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A TOXICITY STUDY ON SIDDHA DRUG- "SURANGUSA PARPAM"

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ABSTRACT

The Siddha system of medicine is the oldest in ancient India and was derived by Tamil Siddhars or spiritual scientists of Tamilnadu. In Siddha system, herbs, metals, minerals and animal origin are used as medicines since thousands of years. This research is toxicity study on siddha drug- "surangusa parpam" this drug ingredients are: Manosilai (Arsenic disulphide), Milagu (Piper nigrum) and Sangu (Conch). This research drug is reference from; *Anubogavaithiyanavaneetham* Part III. Evaluate the Safty profile of Surangusa parpam in in-vivo model is main objective of this research. In this research findings are, **physico-chemical analysis** of Surangusa Parpam, the pH was found to be 6.7. This shows it is slightly acidic and loss on drying at 105^0C was 8.21 % w/w. In **HR SEM** analysis, the particle size of Surangusaparpam was found to be 1-3□ (micron). In **ICP-OES** study, heavy metals like As, Pb, Cd, Hg were found below detection limit (WHO guidelines) in Surangusaparpam. It also shows the presence of Calcium, Iron, Potassium, Magnesium, Sodium, Sulphur, Phosphorus and zinc. In **acute oral toxicity study (OECD-423)**, there were no abnormal signs developed in all test groups. No mortality was observed in all groups. In 28 days **repeated oral toxicity study (OECD-407)**, the experimental animal's blood and histopathological study was evaluated and results were normal in control, Low dose, Mid dose and High dose groups. The kidney shows tubular casts in all test groups. The liver shows mild focal degeneration and mild bile duct hyperplasia in high dose group. From the above results, the drug shows minimum toxicity in high dose groups. Therefore, the indented adult dose of **Surangusa Parpam** becomes **safe for human administration**.

KEYWORDS: *Manosilai* (Arsenic disulphide), *Milagu* (Piper nigrum) *Sangu* (Conch) and *Surangusa Parpam*.

INTRODUCTION

The Siddhars believed that the human anatomy and physiology, the factors causing diseases, the materials used for the treatment and to cure the diseases and food consumed by the living organism, all these factors fall within the five primordial categories.

Surangusa parpam is one of the Siddha drug mentioned in the Siddha text, Anuboga vaithiya navaneetham Part III, pg.no. 90, is useful to treat Kaba dieases like Kasam (cough, asthma), Suram (fever) and Ulaimanthai (Intestinal TB) etc. The ingredients of ***Surangusa parpam*** are Manosilai (Arsenic di-sulphide), Sangu (conch), Milagu (pepper). Till now, there is no toxicity evaluation was done about ***Surangusa parpam.***

Toxicological screening is very important for the extension of the therapeutic potential of existing molecules. The US Food and Drug administration (FDA) states that, it is essential to screen new molecules for pharmacological activity and toxicity potential in animals (21CFR part 314). The toxic effects of chemicals, food substances, pharmaceuticals etc, have attained great significance in the 21st century. Toxicity tests are mostly used to examine specific adverse events or specific end points such as cancer, cardiotoxicity, skin and eye irritation. Preclinical toxicity testing helps to calculate "No Observed Adverse Effect Level" (NOAEL) which is needed to initiate the clinical evaluation.

The present study is aimed to do physico-chemical analysis, heavy metal analysis and particle size analysis and to access the toxicity profile of **Surangusa parpam** in animal model as per OECD guidelines.

Aim is to evaluate the Safety profile of **"*Surangusa Parpam*"** on animal model.
Objectives are To evaluate the physical and chemical analysis of **"*Surangusa Parpam",*** To study the qualitative and quantitative analysis of the test drug ***Surangusa Parpam,*** Acute oral toxicity study of ***Surangusa Parpam*** by OECD – 423 Guideline, 28 days Repeated oral toxicity study of ***Surangusa Parpam*** by OECD – 407 Guideline.

MATERIALS AND METHODS

Test drug: Surangusa parpam

Surangusa parpam contains the following ingredients:

Manosilai(Arsenic disulphide) - 4 varagan(14gm).
Sangu (Conch) - 4 varagan(14gm).

Milagu (Piper nigrum) - 4 varagan(14gm)

Collection

The raw drugs are obtained from the standard raw drug stores, in Chennai.

Authentication

Drugs were identified and authenticated from dept. of Pharmacognosy in Siddha Central Research Institute, Chennai and Botanist in National Institute of Siddha, Chennai.

