



Research Article

ACUTE AND SUB ACUTE TOXICITY STUDY OF ABHRAKA BHASMA- INCINERATED MICA ASH

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ABSTRACT

Among the various *Ras dravyas* (mineral drugs), *Abhraka Bhasma* (incinerated mica ash) is widely used in therapeutics. Many herbal and other organic materials have been quoted in reference for various procedures in preparing *Abhraka bhasma*. It is wonderful that different pharmacological action has been attributed to different *Dravyas* used in the pharmaceutical processing of *Abhraka Bhasma*. However, to establish the safety of such metallic and mineral formulation it is the need of the hour to generate scientific data for such drugs. In the present study two samples of *Abhraka Bhasma* were prepared using two different methods. The safety profile of *Abhraka Bhasma* samples (AB-1 & AB-2) were evaluated by conducting acute and subacute toxicity study as per OECD Guidelines. Both acute and sub-acute toxicity study demonstrated safety of AB-1 and AB-2 when administered at therapeutic dose, TED X5 dose and TED X10 dose. Even though the sample AB-1 was prepared using a smaller number of *Putra*, it was sufficient for preparing good quality of *Bhasma* and was non-toxic.

INTRODUCTION

The use of metal and mineral drugs in therapeutics has been started from the period of classical texts. However, their use in therapeutics has been well flourished only after the development of *Rasa Shastra*. The scholars of *Rasa Shastra* have preferred the minerals over the herbals because of their supremacy, in terms of providing quick relief in lesser doses, to treat even the incurable disorders.^[1]

Rasa Shastra (iatrochemistry) is not only aimed at *Dhatuvada* i.e., converting the lower metals into noble ones but also advocates a definite and concrete ideology in managing the disease conditions-*Dehavada*, which is evident by the various references for therapeutics available for every member of the *Rasa* group.

Among the various *Ras dravyas* (mineral drugs), *Abhraka* (mica) occupies a significant position in both streams, *Dhatuvada* as well as *Dehavada*.

The importance of *Abhraka* in mercurial processing is clearly depicted in one of the earliest treatise *Rasa Hridya Tantra*, that there is no other agent except mica to clip the wings of mercury (*Pakshachchedana*) which is imminent for swooning and binding of mercury^[2,3]. Utility of *Abhraka bhasma* is well established through its continuous use as an excellent medicine since medieval period. Many herbal and other organic materials have been quoted in reference for various procedures in preparing *Abhraka bhasma*. It is wonderful that different pharmacological action has been attributed to different *Dravyas* used in the pharmaceutical processing of *Abhraka Bhasma*. However, to establish the safety of such metallic and mineral formulation it is the need of the hour to generate scientific data for such drugs. Also, classical text of *Rasa shastra* mentions different cycle of *Putra* (incineration) and trituration media for preparations of same *Bhasma*. It is also necessary to find out whether *Bhasma* prepared using different triturating media and different cycle of *Putra* (incineration) are equally safe considering this present study is attempted to evaluate the Safety of *Abhraka bhasma* prepared by different methods.

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MATERIAL AND METHODS

Preparation of *Abhraka Bhasma*

Drug and Chemical

Impure *Abhraka* (mica) was purified through process of heating and quenching in decoction of *Triphala* (*Terminalia chebula*, *Terminalia Bellirica* *Emblica officinalis*)^[4]. After purification *Dhanyabhrikakarana* (insertion of *Abhraka* in sour gruel with rice husk), was done in sour gruel as per R.R.S^[5]. Two samples of *Abhraka bhasma* were prepared as per Ayurveda classics. One sample (AB-1) was prepared by triturating the purified *Abhraka* with *Erand patra Swarasa*^[6] (juice of *Ricinus communis* leaf) and *Guda*^[7] (jaggery) and other sample (AB-2) was prepared by triturating with *Kasmarda Swarasa*^[8,9] (juice of *Cassia occidentalis* leaf).

The prepared samples of *Abhraka Bhasma* were analysed for organoleptic and physico chemical parameters. The safety profile of *Abhraka Bhasma* samples (AB-1 & AB-2) was evaluated by conducting acute and subacute toxicity study as per OECD guidelines.

