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Research Article

Acute and Sub-Acute Toxicity Study of Śilāsindhūra

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Abstract

Śilāsindhūra is an important Rasakalpa told in Rasashastra, which contains Śuddha Pārada, Śuddha Gandhak and Śuddha Manahśila in an equal quantity. After adopting standard Pharmaceutico-analytical procedures, the kalpa was prepared and subjected to Acute and Sub-Acute Toxicity study. The present study was intended to carry an experiment on Swiss albino rats and asses the toxicity ratio in terms of acute and Sub-acute toxicity. All the studies reveal that the given sample of Śilāsindhūra does not show any toxicity in mice.

Key words- Śilāsindhūra, Toxicity study, Manahśila, Procedure.

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INTRODUCTION

The rasa dravyas like Pārada, Gandhaka, Manahśila are proven toxic materials. [i,ii] The present medicine was prepared out of these ingredients ,after adopting classical śōdhana procedures of rasa dravyas. Kūpipakwa rasāyana is the method of preparation of Śilāsindhūra. [iii,iv,v]. The Pharmaceutico-analytical standards had shown good results. [vi]. The further toxicity study was carried to assess the safety of drug in mice. The tests like LD50, Acute and Sub-acute toxicity of Śilāsindhūra were carried on healthy Swiss Albino rats at Indian Drug Research Association and Laboratory, Pune. The study shows that there was no toxicity found in all groups of rats. Hence the Śilāsindhūra can be used in Humans at the dose of 77.58mg per day.

AIMS & OBJECTIVES

To assess the LD 50 dose and Toxic effects of standard Śilāsindhūra in healthy Swiss Albino rats & to determine the respective medicinal dose in Human.

The objectives of present study are:

a) Determination of LD 50 dose in Mice.
b) To examine the oral acute toxicity study in Mice.
c) To examine the sub-acute oral toxicity study in Mice.

MATERIALS & METHODS

The Śilāsindhūra was prepared in the L.K.R.Ayurved college Pharmacy. The prepared Śilāsindhūra shown standard results in Analysis [vi]. This śilāsindhūra was subjected for further experimental study.
For this study the healthy Swiss Albino Mice were used. The study was carried at Indian Drug Research Association and Laboratory, Pune. The Animals were procured from the animal house of National Toxicological centre, Pune.
The present study was subjected to assess the LD 50 dose in Mice. Also to examine the oral acute toxicity and sub-acute oral toxicity study in Mice.
Following methods were adopted in the intention to complete the research work.

i) Collection of literature. - The literature was obtained from classical books on Rasashastra, Bhaishajya kalpana and Ayurveda [iii,iv,vii]. Also the modern books on Pharmacy, Pharmacology [viii], scientific books, science magazines, Thesis, websites were referred.
ii) Determination of LD 50 dose in Mice.
iii) To examine the oral acute toxicity study in Mice.
iv)To examine the sub-acute oral toxicity study in Mice.
The prepared Śilāsindhūra after receiving satisfactory Pharmaceutico-analytical results was tested for above study. This experimental study was carried at Indian Drug Research Association and Laboratory, Pune. The animals were supplied by National Toxicological centre, Pune.

The Methodology of experimental study is as follows.

Estimation of LD 50 of Śilāsindhūra in Mice.	
Animals used	Healthy Swiss Albino mice of either sex.
Weight of the mice	Ranging from 15 gm to 25 gm.
Number of animals used	50
Number of groups	5 (10 animals in each groups)
Number of doses	5 (Doses ranging from 2mg/kg to 10.12 mg/kg.)
Route of administration	Oral.
Observation period	24 hrs.

OBSERVATION

Observation for LD50 of Śilāsindhūra in mice -

No. of groups	No. of animals in each group.	Dose in mg/kg.	Mortality.
A	10	2mg/kg	0 %
B	10	3.6 mg/kg	0 %
C	10	5.5 mg/kg	0 %
D	10	7.75 mg/kg	0 %
E	10	10.12 mg/kg	0 %

To examine the oral acute toxicity study in Mice.	
Animals used	Albino mice
Weight of the mice	Ranging from 15 gm to 25 gm.
Number of animals used	40
Number of groups	4 (10 animals in each groups.)
Dose and Administration	Control Group I - 10ml/kg Normal saline
	Trial Group II- 6 mg/kg (Below non lethal)
	Trial Group III- 10 mg/kg (Nonlethal)
	Trial Group IV- 5 mg/kg (Above non lethal).

Single dose treatment as per selected doses and observation of animals for next 14 days.
Parameters observed - Animals were observed for next 14 days for body weight, mortality, CNS effects, ill health, hematological examination & behavioral

changes. Also at the end of 14 days one animal from each group was scarified for histopathological examination of vital organs.

