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Original Article

Effect of Shodhana Treatment on Chronic Toxicity and Recovery of Aconite

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ABSTRACT

Aconite is one of the poisonous plants used therapeutically in practice of Ayurveda after proper treatment called as 'Shodhana'. To determine the effect of Shodhana treatment on chronic toxicity and to assess the effect of recovery period after chronic toxicity of aconite. Raw aconite (RV), urine treated aconite (SM), and milk treated aconite (SD) were administered in 6.25 mg/kg dose in Charles Foster strain albino rats for 90 days for chronic toxicity. Six rats from each were kept for another 30 days without test drugs treatment to observe recovery from chronic toxicity. RV was found to be highly toxic in chronic exposure, SM had no apparent toxicity, but SD had mild toxicity in kidney. The toxicities of RV and SD were reversible, but sudden withdrawal of SM caused adverse effects, suggestive of tapering withdrawal. Shodhana treatments remove toxic effects from raw aconite. Chronic toxicity of aconite is reversible. Confirmed the arrangement of abstract

Key words: *Aconitum chasmanthum*, cow's urine, cow's milk, recovery, shodhana

INTRODUCTION

The poisonous plants those are transformed into drugs must have excellent therapeutic efficacy and must be safe. Those poisonous plants are used widely for therapeutic purpose in the Ayurvedic system of medicine after proper processing called as 'Shodhana'.[1] Unfortunately, those poisonous plants have the potential to produce notorious toxic effects, even death also, if those are not processed properly or if are taken in a large dose. Therefore, during transmutation of the poisonous plants to drugs, it is essential to evaluate the margin of safety between the dose level that produces the therapeutic effects and that produces the toxic effects. To provide the benefit to risk assessment, animal experimentation is the only way through which this assessment can be made.

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Aconite (Vatsanabha) is one of such poisonous plant used abundantly in practice of Ayurveda after proper Shodhana treatment. It is indicated to treat the diseases like Jwara (pyrexia), Vatavyadhi (arthritis), Pandu (anemia), Shwasa (asthma), Kustha (skin disorders), etc., and is also used as Rasayana (immunomodulator).[2] The accidental ingestion of crude aconite roots may cause various toxic effects, which include feeling of constriction in the throat, pain and tenderness in the abdomen, ringing in the ear with impairment of the hearing capacity, limbs becoming weak, and inability to stand or walk. Twitching of the muscle and convulsions may also occur. The breathing is rapid at first, but soon becomes slow, labored, and shallow. Tachyarrhythmias including ventricular tachycardia and fibrillation are developed in most of the patients.[3] Two deaths are reported after accidental herb-induced aconite poisoning.[4]

One of the recommendations of the World Health Organization (WHO) guidelines for conducting toxicity

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study is to observe the recovery of the experimental animals from toxicity after a certain interval of toxicity study.[5] Hence, this study was planned to observe the chronic toxicity of raw aconite (RV), processed aconite by cow's urine (SM), and prsocessed aconite by cow's milk (SD); and after a prolong exposure to higher dose of aconite, if the animals recovered from the toxic effect or not. Emphasis has been given to observe the likely impact of Shodhana treatment on toxic effect of aconite. The present study conforms to the guidelines laid by the Institutional Animals Ethics Committee (IAEC-06-08/02).