The study was conducted on mature Wistar strain male albino rats, weighing 150-200g obtained from animal house, National institute of Ayurveda, Jaipur. Animals were acclimatized for a period of seven days in laboratory conditions prior to the experiments. Rats were housed in poly propylene cages (six rats per cage), at an ambient temperature of 25±2°C with 12 hr light: 12 hr dark cycle in the animal house of National Institute of Ayurveda, Jaipur. The animals were provided with standard pellet diet and water *ad libitum*. Ethical clearance was obtained from Institutional Animal Ethics Committee, before conducting the experiment (IAEC Clearance no: NIA/IAEC/2021/01). The principles of Laboratory Animal Care were followed throughout the duration of the experiment.

Dose Fixation

As per classical guideline, the therapeutic clinical dose of AB is 125 to 250mg twice a day the suitable dose for rat was calculated by referring to table of Paget and Barnes and the dose was found to be 22.5mg/kg body weight. The test drug was administered orally. The test formulation was administered in a single dose by gavages using oral feeding needles. Animal was kept fasting prior to dosing. Following the period of fasting, the weight of each animal was measured and the test formulation was administered.

Acute Toxicity Study

Acute oral toxicity of *Abhraka Bhasma* (AB1 and AB2) were conducted according to OECD guideline 423^[10]. Three animals were selected for each group.

Group 1A, 1B, 1C were selected for acute toxicity study of AB1 and Group 2A, 2B, 2C were selected for acute toxicity study of AB2 and were administered test drug at doses of 50, 300, and 2000mg/kg in 5% gumacacia suspension. Animal were observed for behavioral changes, sign of toxicity and mortality continuously for first six hour and then periodically up to 14 days continuously. Animals were observed individually after dosing during the first 30 minutes, and periodically during the first 24 hours, with special attention was given during the first 4 hours and daily thereafter, for a total of 14 days. Observations included changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. Body weight was recorded on 1st, 7th, 14th day. Single dose was administered and behavior, hematological and histopathological evaluation was done according to OECD Guideline.

Sub-acute Toxicity study

Subacute toxicity of *Abhraka Bhasma* was conducted as per OECD guidelines 407^[11]. Study design: Ten Wistar albino rats animals were selected for each group, consisting of 5 male & 5 female rats. Animals of control group received vehicle (5% gum acacia solution). Group I to III received AB-1 at TED (22.5mg/kg), TEDX5 (112.5mg/kg/) TEDX10 (225mg/kg/) group IV to VI received AB-2 at TED, TEDX5, TEDX10 Dose levels, respectively.

Test drugs were administered for 28 days using oral gavage. During the study period, the animals were observed for normal physiological functions, behavioral variations and alterations in biochemical parameters. On the 28th day the final weight of the rats were measured and then they were anesthetized under halothane and blood samples collected from each animal by cardiac puncture for hematological and biochemical analysis. After collection of blood samples, the rats were sacrificed, and gross pathological observations were performed on liver and kidney to check for any gross lesions.

Statistical Analysis

All values were expressed as Mean±SEM. Statistical Analysis was performed by one way analysis of variance (ANOVA) followed by Dunnet Multiple comparison. P value <0.05 were considered significant. Graph pad prism (version 5.4) was used in statistical analysis.

RESULTS**Acute Toxicity Study**

In the present study observation of acute toxicity was carried out according to the OECD guidelines 423. Animals were administered *Abhraka bhasma* (AB-1, AB-2) at a dose of 50, 300, 2000mg/kg/oral as single dose. Animals were monitored individually after dosing at least once during the first 30 minutes, and periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days. Observations included changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, spontaneous motor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. During the study period no mortality was seen in the experimental animals of all six groups who were administered test drugs and none of the animal showed any signs of respiratory depression, narcosis and catatonia, and other toxic signs during the experimental study. There was no loss of fur, change in colour of fur, skin colour of any rats. Food consumption and water intake was found normal. No

variations were observed in the hematological and biochemical parameters also. Toxicological evaluation of acute toxicity study revealed that 2 samples of *Abhraka bhasma* are essentially non-toxic and safe after oral administration.

Sub acute Toxicity

The purpose of subacute toxicity study was to assess the toxicity potential of AB-1 and AB-2 when dosed for 28 days by oral route in Wistar albino rats as per the OECD 407 guideline. The study design included 3 groups each for 2 test drugs and a control group resulting 7 groups consisting of 3 male and 3 female rats. Vehicle control group was dose with 5% gum acacia solution, low dose was therapeutic dose with 22.5mg/kg, mid-dose (T.D.X 5) with 112.5mg/kg, high dose (T.D.X10) with 225mg/kg orally for 28 days.

