



Research Article

STANDARDIZATION OF SIDDHA HERBO-MINERAL DRUG AS NANO MEDICINE THROUGH FTIR, ICP-OES AND SEM

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ABSTRACT

Nano medicine in Siddha, is a unique concept and great advancement of Siddhar science. It was clearly explained and documented by many Siddhars by their medicine preparatory and testing methods. They have created many medicines with the use of metals and minerals because of its minimal quantity to avail the high potency results. To reverse the toxicity and adverse reactions they want to convert those heavy metals into Nano particles to modify the physical and chemical characters of the elements. By Drug Delivery Systems (DDS) we can control the Pharmacokinetics, Pharmacodynamics, non-specific toxicity, immunogenicity and makes bio-recognition and efficacy of drugs. This type of DDS is a major lacuna in our system. To overcome this, now we approach our drug as Novel Drug Delivery System (NDDS). Thirumoolar's hypothesis about Atomic theory has been reinstated as nanotechnology in this decade. Nano science and technology may be new to the world but Indian systems of Medicines have been using this technology to make *Parpam*, *Chendharam* etc. The physico chemical, Phyto chemical analysis, The FTIR and ICP-OES studies of trial drug *Rasa Mezhugu* strongly suggesting the safety of the drug by proving heavy metals are in below detectable levels. The active principle *Rasam* is also within 3ppm as per the admissible level for the medicines. With the help of SEM, the trial drug consists of particles with in 1 to 100nm in size. By this we came to know that the drug has been finished perfectly and able to produce good therapeutic values. By approaching in NDDS, the trial drug increase the therapeutic value, bioavailability and act as smart drug.

**KEYWORDS:** *Siddha*, Nano, FTIR, SEM, *Rasa mezhugu*.

INTRODUCTION

Siddhar's are the ancient scientists those who dealing with metallurgy and having the great knowledge on physical and chemical properties of all metals and minerals used in the Siddha system. Not only the medicinal values of the drugs they have documented all the adverse drug reactions and how to manage the complications with simple herbal remedies. In the hierarchy preparations like *Parpam*, *Chenthooram*, *Chunnam*, *Kattu* and *Kalangu* are consciously framed as Nano medicines to provide high pharmacological value and low toxic effect when those metals and minerals are therapeutically used<sup>[1]</sup>. The great Siddhar Thirumoolar clearly explained the size of a Nano particle up to 10<sup>-10</sup>. In Siddha system the metal and mineral preparations are very consciously made into Nano particles with 'Sathru' (antagonist) 'Mithru' (agonist) drugs to nullify the toxicity and increase the potency respectively. By this, the heavy metals like mercury are modified to provide the safe therapeutic value in very low doses. Because the Nano particles are

having very different physical and chemical properties than that of its own mineral form, also it was proved that these kind heavy metals are not having much toxicity and providing good bio availability.

As per the Siddha literature the mercury has all the six tastes and it has the potency of both heat and cold. So, mercury is a highly efficacious drug to act on all the three deranged humours of human body. When it is treated with some kind of herbals and cane jaggery, it becomes a wax like substance called as '*Mezhugu*'<sup>[2]</sup>. These kinds of medicines were useful in the treatment of some chronic diseases like Rheumatoid arthritis, Hemiplegia, Spondylitis etc. This trial drug *Rasa Mezhugu* is also one among them, so it needed the standardisation and scientific validation. Various Siddha literatures like '*Yugi muni Vadha Kaviyam*' were also explained 80 types of *Vadha* diseases. In those this type of Rheumatoid

arthritis is classified as *Uthara Vatha Suronitham*, *Paithiyavathasuronitham* and *Vali azhal Keelvayu*<sup>[3]</sup>.

By the revised World Health Organization (WHO) criteria for the diagnosis of Rheumatoid arthritis, giving a prevalence of 0.75%, projected to the whole population, this would give a total of about seven million patients in India. The prevalence of RA in India is quite similar to that reported from the developed countries. It is higher than that was reported from China, Indonesia, Philippines and rural Africa. These findings are in keeping with the fact that the north Indian population is genetically closer to the Caucasians than to other ethnic groups<sup>[4]</sup>.

## MATERIALS AND METHODS

### Ingredients

1. *Vaalai Rasam* (Purified Mercury) - 2 parts
2. China Root (*Smilax china*) - 2 parts
3. Long Pepper (*Piper longum*) - 2 parts
4. Clove (*Syzygium aromaticum*) - 2 parts
5. Jaggery - Sugar cane (*Saccharum Officinarum*)- 4 parts

### Identification and Authentication

These purchased herbal and mineral drugs were identified for its quality by comparing with the Raw materials kept in the Gunapadam lab, Govt. Siddha Medical College, Chennai. After identification the raw materials were authenticated by the Gunapadam department and the Botanist from the Medicinal Botany Department of Govt. Siddha Medical College, Chennai.

