

**Research Article****EVALUATION OF ANTIFIBROID POTENTIAL OF THE FRUITS OF *RAUWOLFIA VOMITORIA* L. (APOCYNACEAE)*****Mikailu Suleiman and Noela Chinaza Akabueze**

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Received 19th December 2024; Accepted 24th January 2025; Published online 27th February 2025

Abstract

Introduction: The threat posed by uterine fibroid on women is on the rise, especially in African and African-American women. This study therefore aimed at evaluating the antifibrotic effect of *Rauwolfia vomitoria* (L.), Apocynaceae in Wistar Rats. **Methods:** Dried fruits of *R. vomitoria* were purchased from Oja-Oba Market, Kwara State, and pulverized. Phytochemical screening was conducted on the powder using standard methods. The powder was assessed for acute toxicity in rats using Lorke's method. The uterine fibroid was induced in the Wistar rats for thirty days using Monosodium Glutamate (MSG) and then treated for thirty days with the powdered *Rauwolfia vomitoria* at 400mg/kg, 800mg/kg, and 1200mg/kg. Danazol was used as a standard drug at 100mg/kg. The uterus weight ratio (uterus weight/weight of rats) was recorded. The estradiol, albumin, and total protein were assessed using standard kits after the rats were sacrificed. **Results:** Phytochemical screening revealed the presence of triterpenoids, tannins, anthraquinone glycosides, and alkaloids. Acute toxicity showed a Median Lethal Dose (LD₅₀) of 5000mg/kg. The weight ratio of the uterus did not show any significant difference when compared to the control. The estradiol showed a significant ($p < 0.05$) reduction in the treatment groups compared to the untreated control. Albumin and total protein of the treated groups did not show any significant difference ($p < 0.05$) from the control. **Conclusion:** *Rauwolfia vomitoria* is safe at 5000mg/kg and effective at 400mg/kg. And the estradiol of the animals is effectively reduced indicating the ameliorating effect of fibroid.

Keywords: Fibroids, *Rauwolfia vomitoria*, fruits, Estradiol.

INTRODUCTION

Fibroids, also known as uterine leiomyomas, are benign tumors that develop within the smooth muscle of the uterus. These growths are common among women of reproductive age, with the majority experiencing no symptoms. However, in some cases, fibroids can lead to significant clinical problems such as heavy menstrual bleeding, pelvic pain, urinary frequency, and complications during pregnancy [1]. Although fibroids are generally non-cancerous, their presence can severely impact the quality of life of affected individuals, leading to potential long-term reproductive and health issues. Current therapeutic approaches to managing fibroids include medical treatments, surgical interventions, and in some cases, hysterectomy [2]. However, these treatments are often associated with side effects, high costs, and the risk of recurrence, highlighting the need for alternative, safer, and more effective treatment options. *Rauwolfia vomitoria*, a notable species member of the Apocynaceae family, is a plant of significant interest due to its rich history in traditional medicine. This plant is native to tropical regions of West Africa, including countries such as Nigeria, Ghana, and Cameroon. It is a small to medium-sized shrub, typically reaching up to 1.5 meters in height, and is characterized by its glossy, dark green leaves and small, tubular flowers. The plant thrives in forested areas and is often found growing in moist, shaded regions. It is known by various local names, including "the poisonous root" or "vomiting root". Among its bioactive components, reserpine, an alkaloid compound, has garnered attention for its therapeutic effects, particularly in the treatment of hypertension and psychiatric disorders [3].

Local communities utilize the root extract for treating a range of health conditions, including hypertension, insomnia, anxiety, and various infectious diseases [4],[5]. Despite its widespread use in folk medicine, scientific investigations into the pharmacological potential of *Rauwolfia vomitoria*, particularly its antifibroid properties, remain limited. Preliminary studies suggest that certain bioactive compounds found in the fruits of *R. vomitoria* may possess anti-inflammatory, antioxidant, and anticancer properties, which could be relevant in the context of fibroid treatment [4], [6]. However, there is a lack of comprehensive scientific validation regarding the efficacy of *R. vomitoria*'s fruit extracts in addressing fibroid-related issues. This gap in research provides a compelling rationale for this study, which aims to evaluate the antifibroid potential of the fruits of *R. vomitoria* by investigating its biochemical effects and exploring the plant's mechanisms of action, this research seeks to contribute valuable insights into the therapeutic potential of *R. vomitoria* for fibroid management.