All rats were observed for clinical signs, changes in body weight, food consumption, hematology, clinical chemistry and gross pathology. Blood samples were collected on day 29 prior to sacrifice of the animals after overnight fasting. The animals were humanely sacrificed and subjected to a detailed necropsy. There were no test substance-related clinical signs or mortality observed at any of the tested groups.

Table 1: Effect of Test drugs on Haematological Parameters in Acute Toxicity Study of Sample (AB-1)

CBC Parameters	Group 1A Mean \pm SEM	Group 1 B Mean \pm SEM	Group 1C Mean \pm SEM
WBC	3.10 \pm 0.06	4.03 \pm 1.22	6.50 \pm 1.30
LYM%	48.70 \pm 9.48	66.63 \pm 10.07	52.13 \pm 5.49
MID%	9.10 \pm 1.08	6.67 \pm 0.41	10.50 \pm 0.52
NEUT%	42.20 \pm 10.30	26.70 \pm 9.70	37.37 \pm 5.27
LYM#	1.53 \pm 0.32	2.93 \pm 1.12	2.70 \pm 0.32
MID#	0.27 \pm 0.03	0.27 \pm 0.09	0.57 \pm 0.03
NEUT#	1.30 \pm 0.30	0.83 \pm 0.03	1.90 \pm 0.26
RBC	5.95 \pm 0.09	7.07 \pm 0.83	6.43 \pm 0.06
HGB	11.37 \pm 0.03	12.73 \pm 1.03	12.00 \pm 0.06
HCT	33.07 \pm 0.35	36.87 \pm 1.77	36.37 \pm 0.34
MCV	55.40 \pm 1.10	56.07 \pm 0.23	56.67 \pm 0.07
MCH	18.93 \pm 0.35	18.10 \pm 0.61	18.63 \pm 0.09
MCHC	34.33 \pm 0.27	32.37 \pm 0.95	32.90 \pm 0.20
RDW-SD	30.60 \pm 3.69	28.50 \pm 0.60	29.70 \pm 0.00
RDW-CV	14.40 \pm 0.06	14.90 \pm 0.40	15.37 \pm 0.03
PLT	445.67 \pm 23.31	488.67 \pm 138.69	285.00 \pm 14.29
MPV	8.23 \pm 0.68	9.37 \pm 0.62	5.63 \pm 2.62
PDW	15.57 \pm 0.52	16.43 \pm 0.33	16.13 \pm 0.13
PCT	0.37 \pm 0.05	0.47 \pm 0.17	0.23 \pm 0.01
P-LCR	17.63 \pm 6.84	28.07 \pm 5.82	18.80 \pm 0.26

Table 2: Effect of Test drugs on haematological parameters in Acute toxicity Study of Sample (AB-2)

CBC Parameters	Group 2A Mean \pm SEM	Group 2 B Mean \pm SEM	Group 2 C Mean \pm SEM
WBC	4.13 \pm 2.13	5.70 \pm 1.35	8.80 \pm 0.06
LYM%	66.70 \pm 11.55	35.93 \pm 14.31	59.27 \pm 0.30
MID%	7.47 \pm 3.83	7.27 \pm 2.54	10.50 \pm 0.42
NEUT%	25.83 \pm 7.93	56.80 \pm 12.02	30.23 \pm 0.23
LYM#	2.30 \pm 0.70	1.63 \pm 0.18	5.23 \pm 0.07
MID#	0.43 \pm 0.38	0.47 \pm 0.20	0.93 \pm 0.03
NEUT#	1.40 \pm 1.05	3.60 \pm 1.31	2.63 \pm 0.03
RBC	6.24 \pm 0.16	6.38 \pm 0.26	5.74 \pm 0.05
HGB	11.90 \pm 0.10	11.60 \pm 0.56	10.77 \pm 0.07
HCT	36.63 \pm 0.34	35.23 \pm 1.18	32.57 \pm 0.27
MCV	58.93 \pm 1.91	55.33 \pm 0.48	56.87 \pm 0.07
MCH	19.07 \pm 0.53	18.13 \pm 0.12	18.73 \pm 0.23
MCHC	32.47 \pm 0.52	32.87 \pm 0.49	33.03 \pm 0.38
RDW-SD	30.33 \pm 1.62	26.00 \pm 0.00	27.90 \pm 0.00
RDW-CV	15.03 \pm 0.34	13.77 \pm 0.13	14.37 \pm 0.03
PLT	649.00 \pm 10.82	432.67 \pm 91.67	718.67 \pm 31.26
MPV	8.43 \pm 0.15	8.80 \pm 0.35	7.83 \pm 0.03
PDW	15.10 \pm 0.35	16.03 \pm 0.67	14.63 \pm 0.03
PCT	0.54 \pm 0.01	0.37 \pm 0.06	0.56 \pm 0.03
P-LCR	15.77 \pm 2.08	22.17 \pm 4.88	10.67 \pm 0.13

