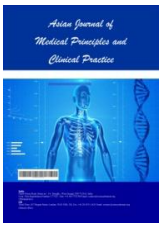

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Toxicological Effects of Overdose of Some Herbal Bitters Commonly Consumed in South Southern Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author KNEA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KNEA, ONB and NPB managed the analyses of the study. Authors BHO, RRU and QES managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The aim of this study was to evaluate the toxicological effects of overdose of Action Bitters and Goko Cleanser on hepatic, renal and haematological indices.
Methodology: Thirty-five (35) male albino wistar rats were divided into seven groups of five rats each. The six treatment groups were given the herbal extracts for four weeks while the control group was given distilled water. The study was carried in the Department of Medical Laboratory Science, Rivers State University, Port Harcourt, between June and August, 2019. Biochemical parameters were assayed using Mindray biochemistry analyzer while haematological parameters were assayed using Sysmex analyzer.

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Results: There were significant increases in hepatic parameters (AST, ALT and ALP), renal parameters (Urea and Creatinine) and significant decreases in haematological indices (PCV and HB) in the treated groups, except for the normal dose weekly treatment group.
Conclusion: Long-term use or overdose of the herbal mixtures can lead to alterations in hepatic, renal and haematological indices.

Keywords: Action bitters; Goko Cleanser; herbal medicine; toxicological effects; overdose; Nigeria.

1. INTRODUCTION

Herbal medicines are herbal preparations or products which contain plant parts or some other plant materials as active ingredients [1]. Bitters are herbal infusions that are made mainly from aromatics and botanicals, and includes any combination of herbs, roots, barks, leaves or other parts of plants [2]. It has been reported that about 80% of the population in the developing countries use traditional medicine [3] and bitters are an example of herbal formulations that have gained such wide acceptance and use.

Herbal bitters are usually poly-herbal liquid preparations which contain bitter herbs. Apart from the liquid forms, bitters can also be manufactured in other dosage forms (capsules, tablets and tinctures) depending on the manufacturer. Generally, they are used as carminatives, aperitifs and to improve digestion [4]. Bitters are being used in different healing systems [5], as they are believed promote digestion, appetite [6], libido, as well as boost body energy. They are also attributed with some medicinal effects; as they are believed to be effective in management of allergies, anaemia, metabolic and immunological conditions, improving immunity, wound healing, and blood clotting [6].

Herbal Bitters contain herbal extracts and alcohol, and are largely consumed by especially young people, because they are believed to restore and boost sexual energy [7].

2. MATERIALS AND METHODS

2.1 Experimental Animals

Thirty-five (35) male Albino Wistar rats, weighing 120-130 g, were used for this study. They were housed under standard conditions and were allowed access to feed and water *ad libitum.*

2.2 Herbal Formulations

The two herbal mixtures used for this study were Action Bitters (a product of Intercontinental Distillers Limited, Nigeria) and Goko Cleanser (a product of Goko Herbs W.A. Limited, Nigeria).

2.3 Dose Determination

The doses were calculated using OECD's Guidelines (OECD, 2001) [8].

The daily doses were extrapolated from the manufacturers' dose of 100 ml/70 kg body weight.

2.4 Experimental Design

Thirty-five (35) rats were divided into five (5) groups (you have seven groups) of five (5) rats each as follows:

Group A1 rats received 0.1 ml/kg body weight of Action Bitters orally once daily for four weeks.

Group A2 rats received 0.1 ml/kg body weight of Goko Cleanser orally once daily for four weeks.

Group B1 rats received 0.2 ml/kg of Action Bitters orally once daily for four weeks.

Group B2 rats received 0.2 ml/kg of the Goko Cleanser orally once daily for four weeks.

Group C1 rats received 0.2 ml/kg of the Action Bitters orally once weekly for four weeks.

Group C2 rats received 0.2 ml/kg of the Goko Cleanser orally once weekly for four weeks.

Group D served as control group, and received distilled water.

