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SUB-ACUTE TOXICITY STUDY OF MERCURIAL COMPOUND RASAKARPURA

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ABSTRACT

Heavy metal toxicity is a global issue, most of the people are not having idea about *Ayurvedic* metallic preparations, they think that these causes damages of liver, kidney, brain etc. but this is a myth and not true as per text. Therefore, it is necessary to proved by experimental study. The present study has been done on *Rasakarpura* which is one of the *Kupipakwa* Mercurial preparations and which was first cited in 12th Century AD. From 12th Century to present era lot of modifications have been made by the *Rasacharyas* in the preparation of *Rasakarpura* along with its ingredients. For the present study five samples of *Rasakarpura* coded as RK-1, RK-2, RK-3, RK-4 & RK-5 were prepared and subjected to sub acute toxicity study through Histopathological and Biochemical studies in albino rats. The observations and results shown Hepatotoxicity is more in R.K-4, moderate in R.K-2 and less in R.K-5, R.K-3 andRK-1. The Renal toxicity was also seen more in R.K-4, moderate in R.K-5, less in R.K-1 and R.K-2 and not seen in R.K-3 whereas cerebral toxicity was more in R.K-2, moderate in R.K-5 and R.K-1 and in R.K-3 and R.K-4 it was less. Observations were showed that R.B.C, H.B% less compare to control group. Histopathological results shown R.K-3 was safer and R.K-2 was showing more toxic result whereas biochemical report shown R.K-2 was more toxic and R.K -3 was having less toxicity.

Keywords: *Ayurvedic,* toxicity, *Kupipakwa,* Hepatotoxicity, Histopathological, Biochemical

INTRODUCTION

Rasashastra is an important branch which plays wide role in curing diseases with minute dose. Various *Rasaoushadis* are having toxic effects when followed improper preparation. Heavy metal toxicity is global issue, most of the people are not having idea about *Ayurvedic* metallic preparations, and they think that liver, kidney and brain etc. will get damage by using such type of preparations which is not correct on the basis of *Rasa* classics. Before administrating such type of preparations,

scholars should know the processing and adhered strictly by adopting different procedures like *Shodhana* (purification), *Bhavana* (Triturating with antitoxic, antichelating juices and decoctions), *Marana* (incineration) etc. Here, the study has been done on *Rasakarpura* which is one of the *Kupipakwa* preparations.

First explanation of the preparation *Rasakarpura* can be seen in name of *Ghanasara rasa* in the classical text *Rasa Prakasha Sudhakara* of 13th Century A.D[1]. by Sri. *Yashodhara Bhatta*. Later there is chronological development in its preparation, developed by later authors such as *Rasendrachintamani*, *Rasendra Sara Sangraha*, *Ayurveda Prakasha*, *Bhavaprakasha*, *Rasa Tarangini*, *Rasamrita* etc. Each author has designed this unique formula as per his utility and administration. In general *Rasakarpura* is place in the category of *Sa-agni*, *Nirgandha*, *Bahirdhuma* classification of *kupipakwa* (*Murchana*) preparation i.e. processing of *Parada*, *Gandhakamla* and *Saindhavalavana* with *Agnisamskarakupipakwa* method results in the formation of *Karpuravatswetavarnaaushadha* that is *Rasakarpura*. When used along with different *Sahapana* and *Anupana* with appropriate *Matra*, it cures various disorders whereas action can be assessed on viewing its multiple indications that is *Twak-vikara*, *Kriminashana*, *Ruchikara* etc. Keeping its immense qualities in view an experimental study was carried out on albino rats with following aims and objectives-

1) To compare sub acute toxicity study of five different samples of *Rasakarpura* through histopathological findings.
2) To find out biochemical changes in the experimental subjects.
3) To form a basis for providing further long term chronic study by providing guidance on likely tolerated doses and assure the safety of *Rasakarpura* prepared with five methods.

Material & Methods-

The five samples of *Rasakarpura* R.K-1, R.K-2, R.K-3, R.K-4, R.K-5 were prepared in accordance with *Kupi* method (*Rastarangini*)[2], *Anubhuta* method[3], *Kupi* method (*Rasmitra*)[4], *Sthaliyantra* method (*Paradasamhita*)[5], *Damaruyantra* method (*Yogatarangini*)[6] respectively.