Table 3: Effect of test drugs on Biochemical parameters in Acute toxicity Study of Sample (AB-1)

Biochemical Observation (RFT, LFT)	Group 1A Mean \pm SEM	Group 1 B Mean \pm SEM	Group 1C Mean \pm SEM
Renal Function Test			
Blood Urea	44.73 \pm 1.79	44.6 \pm 2.36	46.1 \pm 1.01
Serum Creatinine	0.31 \pm 0.02	0.31 \pm 0.02	0.26 \pm 0.02
Liver Function Test			
Total S. Bilirubin (mg/dl)	0.15 \pm 0.01	0.16 \pm 0.01	0.15 \pm 0.02
Direct Bilirubin (mg/dl)	0.25 \pm 0.05	0.46 \pm 0.08	0.30 \pm 0.06
SGOT (IU/ml)	140.37 \pm 5.51	141.53 \pm 5.58	133.20 \pm 5.89
SGPT (IU/ml)	89.40 \pm 3.07	92.53 \pm 1.99	92.73 \pm 2.04
Serum Alkaline Phosphates	113.40 \pm 1.57	116.33 \pm 2.46	117.77 \pm 1.60

Table 4: Effect of test drugs on Biochemical parameters in Acute toxicity Study of Sample (AB-2)

Biochemical Observation (RFT, LFT)	Group 2A Mean \pm SEM	Group 2 B Mean \pm SEM	Group 2 C Mean \pm SEM
Renal Function Test			
Blood Urea	44.73 \pm 2.48	43.8 \pm 1.57	45.17 \pm 2.38
Serum Creatinine	0.30 \pm 0.03	0.31 \pm 0.03	0.31 \pm 0.02

Liver Function Test			
Total S. Bilirubin (mg/dl)	0.15±0.02	0.12±0.01	0.14±0.02
Direct Bilirubin (mg/dl)	0.45±0.11	0.37±0.05	0.40±0.05
SGOT (IU/ml)	133.57±6.21	142.80±1.04	142.97±1.41
SGPT (IU/ml)	94.33±2.87	91.90±2.75	93.87±1.42
Serum Alkaline Phosphates	116.40±4.69	115.17±4.85	120.03±2.51

Table 5: Effect of test drugs on haematological parameters in Sub Acute toxicity Study of sample (AB-1)

CBC Parameters	Group 1(Control) Mean ±SEM	Group 2(AB1 TED) Mean ±SEM	Group 3 Mean ±SEM	Group 4 Mean ±SEM
WBC	3.92±0.54	3.63±0.66	4.68±0.83	3.37±0.71
LYM%	46.66±5.90	49.87±5.63	47.75±5.03	51.21±4.29
MID%	10.65±1.04	8.71±0.59	9.73±0.96	11.7±1.68
NEUT%	38.19±4.32	41.42±5.15	42.52±5.22	37.09±3.31
LYM#	3.07±0.93	1.66±0.45	1.97±0.24	1.78±0.43
MID#	0.39±0.05	0.32±0.05	0.44±0.08	0.39±0.08
NEUT#	1.46±0.17	1.33±0.22	2.27±0.61	1.28±0.30
RBC	6.842±0.53	7.23±0.30	6.448±0.25	6.1±0.40
HGB	11.37±0.72	12.11±0.39	10.66±0.40	10.23±0.65
HCT	38.149±3.33	40.39±1.98	36.17±1.44	34.31±2.33
MCV	56.41±0.76	55.95±1.36	56.17±0.31	56.14±0.74
MCH	16.72±0.38	16.64±0.35	16.5±0.11	16.74±0.25
MCHC	29.73±0.62	29.19±0.38	29.46±0.21	29.94±0.33
RDW-SD	27.98±0.74	27.69±0.76	27.7±0.52	26.57±0.29
RDW-CV	14.36±0.32	14.28±0.29	14.43±0.25	13.87±0.15
PLT	454.4±45.08	420.64±105.10	400.7±24.97	367.9±53.74
MPV	11.03±1.36	63.43±53.07	9.26±0.78	10.23±1.06
PDW	15.81±0.24	15.17±1.11	15.97±0.26	16.35±0.34
PCT	3.948±3.45	2.07±1.52	0.359±0.03	0.356±0.06
P-LCR	31.36±6.47	27.14±6.29	23.55±4.89	28.68±4.98

