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Quality assessment of commercial formulations of tin based herbal drug by physico-chemical fingerprints

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Abstract

The Tin based herbal drug *Vanga Parpam* is extensively used for treating urino genital infections, Odema, Polydepsia and Dyspepsia effectively. There are no reports of physico chemical fingerprints for the tin based drug available. Proper characterization techniques are required for checking the quality of the commercial samples, in terms of the physical and chemical constitution to meet the expected criteria to support its use worldwide. Two popular commercial brands such drug were characterized and compared in terms of morphology, composition, crystal lattice, and oxidation state of the active metal. Physico-chemical fingerprints were generated for the samples using analytical techniques like Powder X ray crystallography, Scanning Electron Microscopy, Energy Dispersive X ray Analysis and Inductively Coupled Plasma Optical Emission Spectroscopy and Fourier Transformed Infra Red spectroscopy. It was found that the percentage of tin varied drastically in both brands along with a difference in the percentage composition of other elements and surface morphology which would have significant impact on the therapeutic efficacy and pharmacological activity of the drug samples. The current study appropriately substantiated the need for the use of modern analytical techniques in the establishment of quality and safety assurance of such potent drug.

Keywords: Metallo herbal drug, *Vanga parrpam*, tinoxide,quality control, fingerprints, standardisation

Introduction

Metallo herbal drugs have been used in the treatment of various infectious diseases by the Indian System of Medicine as minerals and metals play a vital role in the human metabolism The process of preparation of the medicinal formulations generally involves, plants and minerals and several alchemical operations like calcinations, sublimation, distillation, fusion, fermentation, etc, in an eco-friendly environment. Such medicines which contain metals like mercury, silver, arsenic, tin, lead, sulphur, gold can treat effectively all types of infectious diseases and chronic ailments in small dosages without side effects. Most of the medicines are prepared by the trituration of the metals with herbal juices to bring down the metal toxicity and particle size in such a way that there is a balance of micro and nano size so as to increase the bioavailability to the human system. The oxide formulation of 'Parpam' ('*Bhasma' in Ayurveda*) is one of the significant processes and its method of preparation involves the conversion of metal to its respective oxides through repeated calcinations (Wadekar *et al*., 2006). These repeated calcinaions with herbal juices tend to detoxify the metal (Patel, 1986).

There is lack of analytical data on the finished commercial drugs available in the market due to variation in the sources of the raw material, the processing techniques and packaging. The reasons for the lack of such data include not only national health care policies, but also a lack of adequate or accepted research methodology for evaluating traditional medicines (WHO, 1978). But it is possible to generate a physico-chemical fingerprint for the standardization of these drugs with reference to authentic drugs, for monitoring variation between preparations from different brands and for evaluating batch to batch changes during long term storage (Sudha *et al*., 2009).

Vanga Parpam, a tin based Siddha formulation, is widely used for the treatment of Oedema, Polydepsia and Urino genital infections and Dyspepsia (Siddha Materia Medica,1988) in the dosage of 65- 130 mg with butter or ghee or honey as adjuvant. There has been no authentic and comprehensive report on the constitution of this drug and the scientific basis of its application in treating the infectious diseases. Proper characterization techniques are required for checking the quality to meet the criteria to support its use worldwide.

The aims of the present study are to analyze and compare the two popular commercial brands of the drug of *Vanga parpam* available in the market using several modern analytical techniques in the following way: To characterize the bulk property of the drug samples using Fourier Transformed Infra Red, Energy-dispersive X-ray Spectroscopy, Inductively Coupled Plasma- Optical Electron Spectroscopy (ICP-OES) techniques. To identify the phase and crystallinity of the active pharmaceutical ingredient using Powder X Ray Diffraction. To study the thermal stability of the drug samples and further validate the results of the above mentioned analysis.To obtain the surface morphology of samples through Scanning Electron Microscope(SEM).

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Materials and methods

The two popular brands of the samples of the tin oxide based drug, *Vanga parpam* that were prepared according to the *Siddha* texts (Gunapadam) were purchased from the market and named *as* VPX1 and VPX2. The information on the actual materials used and the calcinations method followed in the preparation of the drugs was not available. They were prescribed in the dosage of 100 to 130 mg per day along with an adjuvant like milk, honey or ghee.

Instrumental analysis

The drug samples VPX1 and VPX2 were subjected to physico-chemical characterization using the following instrumental techniques.

FT-IR spectra were recorded using a Perkin-Elmer 360 model IR double beam spectrophotometer. The spectra were collected from wavelength of 4000 cm^{-1} to 400 cm^{-1} with 4cm^{-1} resolution over 40 scans. All spectra were collected against the background spectra of KBr.