Table 1: Showing ingredients of *Rasakarpura* samples

S.No	Drug/Ingredient	R K-1	R K-2	R K-3	R K-4	R K-5
1.	*Hingula* (HgS)for *Parada*	(1500g for all formulations)				
2.	Extracted *Parada* (Hg)	48g	180g	124g	100g	120g
3.	H_2SO_4	72 g	100g	-	-	-
4.	*Saindava Lavana* (Rock salt)	64 g	100g	50g	100g	85g
5.	*Navasadara* (NH_4CL)	-	-	50g	-	-
6.	*Sphatika* (K_2SO_4 $(Al_2SO_4)_3$ 24 H_2O)	-	-	50g	50g	85g
7.	*Tuttha* ($CuSO_4$ $5H_2O$)	-	-	50g	-	-
8.	*Kasisa* ($FeSO_4$ $7H_2O$)	-	-	50g	100g	-
9.	*Gaireeka* (Fe_2O_3)	-	-	-	-	85g
10.	*Tankana* ($Na_2B_4O_7.7H_2O$)	-	-	50g	-	
11.	*Malla* (AS_2O_3)	-	-	24g	-	
12.	*Valmeekamrithika* (Ant hill mud)	-	-	-	-	85g
13.	*Istikachurana* (Brick powder)	-	-	-	-	85g
14.	*Soraka* (KNO_3)	-	-	50g	-	

Principle of Sub- acute toxicity:

- Test in which animals are dosed daily, the animals are maintained at the maximum tolerated dose for a period of 3 weeks to allow development of any pathological changes and then killed and subjected to pathological and histological examination.
- The normal adult dose in human is 125 mg for samples as per different classics so the suitable dose for rats was calculated by referring to table of Paget and Barne's and as per D.R. Lawrence it was taken as 10 times that of the therapeutic dose viz.

Animal Dose:

Human dose x body surface area ratio convertibility factor= 125 mg x 0.018 = 2.25mg /200 g of rat. For converting to mg/kg- the above dose is multiplied by suitable factor i.e. 10. The above Animal dose was fixed as 22.5 mg/200 g of rat.

Table 2: Showing Maximum tolerated dose (MTD) of samples

Name of trial group	Sample Name	Maximum tolerated dose (MTD) of rat	Vehicle
Trial Group I-A	R.K- I	37mg/200g b.w.	1ml of 2% G.C solution
Trial Group I-B	R.K- I	6.7mg/200g b.w	„
Trial Group II	R.K –II	22.5mg/200g b.w	„
Trial Group III	R.K- III	22.5mg/200g b.w	„
Trial Group IV	R.K- IV	22.5mg/200g b.w	„
Trial Group V	R.K- V	22.5mg/200g b.w	„
Control Group IV	-	-	„

Notes: b.w. – Body Weight, G.C. - Gum acacia

1. Here *Rasakarpoora*-1A is having the MTD, so we should fix this dose 37mg for Sub-acute Toxicity study for 5 days, rats were died without taking food and water, then samples of Kidney, Brain, liver were sent for the histological examinations.
2. Here *Rasakarpoora*-1B is taken by following DR Lawrence conversion method for fixation of dose to the Sub–acute toxicity study i.e. 37×0.018 =0.666 × 10 =6.66mg/200gm body weight, this dose was given for 6 rats for 21 days, then samples of Kidney, Brain, liver were sent for the histological examinations.
3. Here in this instance as the maximum tolerated dose was not traced out, for four(R.K-2, 3, 4, and R.K-5) samples so for designing the Sub-acute study the reference from D.R. Lawrence has been taken as it says that where there is no MTD, ten times that of the therapeutic dose may be used. 6th group of equal number of rats are fed with normal food and water.