### Purification Methods

All the raw drugs used in this trial were exactly purified as per the Siddha literatures. These methods were so carefully performed to attain the maximum purified ingredients.

Experimentally a little amount of mercury was ground with equal amount of all the other *Churnams* separately to know the substance that denatures the heavy metal character. It occurred when it was ground with *Lavanga churnam* and the mercury seemed to be denatured completely.

*Vaalai Rasam* (pure form of mercury) was ground with the clove *Churnam* first in order to denature the ill effects of the heavy metal. After this the long pepper *Churnam* was added and ground till they get finely mixed and then the china root *Churnam* was added and ground in a mortar. After getting a well blend mixture of those, Cane jaggery was added and grounded till getting a *Mezhugu* consistency<sup>[5]</sup>. Then the *Mezhugu* was carefully collected and stored in a labelled airtight container

and kept carefully in the absence of sunlight for 1 month for customizing the drug.

### Physico-Chemical Analysis

The physico-chemical analysis and elemental analysis of this herbo mineral formulation have been done at SAIF (Sophisticated Analytical Instrument Facility) in IIT, Madras, Guindy Campus, Chennai.

In this analysis, the trial formulation is subjected to various physico-chemical parameters for the standardization. The results are exhibited in the Table 1 and 2.

### Elemental Analysis

Fourier Transform Infrared Spectroscopy (FTIR)

#### Instrument Details:

Model: Spectrum one: FT-IR Spectrometer

Scan Range: MIR 450-4000 cm<sup>-1</sup>

Resolution: 1.0 cm<sup>-1</sup>

Sample required: 50mg, solid or liquid.

Fourier Transform Infrared Spectroscopy (FTIR) is an analytical technique used to identify mainly organic materials. FTIR analysis results in absorption spectra which provide information about the chemical bonds and molecular structure of a material. The FTIR spectrum is equivalent to the "fingerprint" of the material and can be compared with catalogued FTIR spectra to identify the material. FTIR spectrum analysis is very helpful to identify the presence of functional groups. Characterization of herbal formulations is essential to identify the lead molecule for further research to elucidate the structure of functional compounds which is reasonable for its therapeutic value<sup>[6]</sup>.

### Fourier Transforms Infrared Spectroscopy Analytical Capabilities

Identifies chemical bond functional groups by the absorption of infrared radiation which excites vibrational modes in the bond. Especially capable of identifying the chemical bonds of organic materials. Detects and identifies organic contaminants, identifies water, phosphates, sulphates, nitrates, nitrites, and ammonium ions useful with solids, liquids, or gases.

The interpretation of infrared spectra involves the correlation of absorption bands in the spectrum of an unknown compound with the known absorption frequencies for types of bonds. This table will help users become more familiar with the process. Significant for the identification of the source of an absorption band are intensity (weak, medium or strong), shape (broad or sharp), and position (cm<sup>-1</sup>) in the spectrum. The results of FTIR are discussed in graph.

### Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES)

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) also referred to as inductively coupled plasma optical emission spectrometry (ICP-OES), is an analytical technique used for the detection of trace metals. It is a type of emission spectroscopy that uses the inductively coupled plasma to produce excited atoms and ions that emit electromagnetic radiation at wavelengths characteristic of a particular element.

The intensity of this emission is indicative of the concentration of the element within the sample. The results are provided in the Table 3.

### Scanning Electron Microscope (SEM)

**Resolution:** 1.2nm gold particle separation on a carbon substrate

**Magnification:** From a min of 12x to greater than 1, 00,000 X

The Scanning Electron Microscope (SEM) is a microscope that uses electrons rather than light to form an image. There are many advantages to using the SEM instead of a light microscope. The SEM has a large depth of field, which allows a large amount of the sample to be in focus at one time.

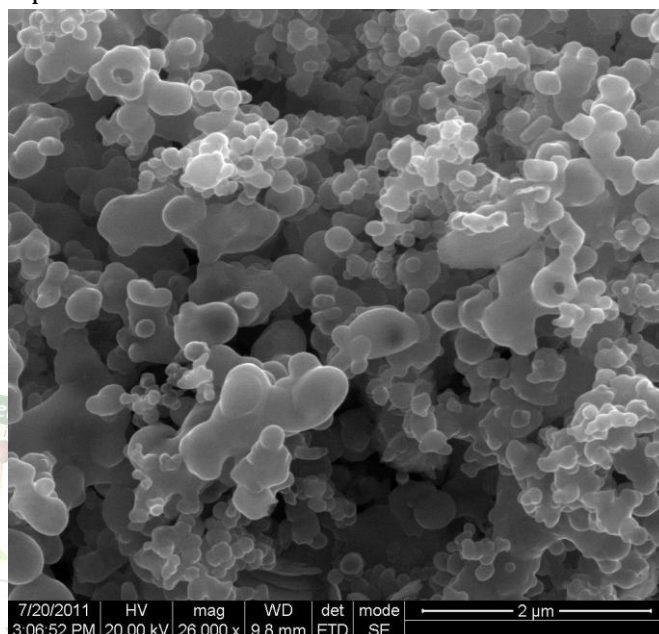
The SEM also produces images of high resolution, which means that closely spaced features can be examined at a high magnification. Preparation of the samples is relatively easy since most SEM one require the very minimal sample to be conductive.

