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Studies on standardization and purification processes of *VEERAM*

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In *Siddha* system of medicine *Veeram* is one of the toxins among the sixty four known toxins. Geologically it is called Calomel. It is a very toxic material therapeutically, these arsenic based medicines are used in Siddha system. Natural substances of milk, tender coconut water, bitter guard and lemon juice are used to purify the *veeram*. This research work analyzed the raw *veeram* and products obtained after purification. Geochemical, physico-chemical analysis, instrumentation techniques of XRF, TG-DTA, FE-SEM, EDAX and particle size analyzer. Among physicochemical parameters total ash value was low. Loss on drying increased in the products in the various intermediate stages which due to the impact of plant agents used in the process. XRF results revealed mercury is present in major concentration. Raw *veeram* showed 77.14% of mercury. In the raw *veeram* particles observed were distributed within the range of 0.0920 µm–0.948 µm. FE-SEM analysis suggested that the bitter gourd treated *veeram* consisted of individual particles with a size ranging from 94 nm to 144 nm. Milk treated samples when subjected to analysis revealed increased particle size which may be attributed to aggregation. Lemon juice treated samples showed particle size in the range of 82 nm to 96 nm and in tender coconut range was 78 nm to 91 nm. In the EDAX raw and other samples showed peak for mercury and chloride. TG-DTA analysis showed that the raw *veeram* sample had a sublimation temperature of 220°C where as in other treated samples sublimation temperature was reduced compared to raw *veeram*. The from the stydy depict that these purification processes forms new organic substances and transformation of the starting toxic metal. These processes have an important role in the formation of complexes and in altering toxic state to non-toxic state.

Keywords: Geochemical, Instrumentation techniques, Physico-chemical analysis, *Veeram*

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In *Siddha* medical system arsenics are called *Paadaanam*. In Tamil language, it means toxins. *Siddhar Bhogar* classified the toxins into sixty four numbers in his book "*Bhogar karasara thurai*"[1]. Toxins are classified in two groups namely natural toxins and synthetic toxins, thirty two kinds of each[2].

The raw *veeram* called as corrosive sulphate is chemically identified as mercuric chloride ($HgCl_2$) occur as crystals or as white crystalline powder form, soluble in water, ether and ethanol[3]. In *Siddha* medical system, *veeram* is otherwise called as *sawveeram, poovinthu, sarakku chunnam* and *parangi pasanam*[1-3]. In Sanskrit it is called *sawveera.* In other regional languages such as Telugu, Kannada, Malayalam it is known as is *sawveera pasanam*[4].

It is a very toxic material hence used in combination with other drugs after proper processing and purification. Common natural substances used to purify the *veeram* are milk, tender coconut water, bitter guard and lemon juice[5]. Therapeutically it is used in very small doses as alterative, antiseptic and caustic. Internally this arsenic based medicines are used for rheumatoid arthritis, generalized body pain, syphilis or gonorrhea, and gastric ulcer and also cancer[1]. Many arsenic based medicines are available in *Siddha* system of medicine and practically used safely for curing various diseases. *In vivo* toxicity research carried out by Murugan *et al*.[6] proved this concept.

Traditional system explains its toxic symptoms which include bitter taste, sore throat, increased salivary - secretion, swelling in abdomen and face, blisters in skin and finally tightness in chest and breathing difficulties which may lead to death[1,7]. Herbal antidotes like *Tribulus terrestris* plant juice or *Indigofera tinctoria* root paste or *Vernonia cinerea* plant juice or coconut toddy have also been mentioned[7,8].

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Veeram is found as a main ingredient in many *Siddha* formulations such as Thirithoda mathirai, amirtha vennai, sawveera centuram, ayaveera centuram, chanda marutha centuram, ashta bairava kuligai, emathanda kuligai, maha veera mezhugu, pancha sutha mezhugu and ghanthaga sudar thylam[9,10].

Present standardization and chemical characterization studies on purification process of *veeram* is a small step towards proving safety of *Siddha* mercurial preparations. Chemical standardization of *veeram* based prepared formulations Chemical standardization research work was already done by Sathish *et al*.[11], and Dharsana *et al.*[12]. In this paper, some advanced techniques were used for the characterization of intermediates obtained in all the four methods mentioned in S*iddha* system and attempts were made scientifically to prove the safety.

Materials and Methods

Veeram was bought from Chennai market raw drug merchant and verified with the database (7487-94-7 CAS Data Base). Ficture was shown in Figure 1. Detoxified materials of bitter gourd, lemon and tender coconut were procured from vegetable market, Thanjavur, Tamil Nadu and milk was brought from SASTRA University Gosala, SASTRA University, Thanjavur.

