WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 17, 1444-1450. Research Article ISSN 2277– 7105

ACUTE ORAL TOXICITY AND HISTOPATHOLOGICAL EVALUATION OF SIDDHA DRUG SARVANGA VATHA CHOORANAM (SVC) IN WISTAR RATS

A. Janakiram[1]*, B. Shalini[2], Dr. N. J. Muthukumar[3] and Prof. Dr. V. Banumathi[4]

[1]Resident Medical Officer, National Institute of Siddha, Tambaram Sanatorium, Chennai.

[2]PG Scholar Dept. of. Kuzhanthai maruthuvam, NIS, Chennai.

[3]Associate professor, Dept.of. Sirappu maruthuvam, NIS, Chennai.

[4]The Director, NIS, Chennai.

Article Received on
22 August 2018,

Revised on 12 Sept. 2018,
Accepted on 02 Octo. 2018,

DOI:10.20959/wjpr201817-13489

***Corresponding Author**
A. Janakiram
Resident Medical Officer, National Institute of Siddha, Tambaram Sanatorium, Chennai.

ABSTRACT

In Siddha system of medicine, one among the ancient traditional medical system of India, that has been practiced for 2000 years and above. *Osteoarthritis* (OA),[1] is a chronic degenerative disorder of multifactorial etiology characterized by loss of articular cartilage and periarticular bone remodeling. Siddha medicine *Sarvanga vatha chooranam (SVC*),[2] is a good remedy for *Osteoarthritis*. SVC is an Herbal formulation in the reference text of *Chikicha rathna deepam part-II Vaithya chinthamani.*[3] it has been used for the treatment of Osteoarthritis (OA). In this study has aimed to evaluate safety and efficacy of the trail drug SVC in female wistar rats (Nulliparous, Non-Pregnant). Acute oral toxicity was performed as per organization for economic co-operation for the development (OECD),[4] guidelines 423 method. Acute toxicity studies were carried out in 5 groups of 15 female wistar rats, a dose of 100mg, 250mg, 500mg, 1000 mg, 2000mg of SVC was administered and monitored for any toxicity effects. After 14 days the animals were sacrificed and the histopathological analysis of the liver, lung, kidney, spleen, of treated groups did not show any significant sign of toxicity. SVC was Non-toxic in acute toxicity study. Studies on the role of elements in health and disease have now become of global importance with rise of research. The present study was undertaken to assess the safety of *Sarvanga vatha chooranam* in Wistar rats.

KEYWORDS: *Siddha system, Sarvanga vatha chooranam, Osteoarthritis, Acute oral toxicity, Histopathology, Azhal keel vaayu.*

INTRODUCTION

Siddha system of medicine dates back to many centuries. It has been practiced by Tamil vaithiyars (native healers of Tamilnadu) who taught people an impeccable life style that trails in societies of Tamilnadu. Osteoarthritis (OA) is a chronic degenerative disorder of multifactorial etiology characterized by loss of articular cartilage and periarticular bone remodeling. The liability of inimical effects while administering the metals and minerals containing traditional medicines is to be explored for its safeness. In Siddha system of medicine, the raw materials like plants, minerals, and animal resources are acquired from the natural surroundings.[5]

Siddha literatures have prescribed many medicines for the treatment of *Azhal keel vaayu*. *Sarvanga vatha chooranam* is one of the classical formulations in Siddha system of medicine, with wide range of therapeutic uses. Chooranam is one of the 32 types of internal medicines in Siddha system of medicine. However, many issues related to a lack of scientific evidence about the efficacy and safety of the drugs remains unresolved. The pre-clinical toxicity screening is essential for determining a safe dose for the human trails. Acute oral toxicity was performed as per organization for economic co-operation for the development (OECD) guidelines 423 method. Acute toxicity studies were carried out in 5 groups of 15 female wistar rats, a dose of 100 mg, 250mg, 500mg, 1000 mg, 2000mg of SVC was administered and monitored for any toxicity effects. After 14 days the animals were sacrificed and the histopathological analysis of the liver, lung, kidney, spleen, of treated groups did not show any significant sign of toxicity. SVC was Non-toxic in acute toxicity study. Studies on the role of elements in health and disease have now become of global importance with rise of research. The present study was undertaken to assess the safety of *Sarvanga vatha chooranam* in Wistar rats.

