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# Effects Of *Rhaptopetalum coriaceum* Oliv Stem Bark Extract On Serum Enzyme Activities And Histopathological Changes In Rats

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## ABSTRACT

Daily oral administration of graded doses of ethanolic extract stem bark of Rhaptopetalum coriaceum Oliv administered to rats for three weeks produced a significant ($P<0.05$) increase in serum glutamate oxalotransaminase (SGOT), pyruvate transaminase levels (SGPT) and a decrease in serum alkaline phosphatase (ALP). The extract was found to produce pathological lesions of the liver, kidney and lung. These lesions include: vascular congestion and hepatic necrosis in the liver, tubular necrosis in the kidney and pulmonary congestion with exaggerated alveolar epithelium in the lungs. These results suggests that users of this local remedy as hypotensive agent.

**Keywords**: Rhaptopetalium coriacum oliv, serum enzymes, pathology rats.

Rhaptopetalum coriaceum Oliv is a plant whose stem bark is used for the treatment of hypertension in folklore medicine (Oliver, 1960). It hs been evaluated and found to relax vascular smooth muscle, therefore supporting its traditional claim as a potential hypotensive agen (Ajagbonna et al 1998). It is however known that most of the herbs used in traditional medicine especially in Nigeria have not been subjected to a detailed comprehensive toxicity tests.

In our earlier study, we reported a disturbance in the anion – cation balance in rats treated with Rhaptopetalium coriaceum extract (Ajagbonna nd Onwuchekwa, 2001). Similarly, since changes in liver enzymes test is usually an indication of tissue destruction, the present study therefore report the effect of chronic treatment of Rhaptopetalum coriaceum extract on serum enzymes and pathological changes on some selected tissues with a view to assessing further the toxicity or safety of this plant to its numerous users who take the plant without a defined treatment regimen.

## MATERIALS AND METHODS

**Animals:**

Sprague – Dawley rats weighing between 130-132g were obtained from the animal house of the Faculty of Science of Usmanu Danfodiyo University, Sokoto and kept in a well-ventilated rate cages with free access to water and feeds (ad libitum). They were left in this environment for two weeks to acclimatize.

**Extraction:**

About 500g of the stem bank of Rhaptopetalum coriaceum was air-dried, coarsely grounded with pestle and mortar and extracted using two successive overnight maceration with occasional stirring or agitation in 70 percent ethanol on a mechanical shaker. The ethanolic extract was filtered through a Whatman No. 1 filter paper and concentrated to a solid residue in a rotary evaporator under pressure. The residue extract, about 30g recovered was now stored in a desiccators and from this, a fresh stock solution was prepared on each day of the experiment.

**Toxicity Study:**

Forty-eight Sprague-Dawley rats were randomly divided into 4 groups of 12 rats each. Group 1 (control) received ordinary distilled water, while groups 2,3 and 4 received solution of 10, 30 and 60mg/kg weight of the plant extract respectively. These solutions were given daily with the help of gastric tube (B.M.I. feeding tube, size 8) for three weeks. The weight of the animals were taken prior to the administration of the plant extract and

subsequently every two days for three weeks of the experiment. Similarly the effect of the extract on feed in take was also noted.

**Serum enzymes:**

An average of four rats were randomly selected weekly from each group and blood collected from the animal tail snipping into a vacutainer, the serum was subsequently centrifuged out from this and used for the determination of alkaline phosphatase, serum glutamate oxalotransaminase and pyruvate transaminase according to method Reitman and Frankel (1957) using the sigma kits.

**Histopatholgoy:**

Following administration of the graded doses of the extract to rats in the different groups, all the animals were monitored daily for any untoward reactions throughout the period of study. Three rats were sacrificed weekly from each group and post mortem carried out. Organs like liver, lung and kidney were excised. These were examined macroscopically and thereafter immediately fixed in 10% formalin. Thin sections of the fixed specimens were prepared by standard techniques and stained routinely with haematoxylin and eosin (H &E). They were examined under light microscope for nay lesions that might have developed during the period of therapy.

**Statistics:**

The data collected in the study was subjected to analysis of variance. Statistical significance was considered when $P<0.05$ values are presented as mean $\pm$ S.E.M. (Standard error of mean).

## RESULTS AND DISCUSSIONS

The test animals during the period of plant administration were observed in this study to consume RCO extract and food at about the same rate as the control (Data not shown).

Similarly, the extract at the doses used in this study did not affect the weight of the treated animal differently from the control because there were increases in body weight throughout the duration of study in control and treated groups.

Rhaptopetalum coriaceum oliv extract significantly ($P<0.05$) decreased the level of serum alkaline phosphatase (Table 1). Low level of this enzymes is not much of clinical significance but the persistent low level throughout the study in the extract treated group may be due to hypophosphatemia and some time decreased level of vitamin C. The low level of this enzyme may also suggest that the extract does not cause damage to bone (Tilkan, 1979, Tietz, 1994).

