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UNRAVELING ANCIENT MEDICINAL FORMULATION SECRETS: PREPARATION OF *GANDHAGAPARPAM*

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ABSTRACT

Gandhaga parpam is a Siddha formulation prescribed for the treatment of leucoderma, eczema, stomach disorders, venereal chronic diseases, poisonous bites and rheumatic fever. *Gandhaga parpam* has been prepared following the methods described in the ancient texts. The first step is the purification of crude sulphur, in which the crude sulphur is added to a mixture of curd & henna, placed in a *sarava samputa* and heated using cow dung cakes. This is repeated seven times. A maximum temperature of 350 °C is reached during heating in about 3 hours. The purified sulphur is triturated with *Allium sativam* extract for about 15 times, followed by tirturation with *Zingiber officinalis* for 15 times. The paste is made into pellets and dried under sun, followed by heating with ash of *Terminalia arjuna* bark for about 18 hours. The intermediates obtained during each purification step were characterized for morphology, elemental composition and crystallinity using scanning electron Microscopy, X-ray fluorescence spectroscopy and X-ray diffractometry. Our studies show that a properly prepared *Gandhaga parpam* exhibits a morphology comprising nanoscale features. Calcium (46.66%) is found to be the major component in the product. This is attributed to burning with ash of *Terminalia arjuna* bark which contains calcium in higher concentration. Increased levels of potassium, chlorine, magnesium, silicon, iron, aluminium has also been observed. Phosphorus, strontium, sodium, tin, lead zinc, copper, bromine have been incorporated in the product due to the addition of garlic and ginger. Titanium and molybdenum are absent in the product, while the levels of lead and bromine are well below the permissible limit.

Keywords: *Siddha*, *Gandhagaparpam*, nanoscale features, *Allium cepa*, *Zingiberofficinalis*

INTRODUCTION

Siddha is one of the ancient systems of medicine dating back to B.C. 10000 to B.C. 4000[1]. This system of medicine originated in Tamil Nadu, located in the southern part of India[2]. *Siddha* medicine derives its medicinal ingredients from plants, animals and minerals [1]. *Siddha* system of medicine was formulated by '*siddhars*' (18 in number), who possessed commendable knowledge in the field of science and medicine[2, 3]. In *Siddha* system, diagnosis is performed by examination of eight important sites/features: pulse, eyes, voice, touch, color, tongue, faeces and urine[2, 3]. The treatment in *Siddha* system of medicine lays emphasis on pediatrics, toxicology and ophthalmology[3]. Among plants, animals and minerals that constitute the *siddha* drugs, preparations based on minerals and metals are used in majority in preference to preparations from plants[3]. Though metals are used in *Siddha* medicines, they are subjected to rigorous treatments involving different steps before being converted to a therapeutic form.

In *Siddha* system, the human body is considered to be a balance between the three humours which are vata, pita and kapha[3]. A healthy body requires equilibrium of humours while a perturbation of this equilibrium leads to sickness[4]. The source of three humours, tissues and waste products is food[3]. Despite the prevalence of this system of medicine since ancient times, this is less popular compared to other traditional systems of medicine like Ayurveda, Kampo (Japanese system) etc.[2]. Medicines derived from plant extracts are still utilized by about 75 % of the global population[5]. *Gandhagaparpam* is used in the treatment of skin and stomach disorders apart from being the cure for venereal chronic diseases and poisonous bites. In the present work, the preparation of *gandhagaparpam* has been carried out based on the procedure detailed in the *Siddha* texts. The intermediates from each preparation step have been characterized using modern analytical tools to understand the physico-chemical transformation that occur during the purification steps, apart from identifying rationale for the use of certain purifying agents.

MATERIALS & METHODS

Preparation of *gandhagaparpam*

The preparation of *gandhagaparpam* involves (i) detoxification of sulphur (ii) purification of sulphur and (iii) preparation of parpam. The process flow diagram for the preparation of *gandhagaparpam* is shown in Figure 1.