MATERIALS AND METHODS

Plant material

Aconitum chasmanthum Holmes ex Stapf. species of aconite (as it is mentioned as official Vatsanabha)[6] was identified and taken for this study. It was collected from Sakut market of Rajasthan, and was identified by the botanist of Institute of Ayurvedic Medicinal Plant Sciences, Gujarat Ayurved University, Jamnagar. The reference sample was kept in the department of Rasashastra and Bhaishajya Kalpana, I.P.G.T.and R.A., Gujarat Ayurved University. Shodhana treatment was carried out in department of Rasashastra and Bhaishajya Kalpana laboratory. Shodhana procedure was performed by two different methods by using two different media, cow's urine and cow's milk. For this purpose, root tubers were made into coarse powder (mesh size 2 – 8) form. The powder was taken in a tray and was immersed in cow's urine and was kept under sunlight. The treatment was continued for 3 days; everyday fresh urine was used.[7] Total, 6 l of urine was used for treatment of 200 g of aconite powder. In another method, the powder was taken in a swing made up of cloth and was subjected for boiling under the bath of cow's milk for duration of five hours.[8] Swing was completely sunk under media by continuous supply of milk, and a total of 3.6 l of milk was used for Shodhana of 200 g powder. The therapeutic dose of aconite mentioned in classics of Ayurveda is 8 mg to 16 mg/day.[9] In the present study, human dose of aconite has been decided to be 15 mg/day. The dose for experimental study of the drugs was 1.25 mg/kg, calculated by extrapolating the human dose to animal dose based on the body surface area ratio. Drug suspension was prepared in 3% gum acacia solution (1 ml in 50 ml distilled water). Suspensions of the test drugs (RV, SM, and SD) were prepared in 1.35 mg/ml concentration.

Animals

Charles Foster strain albino rats of either sex weighing between 180 to 250 g were used for this experiment. They were obtained from the animal house attached to the pharmacology laboratory. They were housed in breeding cases at an ambient temperature with a natural day and night cycles. The animals had free access of Amrut brand rat pellet feed supplied by Pranav Agro Industries and tap water.

Study protocol for chronic toxicity

A total of 42 rats were taken and divided into 4 groups. Group I was comprised of 6 rats; and group II, group III, and group IV were comprised of 12 animals in each group. Each group contained equal number of male and female rats. Group I was designated as control group and received vehicle (1 ml 3% gum acacia solution in 100 ml distilled water) used for preparation of the suspension of test drugs. Animals of group II, group III, and group IV were treated with suspensions of RV, SM, and SD, respectively, in 6.25 mg/kg dose. The dose of the test drugs administered was 5 times more than therapeutic effective dose.

The schedule was continued for 90 days with daily single dose of test drugs and vehicle. Gross case behavior was observed throughout the study period. On the 91st day, 6 rats from each group were sacrificed by stunning; blood was collected from jugular vein for hematological and biochemical tests. All vital organs were collected for histopathological study and body weight of rats before sacrificing was recorded.

Study protocol for recovery study

Six rats, equal number of male and female from each RV, SM, and SD treated groups were kept for recovery study and named as RV(R), SM(R), and SD(R). During this recovery period, no drug was administered, and only normal diet and tap water was given.

This schedule was continued for 30 days. Gross behavior was observed throughout the period of study. On the 31st day, rats were sacrificed by stunning; blood was collected from jugular vein for hematological and biochemical test. All vital organs were collected for histopathological study.

Measurement of hematological and biochemical parameters

Hematological parameters like hemoglobin percentage, total RBC count, hematocrit value, red cell distribution width, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, total WBC count, differential WBC count, platelet count, etc., were determined by using an automatic hematological analyzer.

For biochemical analysis, blood was centrifuged at 1000 rpm for 10 min to obtain serum. Serum sugar, urea, creatinine, cholesterol, triglyceride, bilirubin, total protein, albumin, globulin, serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), and alkaline phosphatase were estimated enzymatically

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using specific kits by measuring the optical density of the reaction products at the corresponding wavelength with a spectrophotometer.

Morphological and histopathological studies

Liver, heart, lung, spleen, fore, mid and hind brain, thymus, trachea, jejunum, kidney, adrenal gland, lymph node, testis, prostate, seminal vesicles, and uterus were removed and dissected carefully.

The organs were transferred to 10% formaldehyde solution for preservation; the sections were cut, taken on slide, and were stained by serially placing them in xylol, acetone, 95% alcohol, running water, hematoxylin to stain the cytoplasm of the cells and eosin to satin the nuclei, and mounted by using diphenly pthalein xylene (DPX), a cover slip is placed which are studied under the binocular research Carl-Zeiss microscope (Germany) at various magnifications to note down the changes in the microscopic features of the tissues studied.

Statistical analysis

All the values were expressed as mean ± SEM (standard error of mean). The data was analyzed by unpaired '*t*' test and by one way analysis of variance (ANOVA). A level of $P<0.05$ and $P<0.01$ was considered as statistically significant and highly significant, respectively. Level of significance was noted and interpreted accordingly.