MATERIALS AND METHOD

The drugs were purchased from the local market in Thirunelveli Town and authenticated by the Department of pharmacology, Government siddha medical college, Palayamkottai, Tamilnadu, India. The drugs were purified and the medicine was prepared as per the methodology in the Siddha text *Chikicha rathna deepam part-II Vaithiya chinthamani.*[3]

Table: 1

S. No.	Tamil Name	Botanical Name	Part Used
1	*Kondrai pattai*	*Cassia fistula*	Bark
2	*Mavilinga pattai*	*Crateva magna*	Bark
3	*Chitramoola pattai*	*Plumbago zeylanica*	Bark
4	*Kandankathiri ver*	*Solanum surattense*	Root
5	*Sangam ver*	*Azima tetracantha*	Root
6	*Vadhamadaki ver*	*Cleodenrum phlomidis*	Root
7	*Poothakarappan pattai*	*Sterculia foetida*	Bark
8	*Perungayam*	*Ferula asafetida*	Gum
9	*Vellarugu*	*Enicostemma axillare*	Whole plant
10	*Thuthuvalai*	*Solanum trilobatum*	Whole plant
11	*Chukku*	*Zingiber officinale*	Dried rhizome
Minerals			
12	**Tamil Name**	**English Name**	
13	*Induppu*	*Rock salt*	
14	*Vediuppu*	*Potassium nitrate*	
15	*Valaiyaluppu*	*Rock salt*	
16	*Kalluppu*	*Rock salt*	

Purification of raw drugs

1. *Induppu* dissolved in kaadi and filtered then dried in sunlight.
2. *Vediuppu* dissolved in cow`s urine or lemon juice and then dried in sunlight.
3. *Valayaluppu* dissolved in kaadi then dried in sunlight.
4. *Kalluppu* dissolved in kaadi and filtered then dried in sunlight.
5. *Chukku* soaked in lime water and then dried.
6. *Perungayam* is fried and then powdered.
7. *Chitramoola pattai:* Remove the inner nerves of bark and take only the outer bark. Powder the bark. Take milk in a pot and upper part of the pot was tied with a cotton cloth (eadu). Bark powder is placed above the cloth and then closed by another pot. Boil 3 hours and take the powder and dry it.
8. *Kontra pattai, mavilinga pattai, poothakarappan pattai*: Common purification method for bark- remove outer bark layer.
9. *Kandankathiri ver, sangam ver, vadhamadaki ver:* Common purification methods for roots are washed with river water.
10. Thuthuvalai, vellarugu: Dried on the sunlight.

Preparation: Purified raw drugs are taken & powdered separately. Then the powders of all the drugs mixed well.

Drug storage: The trial drug *Sarvanga vatha chooranam* is stored in clean dry air tight container.

ACUTE ORAL TOXICITY

Acute toxicity study of SVC was done adhering to the guidelines of OECD 423 method. The study was done in KMCH college of pharmacy, Coimbatore, after obtaining the needed approval for the study from the Institutional Animal Ethics Committee (IAEC) (Ref no: KMCRET/MD(S)/05/2016-17). Fifteen healthy young adult female wistar rats, nulliparous and non-pregnant weighing about 150-200gm were selected for the study. The rats were divided into 5 groups, with 3 animals in each group. 2000mg/kg dosage of the test drug in 200gm body weight was given in a single dose of 1ml. Honey was used as the vehicle for per oral administration of the drug through oral gavage.[5]

Study procedure: Acute oral toxicity was performed as per organization for economic co-operation for development (OECD) guideline 423 methods. The *Sarvanga vatha chooranam* was administered in a single dose by tuberculin syringe. Animals are fasted 3 hr prior to dosing (food was withheld for 3 hr but not water). Following the period of fasting animals was weighed and test substance was administered orally at a dose of 100mg, 250mg, 500mg, 1000mg and 2000mg/kg. After the *Sarvanga vatha chooranam* administration, food was withheld 2 hr in mice. Animals are observed individually after at least once during the first 30 minutes, periodically during the first 24 hrs, with special attention given during the first 4 hrs, and daily thereafter, for a total of 14 days.

