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Research Paper

Effects of Agro-based Adsorbents on the Biochemical Profiles of Wistar Rats Exposed to Cyanide

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ABSTRACT

Background: Cyanide is a very toxic chemical that reacts with the ferric cytochrome oxidase in the mitochondrial system to form a stable complex. This complex inhibits the process of oxidative phosphorylation, thereby interrupting aerobic respiration in the organism. It is postulated that activated charcoal (AC) intercepts the ingested cyanide in the gastrointestinal tract before it is absorbed into the system.

Methods: A single dose of 3 mg/kg body weight of potassium cyanide (KCN) was orally administered to the rats in each of the five groups, each consisting of 6 rats. After 15 minutes, all rats in each group were given AC from different agro-based materials. The control group (group 1) received standard commercial AC orally at 1 g/kg. group 2 received AC from plantain peels, group 3 received AC from castor oil seed shell, group 4 received AC from coconut shell and group 5 received a combination of AC from plantain peels, castor oil seed shell, and coconut shell. Blood samples were collected sequentially from rats in each group for biochemical assays using standard procedures.

Results: The control group, which received KCN and standard commercial AC, exhibited the highest alanine transaminase (ALT) value (60.09±0.10 U/L) on day seven. Similarly, the highest aspartate transaminase (AST) value (196.28±0.72 U/L) was observed in the control group. Alkaline phosphate (ALP) levels followed a similar pattern. On day seven, the serum creatinine levels were 3.81±0.11 mg/dL for group 1 and 3.45±0.05 mg/dL for group 5. Subsequently, all biochemical parameters decreased after day 7, with the lowest levels recorded in rats that received AC derived from coconut shells.

Conclusion: The administration of locally prepared agro-based adsorbents to Wistar rats after exposure to sublethal doses of cyanide significantly mitigated the effects of the cyanide on the liver, kidneys, and heart, as indicated by the biochemical parameters of the albino Wistar rats in the study.

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Introduction

Cyanide is especially toxic to cells and organs with high metabolic demands. These toxic effects lead to tremors, respiratory system depression, tonic-clonic seizures, loss of consciousness, and ultimately, fatality [1-4]. At physiological pH, a larger proportion of the molecule exists in the non-dissociated form, facilitating its ability to traverse cell membranes for absorption into the system, thereby inducing toxicity [5-7].

Exposure to cyanide markedly caused a significant reduction in the generation of energy products and adenosine triphosphate both in living cells and tissue cultures [7-9]. The inhibition of mitochondrial Complex IV is clearly evident in various tissues ex vivo [10-14]. Protecting animals from the toxic effects of cyanide is achievable by diverting the cyanide before it interacts with the cytochrome enzyme [15, 16]. Agricultural waste is typically an ideal option for producing commercial activated charcoal (AC) due to its high specific surface area, stability, effective adsorption capacities, straightforward production process, and cost-effectiveness [17, 18].

AC is the most frequently used non-specific binding agent in clinical practice [19]. Several distinctive qualities contribute to the effectiveness of activated carbons, such as pore structure, functional groups, ash content, carbon yield, bulk density, methylene blue number, and iodine number [20-23].

Materials and Methods

The chemicals used were of technical and analytical grade, purchased by Sigma Aldrich, Germany. The doses of the potassium cyanide (KCN) and AC used in the study were selected based on previous studies [24, 25].

Preparation of samples

All agricultural biomass for the preparation of AC (plantain peels, coconut shells, edible clay, rice husks, and castor oil seed shells) was processed using the method outlined by Subramani and Revathi [26] with minor modifications.

Chemical activation and carbonization

Each sample was divided into three portions of 50 g each and serially activated with 100 mL of 10% 0.5 mol /dm^3 $ZnCl_2$, 500 mL of 0.3 mol/dm^3 H_3PO_4 and 500 mL of 0.5 mol/dm^3 HNO_3 [26].

The in vivo experimental design

Thirty male Wistar rats weighing 180-200 g were used in this experiment. The rats were randomly divided into five groups of six rats each. Each group received a single dose of one of the carbon samples, standard commercial AC, or a combination of the three prepared adsorbents at a dose of 1 g/kg following the administration of KCN at a dose of 3 mg/kg via an orogastric gavage tube. Blood samples were collected via ocular puncture from the rats at baseline, day 2, day 7, day 14 and day 21 for biochemical analysis.

The groups were as follows:

Group 1: This group received feed, water, KCN and standard AC; group 2: This group received KCN and activated carbon samples prepared from plantain peels activated with zinc chloride; group 3: This group received KCN and activated carbon samples prepared from castor oil seed shells activated with nitric acid; group 4: This group received KCN and activated carbon samples prepared from coconut shells activated with phosphoric acid; group 5: This group received a combination of the three locally prepared AC samples.