Method of detoxification

In the present work four processes of *veeram* detoxification methods were studied namely bitter gourd treatment (BV), milk treatment (MV), lemon juice treatment (LV) and tender coconut treatment (TV).

Fig. 1 — Raw *Veeram*

In the BV treatment, bitter guard was cut horizontally and the sample (50 g) was kept in- centre portion then was tied tightly together with the use of a thread and placed in an earthen-vessel which is filled with lemon juice (1250 mL). The bitter guard underwent a process of purification called *thula yanthra murai.* In this procedure, purifying material was tied as a bundle and boiled in a vessel containing fluid sample and - suspended - with the help of a thread in to the liquid or boiled in the steam. The other end of the thread was tied to the rod. The pot was then kept on the stove and heated[13]. The sample was then boiled for one hour with the lemon steam.

The MV method the sample was soaked in cow's milk in an earthen pot, kept under sun light till the milk was fully dried to get the purified form.

LV treatment - followed the *thula yanthram* method. In this method lemon juice was used instead of tender coconut.

TV treatment also followed the *thula yanthram* method. In this method sample is subjected directly with tender coconut steam. Sample was tied in a gada cloth using thread and heated with tender coconut steam.

Geochemical analysis

Specific gravity

Specific gravity is the relative weight of a sample compared to that of the weight of an equal volume of purified water. Specific gravity of the sample is determined by the formula:

$$\text{Specific gravity} = \frac{\text{Weight of sample in air}}{\text{Loss of Weight of sample in purified water}}$$

Hardness

Scratched the smooth surface firmly with sharp edge of the sample specified in Moh's Scale of Hardness, and observed, whether this sample can scratch the mineral under question. If not, another reference mineral was taken with higher hardness and observed the scratch again. The scratching process was repeated with the sample in increasing order of hardness, one by one, to determine correct hardness of the sample under question.

Method of physicochemical analysis

Physiochemical parameters were determined three times as per the standard procedures of Ayurvedic Pharmacopoeia of India and WHO Quality control methods for medicinal plant material[14,15].

Loss on drying (LOD)

LOD was calculated by geting 1 g of powdered drug in a tare weighed plate and located in the hot air oven at a hotness of 105°C. LOD was measured according to the formula: Weight of the dish before heating – Weight of the dish after heating / Weight of the sample × A100.

Total ash

Assessment of the total ash of raw *veeram* and processed *veeram* were done as per the standard procedures[16]. Crushed materials (1 g) was put in to a pre-weighed silica crucible and heated in the muffle furnace at 400°C for about 3 h. Then the crucible was carefully located in a desiccator and permitted to cool at surrounding temperature and the weight was finally calculated. The proportion of weight of the total ash was calculated using the formula (weight of the ash / weight of the drug × 100).

Acid insoluble ash

The proportion of acid unsolvable ash was measured using the formula: Weight of the residue / Weight of the powder × A100, where the mass of the remains is the net weight of ash.

Water soluble ash

The water soluble extractives of the samples were tested according to the same methodology. Dry material (1 g) was put in a glassware and 50 mL of water was added and shaken well physically. The beaker was set aside for one day and after that 10 mL of the solution was taken and kept in hot air oven at 105°C. The percentage weight of the ash was then measured.

Instrumental analysis

XRF spectrometer

The mineral composition of raw *veeram* and detoxified *veeram* were determined employing XRF spectrometer (S8 Tiger, Bruker AXS, Germany) using a 4 kW rhodium anode X-ray tube. The purpose of X-ray fluorescence is to examine chemical compounds both qualitatively and quantitatively by determining their characteristic radiation. In this procedure, the chemical compounds in the materials are passed via X-rays. The X-ray spectrum acquired during the above method revealed a number of characteristic peaks. The energy of the peaks led to the identification of the elements present in the testing materials.

Particle size analysis

Measurement of standard particle size of raw *veeram* and detoxified *veeram* were carried out by the Microtrac particle size analyzer (Microtrac Blue wave, S3500, USA) that uses three precisely placed red laser diodes to exactly characterize particles. The patented Tri-Laser System gives exact, consistent and repeatable particle size analysis for a varied range of submissions by utilizing the confirmed theory of Mie compensation for spherical particles and the proprietary principle of modified Mie calculations for non-spherical particles. The S3500 measures particle size from 0.02 to 2800 microns.