### Physico Chemical Analysis

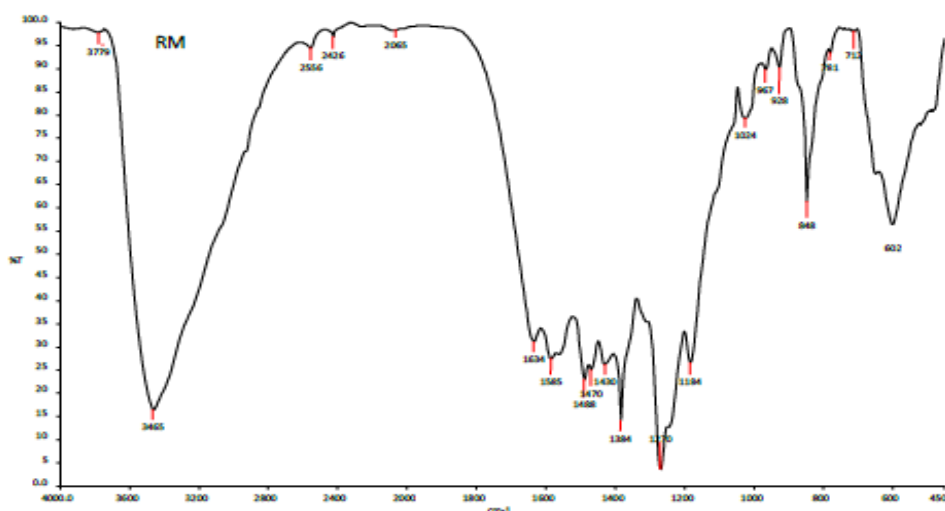
With these salient features of this instrument made the big advantage in Siddha system to prove the Siddhar's knowledge are certainly amazing by illustrating the Siddha medicines are in nano particle size. So, they are absorbed easily and not producing any toxic effects. Also it produces promisingly good result in the treatment of ailments.

### Sem Picture of *Rasa Mezhu*

In this SEM picture the particles are magnified upto 26000x and within 2µm lot of clearly arranged cells are seen. Further interpretation is explained in the results.



FTIR of *Rasa Mezhu*:



**RESULTS****Table1: Colour Characters of Herbo Mineral**

S.No	Sample	Colour-Under ordinary light	Colour-Under UV light
1	Powdered material	Brown	Brown

**Table 2: Physico-chemical properties of Herbo Mineral**

S.No	Parameters	Values obtained (%w/w)	Heavy Metals	Result
1	Total ash value	9.76	Lead	BDL
2	Acid insoluble ash	0.94	Cadmium	BDL
3	Water soluble ash	5.6	Mercury	3ppm
4	Moisture content	8.75	Arsenic	BDL
5	Foreign Organic Matter	0.86	Iron	0.5ppm

BDL – Below Detective Level; PPM – Parts Per Million.

**Interpretation**

The colour of the sample is same in both the ordinary light and UV light, which proves that there is no radio active compounds present in that. The total ash value is 9.76% (w/w), acid-insoluble ash value is 0.94% (w/w), most of the total ash is soluble in acid, so acid-insoluble ash value is very low denoting that it fully gets digested in our alimentary without producing any ill effects. Meanwhile, the water-soluble ash value is 5.6% (w/w) and the foreign organic matter is also very low and this proves that it paves no way for the growth of micro organisms. So this study helps to standardize the preparatory method of this herbo-mineral formulation.

By the heavy metal analysis result, it is inferred that all the toxic heavy metals are removed and the mercury is also within the admissible level. With this the Siddhar's admirable formulas are once again proved that the toxic minerals were converted into almost non-toxic medicines.

**RESULTS AND DISCUSSION**

The phyto-steroids quench the pain and the process of the disease by the anti-inflammatory and analgesic quality. The presence of cardiac glycosides avoids the cardiac complications of the disease. Other important essential oil constituents of clove oil include Acetyeugenol, Beta-caryophyllene and Vanillin, Cateogolic acid, Tannins, Gallotannic acid, Methyl salicylate (pain killer) to reduce the pain and

inflammation. It is clear that this herbo-mineral formulation has essential elements that maintain the normalcy of the body counteracting the disease progression. i.e., the calcium helps in increasing the bone density thus preventing the osteoclastic activity. The iron present in this helps to get rid of anaemia caused by the disease. The chloride and carbonate ions help in maintaining the cellular integrity by governing the acid base balance of the cell<sup>[7]</sup>.