Table 6: Effect of test drugs on haematological parameters in Sub Acute toxicity Study of sample (AB-2)

CBC Parameters	Group1 (Control) Mean ±SEM	Group 5 Mean ±SEM	Group 6 Mean ±SEM	Group 7 Mean ±SEM
WBC	3.92±0.54	5.7±0.59	3.81±0.56	3.61±0.59
LYM%	46.66±5.90	54.81±4.01	47.56±1.27	53.91±4.40
MID%	10.65±1.04	10.81±1.66	9±0.68	8.04±0.62
NEUT%	38.19±4.32	34.38±3.48	43.44±1.43	38.05±4.39
LYM#	3.07±0.93	3.25±0.54	1.86±0.30	2.01±0.39
MID#	0.39±0.05	0.58±0.09	0.33±0.05	0.29±0.04
NEUT#	1.46±0.17	1.92±0.15	1.62±0.22	1.31±0.23
RBC	6.842±0.53	6.62±0.33	6.695±0.17	6.879±0.24
HCT	38.149±3.33	36.08±1.65	30.84±0.96	33.45±1.06

MCV	56.41±0.76	54±1.72	46.09±0.47	48.93±1.52
RDW-SD	27.98±0.74	27.32±0.40	25.05±0.42	25.81±0.44
RDW-CV	14.36±0.32	14.06±0.15	13.85±0.14	14.03±0.15
PLT	454.4±45.08	344.5±24.26	363.5±31.81	321.14±59.44
MPV	11.03±1.36	8.44±0.20	9.46±0.62	64.92±52.91
PDW	15.81±0.24	15.64±0.19	16.66±0.29	16.03±1.20
PCT	3.948±3.45	0.287±0.02	0.352±0.06	6.715±4.83
P-LCR	31.36±6.47	18.77±2.07	27.32±2.87	37.127±5.98

Table 7: Effect of test drugs on Biochemical parameters in Sub Acute toxicity Study of sample (AB-1)

Biochemical Observation (RFT, LFT)	Group 1 Mean ±SEM	Group 2 Mean ±SEM	Group 3 Mean ±SEM	Group 4 Mean ±SEM
Renal Function Test				
Blood Urea	43.97±0.88	47.03±1.22	46.87±0.77	46.52±0.84
Serum Creatinine	0.41±0.02	0.34±0.02	0.32±0.02	0.31±0.02
Liver Function Test				
Total S. Bilirubin (mg/dl)	0.17±0.01	0.15±0.01	0.15±0.01	0.14±0.01
Direct Bilirubin (mg/dl)	0.30±0.02	0.25±0.03	0.32±0.02	0.24±0.03
SGOT (IU/ml)	139.48±2.47	135.43±3.83	137.68±2.75	135.22±3.29
SGPT (IU/ml)	88.60±2.47	89.49±2.47	89.50±1.22	88.36±1.65
Serum Alkaline Phosphates	117.02±1.77	119.83±0.88	117.96±1.33	119.42±1.11

Table 8: Effect of test drugs on Biochemical parameters in Sub Acute toxicity Study of sample (AB-2)

Biochemical Observation (RFT, LFT)	Group 1 Mean ±SEM	Group 5 Mean ±SEM	Group 6 Mean ±SEM	Group 7 Mean ±SEM
Renal Function Test				
Blood Urea	43.97±0.88	45.48±0.91	45.90±1.08	46.37±0.82
Serum Creatinine	0.41±0.02	0.36±0.02	0.34±0.02	0.29±0.02
Liver Function Test				
Total S. Bilirubin (mg/dl)	0.17±0.01	0.16±0.01	0.16±0.01	0.15±0.01
Direct Bilirubin (mg/dl)	0.30±0.02	0.23±0.02	0.24±0.02	0.25±0.02
SGOT (IU/ml)	139.48±2.47	134.56±3.65	140.76±1.72	141.03±1.55
SGPT (IU/ml)	88.60±2.47	86.64±1.86	89.84±1.91	90.14±1.39
Serum Alkaline Phosphates	117.02±1.77	117.32±2.35	118.27±1.23	119.34±1.25

DISCUSSION

Determination of food consumption was important in the study of safety of a product with therapeutic purpose as proper intake of nutrients is essential to the physiological status of the animals and to the accomplishment of the proper response to the drug tested instead of a false response due to improper nutritional conditions.