MATERIALS AND METHODS**Plant Materials**

The fruits of *Rauwolfia vomitoria*, Afzel (Apocynaceae) used for the investigation was identified and authenticated in the Herbarium of the Department of Pharmacognosy and Phytotherapy, Faculty of Pharmaceutical Sciences, University of Port-Harcourt. The fruits were plucked, washed, and dried. The dried fruits were then pulverized using a milling machine. The powdered form was kept in an airtight container during the investigation.

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Collection of Experimental Animals

Seventy albino rats (86g-152g) were acquired from the animal house of the Department of Pharmacology and Experimental Toxicology, Faculty of Pharmaceutical Sciences, University of Port-Harcourt. These experimental animals were acclimatized for one week under standard laboratory conditions [7].

Animal Assay

Induction of Fibroid in Experimental Rats and Treatment

Animals were grouped into five groups, each containing ten rats. Each group was administered 1 g/kg monosodium glutamate for 30 days. The individual weight of each rat was recorded before and after the study [8]. Thirty days after the fibroid was induced, two rats were sacrificed, and the uterus was examined for the presence of fibroid before initiating treatment with a standard drug (Danazol 100 mg/kg) and powdered fruits of *Rauwolfia vomitoria* for the next 30 days.

The groupings are as follows;

Group 1: Control group; Induced but not treated

Group 2: Induced and treated with standard drug (Danazol 100mg/kg)

Group 3: Induced and treated with 400mg/kg of powdered fruits of *Rauwolfia vomitoria*

Group 4: Induced and treated with 800mg/kg powdered fruits of *Rauwolfia vomitoria*

Group 5: Induced and treated with 1200mg/kg powdered fruits of *Rauwolfia vomitoria*

The powdered fruits of *Rauwolfia vomitoria* and Danazol used in this study were dissolved in distilled water and administered orally with the aid of a 1 ml syringe. The weights of the animals were recorded before induction, before treatment, and after treatment [9].

Determination of Biochemical Parameters

At the end of the 30-day treatment period, blood from the sacrificed rats was collected into plain tubes and allowed to stand for 45 minutes. The clotted samples were centrifuged at 3000 rpm for 15 minutes to separate plasma, which was transferred into sample tubes. Plasma estradiol, total protein, albumin concentration, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin, gamma-glutamyltransferase (GGT), and kidney parameters (creatinine and urea) were determined using Accubind ELISA microwells (Monobind Inc. CA 92630 USA [10]).

Determination of Body Uterus Weight

The weights of animals were recorded before induction, before treatment, and after treatment. Animals were sacrificed and the uterus weighed. Weight to uterus ratio was calculated using the

Formula:

$$\text{Weight-to-Uterus Ratio} = \frac{\text{Weight of Rat}}{\text{Weight of Uterus}}$$

Statistical analysis

Data obtained from the studies were expressed as mean \pm standard error of mean. The significance between the mean of the treated and the control animals were established by Student's T-test

RESULTS AND DISCUSSION

Ultimately, the development of uterine fibroid therapy stems from the need for viable choices to reduce symptoms associated with this disease. In light of rising healthcare costs, patients looking for economical approaches to health may consider a combination of conventional medicine and supplemental approaches. Many medicinal plants have been reported to have a positive effect on the treatment of uterine fibroids in African traditional medicine. One of such plant is *R. vomitoria*. This study tries to assess this claim and also compare treatment with the plant fruits to the treatment using standard drugs to investigate if the plant can have any significant use in the modern treatment of uterine fibroids. The safety profile of the *R. vomitoria* fruit has been established in our earlier studies. The phytochemicals of the fruits have also been reported [11],[12]. Many compounds have been investigated as potential biomarkers for the diagnosis and surveillance of uterine leiomyomas. Most of these compounds demonstrate subtle differences among patients when leiomyomas are compared with controls [13]. After the statistical analysis was done using paired sample T-tests to compare the control groups with the test groups in Table 1, it was observed that there was a significant decrease in the estradiol plasma concentration of treatment groups including the standard drug. The observed decrease was concentration dependent. The bioactive form of estrogen (17 β - estradiol) promotes proliferation of fibroids through up-regulation of progesterone receptor expression [14]. Therefore, decreased estradiol of the treated groups may indicate the anti-fibroid effect of the powdered fruits of *R. vomitoria*. The total protein and albumin concentration of the treatments did not exhibit significant difference when compared to group 1.