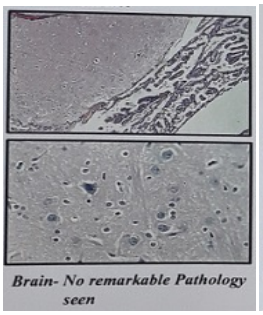
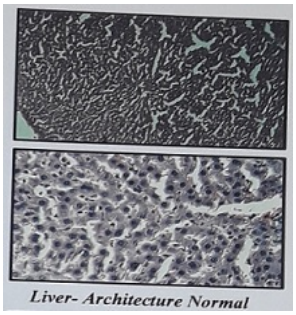
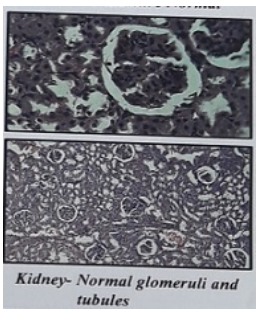
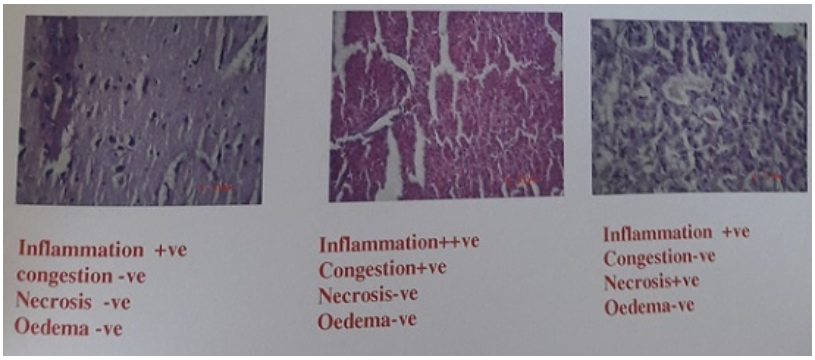
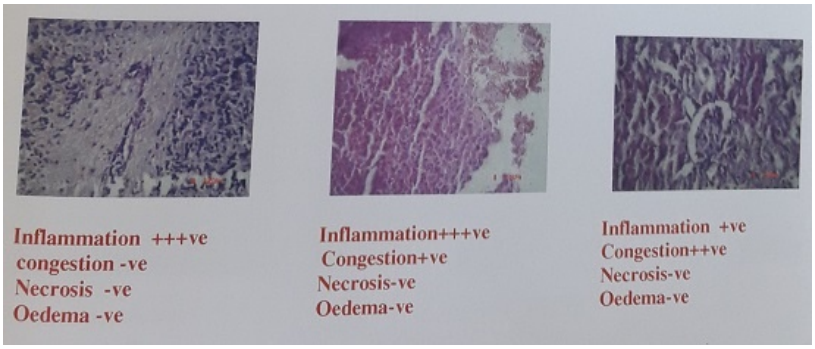
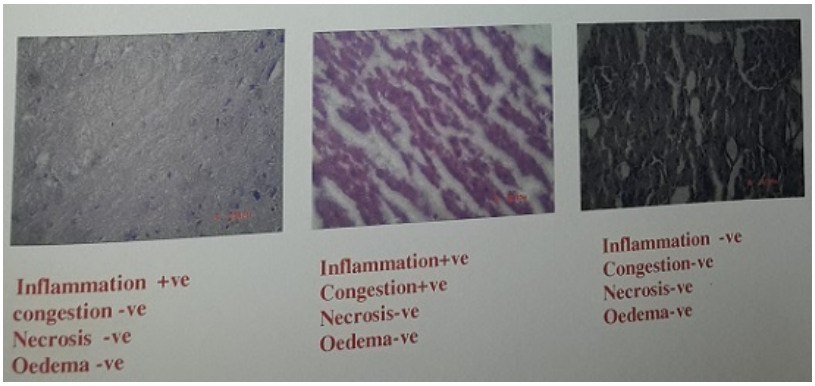
Rats of all groups were starved for 12 hours before the administration of medicine. The dose was administered by syringe and infant feeding tube. 25g of pellet food and 20ml of water was supplied for each rat daily.

Table 3: Showing the drug schedule for Sub-Acute Toxicity Study (MTD)

GROUP	No.of animals	Drug	Dose/200 g b.w	Duration
Trial-IA	6	RK-IA	37 mg/200 g b.w	5 Days
Trial-IB	6	RK-IB	6.7 mg/200 g b.w	21 Days
Trial-II	6	RK-II	22.5 mg/200 g b.w	21 Days
Trial-III	6	RK-III	22.5 mg/200 g b.w	21 Days
Trial-1V	6	RK –IV	22.5 mg/200 g b.w	21 Days
Trial-V	6	RK-V	22.5 mg/200 g b.w	21 Days
Trial-VI	6	Control Group	1 ml of 2% G.C.	21 Days

