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Research Article

The effect of *Rauwolfia vomitoria* extract on liver enzymes of potassium induced hepatotoxicity in adult wistar rats

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Abstract

The effects of *Rauwolfia vomitoria* extract on liver enzymes of potassium bromate induced hepatoxicity was carried out. Twenty eight wistar rats weighing between 210 – 270g were used. They were assigned to four groups A, B, C and D with seven rats in each group. Group A serves as control and received 0.4ml of distilled water, group B received 0.55ml of extract of *Rauwolfia vomitoria*, group C received 0.5ml of potassium bromated while group D received 0.55ml of extract and 0.5ml of potassium bromate. The oral administration lasted for twenty eight days between the hours of 12pm -5pm. Twenty four after the last administration, the animals were dissected. Liver tissues were weighed and evaluation of liver enzymes was carried out using randox kit method. The levels of mean asparte aminotransferase (ALT), alanin aminotransferase (ALT) and alkaline phosphotase in group C was significantly higher ($P<0.001$) than the control and groups B and D. This result shows that *Rauwolfia vomitoria* extract combined with potassium bromate suppressed the toxic effect of potassium bromate.

Keywords: *Rauwolfia vomitoria,* liver enzymes, potassium bromate, wistar rats

1. Introduction

Liver is the key organ regulating homeostasis in the body. It is involved with almost all the biochemical pathways related to growth, fight against disease, nutrient supply, energy production and reproduction. Because of its unique metabolism and relationship to the gastrointestinal tract, the liver is an important target for toxicity produced by drugs, xenobiotics and oxidative stress.[3] More than 900 drugs, toxins and herbs have been reported to cause liver injury and drugs account for 20–40% of all instances of fulminant liver failure.[1]

One of the plants of medicinal value from the humid tropics is *Rauwolfia vomitoria.* It is traditionally used in treatment of variety of ailment such as snakebites, fever and nervous disorders. In the absence of reliable liver protection drugs in modern medicine, a large number of medicinal preparations are recommended for the treatment of liver disorders and quite often claimed to offer significant relief. Attempts are being made globally to get scientific evidences for these traditionally reported herbal drugs. This scenario provides a severe necessity to carry out research in the area of hepatotoxicity[1].

The plant, *Rauwolfia vomitoria* belongs to the family apocynacea and its common names include serpent wood, Swizzler stick among others. The commonly used parts for herbal emedies are roots, root bark, leaves and stem bark. It is

called Ira in Igbo, Wadda in Hausa and Utoenyin in Efik.[12,14] The African species of the plant, *Rauwolfia vomitoria* had twice the amount of reserpine of the Indian species, *Rauvolfia serpetina*.[12] Reserpine which is a major constituent of antihypertensive drug is in Rauwolfia vomitoria in large quantity.

From 1931, Indian doctors researched on possible utilization of *Rauwolfia vomitoria* in neuro-psychiatry. The extract from this plant was first extracted by Swiss chemists in 1952 and becomes the first natural neuroteptic. Today, this plant is still the source of a lot of drugs used in psychiatry[2]. In traditional medicine, the roots and leaves of *Rauwolfia vomitoria* are brewed as tea and used in humans for treatment of hypertension, insanity, snakebite and cholera[4].

It adverse effects include; decreased heart rate and blood pressure, which is due to dilation of blood vessels. It also causes low sex drive, increase appetite, weight losss, swellings, stomach upset, hallucination, poor co-ordination, dizziness, impairment of physical abilities and psychotic depression.[14,15]

Over time, it has been discovered that potassium bromate is toxic and is a possible carcinogen in man[5]. Hence, this study aims at investigating the effects of rauwolfia vomitoria extract on liver enzymes of potassium bromate induced hepatotoxicity in adult Wistar rats.

2. Materials and Methods

2.1 Breeding of Animals

Twenty four Wistar rats were obtained from the animals house of the Pharmacy Department, Nnamdi Azikiwe University Agulu, Anambra state, Nigeria and bred in the Animal house of Nnamdi Azikiwe University, Nnewi campus, Anambra State, Nigeria. They were allowed for a period of ten days for acclimatization under normal temperature (27^0C -30^0C) before their weights were taken. They were fed with water and guinea feed pallets from Agro feed mill Nigeria Ltd.

2.2 Drug Preparation

Rawolfia vomitoria leaves were collected from Eket in Akwa Ibom State and was dried in an oven at a temperature of 50^oC and crushed using laboratory blender. Extraction was done using ethanol. Ethanol was poured into the grinded leafs of *Rauwolfia vomitoria* weighing 700g and was allowed to stay for twenty four hours. It was filtered into a stainless basin with a white cloth and placed in a water bath so as to dry up the ethanol. 300mg of this extract /kg body weight was dissolved in 10mls of distilled water and administered to the animals.

Potassium bromate was obtained from the Department of Biochemistry, Nnamdi Azikiwe University, Nnewi campus, Anambra State, Nigeria.