FE-SEM analysis

Field Emission - Scanning Electron Microscopy (JEOL, JSM-6701 F) was used for the study. Electron microscopes are scientific instruments that use a beam of highly energetic electrons to examine objects on a very fine scale. The sample size is less than 12.0 mm x 12.0 mm x 10 mm (height) and side opposite the side of interest, should be smooth (to enable sample increasing). The small sample height is better and should be in dry.

EDAX

Energy-dispersive X-ray spectroscopy is commonly called as EDS or EDAX. It is an x-ray system used to recognize the basic composition of metals and minerals of the sample. The method can be qualitative, semi-quantitative, and quantitative and also give spatial distribution of elements through mapping and chemical characterization of a sample.

TG-DTA

It is thermo gravimetry-differential thermal analyzer. TG-DTA determines change in weight with respect to increase in temperature. It is used to determine thermal stability, sublimation or evaporation temperature and presence of moisture content in samples. DSC similar to DTA is a thermo analytical technique used to determine phase transition, melting point or crystallization temperature of materials. About 2-5 mg of the sample is taken in a alumina cup and heated at the rate of 10°C/min using a TG-DTA instrument (SDT-Q600, TA Instruments, USA).

Results and Discussion

Geochemical analysis

Geochemical observations of raw *veeram* is presented in Table 1. The raw *veeram* is chemically identified as mercuric chloride. Geochemical properties of mercuric chloride observed were in agreement with the standards prescribed for mercuric

chloride mentioned in Indian Pharmacopoeia and other text books prescribed for chemical analysis[17].

From the data on the geochemical analysis of the products obtained from various purification processes it is concluded that all purifying agents produced similar effects. Data displayed in Table 2. The raw *veeram* has become odoriferous depending upon the purifying agent and also become comparatively less hard. Rajalakshmi *et al.*[18], evaluated the geochemical and physicochemical parameters of sulphur purification processing.

Physicochemical parameters

Physicochemical parameters revealed the purity of the raw material as well as of the various products obtained during intermediate stages of the purifying process, as the total ash value was very low. LOD increased in the products at various intermediary stages which may be due to impact of plant agents used in the process. Using the same method physico-chemical characterization was carried out for an anticancer *Siddha* medicine *veera mezhugu* and lead based Ayurvedic medicine[19,20]. These results are shown in Table 3.

Table 1 — Geochemical analysis Raw *veeram*

Properties	*Veeram*	$Hgcl_2$ Standards
Nature	Crystalline	Crystalline
Color	White	White
Luster	Adamantine	Adamantine
Streak	White	White
Specific Gravity	6.4	5.4
Odor	Odourless	Odourless
Hardness	1.5	1.0
Diaphaneity	Translucent	Translucent
Specific	Dark exposed to light	Dark exposed to light
Probable Mineral	Mercuric Chloride	Mercuric Chloride

Elemental analysis

XRF analysis

Raw, intermediates and final purified *veeram* when analyzed chemically for their elemental composition using X-ray fluorescence spectrophotometry showed variations in the concentration of chemical elements (Table 4). In all the samples mercury is present in major concentration. Raw *veeram* showed 77.14% of mercury. Besides chloride, sulphur, manganese, tin, bromine, germanium, valium, platinum, silica, aluminum, iron and copper. Sample purified with bitter gourd showed absence of copper. In the milk treated sample there was absence of copper but it showed presence of rhodium. In the lemon juice treated samples valium, sulphur and iron were absent, whereas sodium was present. In the tender coconut treated samples, zinc and sodium appeared while

Table 2 — Geochemical data of purified *veeram* with various agents

Properties	BV	MV	LV	TV
Nature	Crystalline	Well Crystalline	Crystalline	Crystalline
Color	Silver White	Silver White	Silver White	Silver White
Luster	Adamantine	Adamantine	Adamantine	Adamantine
Streak	White	White	White	White
Cleavage	Imperfect	Imperfect	Imperfect	Imperfect
Fracture	Conchoidal	Conchoidal	Conchoidal	Conchoidal
Tenacity	Sectile	Sectile	Sectile	Sectile
Specific Gravity	6.4 - 6.5 (Highly intense for crystal clear element)	6.4 - 6.5 (Highly intense for crystal clear element)	6.4 - 6.5 (Highly intense for crystal clear element)	6.4 - 6.5 (Highly intense for crystal clear element)
Odor	Tamarind smell	Milky	Odorless	Odorless
Hardness	1 - 2	1 – 2	1 - 2	1 – 2
Diaphaneity	Translucent	Translucent	Translucent	Translucent
Probable Mineral	Mercuric chloride	Mercuric chloride	Mercuric chloride	Mercuric chloride