OBSERVATIONS AND RESULTS

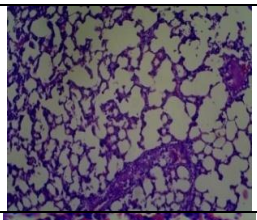
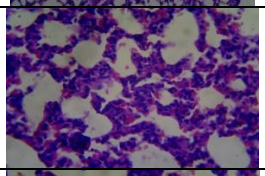
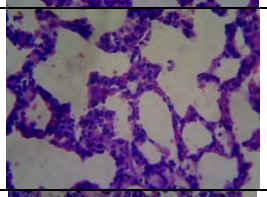
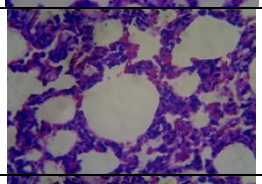
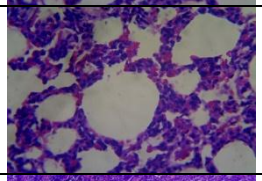
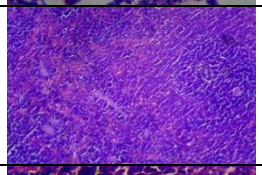
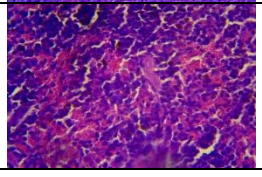
Table 2: Effect of *Sarvanga vatha chooranam* on acute toxicity test in mice.

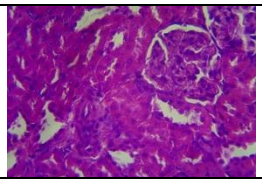
S. N.	Response	Head		Body		Tail	
		Before	After	Before	After	Before	After
1	Alertness	Normal	Normal	Normal	Normal	Normal	Normal
2	Grooming	Absent	Absent	Absent	Absent	Absent	Absent
3	Touch response	Absent	Absent	Absent	Absent	Absent	Absent
4	Torch response	Normal	Normal	Normal	Normal	Normal	Normal
5	Pain response	Normal	Normal	Normal	Normal	Normal	Normal
6	Tremors	Absent	Absent	Absent	Absent	Absent	Absent
7	Convulsion	Absent	Absent	Absent	Absent	Absent	Absent
8	Righting reflux	Normal	Normal	Normal	Normal	Normal	Normal
9	Gripping strength	Normal	Normal	Normal	Normal	Normal	Normal
10	Pinna reflux	Present	Present	Present	Present	Present	Present
11	Corneal reflux	Present	Present	Present	Present	Present	Present
12	Writhing	Absent	Absent	Absent	Absent	Absent	Absent

13	Pupils	Normal	Normal	Normal	Normal	Normal	Normal
14	Urination	Normal	Normal	Normal	Normal	Normal	Normal
15	Salivation	Normal	Normal	Normal	Normal	Normal	Normal
16	Skin color	Normal	Normal	Normal	Normal	Normal	Normal
17	Lacrimation	Normal	Normal	Normal	Normal	Normal	Normal

From acute toxicity study it was observed that the administration of *Sarvanga vatha chooranam* to female wistar rats did not induce drug-related toxicity and mortality in the animals up to 2000mg/kg in 200g female Wistar rats. So No-Observed-Adverse-Effect- Level (NOAEL) of *Sarvanga vatha chooranam* is 2000 mg/kg equal to human dose.

Histopathological Evaluation

S. No.		SPECIMEN	OBSERVATIONS
1	Lung		10x shows normal lung parenchyma
1a			40x shows mild inflammation - not significant
2	Liver		40x shows normal alveoli
2a			40x shows mild interstitial inflammation - not significant
3	Spleen		10x shows normal spleen
3a			40x shows normal white and red bulb
4	kidney		10x shows normal glomeruli and tubules

4a				40x shows normal interstitium.