RESULTS

Analysis of the data related to body weight changes in different groups reveal significant ($P<0.05$) increase in body weight in SM and SD treated groups and statistically non-significant ($P>0.05$) decrease in body weight in RV treated group [Table 1].

Effect of administration of all the test drugs was evaluated on 10 biochemical parameters. In RV treated group, significant change in 2/10 parameters was observed. The observed changes were significant ($P<0.05$) decrease in serum triglyceride level and serum alkaline phosphotase level. In SM administered group, significant ($P<0.05$) decrease in serum alkaline phosphotase level was the significant change. Significant change in 3/10 parameters was found in SD treated group. The observed changes were significant ($P<0.05$) decrease in serum cholesterol level and serum alkaline phosphatase level and significant ($P<0.05$) increase in serum creatinine level.

Table 1: Changes in body weight in control, treated, and recovered rats

Groups	Dose (mg/kg)	Body weight (g)		
		Initial	Final	Change in %
Control	-	218.00 ± 10.67	249.67 ± 17.76	13.94 ± 2.95**
RV	6.75	215.00 ± 08.11	211.67 ± 11.72	01.46 ± 4.20
RV(R)	-	225.00 ± 12.38	252.67 ± 15.57	12.12 ± 1.32**
SM	6.75	233.00 ± 05.99	250.33 ± 09.90	07.28 ± 2.02*
SM(R)	-	250.00 ± 13.49	277.33 ± 18.89	10.67 ± 5.07
SD	6.75	215.33 ± 06.23	229.00 ± 05.81	06.53 ± 2.24*
SD(R)	-	242.67 ± 16.24	262.33 ± 18.17	08.03 ± 0.75**

Values are mean ± SEM of 6 animals (n = 6) in control, toxicity and recovery groups; *$P\leq0.05$; **$P\leq0.01$ by the student's '*t*' test

Analysis of the data after recovery period reveal statistically highly significant ($P<0.01$) increase in blood sugar level in RV(R) group and non-significant ($P>0.05$) increase in SM(R) and SD(R) groups in comparison to their toxicity groups. Serum cholesterol and triglyceride levels were increased significantly ($P<0.05$) in all the recovery groups and increase in serum triglyceride level in RV(R) group was found to be significant. Serum urea and creatinine level was increased in both RV(R) and SM(R) groups, and decreased in SD(R) group. The changes observed in SM(R) group was highly significant ($P<0.01$), and change in serum urea level in SD(R) was statistically significant ($P<0.05$) in comparison to concern toxicity groups [Table 2].

Total, 12 hematological parameters were recorded and calculated from the obtained data. Of the 12 parameters studied, in the RV treated group, highly significant ($P<0.01$) decrease was observed in hemoglobin percentage. No significant change was found in SM treated group. And in SD treated group, significant changes were observed in three parameters i.e., highly significant ($P<0.01$) decrease in red cell distribution width, significant ($P<0.05$) decrease in lymphocyte count, and significant ($P<0.05$) increase in granulocyte count.

Analysis of the data related to red cell count in recovery study reveals increase in hemoglobin percentage in RV(R) and SM(R) groups and decrease in SD(R) group; non-significant ($P>0.05$) increase in total RBC count in all the recovery groups and non-significant ($P>0.05$) increase in hematocrit value in RV(R) and SM(R) groups, and decrease in SD(R) group. After the recovery period, red cell distribution width was increased in SD(R) group, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration was increased in RV(R) and SM(R) groups, and decreased in SD(R) group. Total WBC count was non-significantly ($P>0.05$) increased in all the recovery groups. The monocyte count increased significantly ($P<0.05$) in SM(R) group, but the data was almost similar to that of control group of toxicity study [Table 3].