Method of Purification

Purification of *Manosilai* (Arsensic disulphide)

Red orpiment (35gms) is made into small pieces and kept soaked in 175 gms of fermented butter milk in a clay vessel. It is insolated and kindling frequently. In the evening it is washed in the water. The same procedure is repeated for three times to get purified form.

- *Siddha material medica* Page No: 286

Take equal quantities of limestone and fullers earth and add eight times of water, put the conch into it and boil well to get it purified.

- *Siddha material medica* Page No: 468

Purification of *Milagu*(Piper nigrum)

Piper nigrum is soaked in butter milk for 1 1/2 hours and then it is dried and roasted to get it purified .

- Sarakku suthi seimuraigal page No.13

Method of Preparation

The above ingredients are soaked in goat's urine (2 1/2 palam) and kept for 3 days. On fourth day the contents are rubbed for 3 days with the same urine in which they are kept soaked. Then, they are made into pellets and dried. The dried pellets are placed in a mud plate which is then covered by a similar mud plate. The margins are covered by a mud pasted cloth, dried and then subjected to pudam with cow dung cakes which are 20 times the weight of the sealed mud plates. Again the process is repeated once. Being cooled, the lid is opened and the processed medicine thus obtained is collected and kept in an air tight container.

Dose of drug : 1-2 *kundri* (130-260mg)

Adjuvant : Honey

Therapeutic uses : Kasam, Suram, Ulaimanthai.

Ref: Anuboga vaithiya navaneetham (Part -3) Page No: 90

28 Days Repeated Oral Toxicity Study of Surangusa Parpam OECD-407

Species and strain	:	Wistar albino rats
Sex	:	Male and Female
Age/Weight	:	6 weeks/150-200mg
Test guideline	:	OECD guidelines – 407
Groups/treatment	:	Grouped by randomization
Duration	:	28 days
Number of animals	:	10/group (5/sex)
Route of administration	:	Oral

Groups	No of Rats
Group I Vehicle control (Honey)	10 (5male,5 female)
Group II test drug - low dose X (4.68 mg)	10 (5male,5 female)
Group III test drug - Mid dose 5X (23.4mg)	10 (5male,5female)
Group IV test drug - High dose 10X (46.8mg)	10(5male,5female)

The study will be carried out as per OECD Guideline 407 (Repeated Dose 28-Day Oral Toxicity in Rodents). The animals will be divided in four groups each group consist of 10 animals (5 males and 5 females). One group will serve as control and the other three groups were treated with test drug at three different dose levels (low, mid and high) for 28 days.

RESULTS AND DISCUSSION

Qualitative Analysis: Physico Chemical Analysis

Table: 1 Qualitataive analysis of Surangusa parpam.

S.No	Procedures	Surangusa parpam
1.	Test for Ammonium	-
2.	Test for Sodium	-
3.	Test for Magnesium	+
4.	Test for Aluminium	_
5.	Test for Potassium	_
6.	Test for Calcium	+
7.	Test for Ferrous iron	+
8.	Test for Zinc	_
9.	Test for Arsenic	_
10.	Test for Mercury	_
11.	Test for Lead	-

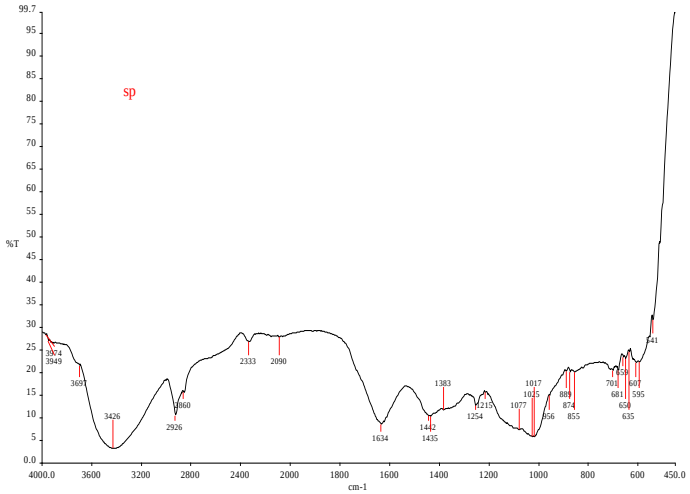
12.	**Test for Sulphate**	**+**
13.	**Test for Chloride**	**-**
14.	**Test for Phosphate**	**+**
15.	**Test for carbonate**	**-**
16.	**Test for Flouride & Oxalate**	**-**
17.	**Test for Starch**	**-**
18.	**Test for Reducing sugar**	**-**
19.	**Test for Alkaloids**	**+**
20.	**Test for Amino acids**	**-**
21.	**Test for Tannic acids**	**-**
22.	**Test for unsaturated compounds**	**+**