The Alanine Transaminase (ALT) of 400mg/kg treatment from Table 2 was significantly lower than the control and standard drug. Although other treatment doses were higher than the control which is suggestive of ineffective of the powder on the ALT of the animals. For the Aspartate Transaminase (AST), from the table of results provided, there is a significant increase in the level of this enzyme after treatment with the standard drug. However, there was a variation in the level of enzymes as the concentration of the powder was increased. This implies that the herb *R. vomitoria* has an unstable effect on the AST enzymes. Alkaline Phosphatase (ALP) are usually measured in the blood to assess the liver and bone health. Its elevation could suggest liver disease. The ALP of the powder treated groups were significantly lower than the control although not as low as the standard drug which also suggest that the enzyme is stable and not affected by the treatment. Albumin from the table of results presented, there was a negligible difference between the control and the treatment groups. On treatment with the powder, the level of albumin maintained a considerably safe range. This implies that the powder has no negative effect on albumin levels. Gamma-glutamyltransferase from the results shown, the untreated control group had a low level of the enzyme.

Table 1. Effect of *R. vomitoria* on estradiol, total protein and albumin plasma concentration

GROUPS	Total protein (g/dl)	Albumin (g/dl)	Estradiol (g/ml)
GROUP 1 (MSG only)	7.36±0.33	4.76±0.17	188.33±25.01
GROUP 2 (STD 100mg/kg)	6.98±0.13	5.15±0.18	*114.33±4.67
GROUP 3 (400mg/kg)	7.19±0.34	5.02±0.5	*90.8±3.34
GROUP 4 (800mg/kg)	8.38±0.46	4.39±0.11	*97.4±2.09
GROUP 5 (1200mg/kg)	8.77±0.56	4.77±0.17	*112.8±2.62

Values are represented as mean ± S.E.M. (standard error of mean)

*Represents the values significantly different from the control (p < 0.05)

Table 2. Effect of *R. vomitoria* on the liver enzymes

GROUPS	GGT (U/L)	BIL (µmol/L)	ALB (g/dl)	AST (U/l)	ALT (U/l)	ALP (IU/L)
GROUP 1 (MSG only)	0.74±0.37	307.4±35.42	4.76±0.17	87.47±17.54	51.04±4.3	153.13±5.44
GROUP 2 (STD 100mg/kg)	*3.33±2.8	*250.34±33.81	5.15±0.18	95.89±2.9	54.18±6.44	*122.57±6.11
GROUP 3 (400mg/kg)	*2.89±2.37	*213.7±57.72	5.02±0.5	19.89±10.8	*44.37±3.73	*132.08±3.9
GROUP 4 (800mg/kg)	*2.22±1.72	*221.96±60.94	4.39±0.11	71.47±8.26	53.82±4.15	*128.55±5.87
GROUP 5 (1200mg/kg)	*3.33±2.81	*205±56.13		56.83±12.02	*59.79±6.23	*135.93±5.23

Values are represented as mean ± S.E.M. (standard error of mean)

*Represents the values significantly different from the control (p < 0.05)

Table 3. Effect of *R. vomitoria* on the Kidney

GROUPS	CREATININE (µmol/L)	UREA (mg/dl)
GROUP 1 (MSG only)	83.22±9.42	109.98±14.39
GROUP 2 (STD 100mg/kg)	*35.5±18.72	133.82±29.83
GROUP 3 (400mg/kg)	*52.09±23.91	*83.86±2.91
GROUP 4 (800mg/kg)	*59.29±22.51	*86.76±3.49
GROUP 5 (1200mg/kg)	90.37±24.28	*88.79±5.22

Values are represented as mean ± S.E.M. (standard error of mean)

*Represents the values significantly different from the control (p < 0.05)

Table 4. Effect of *R. vomitoria* on Electrolytes

GROUPS	NA (mEq/L)	K(mmol/L)	Cl (mmol/L)
GROUP 1 (MSG only)	176.03±2.37	4.91±0.29	111.72±7.14
GROUP 2 (STD 100mg/kg)	178.28±0.68	5.12±0.41	*86.86±2.36
GROUP 3 (400mg/kg)	*135.17±33.93	4.43±1.11	*103.05±6.59
GROUP 3 (800mg/kg)	144.55±36.33	4.31±1.08	*97.46±7.97
GROUP 5 (1200mg/kg)	*174.09±2.26	4.8±1.21	*103.39±5.69

Values are represented as mean ± S.E.M. (standard error of mean)

*Represents the values significantly different from the control (p < 0.05)

Table 5. Differences in rat weight before and after the treatment

GROUPS	Initial weight before induction	Weight before treatment	Weight after treatment	The weight ratio of the uterus
GROUP 1 (MSG only)	92±4.85	160±2	152±19.67	0.0050±0.0001
GROUP 2 (STD 100mg/kg)	102±2.94	165±1.29	153±14.92	0.0059±0.0021
GROUP 3 (400mg/kg)	112±2.05	172±5.42	151±20.78	0.0046±0.0001
GROUP 3 (800mg/kg)	109±3.63	170±6.79	162±15.84	0.0073±0.0002
GROUP 5 (1200mg/kg)	122±8.00	180±2.94	170±20.51	0.0073±0.0001

Values represent: mean ± standard deviation, n=10; Weight ratio of the uterus = Weight of the uterus/Weight of rats.