Table 3 — Physicochemical parameters of raw *veeram* and treated *veeram* samples

S. No	Sample Name	Loss on Drying (%)	Total ash (%)	Acid insoluble Ash (%)	Water soluble Ash (%)
1	Raw *veeram*	3.4120	0.0291	NA	NA
2	BV	9.1537	0.0165	NA	NA
3	LV	8.2111	0.2253	NA	NA
4	MV	8.1418	0.0717	NA	0.0159
5	TV	17.1501	0.0485	NA	0.0290

platinum, valium and aluminum were absent. The purity of the *veeram* increased approximately by 1% only in milk and lemon juice treated samples. Bitter gourd and lemon juice treating methods have contributed in removing metals like copper and valium, respectively. The data obtained are presented in sequel. In the same way, elemental investigation and XRF description was done for related iron based Siddha medicine and tin based Ayurvedic medicine by Sudheer *et al.*[21] and Saraswathi *et al*[22]. These results are displayed in Table 4.

Table 4 — XRF results of raw *veeram* and treated *veeram* samples

Formula	Z	Raw *veeram*	BV	MV	LV	TV
Hg	80	77.14%	76.88%	78.89%	76.67%	77.61%
Cl	17	21.11%	22.08%	19.39%	21.61%	20.68%
S	16	0.64%	0.0%	0.57%	0.63%	0.69%
Mn	25	0.39%	0.35%	0.34%	0.35%	0.37%
K	19	0.0%	0.0%	0.0%	0.03%	0.0%
Tl	81	0.19%	0.22%	0.21%	0.19%	0.20%
Br	35	0.16%	0.19%	0.19%	0.22%	0.20%
Ge	32	0.11%	0.09%	0.07%	0.11%	0.10%
V	23	0.09%	0.06%	0.10%	0.08%	0.07%
Pt	78	0.06%	0.06%	0.09%	0.07%	0.05%
Si	14	0.05%	0.03%	0.06%	0.0%	0.0%
Al	13	0.02%	0.0%	0.04%	0.0%	0.0%
Fe	26	0.02%	0.02%	0.03%	0.02%	0.01%
Cu	29	0.01%	0.02%	0.01%	0.02%	0.02%
Ni	28	0.0%	0.0%	0.0%	0.01%	0.01%

Particle size analysis data

In the raw *veeram,* particles must have been scattered freely, hence particle size of single crystal could be detected easily. Granular size was mainly distributed within the range of 0.0920 µm – 0.948 µm. In v*eeram* purified with BV sample granular size was mainly distributed within the range of 7.67 µm – 143.5 µm. MV sample structure explained that granular size was mainly distributed within the range of 0.0490 µm – 924.9 µm. LV granular size was mainly distributed within the range of 6.82 µm – 99.58 µm. In v*eeram* purified with TV sample granular size was mainly distributed within the range of 11.59 µm – 121.6 µm (Fig. 2a-e).

