



Effect of Oral Consumption of Action Bitters on Renal Indices of Apparently Healthy Subjects in Port Harcourt Metropolis

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Authors' contributions

This work was carried out in collaboration among all authors. Author HAW designed the study, wrote the protocol and the first draft of the manuscript. Author EE collected the samples. Author IE managed the literature search. Author EASB performed the statistical analysis. All authors managed the analyses of the study, read and approved the final manuscript.

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ABSTRACT

Action bitters has been seen not to have nephro-toxic effects on the kidney. However, this study evaluated the effects of sachet packaged action bitters on the kidney of apparently healthy subjects. Blood sample was collected from 20 subjects. Basal blood sample and the blood samples collected after 2 hours of intake of action bitters by subjects were analyzed. The parameters analyzed include sodium, potassium, urea and creatinine using the colorimetric method of analysis and results subjected further to statistical analysis using the GraphPad Prism Version 8.02. Basal results of the renal indices obtained showed the values to be; 144.16 ± 8.89 mmol/L, 3.81 ± 0.57 mmol/L, 25.70 ± 5.66 mg/dL and 1.05 ± 0.38 mg/dL for sodium, potassium, urea and creatinine

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respectively while the results obtained from the subjects two(2) hours after the intake of action bitters were; 128.18 ± 11.05 mmol/L, 2.93 ± 0.57 mmol/L, 25.34 ± 4.74 mg/dL and 1.51 ± 0.75 mg/dL for sodium, potassium, urea and creatinine values respectively. The comparison of the basal and treated sample showed significant differences in the values of sodium, potassium and creatinine ($P=0.05$) while the urea value was not significantly different. The mean value for sodium and potassium in the treated subjects were significantly decreased when compared to the value gotten at the basal state where the action bitter has not been consumed by the subject whereas the creatinine value was significantly increased in the sample of the treated subjects compared to the value of the basal sample. This implies that exposure to a higher dose of action bitters might be detrimental to renal function in the body hence, the dose of bitters and its consumption by humans should be monitored in order to protect against any adverse effect, and subsequent malfunctioning of the kidney.

Keywords: Action bitters; intake; apparently healthy subjects; renal function.

1. INTRODUCTION

Bitters are made up of numerous groups of chemical compounds extracted from the herbs and roots (medicinal plants) that have the common characteristics of a bitter taste, and act to increase the vital energy centers in the body [1,2]. The use of herbs (medicinal plants) in treatment of ailment has gained much publicity and recognition. Medicinal plants contain in them, parts and substances that can be used for synthesis of useful drugs. This has led to the repackaging of herbal bitters, blend of herbs, spices, roots and seeds as tonic and medicinal products. Bitters have been claimed to help heal piles/hemorrhoids and improve sexual function, enhance blood circulation, purification of blood by the kidneys, blood pressure regulation through arterial dilatation and prevent formation of kidney stones, cleanse the colon of impurities and have also been said to possess anti-tumour properties [3]. Bitters are also said to have anti-inflammatory [4], antibiotic and anti-fungal properties [5,6]. They have been said to ensure good digestion of fats and oils and proper functioning of the excretory system reduce accumulated fat, triglycerides and cholesterol levels thereby conferring on it hypolipidemic properties. They are said to reduce excess body fat, promote healthy weight loss, act as body detoxifier, hepatoprotective and enhancing its functions generally [7,8]. Bitters act on the pancreas thereby helping to normalizing blood sugar levels, promote the production and release of pancreatic enzymes [9].

Traditional diets in times past had more of bitter food as compared to modern diets full of sweeteners, as a result of this, Green (1991) desires that the medicinal side of bitters be seen in the light of preventing what he termed "the

bitter deficiency syndrome" of our era, which in his opinion is the predisposing factor to many ailments of our time [10]. The world's population is gradually diverting to the usage of herbal medicine because of the acclaimed effects in preventing and protecting against some ailments in the body [11]. The National Agency for Food and Drug Administration Control (NAFDAC) have even recognized and approve the sales of these bitters in the open market [12].

Action bitters is an herbal alcoholic beverage (liquid to consume, usually excluding water) that is made up of numerous groups of chemical compounds extracted from herbs and roots having several benefits on human [1]. Many considered these alcoholic bitters as a multipurpose medicine and they use it without considering its effects on the kidneys and/or other organs in the body. The rate of the intake of these alcoholic bitters in the last five years underscores it as an important contributory factor to kidney impairments [13,14]. Hence, it has become a public health intervention to reduce the consequences of the intake of alcoholic bitters. Many people use herbal remedies for the treatment of a wide range of diseases due to the claims of their efficacies by the manufacturers. However, there is little insight as to the mode of action and possible toxic effects of these popular herbal formulations on organs such as liver and kidney. This study aims at determining the effect of the consumption of Action bitters on the kidney of apparently healthy subjects.

2. MATERIALS AND METHODS

2.1 Study Population / Area

A total of 20 apparently healthy subjects who freely gave their consent and permission to

participate in this study were recruited from Port Harcourt. They comprised of 16 male and 4 female subjects. The purpose of the study was carefully explained to the subjects, all exclusion and inclusion criteria were also spelt out and they willingly consented to participate in the study.

2.2 Action Bitters

Action bitters produced by Intercontinental Distillers Limited, Ogun state, Nigeria were purchased from a reputed pharmacy store in Mile 3. The Action bitters were bought as liquid formulations in sachets of about 25 ml liquid content and stored at room temperature before administration to the subjects. The phytochemical component of the Action bitter is shown in Table 1 below.