Detoxification of sulphur

500 mL of curd and 500 g of Henna paste were taken in an earthen vessel whose mouth was closed with a muslin cloth. One kilogram of crude sulphur was placed on the muslin cloth and covered with another earthen vessel. A clay-smeared cloth was used to seal interface between the two earthen vessels purportedly to prevent diffusion of air into the vessels (Fig. 2A). A small pit was made on the ground in such a way that the bottom of the earthen vessel was placed in the pit. The portion of the earthen vessel above the ground was covered with ten cow dung cakes and sent on fire. (Fig.2B). The set up was not disturbed allowing the heating to proceed uninterrupted till the cow dung cakes were completely burnt. The earthen vessel was allowed to cool and sulphur was recovered from the vessel. This process of treating sulphur with curd and henna paste in earthen vessels and heating with cow dung cakes was repeated seven times. The sulphur obtained at this stage is the de-toxified sulphur.

Purification of sulphur

The de-toxified sulphur was triturated with the extract of *Allium cepa* for 12 hours. This was followed by trituration with *Zingiberofficinalis* extract for 12 hours. The trituration is expected to reduce the particle size of the sulphur and facilitate exposure of sulphur for treatment with these aqueous extracts. This is called purified sulphur.

Preparation of *parpam*

The purified sulphur was made into thin flat discs and allowed to dry under sunlight. The dried product was ground for 3 hours. The resultant powder is *gandhagaparpam*.

Characterization of Intermediates and *Gandhagaparpam*

Scanning Electron Microscopy

The surface morphology of the final product was studied using a cold Field Emission Scanning Electron Microscope (JEOL 5701F, JEOL, Japan). A small amount of the sample was mounted on to a brass stub using a carbon tape. A thin layer of gold was sputter coated to render the top surface conducting to overcome charging of the sample.

X-ray diffractometry

The crystallinity of intermediates and that of final product was studied using a powder X-ray diffractometer (D8Focus, Bruker, USA). The powdered sample was irradiated with Cu–Kα radiation and the analysis was performed from 10° to 60° (2θ) with a step size of 0.001 at a scan rate of 1 step/second.

Elemental analysis by X-ray Fluorescence Spectrometry

The elemental composition of the intermediates was determined using X-ray fluorescence spectrometer (S8 Tiger, Bruker AXS, Germany). The samples were pelletized in the form of thin 34 mm diameter discs using a hydraulic press applying a load of 25 ton.