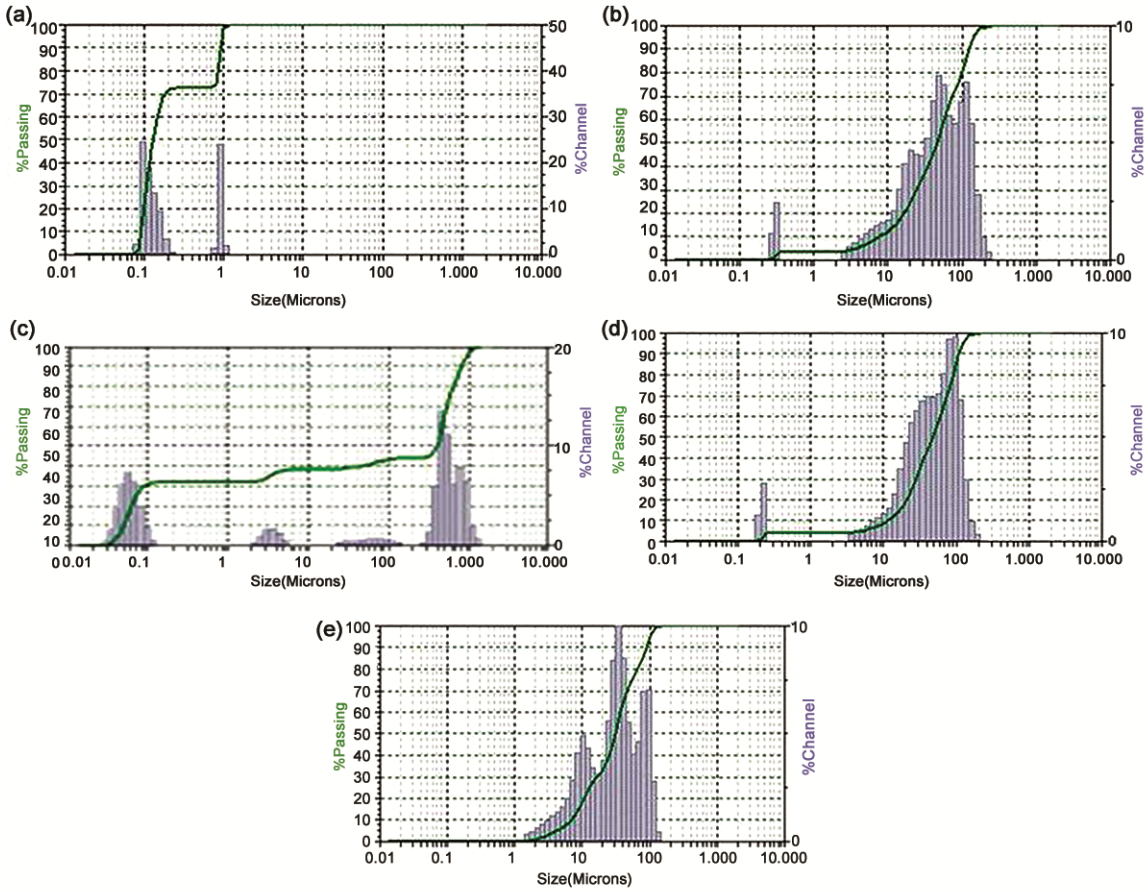

Fig. 2 — Particle size images A - Raw *Veeram,* B – BV, C – MV, D- LV, E- TV

FE-SEM analysis

In the present study FE-SEM analysis of raw *veeram* and processed *veeram* samples were carried out. Similar method of analysis was performed for a borax based *Siddha* formulation by Devi *et al.*[23]. The particle size distribution indicated that the bitter gourd treated *veeram* consisted of individual particles ranging from 94 nm to 144 nm. The milk treated samples showed agglomeration of particles and identification of individual particles were different. The lemon juice treated samples showed marked variation as compared to bitter gourd and milk treated samples. Here different particle morphology like circular, oval and tube like structures were observed. The size ranged from 82 nm to 96 nm. The tender coconut samples showed the presence of individual particles ranging 78 nm to 91 nm. XRD instrumental research article calculate the step size of the *veeram*[24]. The images obtained from the Field Emission Scanning Electron Microscope are presented in Figure-3 (a-e).

Elemental analysis by Energy Dispersive X-Ray analysis

The testing materials were mounted on a brass stub and sputter coated with gold and started into the specimen chamber of the cold FE-SEM (JSM-6701F. JEOL, Japan) under ultra high vacuum for Energy Dispersive X-Ray analysis. Raw *veeram* and *veeram* purified with various purification agents showed peak for mercury and chloride. Similarly in addition of our data EDAX characterization was done for related research work on vanga Bhasma by Saraswathi *et.al*., 2013 and Naga bhasma by Singh *et.al*., 2010[22,25]. The elemental images displayed in Figure 4 (a-e).

TG-DTA

The *veeram* sample had a sublimation temperature of 220°C. This temperature curve figure was shown in Figure 5. Detoxified veeram samples curve figures of BV, LV, MV and TV were shown in Figure 6. No residue was left behind whereas BV sample indicated a significant difference in sublimation temperatures (227°C & 211°C). LV samples indicated decrease in sublimation temperature (204°C & 206°C), which can be attributed as an outcome of treatment with lemon juice. MV and TV samples also showed similar effects. A reduction in temperature was observed in all the samples except BV indicating that treatment was carried out with specific purifying agents that caused a change in their thermal properties. Changes observed in the sample treated with BV were not significant. From the TG-DTA curves it can be observed that treatment with various herbal juices have caused a reduction in sublimation temperature of