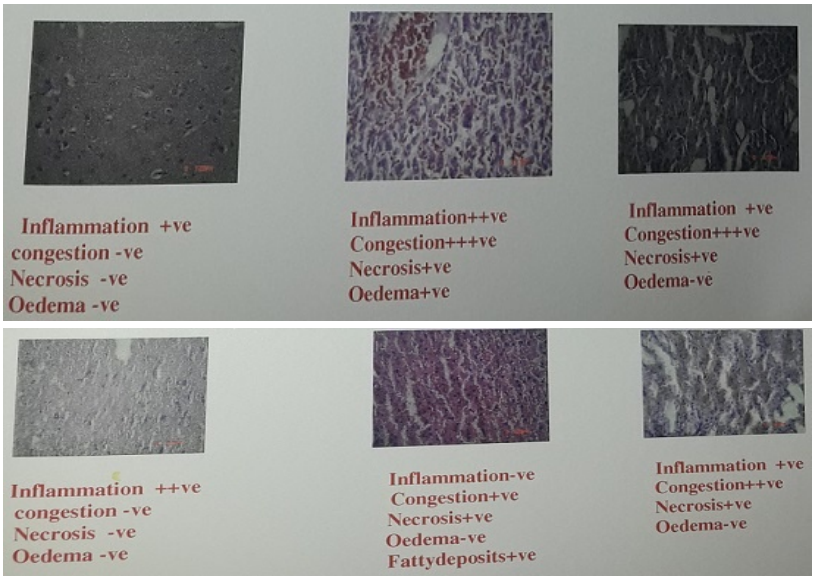
RESULT & DISCUSSION

Histo-pathological study was done in Pathology dept of Government district hospital Udupi- Karnataka.

Group	Brain	Liver	Kidney
Control Group	 Brain- No remarkable Pathology seen	 Liver- Architecture Normal	 Kidney- Normal glomeruli and tubules
RK-1	 Inflammation +ve congestion -ve Necrosis -ve Oedema -ve	Inflammation++ve Congestion+ve Necrosis-ve Oedema-ve	Inflammation +ve Congestion-ve Necrosis+ve Oedema-ve
RK-2	 Inflammation +++ve congestion -ve Necrosis -ve Oedema -ve	Inflammation+++ve Congestion+ve Necrosis-ve Oedema-ve	Inflammation +ve Congestion++ve Necrosis-ve Oedema-ve
RK-3	 Inflammation +ve congestion -ve Necrosis -ve Oedema -ve	Inflammation+ve Congestion+ve Necrosis-ve Oedema-ve	Inflammation -ve Congestion-ve Necrosis-ve Oedema-ve

RK-4

RK-5



Hepatotoxicity of five samples:

- **R.K-1** Inflammation of liver present, congestion slight positive, necrosis & oedema absent and no fatty deposits.
- **R.K-2** Inflammation of liver present more, congestion slight positive, necrosis & oedema absent and no fatty deposits.
- **R.K-3** Inflammation of liver slightly present, congestion slightly present, necrosis & oedema absent and no fatty deposits.
- **R.K-4** Inflammation of liver moderately present, congestion present more, necrosis slightly present, oedema present and no fatty deposits.
- **R.K-5** Inflammation of liver absent, congestion slightly present, necrosis slightly present, oedema absent and fatty deposits positive.

By observing the above result hepatotoxicity was seen more in R.K -4, moderate in R.K -2 and less in R.K -5, R.K-3 andRK-1.

Renal Toxicity of five samples:

- **R.K-1** Inflammation of Kidney present, congestion absent, necrosis positive, oedema absent.
- **R.K-2**Inflammation of Kidney present, moderate congestion, necrosis negative, oedema absent.
- **R.K-3**Inflammation of Kidney absent, congestion, necrosis & oedema absent .
- **R.K-4** Inflammation of Kidney slightly present, congestion present more, necrosis slightly present, oedema absent.
- **R.K-5** Inflammation of Kidney slightly present, congestion moderate, necrosis slightly present, oedema absent.

By observing the above result, renal toxicity was seen more in R.K-4, moderate in R.K-5, less in R.K-1 and R.K-2 and not seen in R.K-3.

Cerebral Toxicity of five samples:

- **R.K-1** Inflammation of Brain present, congestion absent, necrosis & oedema absent.
- **R.K-2** Inflammation of Brain present more, congestion, necrosis & oedema absent.
- **R.K-3** Inflammation of Brain slightly present, congestion, necrosis & oedema absent.
- **R.K-4** Inflammation of Brain slightly present, congestion, necrosis & oedema absent.
- **R.K-5**Inflammation of Brain moderately present, congestion, necrosis & oedema absent.

