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ACUTE TOXICITY STUDY OF PROCESSED SIMPSHAPA IN WISTAR RATS –AN EXPERIMENTAL STUDY

Dr. Adivesh Arakeri*[1], Naik N. Sameer[2] and Hiremath R.R.[3]

[1]PG Scholar, Dept of Kayachikitsa, KLE's Shri BMK Ayurveda Mahavidyalaya, Shahapur, Belgaum, Karnataka.

[2]HOD, Professor, MD (Ayu).P.hd, Dept of Kayachikitsa, KLE's Shri BMK Ayurveda Mahavidyalaya, Shahapur, Belgaum, Karnataka.

[3]Reader, Professor, MD (Ayu).P.hd, Dept of Rasashashtra & Bhaishajya Kalpana, KLE's Shri BMK Ayurveda Mahavidyalaya, Shahapur, Belgaum, Karnataka.

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***Corresponding Author**
Dr. Adivesh Arakeri
PG Scholar, Dept of Kayachikitsa, KLE's Shri BMK Ayurveda Mahavidyalaya, Shahapur, Belgaum, Karnataka.
adivesh@gmail.com

ABSTRACT

Simpshapa is one amongst Salasaraadigana, Aasanadigana and Mushkakadigana It is indicated in prameha & medoroga it effectively does kapha & Medo dhatu shoshana The drugs used in the preparation of Processed Simpshapa were, Simpshapa kanda sara, Simpshapa kanda twak and Simpshapa patra. Only Simpshapa kandasara & kanda twak are described in Prameha and Medo Roga in various Ayurvedic classics. But there are many recent studies available on Anti- Diabetic activity of Simpshapapatra. The description of the toxic signs or complications on combination/ Processing of all three parts together (Processed Simpshapa) are not available in classics and no any such researches are documented till today. In present study, Simpshapa sara is obtained by kastamarjana, to this Sara, bhavana is given with simpshapa kanda twak & patra, later dried in shade. The processed shimpshapa Choorna is administered to female wister rats and observed for 14 days. **Results:** No mortality, any toxic Signs were seen in the dose of 5000mg/ kg body weight in any rats during the experimental study. None of the animal showed any Signs of respiratory depression, Necrosis and catatonia and other toxic signs during the experimental study. No signs of diarrhea, bloody stool, mucous in stool etc were observed. Food consumption (10-12g/rat) and water intake (15-20ml/rat) was found normal throughout the completion of the study. All the animals were found active throughout the experimental study.

KEYWORDS: Simpshapa, Acute toxicity study, Prameha, Medoroga, Kandasara.

INTRODUCTION

Simpshapa[1] is one amongst Salasaraadi gana[2], Aasanadi gana[3] and Mushkakadi gana.[4, 5] It is indicated in prameha & medoroga[6] as it effectively does kapha & medodhatu shoshana[7] In Samhitas various single herbal drugs are described in Madhumeha and effectively proved as anti-diabetic without complications. Evaluation of effective formulation is current need by using potent plants to treat Diabetes mellitus. In present study, Simpshapasara is obtained by kastamarjana with water, to this prepared Sara, bhavana is given with simpshapakandatwak & patra, later shade dried. As it is proprietary combination hence safety is must, so safety was done in 5 female Wistar rats. The guideline followed for safety is OECD (420)[8], the references of research articles, Vogelect are Followed or efficacy study.

OBJECTIVE

- To evaluate safety of processed Simpshapa in female Wistar Rats.

MATERIALS AND METHODS

Wistar rats weighing 150-200 gm were procured from animal house, K.L.E.U's Jawaharlal Nehru Medical College, Belgaum, Karnataka and Experimental study was conducted at the Animal house K.L.E.U'S Shri B.M.K. Ayurveda Mahavidyalaya Belgaum. All animals were housed in colony cages at an ambient temperature 22°C ± 3°C and 45-55% relative humidity with 12/12 hr natural light & dark cycle. All animals were acclimatized in the laboratory about a week before commencement of the study. They fed with free access of standard pellet diet (Amruta feeds, VRK's Scientist's Choice Laboratory Animal Feed, Baramati, supplied by Sai Durga Feeds and Foods, Bangalore) and fresh water ad libitum. Floor bed was changed every day, to maintain hygienic condition. The experiment protocol has been approved by the Institutional Animal Ethics Committee BMK/IAEC/Res-12/2012.

EXPERIMENTAL DESIGN

Acute toxicity study

Five female Wistar rats were taken for the toxicity study. To easy identification each animal marking was given by the saturated picric acid as follows

1. Unmarked
2. Head

3. Neck
4. Body
5. Tail.

Selection of Dose: (OECD 420)

- 5000mg/kg body weight

Table no 1: Initial weight of all 5 animals

	Animal marking	Initial weight
1.	Unmarked	168gms
2.	Head	161 gms
3.	Neck	152 gms
4.	Body	157 gms
5.	Tail	140 gms

Dose calculation

1. Unmarked

5000mg for 1000mg body weight

For 168mg =?