Table 1. Phytochemical analysis of action bitters sachet

Components	Qualitative Strength
Alkaloids	+++
Flavonoids	++
Tannins	+
Cardiac glycosides	-
Phenols	++
Cardenolides	+
Terpenoids	-
Diterpenoids	-
Carbohydrate	
Sterols	-
Phlobatanins	+
Quinones	+
Oxalate	-

Table 1 shows the qualitative analysis of Action bitters.

2.3 Administration of the Action Bitters / Blood Collection

The subjects were made to fast overnight at least for a minimum of 7-8 hours. A 5 ml of blood was collected from the vein of each subject under

aseptic procedures. A basal sample was first collected, then after giving the subjects a sachet of the action bitters, they were asked to wait for a period of 2 hours before the next sample was collected. The blood was transferred into a heparinized vial, mixed properly, centrifuged and the plasma was separated into plain vials, preserved in the refrigerator for analysis of renal function indices.

2.4 Methods

Blood urea was analyzed using the Berthelot's Urease method [15]. Creatinine was estimated using Jaffe's method [16], while sodium estimation was done using colorimetric method [17] and potassium by colorimetric method [18]. Quality control sera were assayed along with the parameters analyzed. Standard operating procedures (SOP) were adhered to and good laboratory practices were observed. All the machines were checked and calibrated before usage. Readings were in triplicates and results expressed as mean \pm standard deviation using the GraphPad prism version 8.02. Values were considered significant at $P=0.05$.

3. RESULTS

The results of the analysis done in the blood samples collected are shown in Table 2.

Table 2 shows results of renal indices obtained in the subjects. The comparative analysis of the basal and 2 hours after intake of action bitters indicated significant difference in sodium, potassium and creatinine levels, while no significant difference was observed in the urea level.

4. DISCUSSION

The kidney is seen to be the site of accumulation of chemicals; hence urea and creatinine are sensitive and reliable biochemical indices for evaluation of renal function [19]. The significant

Table 2. kidney function test parameters of basal and that of 2 hours post sample of apparently healthy subjects

Parameters	Basal	2 hours after intake of Action bitters	T value	P value	Remark
Sodium (mmol/L)	144.16 \pm 8.89	128.18 \pm 11.05	0.1882	0.0001	S
Potassium (mmol/L)	3.81 \pm 0.57	2.93 \pm 0.57	0.4234	0.0001	S
Urea (mg/dL)	25.70 \pm 5.66	25.34 \pm 4.74	0.4057	0.8257	NS
Creatinine (mg/dL)	1.05 \pm 0.38	1.51 \pm 0.75	0.7362	0.0188	S

P=0.05 indicates significant difference, NS-Non significant, S=Significant

reduction seen in sodium value might suggest a significant effect on sodium pump that maintains the constancy of the extracellular concentration of potassium probably due to water deprivation.

Therefore, the significant reduction in sodium concentration after 2 hours of intake of Action bitters might be adduced to increased excretion of sodium resulting from rise in glomerular filtration rate (GFR). While the significant reduction in potassium level after 2 hours of intake of the herbal mixture may be attributed to decreased sodium re-absorption at the distal tubule of the kidney. The action of flavonoids in the content of this action bitters might be adduced as the reason for the observed decrease in the electrolyte values (potassium and Sodium), because it has been stated by [20] as another mechanism of action in the vasodilation of blood vessels thereby maintaining the action of the Renin-angiotensin aldosterone system in controlling and balancing electrolytes in the body. though in the study by Nwachuku and Elekima [1], there was no significant difference observed in potassium and sodium values of rats given action bitters. The dose or quantity of action bitter taken will reflect on the impart and observation seen in any renal interference of these parameters.

The significant increase seen in creatinine level in this study is in line with the work done in these studies [4,21] but disagreed with the findings of [22]. Extrapolating the results seen in rats to humans as shown in this study, the creatinine values in the subjects were increased as against what Anionye et al. [22] reported in their study, where the creatinine value of the rats treated with Action bitters showed no significant difference. There might be a possibility that the significant increase in creatinine value as observed in the subjects in this study might equally interfere with the renal functions since most people consume Action bitters for the acclaimed purpose of energy boosting. Meanwhile, Anayasor *et al.*, reported increased oxidative stress on the kidneys when anti-oxidant and anti-inflammatory properties of polyherbal preparations such as Swedish bitters, Yoyo bitters, Action bitters etc. were evaluated. This might be a contributing factor to the increased creatinine value observed since the composition of Action bitters are likened to these bitters used in their study [4] and the phytochemical analysis of action bitters (Table 1) shows its components to be rich in alkaloids, flavonoids, phenols amongst others which play vital roles in maintaining oxidative stability [23]

Also, in the study carried out by Elechi-Amadi et al. [24], there was an indication that consumption of action bitters altered the renal indices as an increased creatinine value was also observed. This corroborates with this study where we observed an increased creatinine level of the humans who took the sachet action bitters hence a misuse or overdose might complicate the renal functions if intake is not properly guided. Finally, the non-significant difference seen in urea value is in line with the work [22,25] but disagreed with the findings of the following authors [4,21]. Anionye et al. [22] reported that there was no significant difference in urea level and therefore super bitters did not interfere with renal capacity of the kidney to excrete metabolites though this was carried out in rats however, in this study where human subjects were used, the urea values were not significantly different in the treated group corroborating with the observations in the study. This study also corroborates the study done by Oforibika and uzor in rats where different doses of bitters were administered to rats and the urea levels evaluated showed no significant difference as observed in their study [26].

5. CONCLUSION

Due to the significant decreased levels in the electrolytes (sodium and potassium), Action bitters could be said to be effective in preventing any functional incapability of the renal system. However, they might be able to alter the renal function due to the significant increase observed in the creatinine level which is one of the indices for renal function.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline participant's consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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