Histopathological study shows that among 16 organs studied, significant pathological changes were observed in only two organs i.e., kidney and testis, in RV and SD treated groups. SD seemed to be more toxic than RV to kidney. Peri-arteriolar cell infiltration was the disturbance observed in the cytoarchitecture of kidney in RV treated

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Table 2: Biochemical observations after treatment and recovery period in control, treated, and recovered rats

Parameters	Groups (Dose mg/kg)						
	Control (-)	RV (6.75)	RV(R) (-)	SM (6.75)	SM(R) (-)	SD (6.75)	SD(R) (-)
Blood sugar (mg/dl)	102.16 ± 4.02	099.17 ± 2.27	116.83 ± 2.36**$^{\#\#}$	100.00 ± 3.31	111.33 ± 3.99	099.50 ± 3.82	108.67 ± 2.56
Blood urea (mg/dl)	42.00 ± 3.03	44.33 ± 2.49	52.83 ± 3.65$^{\#\#}$	35.83 ± 0.79	44.83 ± 0.95**	45.17 ± 2.33	39.00 ± 1.06*
Serum creatinine (mg/dl)	0.65 ± 0.02	0.70 ± 0.03	0.72 ± 0.05	0.63 ± 0.02	0.73 ± 0.02**	0.77 ± 0.04*$^{\#\#}$	0.68 ± 0.03
Serum cholesterol (mg/dl)	58.50 ± 5.16	50.67 ± 2.67	53.50 ± 4.26	53.67 ± 4.48	57.83 ± 7.89	45.50 ± 2.64*	52.00 ± 3.18
Serum triglyceride (mg/dl)	218.17 ± 47.49	87.00 ± 17.49*$^{\#\#}$	254.50 ± 72.39*	138.33 ± 33.85	139.17 ± 17.47	110.00 ± 22.48$^{\#}$	128.67 ± 6.93
Serum bilirubin (mg/dl)	0.62 ± 0.07	0.52 ± 0.02	0.65 ± 0.06	0.61 ± 0.03	0.55 ± 0.06	0.60 ± 0.07	0.68 ± 0.10
Serum alk. phos. (mg/dl)	239.17 ± 37.31	150.83 ± 12.99*$^{\#\#}$	97.67 ± 5.23**$^{\#\#}$	138.33 ± 9.86*$^{\#\#}$	96.67 ± 8.71**$^{\#\#}$	135.17 ± 13.00*$^{\#\#}$	101.00 ± 10.86$^{\#\#}$
SGOT (IU/l)	374.33 ± 57.67	291.67 ± 41.45	420.67 ± 48.89	317.33 ± 20.23	357.67 ± 58.92	329.50 ± 55.75	399.93 ± 93.09
SGPT (IU/l)	120.83 ± 10.18	97.17 ± 9.31	100.33 ± 10.22	95.67 ± 7.13	86.17 ± 8.01	95.17 ± 11.65	96.50 ± 14.96
Serum total protein (g/dl)	7.45 ± 0.28	7.38 ± 0.17	7.64 ± 0.17	7.35 ± 0.21	7.47 ± 0.33	7.53 ± 0.14	7.47 ± 0.14

Values are mean ± SEM of 6 animals (n = 6) in control, toxicity and recovery groups; *P≤0.05; **P≤0.01 by the student's 't' test, toxicity groups are compared with control group; recovery groups are compared with respective toxicity groups; $^{\#}P$≤0.05; $^{\#\#}P$≤0.01 by the multiple 't' test, toxicity and recovery groups are compared with control group

Table 3: Hematological observations after treatment and recovery period in control, treated, and recovered rats

