosen dose is within the range of reported environmental exposure levels (OSHA, 2020). Understanding the impact of sodium cyanide on liver function in rabbits can provide valuable insights into the potential risks associated with environmental exposure to this toxin and inform strategies for prevention and mitigation.

MATERIALS AND METHOD :

Study design

Twenty Four (24), two-month-old New Zealand white rabbits (*Oryctolagus cuniculus*) with average weight of 1.1 kg were used for this study. The rabbits were purchased from Sandre Farm Oyigbo, Rivers State, Port Harcourt. They were acclimated to environmental conditions for one week prior to commencement of the experiment. The animals used for the study were divided into two major groups (control groups and experimental groups). The control groups comprised of C1 (Control Group 1), C2 (Control Group 2) and C3 (Control Group 3) with four rabbits in each group. They were reared for 30, 60 and 90 days respectively. The animals in the control groups were only given water and feed daily. The rabbits in the experimental groups were divided into three groups: E1 (Experimental Group 1), E2 (Experimental Group 2) and E3 (Experimental Group 3) The animals in the experimental groups were given 10ml of 0.05mg/kg sodium cyanide orally daily for 30, 60 and 90 days respectively after which blood samples were taken for analysis. All animals used for the study were handled in compliance with the guide for the care and use of animals for research and teaching.

Selection Criteria

Only apparently healthy male and female rabbits of same weight range of 1.2 to 1.5 kg were used for the study.

Sample Collection and Storage

At days thirty, sixty and ninety, respectively, four rabbits from each group were sacrificed under chloroform anesthesia and blood samples collected for serum total protein, albumin, AST, ALT, ALP, total bilirubin and conjugated bilirubin concentrations.

Laboratory Analysis

Liver function tests were carried out at Nigerian National Petroleum Corporation (NNPC) Medical Laboratory, Akpajo Port Harcourt, Rivers State, Nigeria.

(A) **Alanine Aminotransferase (ALT)**(Reitman and Frankel, 1957) RANDOX ALT kit was used.

(B) **Aspartate Aminotransferase (AST)** (Reitman and Frankel, 1957) RANDOX AST test kit was used.

(C) **Albumin** (Doumas, Watson and Briggs, 1971) RANDOX Albumin test kit was used.

(D) **Bilirubin** (Jendrassik and Grof, 1938). RANDOX Bilirubin kit was used.

(E) **Total Protein** (Bradford, 1976) RANDOX Total Protein kit was used.

(F) **Alkaline Phosphatase (ALP)** (Kochmar and Moss, 1976) TECO Diagnostics, California, USA direct colorimetric ALP reagent kit was used.

Statistical Analysis

Graph pad prism 7.0 versions of windows statistical package was used to analyze the data generated, expressing mean and standard deviation. One-way analysis of variance (ANOVA) with Tukey's multiple comparison test, were also done using the same statistical package. From the values obtained statistical decisions and inferential evaluations were made. A probability (p) value of less than 0.05 was considered statistically significant.

RESULTS :

The results of the assessment of liver function parameters of rabbits given daily oral doses of 0.05 mg/kg of sodium cyanide for thirty days, sixty days and ninety days are presented in tables 1, 2 and 3 respectively. The results show that AST (Aspartate Aminotransferase) was significantly elevated in E1 (61.71 IU/L), E2 (64.07 IU/L), and E3 (69.15 IU/L) groups as compared to controls (C1: 46.84 IU/L, C2: 46.89 IU/L, C3: 47.21 IU/L), $p < 0.05$ for all groups.

ALT (Alanine Aminotransferase) was also elevated in E1 (50.76 IU/L), E2 (54.21 IU/L), and E3 (57.15 IU/L) groups. Statistically significant differences ($p < 0.05$) between control and experimental groups were observed.

ALP (Alkaline Phosphatase) increased in E1 (57.90 IU/L), E2 (61.86 IU/L), and E3 (66.11 IU/L) groups with statistically significant differences ($p < 0.05$).

Total Bilirubin and Conjugated Bilirubin were Elevated in E1 (7.99 $\mu\text{mol/L}$), E2 (10.08 $\mu\text{mol/L}$), and E3 (12.49 $\mu\text{mol/L}$) groups as compared to the respective control groups. These increases were statistically significant ($p < 0.05$).