**FTIR results of *Rasa mezhugu***

The absorbance frequency around 3465cm<sup>-1</sup> is corresponding to either for O-H of alcohols/phenols or for N-Hstretch of amines.

The absorbance frequency around 2556, 2426, 2065cm<sup>-1</sup> arises from the C-Hstretch of Alkenes, Alkanes and Aldehydes.

Further the bands around 16349cm<sup>-1</sup> to 1183cm<sup>-1</sup> are corresponding to the bending frequency of Aromatics, Nitro compounds, Aromatic amines N-Hand stretching frequency of C-N of amines.

The band in the 848cm<sup>-1</sup> is corresponding to the bending frequency of Phenyl Ring Substitution Bands of mercury.

Fourier transform infrared spectroscopy (FTIR) data shows oxide forms of potassium, calcium, ferrous and sodium.



## Results of ICP-OES

Table 3: Elements with frequencies

S.No	Elements with frequencies	Availability Mg/l
1.	As193.696	BDL
2.	Ca317.933	8.092
3.	Cd226.502	BDL
4.	Fe238.204	0.472
5.	Hg253.652	3.075
6.	K766.490	7.25
7.	Na589.592	2.638
8.	P213.617	4.081
9.	Pb230.204	BDL
10.	S181.975	15.321

(BDL: Below Detectable Limit)

In the trial substance the heavy toxic metals like As, Cd and Pb are in below detectable level and this infers that they are not present. And the present heavy metal Hg is also in 3ppm, within the admissible level. Also the available sulphur is obtained from the herbals used in this formulation. This helps very much in denaturing the chemical toxicity of mercury. This itself elaborates the intellectual approach in the use of herbs, metals and minerals by the great Siddhars.

**SEM Results**

In this SEM picture of *Rasa Mezugu* shows the partical sizes in a 26000x magnification within a small area of 2 micro meter. So, the particles are present in the range between  $10^{-9}$  to  $10^{-7}$ . The trial drug consists of particles with in 1 to 100nm in size. By this we came to know that the drug has been finished perfectly and able to produce good therapeutic values.

Thirumoolar's hypothesis about Atomic theory has been reinstated as nano technology in this decade. Nano science and technology may be new to the world but ISM have been using this technology to make *Parpam*, *Chendhuram* etc, from time immemorial. Our medicine particles are in oxygen deficient state and clearly identifiable fractions of particles are in the nanometer size range. These properties might impart the therapeutic property<sup>[8]</sup>.

Modern medicine cures a particular disease by targeting exactly the affected zone and transporting the drug to that area known as drug delivery system (DDS). By DDS we can control the PK, PD, non specific toxicity, immunogenicity and makes bio - recognition and efficacy of drugs. This type of DDS is a major lacuna in our system. To

overcome this, now we approach our drug as Novel Drug Delivery System (NDDS).

From the above references, we come to know that our formulations are in nano particle in size and they can be easily fulfill the NDDS. Through the administration of vehicles, our drug can actin the major mechanisms like passive/active target and release as controlled, potential and pulsatile manner and also as protein - peptide/lipid - polymer based drug delivery system.

**CONCLUSION**

The mercury used in this preparation is derived from *Lingam* as the purest form of mercury (*Vaalai Rasam*) is used. Then all the other drugs were purchased and duly authenticated and then subjected to preparation.

The physico-chemical analysis provides proper buffering action and reduces the auto immune activity of cellular destruction. Thus this preparation inhibits the complications and increasing the quality of life of the affected patients.

The FTIR and ICP-OES studies strongly suggesting the safety of the drug by proving heavy metals are in below detectable levels, the active principle *Rasam* is also within 3ppm as per the admissible level for the medicines.

With the help of SEM, the trial drug consists of particles with in 1 to 100nm in size. By this we came to know that the drug has been finished perfectly and able to produce good therapeutic values. By approaching in NDDS, the trial drug increase the therapeutic value, bioavailability and act as smart drug. Since most of Siddha nano particle drug has absorbed in the mucosal level, nano particles improve the drug delivery to the cells even

in cytoplasm and take up these particles easily because of their size.

In this process heavy metal like mercury was denatured and converted into an effective medicine only by grinding with few herbals. Such a transformation of toxic substance into a therapeutic standard is an admirable chemical miracle that was achieved by the Siddhars. The safety of this drug is proved now by the acute and sub-acute toxicity studies done in experimental animals. The result of this study reveals that there are no adverse effects encountered even at the high dose level of 5000mg/kg. This is clear that the Siddhars were the pioneers with extraordinary intelligence in the field of metallurgy and alchemy.

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