Parameters	Groups (Dose mg/kg)						
	Control (-)	RV (6.75)	RV(R) (-)	SM (6.75)	SM(R) (-)	SD (6.75)	SD(R) (-)
Hb (%)	14.10 ± 0.23	12.42 ± 0.42*$^{\#\#}$	13.03 ± 0.33	13.42 ± 0.35	13.43 ± 0.36	14.67 ± 0.48	13.72 ± 0.22
RBC (10^{12}/l)	6.68 ± 0.30	6.35 ± 0.24	6.44 ± 0.33	6.55 ± 0.24	6.62 ± 0.60	6.75 ± 0.41	6.90 ± 0.30
MCV (fL)	77.43 ± 2.50	79.13 ± 0.94	78.58 ± 1.39	77.80 ± 0.77	78.70 ± 1.20	77.48 ± 1.14	79.55 ± 1.13
Hematocrit (%)	51.25 ± 0.97	50.22 ± 1.45	50.60 ± 2.65	50.88 ± 1.60	54.17 ± 3.88	51.42 ± 2.72	50.03 ± 2.08
MCH (Pg)	21.26 ± 0.75	19.63 ± 0.76	20.50 ± 1.12	20.67 ± 1.21	21.09 ± 1.86	22.08 ± 0.87	20.02 ± 0.61
MCHC (g/dl)	31.52 ± 0.10	27.95 ± 1.81	30.51 ± 1.12	30.47 ± 1.08	30.96 ± 1.75	31.89 ± 0.71	29.97 ± 0.71
RDW (%)	6.68 ± 0.21	6.22 ± 0.15	5.42 ± 0.40	6.15 ± 0.38	6.02 ± 0.45	5.77 ± 0.19**	6.13 ± 0.39
TLC (10^9/l)	1.79 ± 0.44	1.37 ± 0.37	2.05 ± 0.32	2.35 ± 0.36	2.37 ± 0.41	2.54 ± 0.46	2.68 ± 0.25
Lymphocyte (%)	66.85 ± 2.93	62.07 ± 2.18	60.85 ± 3.51	61.73 ± 1.87	62.35 ± 4.05	52.43 ± 4.16*$^{\#\#}$	62.28 ± 3.03
Monocyte (%)	2.78 ± 0.30	3.20 ± 0.25	3.38 ± 0.27	2.27 ± 0.16	3.05 ± 0.26*	2.18 ± 0.17	3.65 ± 0.73
Granulocyte (%)	30.37 ± 2.75	34.75 ± 2.00	35.78 ± 3.66	35.98 ± 1.93	34.60 ± 3.85	44.35 ± 4.17*$^{\#\#}$	34.07 ± 2.85
Platelet (10^9/l)	414.33 ± 42.92	346.83 ± 31.29	378.33 ± 51.94	467.83 ± 22.01	337.00 ± 67.41	444.17 ± 26.36	355.50 ± 48.32

Values are mean ± SEM of 6 animals (n = 6) in control, toxicity and recovery groups; *P≤0.05; **P≤0.01 by the student's 't' test; toxicity groups are compared with control group; recovery groups are compared with respective toxicity groups; $^{\#\#}P$≤0.01 by the multiple 't' test, toxicity and recovery groups are compared with control group

group and multiple hemorrhagic spots were observed in SD treated group.

Mild fatty changes and hemorrhagic spots were the pathological changes observed in the cytoarchitecture of liver in SM(R) group. But after the recovery period, almost normal cytoarchitecture of kidney was observed in both RV(R) and SD(R) groups, whereas mild fatty changes in cytoarchitecture of kidney was found in SM(R) group. The prostate was quiescent in RV and SM toxicity groups, and after the recovery, prostate became active in SM(R) group [Figures-1-6].

DISCUSSION

Body weight change is sum of the effects occurring in different parts of the body and decrease in body weight is an index of the toxicant induced decrease. This decrease in body weight observed in RV treated group may be due to toxicant induced degeneration and could be considered as a significant adverse effect. And increase in body weight in SM and SD treated albino rats indicate normal progressive health status of the animals and it is also indicative of the fact that no degenerative changes are occurring during SM and SD administration.

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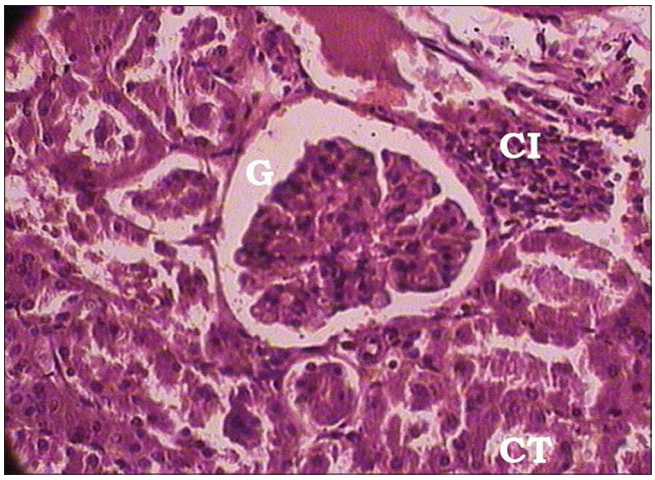