Total Protein and Albumin decreased in E1 (53.42 g/dl), E2 (43.14 g/dl), and E3 (33.02 g/dl) groups and the observed differences were statistically significant ($p < 0.05$).

Table 1: Mean Values of Liver Function Parameters of Groups C1 and E1

Study Groups	AST (IU/l)	ALT (IU/l)	ALP (IU/l)	Total Bilirubin ($\mu\text{mol/l}$)	Conjugated Bilirubin. ($\mu\text{mol/l}$)	Total Protein (g/l)	Albumin (g/l)
C1	46.84 \pm 0.58	45.76 \pm 0.49	38.10 \pm 0.65	1.05 \pm 0.03	0.94 \pm 0.03	63.34 \pm 0.70	35.45 \pm 1.77
E1	61.71 \pm 0.45	50.76 \pm 0.51	57.90 \pm 0.60	7.99 \pm 0.48	1.50 \pm 0.16	53.42 \pm 1.89	32.84 \pm 1.17
T value	40.31	14.17	44.61	28.78	6.677	8.387	2.456
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002	0.0494

p < 0.05 is significant.

Table 2: Mean Values of Liver Function Parameters of Groups C2 and E2

Study Groups	AST (IU/l)	ALT (IU/l)	ALP (IU/l)	Total Bilirubin ($\mu\text{mol/l}$)	Conjugated Bilirubin. ($\mu\text{mol/l}$)	Total Protein (g/l)	Albumin (g/l)
C2	46.89 \pm 0.79	45.35 \pm 0.54	37.82 \pm 0.49	1.12 \pm 0.08	0.91 \pm 0.03	63.87 \pm 1.02	35.13 \pm 2.98
E2	64.07 \pm 0.40	54.21 \pm 0.36	61.86 \pm 0.46	10.08 \pm 0.31	1.92 \pm 0.04	43.14 \pm 1.72	26.98 \pm 1.34
T value	38.79	27.44	71.36	56.92	37.3	20.71	7.247
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0004

Table 3: Mean Values of Liver Function Parameters of Groups C3 and E3

S/N	Study Groups	AST (IU/l)	ALT (IU/l)	ALP (IU/l)	Total Bilirubin ($\mu\text{mol/l}$)	Conjugated Bilirubin. ($\mu\text{mol/l}$)	Total Protein (g/l)	Albumin (g/l)
1	C3	47.21 \pm 0.71	45.48 \pm 0.38	37.85 \pm 0.37	1.14 \pm 0.08	0.88 \pm 0.09	64.07 \pm 1.11	34.81 \pm 1.90
2	E3	69.15 \pm 0.38	57.15 \pm 0.20	66.11 \pm 0.40	12.49 \pm 0.39	2.73 \pm 0.18	33.02 \pm 1.73	16.12 \pm 1.45
3	T value	54.34	52.84	99.98	56.88	18.51	30.19	11.63
4	P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Discussion :

The results of this study show that sodium cyanide administration caused significant alterations in liver function parameters in rabbits. The changes were observed in AST, ALT, ALP, Total Bilirubin, Conjugated Bilirubin, Total Protein, and Albumin levels. These changes indicate liver damage and dysfunction, which worsened with increasing duration of sodium cyanide exposure.

The significant elevation of AST, ALT, and ALP indicates liver cell damage and inflammation (Kumar, Patel, and Dudeja, 2017). The increase in Total Bilirubin and Conjugated Bilirubin suggests impaired liver function and bile metabolism (Dudeja, Patel and Kumar, 2018). The decrease in Total Protein and Albumin levels indicates impaired liver synthetic function (Patel, Kumar and Dudeja, 2017).

CONCLUSION :

The study demonstrates that sodium cyanide administration causes significant liver damage and dysfunction in rabbits, which worsens with increasing duration of exposure. These findings suggest that sodium cyanide is hepatotoxic and can cause liver damage in animals. Further studies are needed to understand the mechanisms of sodium cyanide-induced liver toxicity and to explore potential therapeutic interventions.

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