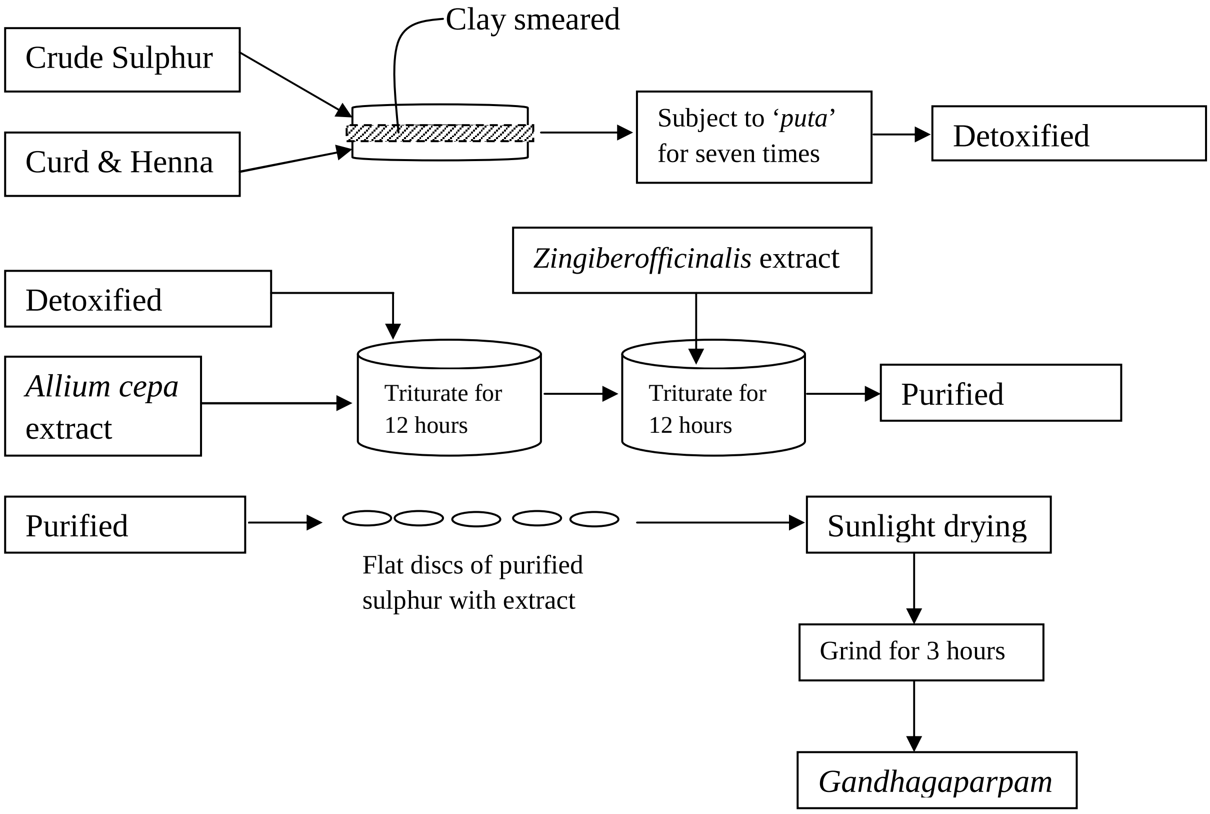

Fig. 1: Process flow diagram for the preparation of *gandhagaparpam*.

Fig. 2: [A] Crude sulphur, curd and henna in earthen vessels sealed with clay smeared cloth; [B] A typical *puta* in progress.

RESULTS & DISCUSSION

It may be recalled that during the purification of sulphur, the crude sulphur was heated with a curd and Henna paste, before being subjected to '*puta*'. The knowledge of temporal variation of temperature during '*puta*' will help identification of possible physico-chemical transformations of sulphur. Figure 3 shows the temporal variation of temperature during the '*puta*' step. It may be observed from Figure 3 that the temperature increases gradually reaching a maximum temperature of about 320-350 °C in 110-130 minutes.

The similarity of temperature profiles for different '*puta*' indicates the suitability of this heating method (by burning cow dung cakes of specified size and mass) to maintain similar temperature profiles during each *puta* cycle.

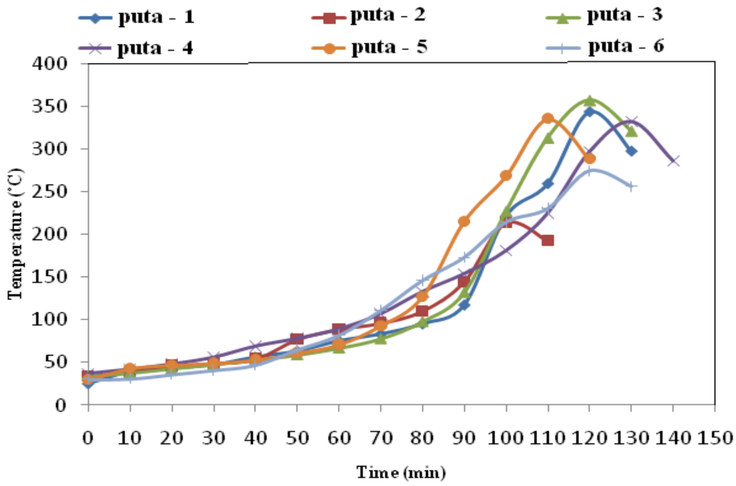

Fig. 3: Temporal variation of temperature during '*puta*'.

Allotropic modifications during purification of sulphur

The melting point of sulphur is 119.2 °C. Hence during the heating phase of '*puta*', sulphur melts and mixes with the mixture of curd & Henna, whereas in the cooling phase sulphur solidifies, during which incorporation of some ingredients from curd & Henna is expected. This could manifest as allotropic modification with the formation of new crystalline phases. Figures 4a & 4b show the X-ray diffractograms of the crude and purified sulphur. The crude sulphur contains (111) and (144) phases, while the purified sulphur contains peaks characteristic of α-S8 (face-centred, orthorhombic) phase of sulphur (PCPDFWIN 89-2600).