Figure 1: Cytoarchitecture of kidney in RV treated group 400× [Cell infiltration (CI) in kidney]

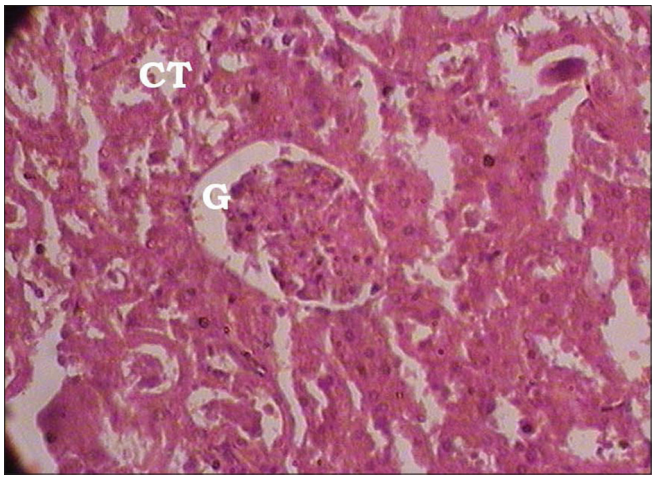


Figure 2: Cytoarchitecture of kidney in RV (R) group 400× [Normal cytoarchitecture]

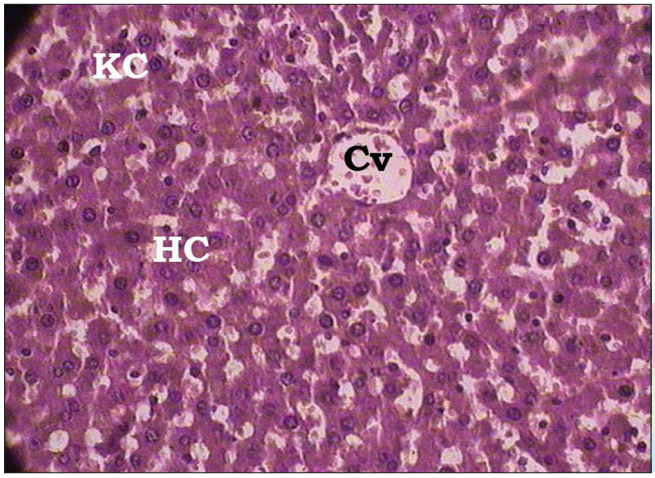


Figure 3: Cytoarchitecture of liver in SM treated group 400× [Normal cytoarchitecture]

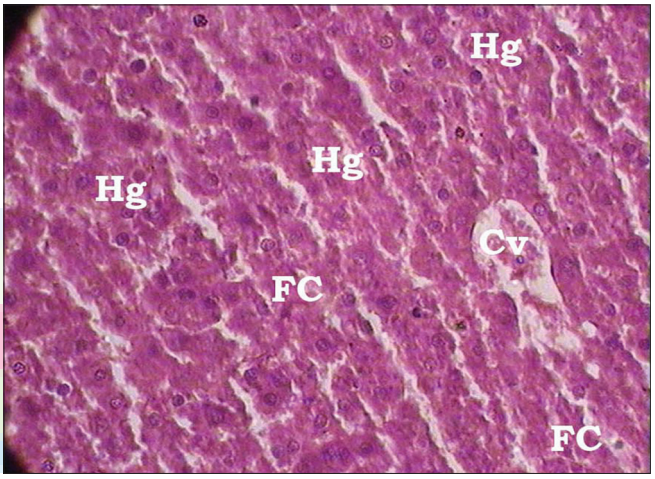


Figure 4: Cytoarchitecture of liver in SM (R) group 400× [Fatty changes (FC) and hemorrhagic spot (Hg) in liver]