168X5000

1000

= 840mg

2. Head

5000mg for 1000mg body weight

For 161mg =?

161X5000

1000

= 805mg

805gm for animal as per dosage of 5000/kg body weight

3. Body

5000mg for 1000mg body weight

For 157mg =?

157X5000

1000

= 785mg.

4. Neck

5000mg for 1000mg body weight

For 152mg =?

152X5000

1000

= 760mg.

5. Tail

5000mg for 1000mg body weight

For 150mg =?

150X5000

1000

= 750mg.

ACUTE TOXICITY STUDY (OECD 420)

Experimental Animals: 5 female Wistar rats of 150-200g

Dose schedule – 5000mg/kg body weight

Duration – 14 days

Preparation of dose

- Processed simpshapa Choorna was taken and measured.
- 1000 mg Ghana was dissolved in 1ml or 10ml distil water respectively
- 1ml solution was taken in 1ml syringe from 10ml and administered to animal.

Table no 2: showing the dose schedule for – Acute toxicity study

5 female rats of 150-200 wt were selected for the study

Animal marked	Dose mg/kg	Duration in days
Head	5000mg	14 days
Neck	5000mg	14 days
Body	5000mg	14 days
Tail	5000mg	14 days
Right limb	5000mg	14 days

OBSERVATIONS

All experimental animals were observed for the duration of 14 days.

- No Mortality was observed in any animals throughout the study
- No evident toxic signs were observed throughout the study.

- No changes on gross behavior at any dose level studies (5000mg/kg B W)
- Weight observation was done daily
- Urine analysis of animals was done before and after drug administration.

Water and food intake was recorded daily till the completion of the study.

Table no 3: showing Food, Water Intake & Weight Gain of Unmarked Animal throughout study

Day	Food (gms)	Water (ml)	Weight (gms)
1.	10	25	168
2.	12	25	170
3.	12	25	171
4.	10	25	172
5.	12	25	173
6.	12	25	173
7.	12	15	171
8.	10	20	172
9.	8	20	173
10.	10	25	174
11.	12	25	176
12.	11	25	175
13.	10	25	174
14.	11	25	174

Table no 4: showing Food, Water intake & weight gain of Head Marked Animal throughout study

Day	Food (gms)	Water (ml)	Weight (gms)
1	12	25	161
2	12	25	168
3	12	25	169
4	08	25	166
5	08	15	163
6	08	15	163
7	10	25	164
8	08	20	161
9	08	20	161
10	08	20	160
11	08	20	160
12	10	25	162
13	10	25	163
14	10	25	164

Table no 4: showing Food, Water intake & weight gain of Body Marked Animal throughout study

Day	Food (gms)	Water (ml)	Weight (gms)
1.	10	25	157
2.	11	25	164
3.	10	20	163
4.	10	20	161
5.	10	20	161
6.	10	20	161
7.	12	20	161
8.	08	20	161
9.	09	20	161
10.	10	20	161
11.	10	25	160
12.	12	25	160
13.	08	29	158
14.	09	20	158

Table no 5: showing Food, Water intake & weight gain of Neck Marked Animal throughout study

Day	Food (gms)	Water (ml)	Weight (gms)
1.	10	20	152
2.	10	20	154
3.	09	18	155
4.	08	20	150
5.	08	20	149
6.	10	20	150
7.	10	25	151
8.	12	25	153
9.	12	25	153
10.	12	25	153
11.	13	25	154
12.	12	25	154
13.	11	25	154
14.	12	25	155

Table no 6: showing Food, Water intake & weight gain of Tail Marked Animal throughout study

Day	Food (gms)	Water (ml)	Weight (gms)
1.	10	25	150
2.	11	25	150
3.	10	20	151
4.	08	20	151
5.	08	20	152
6.	9	18	153
7.	10	20	152

8.	10	25	154
9.	11	20	153
10.	11	20	154
11.	12	25	155
12.	08	20	154
13.	09	20	153
14.	10	25	155

ACUTE TOXICITY STUDY

Acute toxicity

- No mortality was seen in the dose of 5000 mg/ kg body weightin any ratsduring the study.
- None of the animal showed any Signs of respiratory depression, Necrosis 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**

Food consumption and water intake was found normal (i.e 10-12 g/ rat and 15-20 ml/rat) throughout the study.

- **Body Weight**

Weight was increased in all five animals around 5-8gm/rat during the Experimental study.

- **Urine and stool**

No signs of diarrhea, bloody stool, mucous in Stool etc were observed.

All five experimental animals were found active throughout the study.