The treatment lasted for 28 days. On the 29th day, after an overnight fast, the rats were sacrificed by puncture of the jugular vein. Blood samples were collected into plain bottles for biochemical assays and K_3EDTA bottles for haematological assays.

2.5 Biochemical Analysis

The biochemical parameters, alkaline phosphatase (ALP), aspartate transaminase

(AST), alanine transferase (ALP), urea and creatinine were assayed using Mindray biochemistry autoanalyzer (Model BS120, china) while haematological parameters, PCV and heamoglobin were determined using Sysmex KX-21n auto-analyser, Japan.

2.6 Statistical Analysis

Data from this study were analyzed using SPSS version 23. The statistical tool used was ANOVA. P-values less than 0.05 were considered statistically significant. Values are expressed as mean ± SD.

3. RESULTS

The qualitative phytochemical analysis of herbal mixtures shows the presence of carotenoid, saponins, alkaloids, flavonoids and tannins.

The levels of alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transferase (ALT), Urea and Creatinine were significantly higher compared to the levels in control group. However, there were no significant differences in packed cell volume (PCV) and haemoglobin (Hb) levels.

There were no significant differences in the levels of the parameters between the treated groups and the control group.

The levels of all the parameters were significantly higher in the treated rats compared to the levels in the control group.

The levels of ALP, AST, ALT, Urea and Creatinine were significantly higher in the treated rats compared to the levels in control group. However, there were no significant differences in PCV and Hb levels.

4. DISCUSSION

This study evaluated some biochemical and haematological parameters in male albino wistar rats treated with two herbal mixtures in order to investigate their toxicological effects. This study was designed to model the pattern of consumption of the herbal mixtures, that is, regular consumption (normal dose daily and double dose daily) and occasional consumption (normal dose weekly and double dose weekly).

The results from this study indicate that, at normal dose daily treatment with the herbal mixtures there were significantly raised levels of hepatic and renal parameters. However, there were no significant differences in the haematological parameters. The normal dose weekly treatment did not cause any significant changes in the parameters. This is probably because there was sufficient time interval between consecutive consumption to allow for the body to metabolize the herbal mixtures.

The double dose daily treatment produced significant changes in the hepatic, renal and haematological parameters. ALP, AST, ALT, Urea and Creatinine were significantly higher than the control while the PCV and haemoglobin were significantly lower compared to the control. The double dose weekly treatment gave similar increases in ALP, AST and ALT but no significant changes in PCV and haemoglobin levels.

The observed significant increases in the liver enzymes are indications that the herbal mixtures could be toxic at the dose used for this study when frequently consumed. This may mean that there may be alteration in the structure and or function of the liver [9]. Other researchers have reported similar findings [10]. The significant reduction in the haematological parameters indicate that the herbal mixtures can reduce the production of erythrocytes [11].

The changes in the parameters could also be due to systemic inflammation, as herbal bitters have been reported to cause inflammation [12].

Table 1. Qualitative phytochemical analysis

Phytochemical	Action bitters	Goko Cleanser
Carotenoids	+	+
Saponins	+	+
Alkaloids	+	+
Flavonoids	++	+
Tannins	+	+

Table 2. Comparison of Mean ± SD of parameters for normal dose daily of herbal mixtures

Herbal mixture	ALP (U/L)	AST (U/L)	ALT (U/L)	UREA (mmol/L)	CREAT (µmol/L)	PCV(%)	Hb(g/dl)
Action Bitters	65.67± 4.93a	125.67 ± 4.58ab	57.00± 2.65a	5.10± 0.95a	64.67± 3.79ab	40.33 ±4.62	14.63± 1.46
Goko Cleanser	67.00 ± 5.81a	129.00 ± 7.94ab	58.67± 2.89a	5.63± 0.31a	58.00± 5.29 ab	40.67± 4.51	13.23± 1.51
Control	57.33± 1.53	114.33 ± 3.51	41.67± 2.89	4.47± 0.15	54.67± 2.52	42.00± 2.65	13.67± 0.91
p-value	0.001	0.08	0.03	0.04	0.01	0.18	0.46
F-value	27.525	12.273	6.811	6.205	12.027	2.301	0.889