The group treated with the standard drug had a significant increase and on treatment with the powder, there was a steady increase in the level of enzymes which was in the same range as that of the standard drug. This also suggests that the powder has a positive effect on the GGT enzymes. Abnormal bilirubin can indicate various health conditions ranging from jaundice to liver inflammation. However, Table 2 shows that bilirubin of the treated groups are significantly lower than the control group. This indicates the positive effect of the powder and the standard drug on the induced animals. The Creatinine of the standard drug group reduced drastically from its initial high amount with the untreated control group which shows for positive effect of Danazol. However, on treatment with the test anti-fibroid herb, there was a steady increase in creatinine level which should not have been. This suggests the anti-fibroid herb harms the creatinine level. For urea, the control groups had high levels of urea. On treatment with the anti-fibroid herb, there was a significant decrease which shows for positive effect.

However, as the concentration of the test herb increased, the level of urea increased although still within a safe limit. From May 1989 to October 1991, 101 consecutive patients were treated for submucous fibroids using herbs. During the postoperative course, attention was paid to the occurrence of cerebral confusion, nausea (defined by at least one incident of vomiting), and dyspnea. The serum levels of sodium, potassium, and chloride were assessed to ascertain the effects of these herbs on the electrolyte levels [15]. As per a review published in the Current Opinion in Obstetrics & Gynecology, there are receptors for estrogen in your uterus that bind estrogen molecules to the tissue. The resulting cellular process may make the fibroid's growth possible. These estrogen receptors have been found in the fibroids also, that's the reason why fibroids have higher amounts of estrogen hormone than the nearby tissue. Therefore, just like mineralocorticoids, estrogen causes sodium retention by renal tubules. This is normally insignificant even during pregnancy [16]. Since Vasopressin acts on the kidneys to regulate water excretion

and electrolyte balance, it was natural to hypothesize that estrogen might influence Vasopressin secretion. The first questions many neuroendocrinologists asked to address this possibility included: Are plasma levels of Vasopressin responses to electrolyte balance different in males and females? What is the impact of Fibroid on Vasopressin secretion? What happens to plasma Vasopressin levels following estrogen elevation? Unfortunately, experiments to answer these questions have not provided consistent results. This is probably because gonadal steroids act on components of the homeostatic system involved in the regulation of water and electrolyte balance, and which one of these actions predominates is modified by a variety of factors including species, gender, diet, and reproductive and fluid balance status [17]. Since there's a link between the Estrogen level and the Vasopressin then invariably, we can relate it to the effects on the electrolytes because the Vasopressin is directly linked with enhanced water, Cl, Na, and Ca reabsorption and sharply increased net K secretion. This study which involved the effects of *R. vomitoria* on the electrolyte of albino rats showed different electrolyte levels in the biochemical analysis. What was key in the results was the fact that the supposed effects on electrolyte levels were not dose-dependent as the electrolyte level showed different variations. This implied that at different doses, there were contrasting electrolyte levels that did not follow a desired pattern. The K of the standard and control group did not exhibit any difference. Consequently, the Na showed an inverse dose-dependent with the lowest dose (200mg/kg) having the highest reduction while Cl showed an erratic reduction. This indicates that the treatments did not affect the body electrolytes of the animals. Based on the curative study, a reduction in the weight ratio of the uterus of the induced rats was observed at a lower dose of 400mg/kg of the test plant in Table 5 but an increased weight ratio was seen in 800mg/kg and 1200mg/kg. This indicates the effectiveness of the test plant at low doses and the increase in weight in high doses (800mg/kg and 1200mg/kg) as a result of other contributing factors.

Conclusion

The results from the biochemical analysis of the serum of albino rats showed a variation in the electrolyte level although the results were not consistent with dose increase. Conclusively, the Anti-fibroid activities of the Natural products have significant effects on the Electrolyte of the albino rats.

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