Administration of the plant extract was also associated with significant increase ($P<0.05$) in the level of SGOT and SGPT (Table 1). These are liver enzymes and their increased levels are indicative of liver damage (Kaneko, 1980 and Tietz, 1994). In previous studies, these enzymes were found high concentration in hepatic tissue of dogs, cats and primates with elevation of its activity in plasma indicating hepatocellular damage (Tilkan, 1979). Similarly, woodman (1988) observed in his study that increased plasma enzymes activities often seen following liver damage does not only indicate an increase in liver ability to synthesized the enzymes but also a loss of material from damaged hepatocytes, suggesting therefore that increased plasma enzymes usually are an indirect reflection of tissue cellular damage.

In this study, seven days therapy of the graded doses of the extract of RCO did not produce any deleterious effect on the organs examined (Kidney, liver and lung), there were however, a mild vascular congestion on the kidney of the rats receiving the highest dose of 60mg/kg, suggesting a dose dependent effect of the extract.

Tables 2,3 and 4, showed the various lesions produced by the administration of the extract for three weeks.

In rats that received the highest dose for example, the liver showed vascular congestion, hepatic necrosis with karyorhetic nuclei, this iesson observed may have occurred due to metabolism of eh toxic principle contained in the extract in the liver which is the primary organ of biotransformation. The liver of the control group that received ordinary water had neither necrosis nor congestion (Table 2).

Examination of the kidney (Table 3) also revealed acute tabular necrosis and a dose dependent vascular congestion in the rats treated with extract suggesting a decrease functional capacity of the kidney.

This result may not be surprising, since the kidney is the primary organ of excretion so that it may have been exposed to the toxic principle present in the extract. Similarly, in the lung of the treated group there was severe pulmonary congestion with exaggerated alveolar epithelium (Table 4). The component of the plant extract that may be responsible for the observed pathological changes has not been elucidated, however the presence of alkaloids and flavnoid in the decoction (Ajagbonna and Onyeyili, 2002) might have contributed to such pathological effects observed. In a similar study, severe necrosis and congestion have been reported in liver, kidney and lungs of animals treated with crotalaria species containing alkaloid (Nuhu et al, 2000). Furthermore, whether or not these pathological changes are reversible with persistent use of the herbs requires further investigation.

**le 1: Effect of stem bark extract of rhaptopetalum coriaceum oliv on serum enzyme activities in rats treated daily with the extract for three weeks.**

| Parameter | Dose of Extract (mg/kg) | Weeks of Treatment | | |
|---|---|---|---|---|
| | | 1 | 2 | 3 |
| ALP(iu/l) | 0 | 23.2 ±0.60 | 22.3± 0.76 | 23.0 ±0.79 |
| | 10 | 18.5± 0.042 | 19.3± 0 41 | 19.1± 32 |
| | 30 | 16.6 ± 0.71 | 15.8 ±1.07 | 17.0± 0.57 |
| | 60 | 15.8 ±1.40 | 14.6 ±1.20 | 15.5 ±1.40 |
| SGOT(iu/l) | 0 | 50.0 ±1.80 | 49.3 ±2.06 | 51.3± 0.80 |
| | 10 | 48.6± 1.20 | 50.0 ±0.68 | 52.5± 1.20 |
| | 30 | 48.3 ±0.80 | 54.6± 1.40 | 58.0 ±0.60 |
| | 60 | 53.0 ±2.20 | 58.8 ±0.90 | 65.0± 0.90 |
| SGPT(iu/l) | 0 | 22.2± 0.70 | 21.5 ±0.56 | 21.6± 0.84 |
| | 10 | 22.0. ±1.10 | 22.1 ±0.8 | 22.0 ±0.87 |
| | 30 | 21.6 ±0.80 | 21.8 ±1.20 | 29.0± 1.10 |
| | 60 | 22.0± 0.70 | 22.8± 0.70 | 30.8 ±0.65 |

Values are mean ± SEM of six observations

* Values significantly (P<0.05) higher than the control

** Represent values significantly (P<0.05) lower than the control.

**ble 2: Histopathological changes of the liver tissue after three weeks of oral administration of RCO to rats.**

| atment RCO (mg/kg) | Pathological Changes |
|---|---|
| Control) | No visible lesion |
| | Mild vascular congestion and fatty denegation of hepatocytes |
| | Vascular degeneration with focal areas of hepatic necrosis |
| | Wide spread hepatic necrosis with karyorhetic nuclei |

**ble 3: Histopathological changes of the kidney after three weeks oral administration of RCO to rats.**

| atment RCO (mg/kg) | Changes |
|---|---|
| ontrol) | No visible lesion (normal kidney) |
| | Localized mild vascular congestion in the cortex |
| | More generalized vascular congestion in both cortex and medulla |
| | Severe vascular congestion. Severe acute tabular necrosis with both cortex and medulla |

**Table 4: Histopathological changes of the lung tissue after three weeks oral administration of RCO to rats.**

| Treatment RCO (mg/kg) | Changes |
|---|---|
| 0(Control) | No visible lesion |
| 10 | Mild tissue congestion with localized area of pulmonary collapse |
| 30 | Wide spread pulmonary congestion |
| 60 | Severe pulmonary congestion with exaggerated alveolar epithelium |

In conclusion, this study demonstrate that Rhaptopetalum coriacium contain some toxic principles and must therefore be used with some cautions especially in long-term therapy.

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