Food consumption and water intake was found normal (i.e., 10-12gm/rat and 15-20ml/rat) throughout the study. No significant changes were observed in treated groups and this reveals that test

drugs did not adversely affect the basic metabolic processes of the experimental animals.

Body weight is an important indicator of physiological as well as pathological state of animals. After exposure to few possible toxic substances, there will be changes in body weight gain and internal organ weights which would reflect toxicity.^[12] The body weight changes are markers of adverse effects of drugs and chemicals and if the body weight loss observed is more than 10% of initial body weight, it will be considered as statistically significant.^[13]

In the sub acute toxicity study all test groups showed normal progressive weight gain. Percentage change in body weight pattern did not differ significantly from the changes observed in control group.

Haematological parameters can be considered as the most sensitive parameters to evaluate the toxicity of medicines and a blood profile normally gives important information on the reaction of body to damage or stress. In present study there were no statistically significant variations in the haematological parameters after 28 days of administration of test drugs.

In histopathological studies no pathological changes were observed in liver and kidney in all groups. Histopathology of liver of all the groups showed Normal hepatic cells with central vein, sinusoidal dilation, liver lobules and portal. No abnormal changes were detected in the histopathology of kidney of all groups. Normal architecture of tubules, Bowman's capsule and Pycnotic nuclei were seen.

CONCLUSION

The sub-acute toxicity study demonstrated safety of AB-1 and AB-2 when administered at therapeutic dose, TED X5 dose and TED X10 dose. Even though the sample AB-1 was prepared using a smaller number of *Putra*, it was sufficient for preparing good quality of *Bhasma* and was nontoxic.