Lungs: Section from lung shows normal alveoli, bronchioles. Blood vessels show normal. There is presence of mild inflammatory infiltrates composed mainly of lymphocytes seen in the interstitium it is not significant.

Liver: The sections from the liver shows normal lobular architecture. Individual hepatocytes show no significant pathology. Portal triad shows normal morphology. Sinusoids show normal. Central vein is normal.

Spleen: Section studied from the spleen shows normal red pulp. White pulp shows prominent lymphoid aggregates with germinal centre formation. The pencillar artery shows normal. No evidence of toxic changes.

Kidney: Section studied from the kidney shows both cortex and medulla. The Glomeruli show normal morphology. The tubules show no significant pathology. Interstitium shows unremarkable. Blood vessels show unremarkable.

DISCUSSION

Sarvanga vatha chooranam was administered single time at the doses of 100mg, 250mg, 500mg, 1000mg and 2000mg/kg to female Wistar rats and observed for consecutive 14 days after administration. Doses were selected based on the pilot study and literature review. All animals were observed daily once for any abnormal clinical signs. Weekly body weight and food consumption were recorded. No mortality was observed during the entire period of the study. Data obtained in this study indicated no significance physical and behavioral signs of any toxicity due to administration of *Sarvanga vatha chooranam* at the doses of 100mg, 250mg, 500mg, 1000mg and 2000mg/kg to female Wistar rats.

At the 14th day, all animals were observed for functional and behavioral examination. In functional and behavioral examination, home cage activity, hand held activity were observed. Home cage activities like Body position, Respiration, Clonic involuntary movement, Tonic involuntary movement, Palpebral closure, Approach response, Touch response, Pinna reflex, Sound responses, Tail pinch response were observed. Handheld activities like Reactivity, Handling, Palpebral closure, Lacrimation, Salivation, Piloerection, Papillary reflex, abdominal tone, Limb tone were observed. Functional and behavioral examination was normal in all treated groups. Food consumption of all treated animals was found normal as compared to normal group. There are no signifincant abnormalities seen in histopathological examination of siddha drug *Sarvanga vatha chooranam.*

CONCLUSION

The present study was conducted to know single dose toxicity of *Sarvanga vatha Chooranam* on female Wistar rats. The study shows that *Sarvanga vatha chooranam* did not produce any toxic effect at dose of 100mg, 250mg, 500mg, 1000mg and 2000mg/kg to rats. So No-Observed-Adverse-Effect-Level (NOAEL) of *Sarvanga vatha chooranam.* The drug was administered by oral route single time and observed for 14 days. Daily the animals were observed for clinical signs and mortality. There were no physical and behavioral changes observed in Female Wister rats during 14 days. Mortality was not observed in any treatment groups. There are no signifincant abnormalities seen in histopathological examination of siddha drug *Sarvanga vatha chooranam.* This study provides scientific validation for the safety of *Sarvanga vatha Chooranam*

REFERENCES

1. Dicesare PE, Abramson SB. Pathogenesis of osteoarthritis. In: Harris ED, Budd RC, Genovese MC et al (editors). Kelley's Textbook of Rheumatology, volume II, 7th edition, Elsevier Saunders, 2005; 1493-1513.
2. Shekelle P.G, Morton SC, Suttorp MJ, Buscemi N, Friesen C. Challenges in sylematic reviews of complementary and alternative medicine topics, Ann Intern Med, 2005; 142: 1042-1047.
3. Anoop A, Jagadeesan M and Subramanium S. Toxicological studies on Linga chendooram - I, A siddha drug, Indian J Pharma Sci, 2002; 64(1): 53.
4. Vaithya vidhvanmani C.Kannusami pillai; Chikicha rathna deepam part-II Vaithiya cahinthamani, 2007; 164.
5. OECD. Guideline for Testing of Chemicals 423, Acute oral toxicity (acute toxic class method), December 2001.
6. B. Chitra, R. S. Ramaswamy, and V. Suba, Toxicity Evaluation of Purana cantirotaya centhuram, A Siddha medicine in Wistar Rats; International Scholarly Research Notices, 2015; Article ID 473296: 10.