\+ Present - Absent

Arsenic di sulphide (manosilai) as the major ingredient, it was found to be very much higher in before purification sample. But after the purification process, the level of arsenic content was reduced drastically to below 10, then it again reduced in the finished product of Surangusa parpam. Due to the addition of drugs, the biological minerals are added up in the finished product.

FTIR analysis of Surangusa parpam

The schematic graph of FTIR analysis is shown below



DISCUSSION

In this study, the ingredients for **Surangusa parpam** were procured and purified as per Siddha literature. **Surangusaparpam** was subjected to qualitative, quantitative and toxicity studies. Qualitative analysis includes chemical analysis and physico-chemical properties of Surangusaparpam. Quantitative analysis includes FTIR, ICP-OES and HR SEM analysis. Toxicity studies includes both acute and 28 days Repeated oral toxicity studies carried out in rodents as per OECD guideline.

Qualitative analysis of Surangusaparpam shows the presence of magnesium, calcium, iron, sulphate, phosphate, alkaloids and unsaturated compounds.

In physico-chemical analysis, the pH of Surangusaparpam was found to be in the range of 6.7. This shows it is slightly acidic. Thus it can be easily absorbed form the gastrointestinal tract on oral administration. The loss on drying value of Surangusaparpam at 105^0C was found to be 8.21 % w/w, hence the drug will not lose much of its volume on exposure to the atmospheric air at room temperature.

In **HR SEM** analysis, the particle size of Surangusaparpam was analyzed as 1-3□ (micron). This favours the absorption of the drug more active and the drug will have increased bio-availability.

In **ICP-OES** study, heavy metals like As, Pb, Cd, Hg were found below detection limit in Surangusaparpam. It also shows the presence of calcium, iron, potassium, magnesium, sodium, phosphorous, sulphur and zinc.

FTIR analysis shows the presence of functional groups like alcohols, phenols, alkanes, primary amines, alkyl halides, aliphatic amines, aromatics and alkynes.

From the physico-chemical analysis, qualitative and quantitative analysis of Surangusaparpam, the preparation as per the literature ensures the safety of the drug from heavy metals. Even though the formulation contains Arsenic di sulphide (manosilai) as the major ingredient, it was found to be very much higher (263.12) in before purification sample. But after the purification process, the level of arsenic content was reduced drastically to below 10, then it again reduced to 9 in the finished product of Surangusa parpam.

In **Acute oral dose toxicity study** period, there were no abnormal signs developed in 5mg, 50mg, 300 & 2000mg/kg b.w treated animals. No mortality and reduction in body weight of animals were observed in all groups.

In 28 days repeated oral dose toxicity study, the animals were sacrificed on day 29 and the blood samples were collected and sent for investigation. The organs were collected and sent for histopathology study.

All the reports were statistically calculated. There were no significant changes in body weight changes, food and water intake, hematological parameters, renal parameters and liver function test. Gross pathological examination doesn't show any abnormalities in control and test groups. The histopathological study of the organs such as heart, spleen, stomach, brain, nail, bone was normal in control, Low dose, Mid dose and High dose groups. The kidney shows tubular casts in all test groups. The liver shows mild focal degeneration and mild bile duct hyperplasia in high dose group. From the above results, the drug shows minimum toxicity in high dose groups. Therefore, the indented adult dose of **Surangusa parpam** becomes safe for human administration.

CONCLUSION

From the above study it is concluded that,

In **Surangusa parpam,** though arsenic di-sulphide is an ingredient, it was found to below the detection level in the prepared medicine analyzed by sophisticated instrument. It reveals the potential background of Siddhars knowledge in the field of metals, minerals and herbal usage in medicine preparation.

The acute and repeated oral dose toxicity studies of Surangusa parpam is found to be less toxic and the therapeutic dose level mentioned in the literature is a safer dose for human consumption.

Hence further studies on **Surangusa parpam** are to be conducted for its scientific validation and global acceptance.

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