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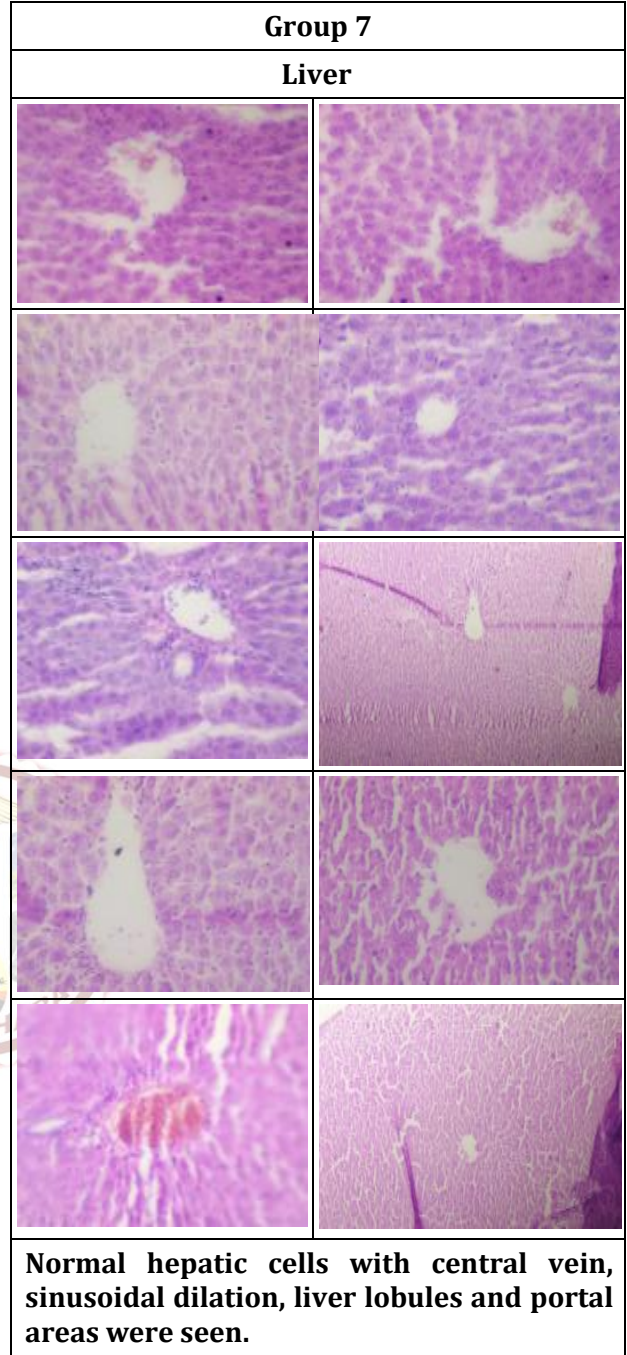
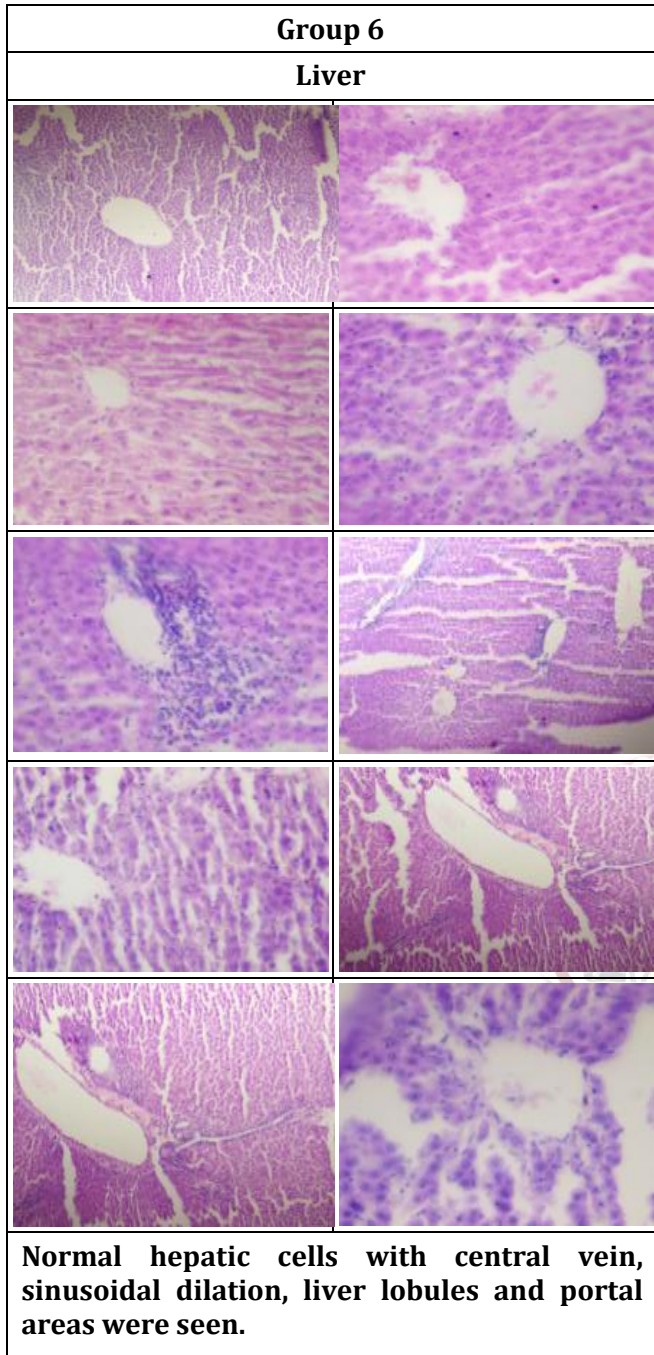
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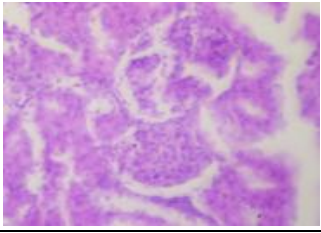
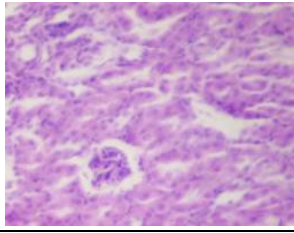
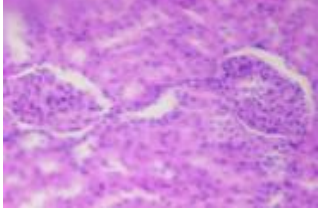
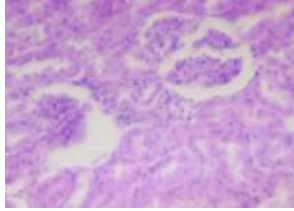
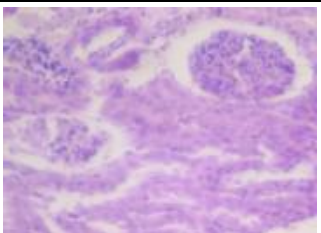
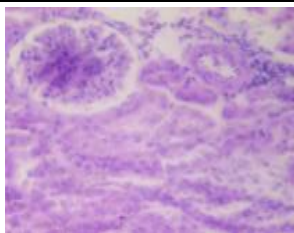
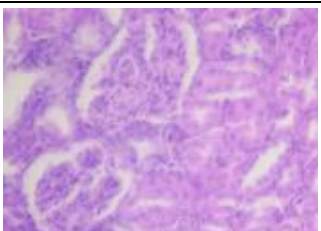
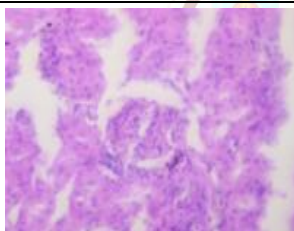
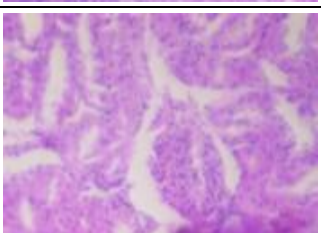
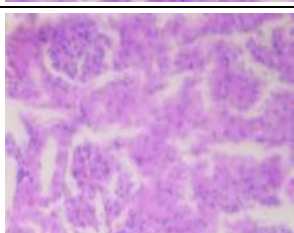
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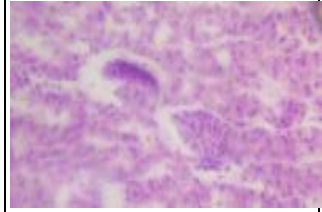