The Randox 240 Biochemistry Analyzer kit was used for the biochemical analysis of the blood samples from the Wistar rats using the manual provided by the manufacturer.

Data analysis

Data were analyzed by one-way analysis of variance (ANOVA), followed by Bonferroni's post-hoc test using SPSS software, version 24. $P<0.05$ were considered to be statistically significant.

Results

Table 1 shows the effect of treating KCN ingestion with the different AC samples on alanine transaminase (ALT) levels in Wistar rats. The highest ALT values across all rat groups were observed on day seven of the experiment. The control group (group 1) recorded the highest ALT level on day 7 at 60.09±0.10 U/L.

Table 2 shows the effect of treating KCN ingestion with the different AC samples on aspartate transaminase (AST) levels in Wistar rats. The AST levels increased from baseline and reached maximum levels in all the groups on day seven of the experiment, and then decreased but did not return to baseline levels. The control

group exhibited the highest AST level on day seven at 196.28±0.72 U/L.

Table 3 shows the effect of treating KCN ingestion with the different activated AC samples on alkaline phosphate (ALP) levels in Wistar rats. The ALP levels increased from baseline and peaked on day seven of the experiment. Subsequently, ALP levels began to decrease but did not return to baseline levels.

Table 4 shows the effect of treating KCN ingestion with different AC samples on the urea levels in Wistar rats. There was a consistent increase in urea levels across all groups, peaking on day seven of the experiment. Following this peak, the values decreased but did not reach baseline levels.

Table 5 depicts the impact of treating KCN ingestion with AC on creatinine levels in Wistar rats. The highest serum creatinine levels were observed on day seven of the experiment. On day seven, the serum creatinine level was 3.81±0.11 mg/dL for group 1 and 3.74±0.02 mg/dL for group 2.

Table 6 shows the effect of treating KCN ingestion with AC on lactate dehydrogenase (LDH) levels in Wistar rats. The highest LDH values across all rat groups were observed on day seven of the experiment.

Table 1. Effect of treating KCN ingestion with different AC samples on ALT levels (U/L) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	16.27±0.01	18.65±0.02	12.95±0.05**	14.49±0.07	19.92±3.02
Day 2	48.75±0.50	43.55±1.00*	47.55±0.20*	43.31±0.20*	47.36±0.10**
Day 7	60.09±0.10	52.02±0.50***	51.40±0.55***	58.16±0.45**	50.08±0.54***
Day 14	36.87±0.10	33.53±0.03***	34.61±0.26***	33.03±0.03***	30.81±0.19***
Day 21	19.57±0.34	24.23±0.44***	18.67±0.33***	18.48±0.48**	21.35±0.34***
F	6811.5	348.1	2639.4	3860.1	83.14
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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Table 2. Effect of treating KCN ingestion with different AC samples on AST levels (U/L) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	82.05±0.05	96.16±0.25***	94.48±0.41***	86.88±0.25	88.66±0.84***
Day 2	178.9±0.64	170.06±0.45***	162.52±0.00***	174.03±0.58**	160.24±0.76***
Day 7	196.28±0.72	186.53±0.70***	183.06±0.80***	180.78±0.43***	176.13±0.12***
Day 14	162.74±0.46	145.55±0.09***	152.15±0.56***	150.06±0.49***	134.71±0.45***
Day 21	100.46±0.32	104.98±0.65***	106.99±0.01***	110.38±0.63***	98.05±0.07***
F	113317.5	4680	10576.0	3448.9	2452.0
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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Table 3. Effect of treating KCN ingestion with different AC samples on ALP levels (U/L) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	94.34±0.34	88.29±0.29	76.03±0.11***	80.15±0.69***	92.53±0.50*
Day 2	140.60±0.20	152.40±0.34***	164.29±0.85***	146.66±0.34***	158.71±0.29***
Day 7	194.39±0.56	184.55±1.15***	188.95±0.45***	190.45±0.65***	180.03±0.80***
Day 14	140.80±0.80	127.20±0.70***	129.2±0.50***	130.77±0.77***	123.39±0.39***
Day 21	104.11±0.32	103.05±0.75***	121.8±0.77***	128.75±0.45***	112.05±0.45***
F	3001.7	23995.6	13720	15454.7	172403
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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Discussion

Our study showed marginally increased levels of ALT enzyme activity in the rats. Other studies have shown abnormally elevated levels of liver enzymes when animals were exposed to cyanide without intervention using antidotes or binding agents [27-29]. Conversely, some studies have reported no increase in liver enzyme levels [30-32].

The AST levels increased from baseline and peaked in all groups on day seven of the experiment, after which its levels declined but did not return to baseline levels. The results presented here indicated lower values compared to those in previous studies that investigated the impact of cyanide on the biochemical parameters in Wistar rats without intervention [30, 31]. In contrast, Anwar et al [31] and Hassan et al [32] reported no disruption in liver enzyme activity after exposing rats to certain toxins.