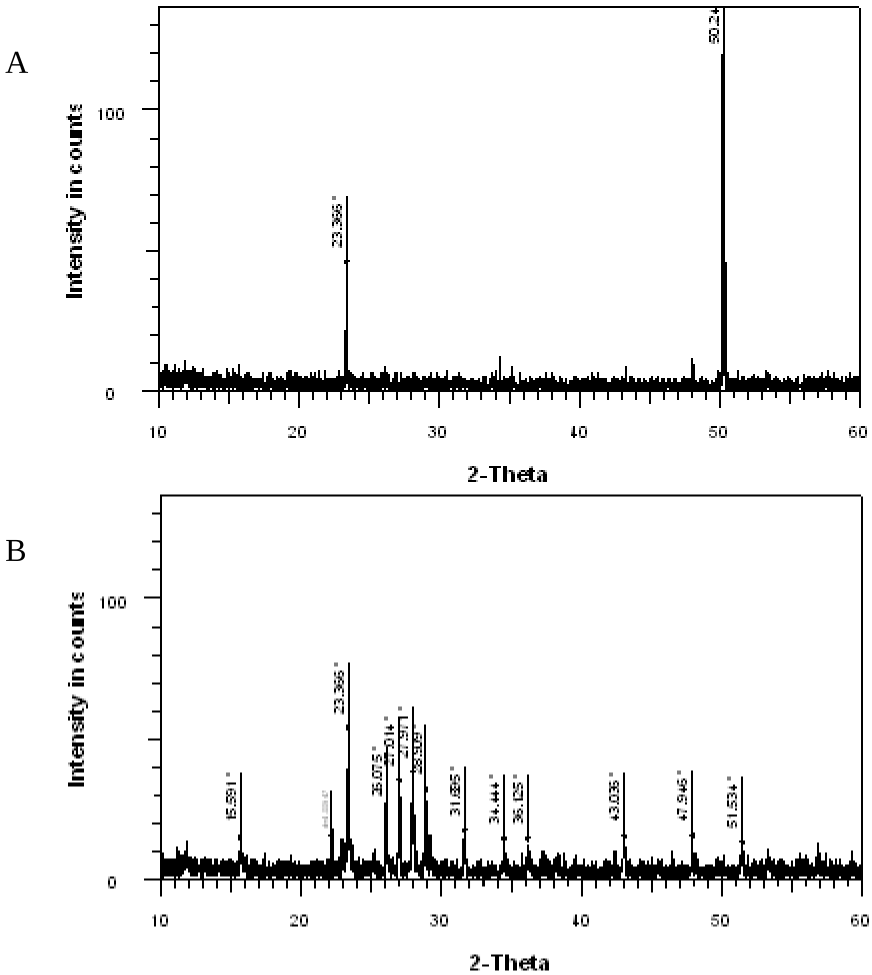

Fig. 4: Powder X-ray diffractograms of [A] Crude sulphur; [B] Purified sulphur.

Chemical changes accompanying purification of sulphur

Apart from the allotropic modification, substantial changes in chemical composition occur during the purification of sulphur. Elemental analyses by X-ray fluorescence spectroscopy (Table 1) reveal significant changes in the percentage of elements like Mg, Si, Al, Fe etc between the crude and that of the purified sulphur. These impurities were most likely leached away during the trituration of phase-transformed sulphur with *Allium cepa* and *Zingiber officinalis* sequentially.

It has been established that the aqueous extract of *Allium cepa* contains sulphoxides like propenyl cysteine sulphoxide [6]. Hence the reduction in composition of elements like Mg, Si, Al and Fe may be attributed to the metal scavenging activity of the aqueous extract of *Allium cepa*.

Though the crude sulphur used was 99.27 % pure, further purification lead to increase in its composition to 99.6 %. We believe that the ancient practitioners of *Siddha* had devised these purification methods utilizing the naturally available materials to increase the purity of raw material and transform the nature of raw material to render it non-toxic.

Preparation of *gandhagaparpam*

During the preparation of *gandhagaparpam*, the purified sulphur still containing water-soluble constituents of *Allium cepa* and *Zingiberofficinalis*, was dried under sunlight. During this period of slow drying under sunlight, reactions occur between the organic constituents of *Allium cepa* & *Zingiberofficinalis* and elemental sulphur, probably resulting in the formation of a complex compound. This could be responsible for the expected potency of the *gandhagaparpam*. This formation of complexes can also be ascertained with the presence of oxygen as the major constituent in the *gandhagaparpam* (Table 2). It is also evident that the heavy metals like Pb, Zn, Cu are present within the permissible limits while toxic elements like As are absent in the final product.