ANOVA followed by Tukey multiple comparisons. Values with different superscripts are significantly different (p<0.05)

Table 3. Comparison of Mean ± SD of parameters for normal dose weekly of herbal mixtures

Herbal mixture	ALP (U/L)	AST (U/L)	ALT (U/L)	UREA (mmol/L)	CREAT (µmol/L)	PCV(%)	Hb(g/dl)
Action Bitters	59.00± 1.00	112.02± 3.46	44.00± 2.65	4.70± 0.53	56.33± 2.52	43.33± 3.51	14.43± 0.75
Goko Cleanser	57.00± 6.00	115.20± 2.00	44.67± 2.89	4.43± 0.58	55.50± 3.00	44.01± 3.46	15.96± 1.10
Control	57.33± 1.53	114.33± 3.51	41.67± 2.89	4.47± 0.15	54.67± 2.52	42.00± 2.65	13.67± 0.91
p-value	0.12	0.50	0.44	0.21	0.11	0.18	0.06
F-value	32.805	0.788	0.944	33.754	22.892	3.968	4.766

ANOVA followed by Tukey multiple comparisons. Values with different superscripts are significantly different (p<0.05)

Table 4. Comparison of Mean ± SD of parameters for double dose daily of herbal mixtures

Herbal mixture	ALP (U/L)	AST (U/L)	ALT (U/L)	UREA (mmol/L)	CREAT (µmol/L)	PCV(%)	Hb(g/dl)
Action Bitters	69.67± 5.51ab	127.67± 2.89a	55.00± 2.00ab	5.57± 0.25a	67.00± 1.73a	39.33± 2.08a	11.07± 0.68a
Goko Cleanser	62.02± 2.10ab	129.00± 6.93a	52.67± 3.06ab	5.27± 0.61a	66.01± 5.20a	38.33± 3.06a	10.10± 1.01a
Control	57.33± 1.53	114.33± 3.51	41.67± 2.89	4.47± 0.15	54.67± 2.52	42.00± 2.65	13.67± 0.91
p-value	<0.001	0.03	0.003	0.01	0.001	0.03	0.03
F-value	57.791	4.034	16.908	9.587	27.312	6.645	6.355

ANOVA followed by Tukey multiple comparison. Values with different superscripts are significantly different (p<0.05)

Table 5. Comparison of Mean ± SD of parameters for double dose weekly of herbal mixtures

Herbal mixture	ALP (U/L)	AST (U/L)	ALT (U/L)	UREA (mmol/L)	CREAT (µmol/L)	PCV(%)	Hb(g/dl)
Action Bitters	64.67± 4.62ab	124.33± 1.53ab	53.00± 7.00a	5.63± 0.31a	68.01± 3.61a	46.67± 2.89	15.23± 0.92
Goko Cleanser	60.33± 5.03ab	122.33± 5.85ab	54.00± 3.46a	5.67± 0.06a	66.67± 5.03a	48.00± 5.00	15.63± 0.95
Control	57.33± 1.53	114.33± 3.51	41.67± 2.89	4.47± 0.15	54.67± 2.52	42.00± 2.65	13.67± 0.91
p-value	<0.001	0.04	0.04	0.001	0.03	0.09	0.09
F-value	36.578	1.239	6.091	29.194	16.545	3.671	3.769

ANOVA, followed by Tukey multiple comparison. Values with different superscripts are significantly different (p<0.05)

5. CONCLUSION

Findings from this study indicate that long-term consumption of the herbal mixture or their abuse can affect the liver, kidney and erythropoiesis. Long-term use or overdose of the herbal mixtures can lead to alterations in hepatic, renal and haematological indices.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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