2.3 Experimental Protocols

The twenty animals were weighed and allocated into five groups of four animals each. The groups were designated as groups A, B, C, and D. Group A animals served as the control and received 0.4ml of distilled water. The experimental groups B, C and D received different doses of drugs as follows: Group B received 0.6ml of extract of *Rauwolfia vomitoria*, Group C received 0.5ml of potassium bromate, Group D received 0.55ml of extract + 0.5ml of potassium bromate. The drugs were administered once in a day between the hours of 12-5pm for a period of twenty eight days. The drugs were administered orally using intubations method. After the twenty eight day, the animals were weighed and their weight recorded.

Twenty four hours after the last administration, the animals were anesthetized under chloroform vapour and were dissected. Blood samples were collected by cardiac puncture using sterile syringes with needles. Blood for serum preparation was collected into sterile plain tubes without an anti-coagulant. Serum samples were separated from the clot by centrifugation at 3,000rpm for 5minutes using bench top centrifuge (MSE, Minor, England). Serum samples were separated into sterile plain tubes and were stored in the refrigerator for analysis. Liver tissues were removed from the animals and weighed. The activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phospotase (ALP) were determined using randox kit method.

3. Result

3.1 Morphometric Analysis of Body Weight

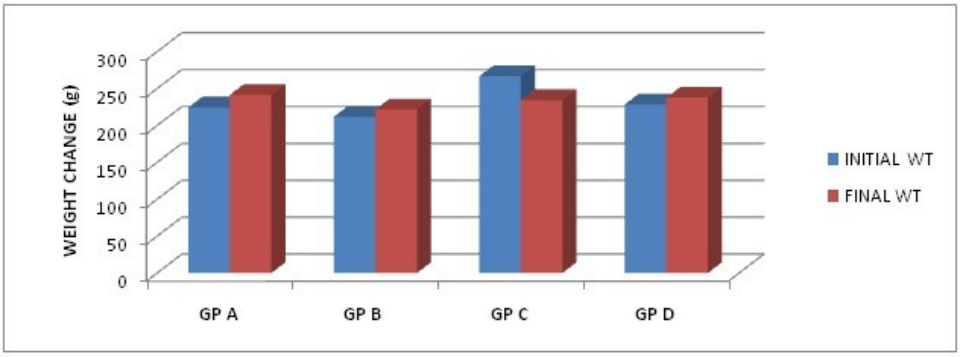
Table 1.0: Comparison of mean initial and final body weight and liver weight in all the groups (A, B, C & D)

Parameters	Group A	Group B	Group C	Group D	F-Ratio	PROB.OF SIG.
Initial Body Weight	224.40±4.79	211.75±4.64	266.75±7.63	228.50±8.96	68.230	<0.0001
Final Body Weight	241.50±6.60	221.50±10.66	234.25±8.53	237.65±10.01	30.510	<0.0001
Liver Weight	5.79±0.044	5.65±0.161	8.53±0.625	5.72±0.072	53.84	<0.0001

(Mean ± SEM given for each measurement)

The final body weight for group A (Control), groups B, and D showed a statistically significant increase (P<0.001). The initial body weight for group C treated with potassium bromate was significantly higher (P<0.001) than the control and other experimental groups (B and D) animals. The weight change for group C showed a statistically significant increase compared with the control and other experimental groups (P<0.001).

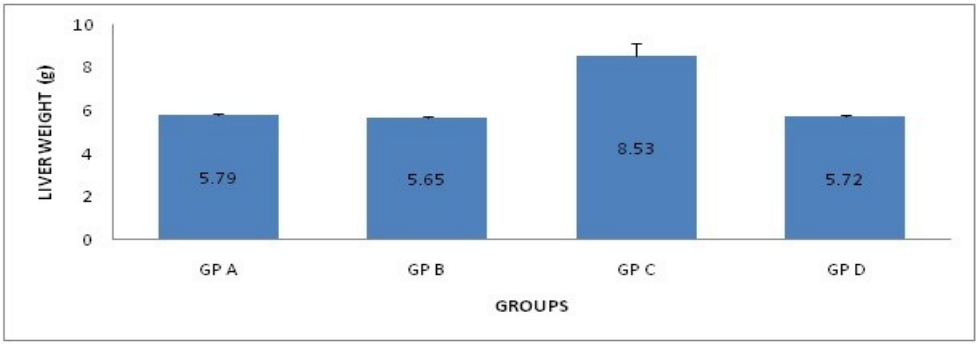
Figure 1.0 : The bar chat representation of the mean initial and final body weight



The weight of animals in group C were significantly higher (P<0.001) than group A (Control) and groups B, D and F. before administration. After the administration, the weight of animals in group A (control) and group B, D increased statistically while the group C animals showed a significant decrease (P<0.001) compared to the weight before administration.