To examine the oral sub-acute toxicity study in Mice.	
Animals used	Albino mice
Number of animals used	40
Weight of the mice	Ranging from 15 gm to 25 gm.
Number of groups	4 (10 animals in each groups.)
Dose and Administration	Control Group I - 10ml/kg Normal saline
	Trial Group II - 6 mg/kg (below non lethal)
	Trial Group III - 10 mg/kg (Non lethal)
	Trial Group IV- 15 mg/kg (Above non lethal).

Daily administration of above calculated dose of Śilāsindhūra O.D for 1 month.

Parameters observed- Animals were observed for next 4 weeks for body weight, mortality, CNS effects, ill health, hematological examination & behavioral changes. Also at the end of 30 days one animal from each group was scarified for histopathological examination of vital organs.

RESULTS

a) Estimation of LD 50 of Śilāsindhūra in Mice.

With the dose used ranging from 2mg/kg to 10.12 mg/kg, no mortality was observed up to dose of 10.12 mg/kg. Hence the maximum nonlethal dose in mice is 10.12mg/kg. The corresponding non-lethal dose in a man of 70 kg is 77.58mg.

b) To examine the oral acute toxicity study in Mice.

General symptoms	Control group	Group II	Group III	Group IV
CNS effects	NAD	NAD	NAD	NAD
Behavioral changes	NAD	NAD	NAD	NAD
Mortality	NIL	NIL	NIL	10%
Body weight	16%	10.8%	6.6%	6.6%

Haematology	Hb%	WBC	N	E	L	M	ESR
Control group	14	7000	35	1	58	6	1.5
Group II	13.5	6430	40	2	49	9	1.9
Group III	13	6000	29	3	62	6	2
Group IV	13.5	5500	27	2	69	2	1

- **Pathological examination.**

The reports of liver, kidney, heart and lung are normal in control group and as well as in other three trial groups.

c)To examine the oral sub-acute toxicity study in Mice.

General symptoms	Control group	Group II	Group III	Group IV
CNS effects	NAD	NAD	NAD	NAD
Behavioral changes	NAD	NAD	NAD	NAD
Mortality	NIL	NIL	10%	20%
Body weight	31.5%	17.39%	18.18%	8%

Haematology	Hb%	WBC	N	E	L	M
Control group	14.3	5100	32	1	60	7
Group II	14.2	9800	41	2	51	6
Group III	13.2	7200	34	0	60	5
Group IV	14.3	6100	44	2	50	4

Haematology	ESR	SGPT	SGOT	Alkaline Phosphate
Control group	2	88	76	980
Group II	4	78	76	1020
Group III	3	68	69	810
Group IV	2	104	89	682

- **Pathological examination.**

The reports of kidney, heart and lung are normal in control group and as well as in other three groups. The liver shows cellular swelling in all groups.

DISCUSSION

On the study of the subject, apart from the literary study, the research work was carried out. All the findings are discussed here.

- The used Śilāsindhūra was of standard quality.
- During estimation of LD50 of Śilāsindhūra all animals were selected as per inclusive an exclusive criterion.
- The animals in control group were given normal saline from oral route.
- The animals in all three trial groups of Acute and Subacute study were given drug Śilāsindhūra in said dosage from oral route. All the animals tolerate the method of oral feeding.

Experimental study-

The LD 50 study resulted into estimation of dose as 10.12 mg / kg.

From the acute toxicity study carried on Swiss Albino mice, the result indicates that the Śilāsindhūra did not produce any mortality up to the dose of 15 mg/kg, when given orally and also no apparent toxic effects could be observed in all subjective parameters like body weight, mortality, CNS effects, ill health and behavioral changes. Also no toxic effects were seen in parameters like hematological, bio-chemical and histopathological study.

From the oral sub-acute toxicity test, findings of different parameters like body weight, mortality, CNS effects, ill health, behavioral changes, hematological, bio-chemical and histopathological study, it can be said that the drug has less toxic effects.[ix]

CONCLUSION

The present study chiefly aimed at experimental study after preparation of Śilāsindhūra and its analytical study. From the total study the conclusion drawn is as follows-

i) Raw materials used are known, authenticate and uncontroversial.
ii) The result of acute toxicity test showed that the drug did not produce any mortality and apparent toxic effects up to the dose 1.5 mg/kg in mice.
iii) The result of sub-acute toxicity test showed some toxic effects like increase in SGPT and slight cellular change like swelling are seen when given in dose of 1.5 mg/kg for continuous one month to the mice.
iv) The Śilāsindhūra can be given in human of 70 kg in lower dose i.e.<77.58 mg.

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