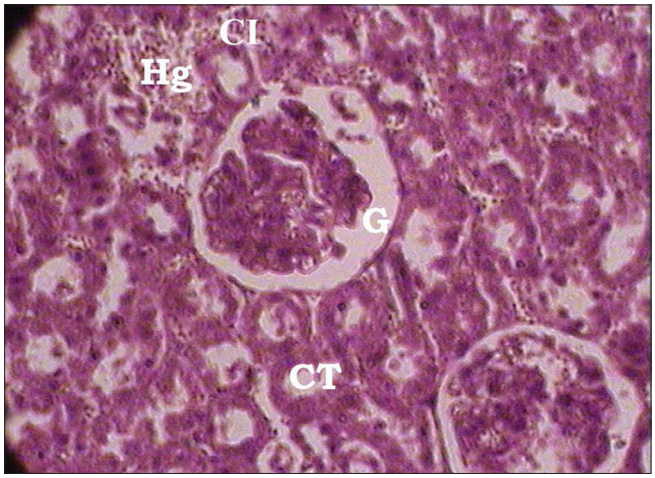


Figure 5: Cytoarchitecture of kidney in SD treated group 400× [Hemorrhagic spot (Hg) and cell infiltration (CI) in kidney]

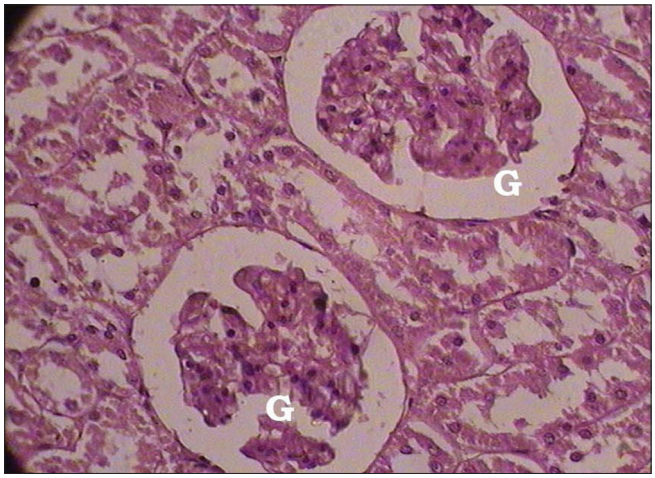


Figure 6: Cytoarchitecture of kidney in SD (R) group 400× [Normal cytoarchitecture]

The observed decrease in triglyceride level in RV treated group may be due to decreased formation of very low density lipoprotein (VLDL) in the liver and its reduced metabolism to inhibit the release of triglyceride. It may also indicate increased utilization of serum triglyceride pool in the body. It is also possible that the observed decrease

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may be due to decreased conversion of chylomicrons to VLDL. The observed decrease in total cholesterol level in SD treated group may be due to enhanced metabolism probably through the hydrolysis of cholesteryl ester and its utilization. The drug may be modulating the biosynthesis and absorption of cholesterol also. Liver injury leads to hypocholesterolemia and in such conditions, decrease is expected in triglyceride level also.[10] In this study, both serum cholesterol and serum triglyceride level was found to be decreased in RV and SD treated groups. Hence, it can be suggested that the observed changes are likely to be pathological in nature.

Both the serum urea and serum creatinine were increased in the RV treated group. Those findings indicate some pathology in kidney. The alkaloids of aconitine group affect the sodium channels on the cell membrane, which can lead to increased uptake of sodium and other ions into the cells.[11] The increased sodium uptake into the cells may lead to plasma sodium depletion, which may cause pathology in kidney and the effect is manifested by increase in serum urea and creatinine level. The increase in serum creatinine found in SD treated group may be considered as pathological; level of creatinine is increased in nephropathy,[10] so there may be some pathology in the kidneys.

The significant decrease in hemoglobin percentage observed in RV treated group may be due to hypoproliferation of red blood cells. The hypoproliferation occurs may be because of impaired renal function. The impaired renal function causes inadequate stimulation of erythropoietin. And the inadequate stimulation of erythropoietin leads to hypoproliferative anemia.[10] The increase in mean corpuscular volume found in RV treated group also supports this phenomenon.