Generally, the highest ALP levels were observed on day seven, while the lowest levels were noted on day 21, apart from the baseline values. T Serum alkaline levels were elevated in other studies that examined the biochemical profiles of rats post-exposure to toxicants [30-33]. However, these findings contrast with those of other studies where the biochemical parameters remained within normal limits during the experiment [32-34].

The lowest urea levels were observed in rats that received the combination of the prepared activated carbon samples. This finding is in agreement with findings from previous studies, in which the urea levels were found to be elevated in the rats exposed to toxic substances,

Table 4. Effect treating KCN ingestion with different AC samples on urea levels (mg/dL) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	20.54±0.54	28.62±0.49***	23.45±0.23***	18.01±0.37*	22.00±0.34***
Day 2	53.12±0.53	58.43±0.56**	58.73±0.14**	69.69±0.26***	72.59±0.31
Day 7	70.80±0.74	62.73±0.56***	66.07±0.35***	77.19±0.82**	74.68±0.18***
Day 14	51.36±0.36	48.69±0.11*	53.66±0.04*	54.61±0.31**	58.99±0.69***
Day 21	38.41±0.41	34.87±0.09**	32.69±0.21*	30.36±0.33**	32.56±0.41**
F	49.0	1339.6	9543.6	5599.7	1816.2
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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Table 5. Effect of treatment with the test and standard AC after KCN ingestion on creatinine levels (mg/dL) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	0.43±0.01	0.60±0.01**	0.54±0.02***	0.51±0.01***	0.58±0.04**
Day 2	0.97±0.02	0.95±0.04	0.94±0.03**	0.95±0.02***	0.90±0.04***
Day 7	3.81±0.11	3.74±0.02*	3.56±0.03**	3.67±0.01**	3.45±0.05***
Day 14	2.92±0.03	2.80±0.03**	2.72±0.03**	2.44±0.04***	2.34±0.01***
Day 21	1.24±0.41	1.27±0.04	1.44±0.01**	1.34±0.02	1.44±0.02**
F	16850	1242.0	183.7	158.3	154.5
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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including cyanide [31, 33, 34]. This outcome is likely attributed to the impact of the prepared adsorbents on the absorption of cyanide into the system.

The results of this study are consistent with findings from previous studies where creatinine levels were also elevated in some rats exposed to cyanide [31, 33]. However, the findings of this study differ from those of other studies, in which there was no increase in the biochemical parameters following the use of scopoletin in cyanide-exposed rats [32, 33]. The increased serum levels of creatinine may result from diminished renal excretion [32-34].

The LDH levels declined after day seven but did not return to baseline levels in all groups of rats. The lowest level on day 21 was observed in rats that received AC prepared from the three agro-based sources. The rise in blood LDH levels in this study was likely due to injuries to the cardiac tissues caused by the cyanide administered to the rats in the experiment. Previous studies, however, recorded a more significant increase in LDH levels [33, 34].

Conclusion

Table 6. Effect of treatment with the test and standard AC after KCN ingestion on LDH levels (U/L) in Wistar rats

Group	Mean±SD				
	1	2	3	4	5
Baseline	150.78±0.45	172.26±0.51***	165.32±0.01***	176.63±0.03***	152.53±0.47***
Day 2	342.79±0.22	268.84±0.69***	320.13±0.14***	294.83±0.73***	282.29±0.22***
Day 7	389.39±0.19	324.08±0.08***	364.18±1.62**	338.35±0.52***	320.64±0.87***
Day 14	247.31±0.08	236.42±1.03***	242.94±0.40***	275.21±0.62***	223.44±0.34***
Day 21	190.10±0.36	184.50±0.50***	178.62±0.62***	203.04±0.42***	156.90±0.46***
F	16850.0	1242.00	183.7	158.3	154.48
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05, **P<0.01, ***P<0.0001 compared to the control group.

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The administration of locally prepared agro-based adsorbents to the Wistar rats after exposure to sub-lethal doses of cyanide significantly alleviated the effects of the cyanide on the liver, kidneys and heart, as demonstrated by the biochemical parameters of the Wistar rats in the study.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the University of Nigeria Teaching Hospital (Code: NHREC/05/01/2008B-FWA00002458-IRB00002323).

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Authors' contributions

Conceptualization and study design: Ofor Casimir Chijioke and Shu Elvis Neba; Data collection: Ofor Casimir Chijioke, Nwakelu Benjamin Nwaforcha, Ohanme Eugene Ohams, and Akuodor Godwin Christian; Writing the original draft: Ofor Casimir Chijioke, Shu Elvis Neba, Ofonakara Uzochukwu, Anele Donatus Onyebuchi and Aja Daniel Ogbonnaya; Review & editing: Ofor Casimir Chijioke and Shu Elvis Neba.

Conflict of interest

The authors declared no conflict of interest.

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