The relative liver weight for group C (potassium bromate administered) were significantly higher (P<0.001) than that of the group A (control) and other experimental groups (B,and D). The values for groups B, D were similar to the group A (control).

Figure 2.0: The bar chart representation of the relative liver weight of the various groups.



The group C (potassium bromate administered) were significantly higher (P<0.001) than the control group (A) and groups B, D.

Table 2. Activities of serum levels of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphotase (ALP)

Liver Enzymes	Group A	Group B	Group C	Group D	F-Ratio	PROB.OF SIG.
AST	83.80±28.55	79.75±13.51	128.14±3.21	94.65±5.07	60.04	<0.0001
ALT	47.02±16.70	36.66±01.22	73.23±6.21	39.63±8.07	12.30	<0.0001
ALP	383.30±21.22	295.83±30.83	483±46.75	347.21±16.29	7.58	< 0.0012

(Mean -+SEM given for each measurement).

From the results obtained from calculations of aspartate aminotrasferase (AST), alanine aminptransferase (ALT) and alkaline phosphotase (ALP), there were a significant decrease (P<0.001) in the AST activity levels at all doses of the drugs relative to the control (A) except in group C treated with potassium bromate. The group C activity level statistically were significantly higher (P<0.001) than the control (A) and other groups.

The alanine aminitrasferase (ALT) activity levels showed a significant decrease (P<0.001) in groups B treated with *rauwolfia vomitoria* extract and D relative to the control (A) except in group C treated with potassium bromate. The alkaline phosphotase (ALP) level in group C were significantly higher than the control group (A) and other groups.

The alkaline phosphotase (ALP) activity levels in groups B, and D were significantly lower (P<0.001) than the control (A). The alkaline phosphotase activity levels in group C were significantly higher (P<0.001) than the control (A) and other groups.

4. Discussion

The results of this study agree with the discovery that potassium bromate is toxic and is a possible carcinogen in tissue[5]. There were no significant difference (P<0.001) in the serum and tissues levels of AST, ALT and ALP in groups B and D compared with the control as shown in table 2.0. There were significant difference (P<0.001) in the serum and tissues levels of AST, ALT and ALP in group C compared with the control and groups B and D. These results indicated that the extract from *Rauwolfia vomitoria* did not bring about cellular damage in the liver during the experimental period. Enzyme activities in the serum and tissues are often used as "maker" to ascertain toxic effects of administered foreign compounds to experimental animals[7]. ALP is a membrane bound enzyme[11] while ALT and AST are cytosolic enzymes[6]. These enzymes are highly concentrated in the liver and kidney and are only found in serum in significant quantities when the cell membrane becomes leaky and even completely ruptured[8,10]. A rise in serum level or decrease in tissue level of these intracellular enzymes is an index of damage to the liver cells[9].

Observation of the body weight difference in groups reveals gradual increase in weight of animals for the control group A. This could have been physiological as the only substance they were exposed to was water and food. Comparing the results of weight difference reveals severe loss of weight by the potassium bromate exposed group. This is probably as a result of loss of appetite by the animals in the group. The groups that were treated with extract of *Rauwolfia vomitoria* only, extract of *Rauwolfia vomitoria* and potassium bromate, showed increase in weight which is similar to the control group. Extract of *Rauwolfia vomitoria* in this instance functions primarily as a dietary supplement enhancing growth. Previous researches cited in literatures of *Rauwolfia vomitoria* did not state pre and post experimental weight, hence weight changes were not determined in their works.

The relative weights of the organ also showed significant differences in groups. There was relative increase in liver weight for the potassium bromate exposed animals compared to the control. This organ weight increase was irrespective of the fact that there was total body weight loss. This could have been pathological and one may deduce that the increase in liver weight was not growth but inflammation. Antioxidant properties of *Rauwolfia vomitoria* could have been responsible for the control or prevention of inflammation in the groups treated with them.

The animals in group D gives a particularly interesting observation about the dynamics of reactions to the presence of various substances in our systems. On administration of extract of *Rauwolfia vomitoria* respectively to the groups, the animals showed increase in overall body weight similar to that of the control. Administration of extract of *Rauwolfia vomitoria* alone did not cause weight loss to the animals compared with the animals in control group By these observation one may deduce that administration of extract of *Rauwolfia vomitoria* may boost the tolerance capacity for mercury induced toxicity

5. Conclusion

The extract of *Rauwolfia vomitoria* did not induce adverse alterations in biochemical parameters of serum aspartate aminitransferase (AST), serum alanine aminotrasferase (ALT) and Alkaline phosphotase (ALP) and no histopathological lessons was observed in the liver tissues of the rats. This study has demonstrated the potential ability of *Rauwolfia vomitoria* to protect against potassium bromate induced toxicity in the liver enzymes of rats. The findings of this study suggests that *Rauwolfia vomitoria* administered to individuals exposed to potassium bromate poisoning in bread could provide some protection against its effects on the liver enzymes.

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