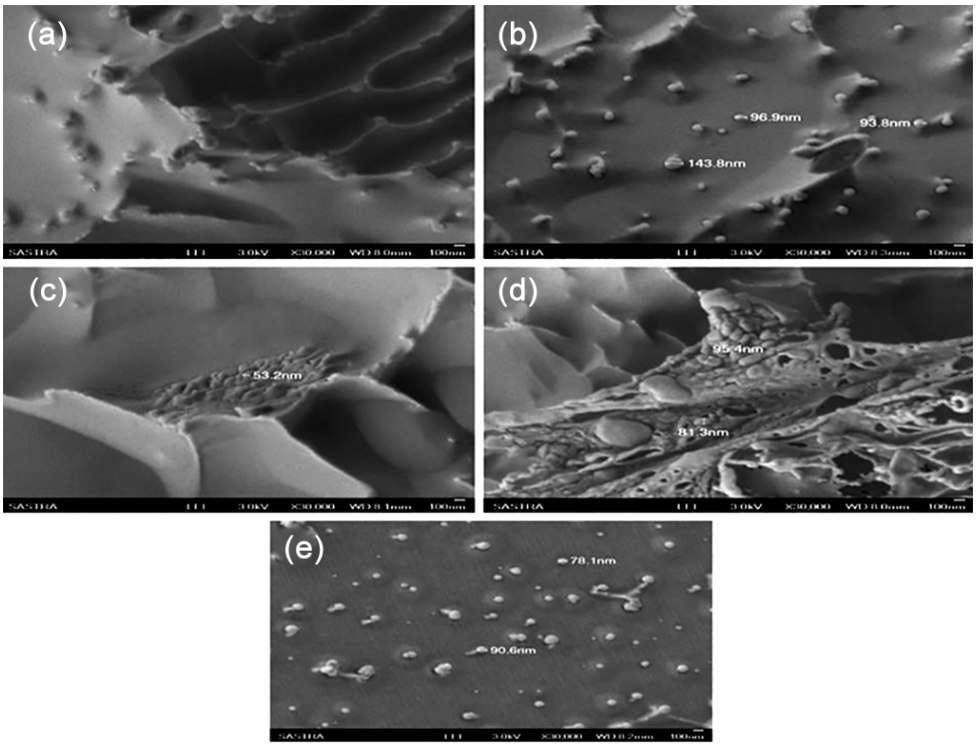

Fig. 3 — SEM analysis – (Image of X30,000 magnified) A - Raw *veeram* B- BV, C- MV, D- LV, E – TV