Table No.7 showing observations

S.L	Observations	unmarked	Head	Neck	Body	Tail
1	Changes in skin:	Nil	Nil	Nil	Nil	Nil
	Blanching	Nil	Nil	Nil	Nil	Nil
	Cyanosis	Nil	Nil	Nil	Nil	Nil
	Erythema	Nil	Nil	Nil	Nil	Nil
	Itching	Nil	Nil	Nil	Nil	Nil
2	Changes in Fur:	Nil	Nil	Nil	Nil	Nil
	Falling of fur	Nil	Nil	Nil	Nil	Nil
	Piloerection	Nil	Nil	Nil	Nil	Nil
	Discoloration	Nil	Nil	Nil	Nil	Nil
3	Changes in Eyes :	Nil	Nil	Nil	Nil	Nil
	Exopthalamus	Nil	Nil	Nil	Nil	Nil
	Redness	Nil	Nil	Nil	Nil	Nil
	Ptosis	Nil	Nil	Nil	Nil	Nil

	Lacrimation	Nil	Nil	Nil	Nil	Nil
	Pupil constricted,	Nil	Nil	Nil	Nil	Nil
	Pupil dilated	Nil	Nil	Nil	Nil	Nil
4	Behavioural pattern:					
	Restlessness	Nil	Nil	Nil	Nil	Nil
	Grooming	Nil	Nil	Nil	Nil	Nil
	Lying flat on belly	Nil	Nil	Nil	Nil	Nil
	Lying flat on side,	Nil	Nil	Nil	Nil	Nil
	Lying flat on back	Nil	Nil	Nil	Nil	Nil
	Sleeping	Nil	Nil	Nil	Nil	Nil
5	Salivation:					
	Viscid	Nil	Nil	Nil	Nil	Nil
	Watery	Nil	Nil	Nil	Nil	Nil
6	Respiration:					
	Depression Stimulation	Nil	Nil	Nil	Nil	Nil
	Failure	Nil	Nil	Nil	Nil	Nil
7	Increased motor activity Decreased motor activity:					
	Muscle relaxation Analgesia	Nil	Nil	Nil	Nil	Nil
	Arching	Nil	Nil	Nil	Nil	Nil
	Rolling	Nil	Nil	Nil	Nil	Nil
8	Central nervous system					
	Defecation	Nil	Nil	Nil	Nil	Nil
	Urination	Nil	Nil	Nil	Nil	Nil
	Squatting	Nil	Nil	Nil	Nil	Nil
	Ataxic gait	Nil	Nil	Nil	Nil	Nil
	Tremors	Nil	Nil	Nil	Nil	Nil
	Timidity	Nil	Nil	Nil	Nil	Nil
	Writhing	Nil	Nil	Nil	Nil	Nil
	Paresis of hind limbs	Nil	Nil	Nil	Nil	Nil
	Paresis of forepaws	Nil	Nil	Nil	Nil	Nil
	Twitches	Nil	Nil	Nil	Nil	Nil
9	Convulsions:-					
	Colonic	Nil	Nil	Nil	Nil	Nil
	Tonic	Nil	Nil	Nil	Nil	Nil
	Rolling	Nil	Nil	Nil	Nil	Nil

DISCUSSION AND CONCLUSION

The drugs used in the preparation of Processed Simpshapa were, Simpshapa kandasara, Simpshapa kanda twak and Simpshapa patra. Only Simpshapa kanda sara & kanda twak are described in Prameha and Medo Roga in various Ayurvedic classics. But there are many recent studies available on Anti- Diabetic activity of Simpshapapatra.[9]

The description of the toxic signs or complications on combination/ Processsing of all three parts together (Processed Simpshapa) are not available in classics and no any such researches are documented till today. In present study, Processed Simpshapa:

Step-1. The Simpshapa Kaasta Maarjana (rubbing) was done with help of water and paste was prepared and then dehydrated, sara Choorna was obtained.

Step-2. Kwatha of Simpshapa kandatwak & patra was prepared as per general rule (1:16 and reduced to 1/8 th).[10]

Step-3. The dehydrated powder was given Bhavana with above prepared kwatha for one time and it was shade dried.

Hence, safety study was conducted on Wistar female rat.

ACUTE TOXICITY STUDY (OECD 420)

For safety study OECD 420 was followed up to the dose of 5000mg/ kg body weight on Wistar female rats. No mortality, toxic signs were observed for the duration of 14 days. No changes were observed in gross behavior of rats.

No mortality, any toxic Signs were seen in the dose of 5000mg/ kg body weight in any rats during the experimental study. None of the animal showed any Signs of respiratory depression, Necrosis and catatonia and other toxic signs during the experimental study. No signs of diarrhea, bloody stool, mucous in stool etc were observed. Food consumption (10-12g/rat) and water intake (15-20ml/rat) was found normal throughout the completion of the study. All the animals were found active throughout the experimental study.

CONCLUSION

Safety study of processed Simpshapa was done as per OECD (420) up to the dose of 5000mg/kg body weight. No mortality and toxic signs were observed in any animals during experimental study. Hence processed simpshapa proved to be safe.

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