By observing the above results, cerebral toxicity was seen more in R.K-2, moderate in R.K-5 and R.K-1 and less in R.K-3 and R.K-4.

Discussion on Heamogram Study:

Table 4: Showing Heamogram results of different groups of *Rasakarpura*

Parameters	Control group	Trial group- I	Trial group- II	Trial group- III	Trial group- IV	Trial group-V
HB g %	17.4	13.1	10.2	13.2	14.7	13.1
TLC cells/ Cu mm	9600	4800	3800	3200	5700	1400
DLC N-L-M.C	N-35% L-59% M.C-06	N-0 L-0 M.C-4	N-60 L-34 M.C.-6	N-30 L-65 M.C.-5	N-39 L-58 M.C-3	N-43 L-50 M.C-7
RBC Million for Cu.mm	8.15	6.37	4.78	5.94	6.75	6.60
PCV%	44.8	34.7	26.7	33.2	58.3	33.9
MCV - Fl	55.0	54.6	56.0	56	56.8	51.5
MCHp g	21.3	20.5	21.3	22.2	21.7	19.8
RDW -CV-% -SD-f	C.V-13 SD-26.3fl	C.V-14.8 SD-29.1	C.V-13.2 SD-27.1	C.V-14.5 SD-29.1	C.V-13.7 SD-29.1	C.V-15.3 SD-26.3
Platelet Count Lakhs/Cu mm	2.78	1.05	2.07	6.39	3.27	7.08

1. H.B% was less compared to control group in all groups.
2. TLC was very less in R.K-5 less in remaining all groups compares to Control group.
3. DLC was very less in R.K-1 more or less in remaining all groups compare to control group.
4. R.B.C was less compare to control group in all groups.
5. P.C.V more or less in Remaining all groups compare to control group.
6. M.C.V was equal in all groups compare to control group.
7. M.C.H was equal in all groups compare to control group.
8. Platelets were less in R.K-1 more or less in remaining all groups compares to control group.

Hematological changes in R.K-1 and R.K-5 was having slight changes compare to other groups.

Discussion on Biochemical Study:

Table 5: Showing Biochemical results of different groups of *Rasakarpura*

Parameters	Control group	Trial group- I	Trial group- II	Trial group- III	Trial group- IV	Trial group-V
RBS-mg%	93.0	80.7	80.5	128.9	85.0	137.9
Urea-mg%	53.2	39.0	44.0	34.7	41.1	41.0
S. Cr-mg%	0.4	0.33	0.25	0.22	0.27	0.22
S.Chol mg%	100.0	81.1	82.0	74.0	77.0	72.0
T.G mg%	122.0	144.0	146.0	113.0	108.0	126.0
SGOT IU/L	278.0	261.0	295.0	147.0	345.0	179.0
SGPT IU/L	81.0	96.0	106.0	72.0	118.0	83.0
Al.P IU/L	493	561	367	657	482	627
BilirubinT-mg%	0.38	0.47	0.56	0.35	0.43	0.36

BilirubinD-mg%	0.14	0.19	0.21	0.20	0.19	0.11
Total protein-g%	6.27	5.71	5.31	5.2	6.09	5.64
Albumin-g%	4.17	3.79	3.59	3.60	3.85	3.81

Inference:

1. R.B.S was more compare to control group in R.K-3(128.9), R.K-5(137.9)
2. R.B.S was less compare to control group in R.K-4(85), R.K-2(80.5), andR.K-1 (80.7)
3. Blood urea was less compare to control group in all groups
4. S.Cr was less compare to control group in all groups
5. S.Chol was less compare to control group in all groups
6. T.G in R.K-2 was more compare to control group
7. S.G.O.T in R.K-2 was more compare to control group
8. S.G.P.T in R.K-1, R.K-2, R.K-4 was more compare to control group
9. Bilirubin-T R.K-1, R.K-2, R.K-4 was more compare to control group
10. Bilirubin-D R.K-1, R.K-2, R.K-3,R.K-4 was more compare to control group
11. Total Protein was less compare to control group in all groups
12. Albumin was less compare to control group in all groups

CONCLUSION

Histopatological Conclusion:

By observing total result R.K-3 was safer. R.K-5 and R.K-4 in minimum period was moderately safe. R.K -1 was slight safe and R.K-2 was showing more toxic result.

Biochemical Conclusion:

By observing the biochemical report R.K-2 was more toxic. R.K-1, R.K-4, were moderately toxic and R.K -3 was having less toxicity.

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