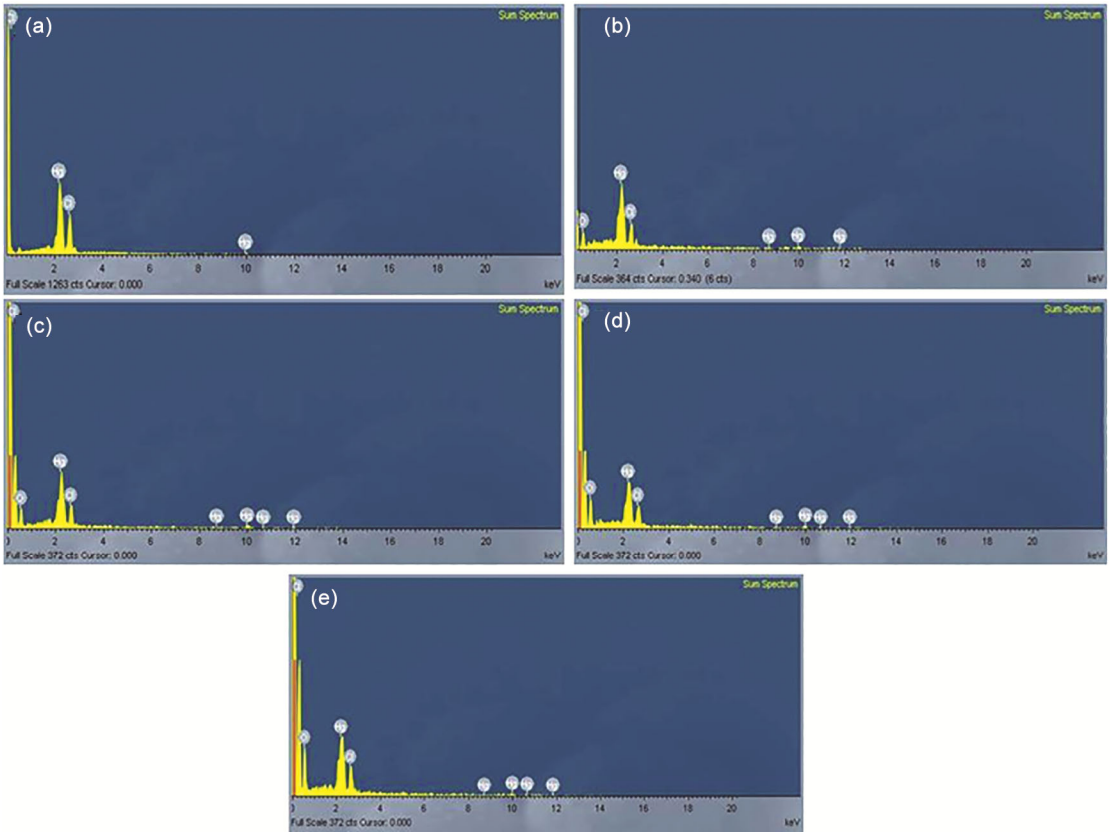

Fig. 4 — EDAX Images A - Raw *veeram* B - BV, C - MV, D - LV, E – TV

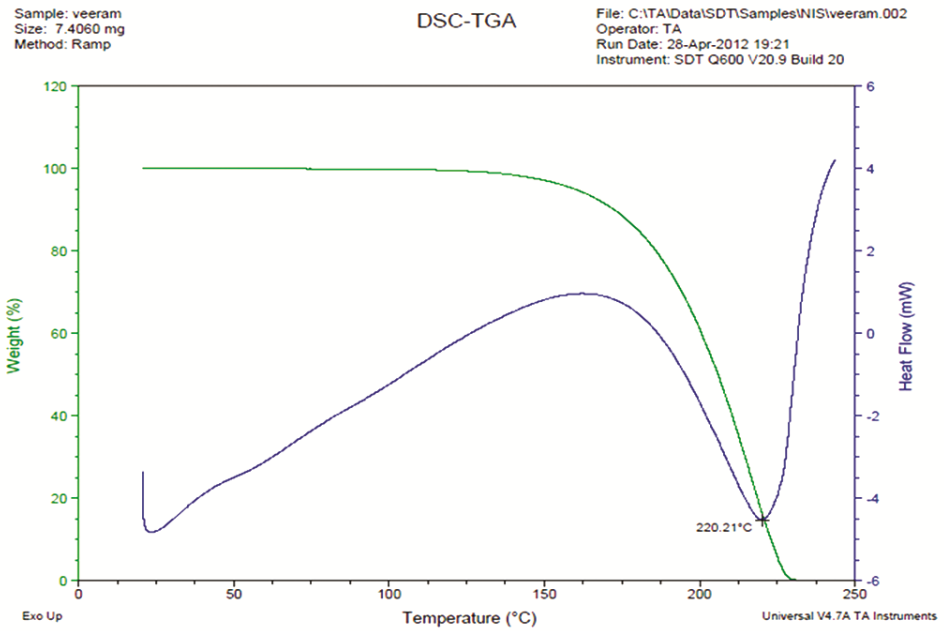

Fig. 5 — TG-DTA curve of Raw *veeram*

veeram compared to untreated *veeram*. This indicates a possible transformation in the treated samples of mercuric chloride (*veeram*). In metallic preparations the temperature was so high as much as 450°C to750°C compared to arsenics[26]. Garg *et al.*[27], conformed these thermal treatments results in their research work.