Among the red cells indices, red cells distribution width was decreased significantly in SD treated group. Red cells distribution width varies due to difference in size of the red cells. The decrease in red cells distribution width may be indicative of homogeneous distribution of red cells in the animals of SD treated group. The significant increase in granulocyte count and significant decrease in lymphocyte count along with increase in total WBC count may indicate occurrence of acute inflammation in this group.

The biochemical and hematological changes observed in RV and SD treated groups are supported by the findings of histopathological study. Pathological changes in the cytoarchitecture of kidney were observed in RV and SD treated groups. And again, these changes may be due to presence of aconitine group of alkaloids, which may alter sodium metabolism leads to pathological changes in the kidney.

Increase in blood sugar and blood urea level found in RV(R) group clearly indicates persistent liver injury after the recovery period in RV administered group. Liver is the main organ for carbohydrate and urea metabolism.[12] In the toxicity study, no injury in liver tissue was found, but after the recovery period injury in hepatic tissues was observed. This hepatic functional derangement may be the cause of the hyperglycemia observed after the recovery period of all the test drugs administered groups.

Serum creatinine level was already increased in RV toxicity group and further increase after recovery period is indicative of persistent pathology in kidney. Serum creatinine level was decreased in SM toxicity study, but a huge (15.87%) highly significant increase after the recovery period indicates the occurrence of pathological condition in kidney. Both serum urea and creatinine were increased in SD toxicity group, and decrease in both the parameters after recovery period could be considered recovery from the earlier trend.

The reversals in the observed changes in red blood cell count and red cell indices indicate significant recovery from the impact of the test drugs on the red blood cell count and indices during the recovery period. A significant increase in granulocyte count observed in SD toxicity group was reversed after the recovery period and decrease in granulocyte count was found. It indicates a successful recovery from an acute inflammatory condition occurred during toxicity study of SD group after recovery period.

The body weight was increased significantly in all the recovery groups. The body weight was decreased during toxicity study in RV treated group, but it was increased highly significantly ($P<0.01$) after the recovery period which indicates reversal of toxicant induced tissue degenerative changes. The reversal could be considered as significant effect.

Among 16 organs studied in chronic toxicity study, significant pathological changes were observed only in 4 organs i.e., liver, kidney, testis, and prostate. So after the recovery, histopathological study of these four organs was carried out. The histopathology of liver in SM(R) group indicates there was existence of persisting pathology. After recovery period, almost normal cytoarchitecture of kidney observed in both RV(R) and SD(R) groups indicates reversal of toxicant induced pathological changes in kidney. All these changes were suggestive of partial recovery from the renal toxicity of all the test drugs, but existence of persisting hepato-toxicity, which was found in chronic toxicity study.

Analysis of the data of the chronic toxicity study reveals all of the test drugs do not show serious toxic effects in biochemical, hematological and histopathological parameters, and vital organs. However, moderate toxicity in RV and SD groups were seen in liver and kidney. This indicates that they should be administered carefully in persons with functional insufficiency of these organs. It is observed that the changes in the parameters were less in treated

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aconite groups in comparison to raw aconite group, may be due to conversion of the alkaloid aconitine to aconine after Shodhana treatment.[13] Aconitine affects sodium channels on the cell membrane, but aonine is antagonistic to aconitine.[14]

The observed changes as discussed above are reversible to some extent in kidney as well as in liver. Analysis of the data of the recovery study reveals that rats of all recovery groups have shown partial to significant recovery with respect to biochemical, hematological, ponderal, and histopathological parameters. The obtained data from the recovery study are suggestive of partial to complete recovery after stoppage of test drugs in RV(R) and SD(R) groups. Some persisting pathological conditions observed in SM(R) group indicates sudden withdrawal of test drug could cause adverse effects and are suggestive of tapering withdrawal of the test drug.

The study revealed that administration of raw aconite leads to impairment in kidney and liver functions; treated aconite in cow's milk causes toxicity in kidney, but Shodhana treatment in cow's urine reduces the toxic effect of aconite significantly. The toxicity of aconite is reversal after certain period of withdrawal.

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