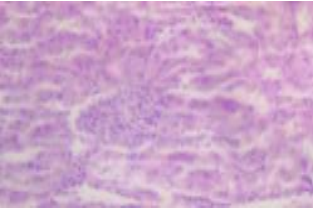
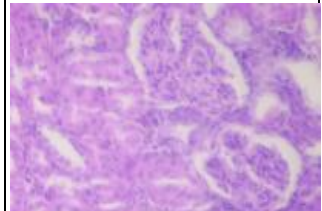
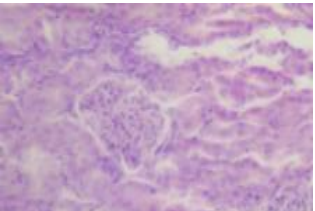
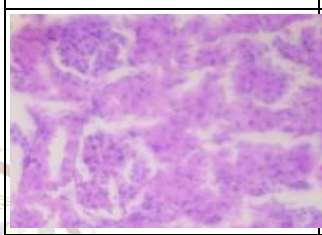
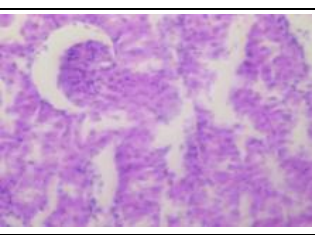
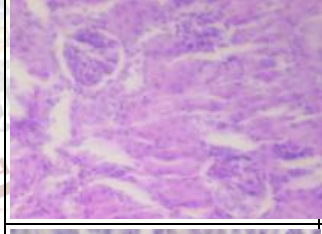
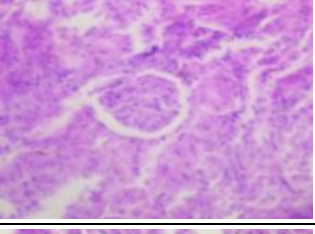
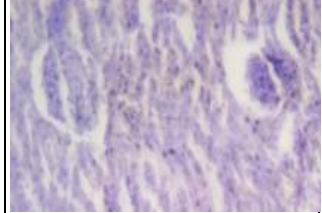
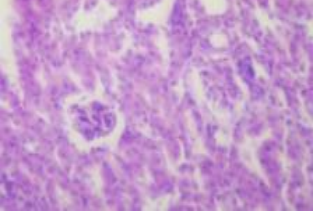
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Group 6	
Kidney	
	
	
	
	
	
<p>Normal architecture of tubules, Bowman's capsule and Pycnotic nuclei were seen.</p>	

Group 7	
Kidney	
	
	
	
	
	
<p>Normal architecture of tubules, Bowman's capsule and Pycnotic nuclei were seen.</p>	