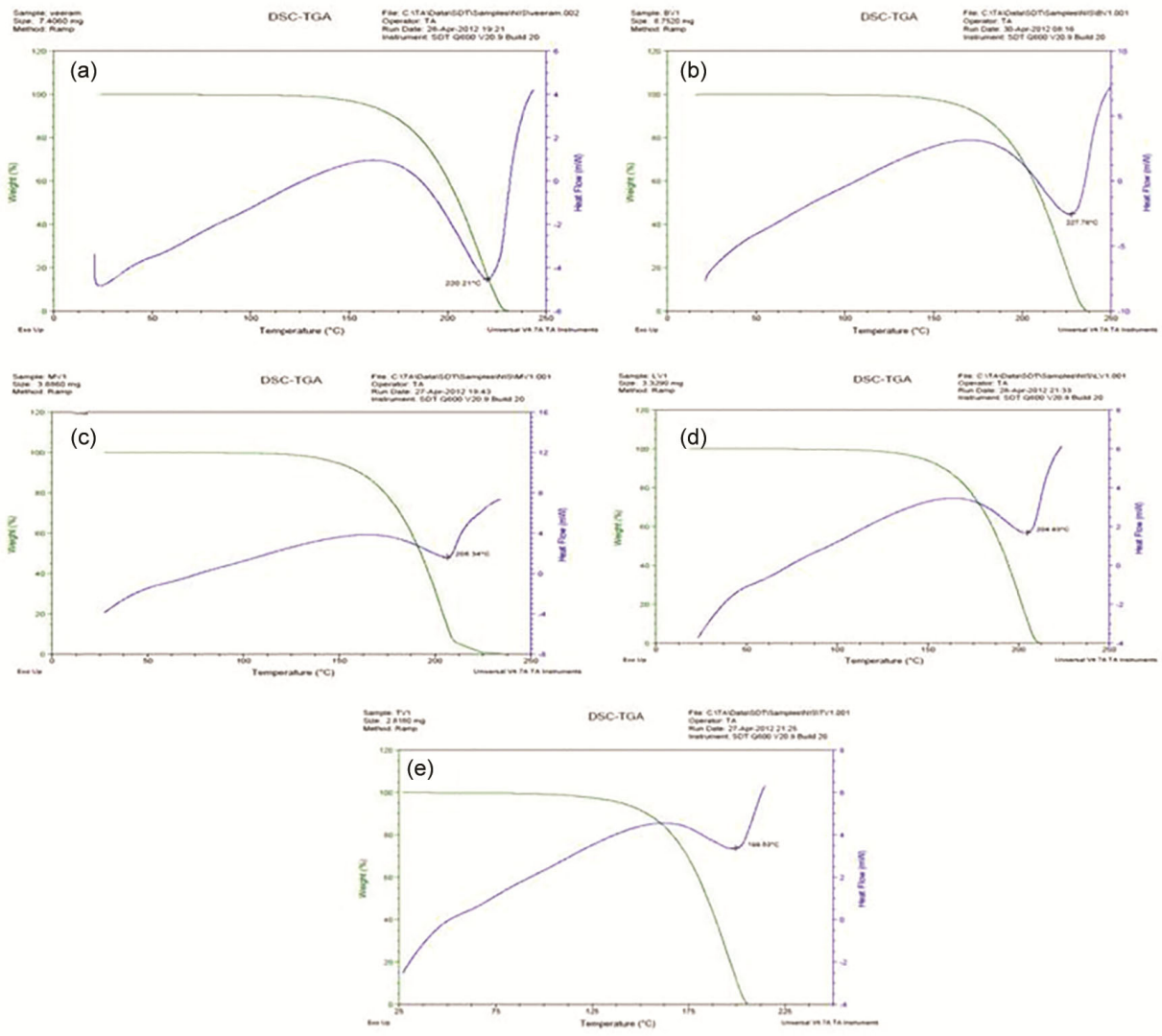

Fig. 6 — TG-DTA curve of A-BV, B-MV, C-LV, D-TV

Conclusion

From the geochemical analysis data it is concluded that all purifying agents produced only similar effects. Physicochemical parameters revealed that the total ash value was very low which was also supported by TG-DTA data. Loss on drying increased in the products in the various intermediary stages which may be due to impact of plant agents used in the processes. XRF results suggested that purity of mercury increased by 1% in MV and LV samples. Zinc and sodium were found to be present in TV samples. MV sample showed presence of rhodium, sodium was present in LV samples and copper was absent in BV sample.

Particle size analysis revealed that in the TV samples, size was in the range of 11.59 µm – 121.6 µm while in the MV samples size was mainly distributed in the range of 0.0490 µm – 924.9 µm. This may be due to presence of agglomerated particles. FE-SEM analysis also confirmed the data. In LV, particle size was found to occur within the range of 6.82 µm – 99.58 µm and in BV particle size is in the range of 7.67 µm – 143.5 µm. Milk treated samples cannot perform good activity as the particles were agglomerated. Individual particles did not exist. In these samples drug's absorption may be problematic. Further milk treated samples showed the presence of rhodium. Bitter gourd proceesed *veeram* confirmed absence of heavy metals and better size reduction. Lemon juice treated samples showed absence of heavy metals and increased purity of mercury. To conclude, of the four methods of

purification from the chemical characterization point of view lemon juice proceesed *veeram* explains best followed by tender coconut treated and least by bitter gourd treatment. Compared to bitter gourd, tender coconut shows better particle range 78 nm to 91 nm where as it is 94 nm to 144 nm in bitter gourd. Milk treatment stands last due to presence of rhodium and agglomerated particles.

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Conflict of Interest

Authors declare that they do not have any conflict of interest.

Authors' Contributions

All the authors worked together to complete this manuscript. Authors M R and M N J procured the material and did the process as per the text. S S collected the processed samples and followed the analysing work and collected data and R P draught of the manuscript and followed the corresponding works. The study analyses were overseen and guided by B P. The manuscript was read and approved by all authors.

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