The scanning electron micrograph of *gandhagaparpam* (Figure 5) reveals the presence of high-aspect ratio nanostructures with fibre-like morphology, which are expected to improve therapeutic activity[7,8]. The surface area of particles depends on the particle size and shape. Finer particles and those with high aspect ratio possess higher surface area compared to those of spherical, coarse particles [9,10,11,12]. The high aspect ratio structures present in *gandhagaparpam* ensure the availability of high surface area for interaction of *parpam* with the fluid. It may be recalled that the interaction between a fluid and solid particles occur through the interface. The external surface area of the particles is the interfacial area between the fluid and solid particles[13] and hence higher the particle surface area more is the interaction with the fluid. In the case of *gandhagaparpam*, this could manifest as the improved therapeutic activity. This aspect needs further investigation.

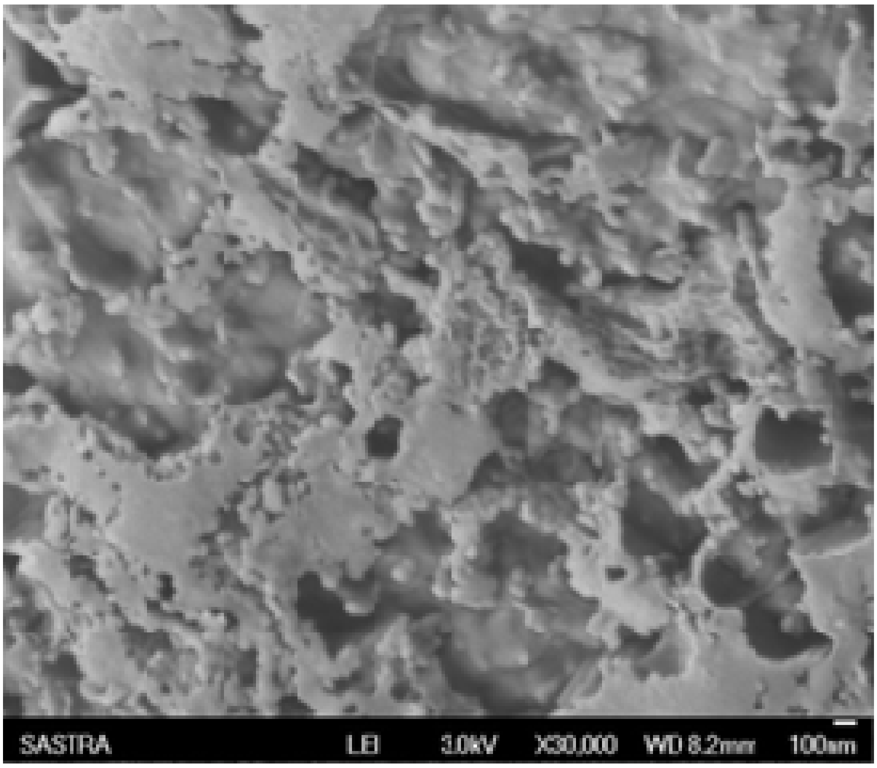

Fig. 5: Scanning electron micrograph of *gandhagaparpam*.

Table 1: showing Elemental analysis of the crude and purified sulphur

Element	Mass percentage in Crude Sulphur	Mass percentage in Purified Sulphur
Sulphur	99.27±0.085	99.61±0.095
Calcium	0.16±0.010	0.03±0.026
Magnesium	0.27±0.153	0.22±0.096
Silicon	0.13±0.015	0.03±0.006
Aluminium	0.06±0.014	0.01±0.014
Iron	0.06±0.006	0.02±0.000
Chlorine	0.03±0.031	0.05±0.025
Potassium	0.03±0.000	0.02±0.029
Titanium	0.01±0.000	-
Molybdenum	0.01±0.001	0.01±0.002

Table 2: showing Elemental analysis of the *gandhagaparpam*

Element	Mass percentage
Oxygen	58.57
Sulphur	38.28
Potassium	1.60
Chlorine	0.47
Magnesium	0.25
Calcium	0.06
Aluminium	0.05
Sodium	0.13
Iron	0.04
Lead	0.01
Manganese	0.01
Silicon	0.27
Copper	0.00
Phosphorus	0.26
Zinc	0.00

CONCLUSION

Gandhagaparpam has been prepared following the procedure described in the *Siddha* texts. The role of curd, Henna, *Allium cepa* and *Zingiberofficinalis* in the purification of sulphur and in the elemental composition of *gandhagaparpam* has been elucidated. Substantial allotropic modification of sulphur, as a result of treatment with curd and henna, results in its improved reactivity with phyto-constituents. The nanoscale structures on the parpam may aid in its therapeutic activity.

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