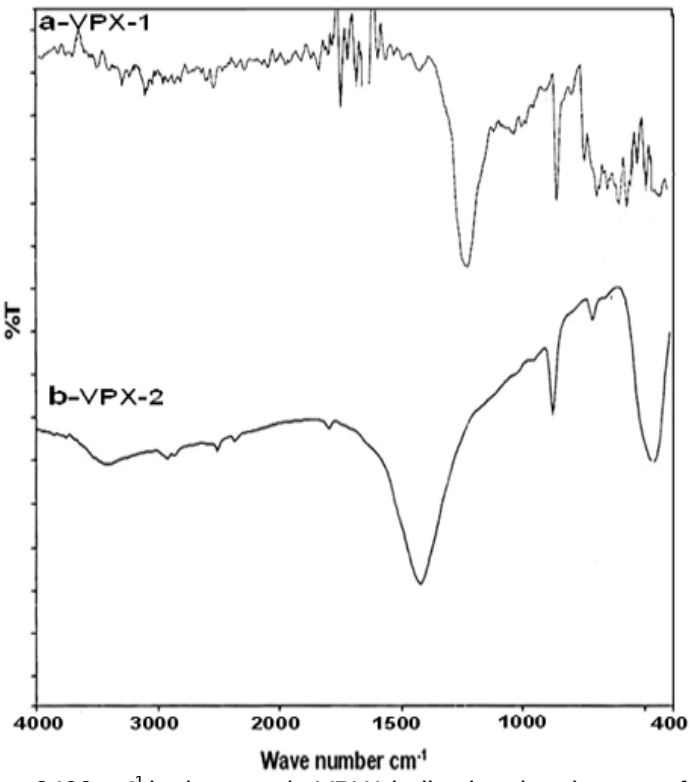
Assessment of metallic constitution was made by ICP-OES analysis using Perkin-Elmer 5300DV ICP-OES. Thermal properties of the drug samples were investigated on Meltzer TA 4000. The thermo gravimetric analysis (TGA)were carried out at the rate of 20°C/ min. TGA curves were obtained by heating the drug samples in the temperature range 0˚ C - 600˚ C. The powder X-ray diffraction patterns of the solid samples were recorded on Rigaku CD MAX 2 VCc model of X ray diffractometer using Cu Kα radiation filtered by nickel foil over the range of diffraction angle 20-80˚. The wavelength of the radiation used was 1.5405 A˚. The bulk elemental composition of the samples was found out by EDAX (EDAX Inc, Mahwah, NJ, USA) which was attached with Environmental Scanning Electron Microscope (ESEM) (Quanta 200, FEI, Hillsboro, Oregon, USA). The elements measured were O, Si, S, Ca, Mn, Fe, Cu, Zn, and Sn. SEM images were obtained with a JOEL-JSM-6360 instrument, USA.

Results and discussion

Both the samples were colourless, consisting of very fine and fine particles as confirmed by the presence of particle in the furrows and depressions of thumb and forefinger when rubbed (The Siddha Pharmacopoeia of India, 2010). The samples were sparingly soluble in water. The pH of the samples was close to 6.9.

The FTIR spectra of the two samples were shown in Fig.1. On comparison of the band position, their shape and intensity of the IR spectra of the two samples with those of the standard SnO_2 we could infer that SnO_2 was the common constituent in both the samples. The characteristic peaks in the wavelength regions of 625 - 665 cm^{-1} and 1040 - 1060 cm^{-1} corresponds to O-Sn-O bridge of the functional group of SnO_2. The number of small peaks in the range between 400 - 555 cm^{-1} displayed by the two samples confirms the presence of SnO2 (Nakamoto, 1986; Davydov & Sheppard, 2003; Zhang & Gao, 2004). There was no intense broad peak

Fig. 1. FTIR analysis of Vanga parpam samples VPX 1 (a) & VPX 2 (b)



at 3400cm^{-1} in the sample VPX1 indicating the absence of moisture, while the broad peaks at 3400 cm^{-1} in the sampleVPX2 is due to the characteristic OH stretching vibrational bands due to adsorbed water in the sample. Both the samples showed prominent peaks at 1421 cm^{-1} which was due to $CO3^{2-}$ from $CaCO_3$. The source of Calcium carbonate would have been due to addition of lime water during the calcinations process.

Table 1. ICP- OES analysis of Vanga Parpam samples (VPX-1 and VPX-2)

Elements	VPX-1 (mg/L)	VPX-2 (mg/L)
Ca	85.60	51.14
Cu	0.08	0.01
Fe	0.53	1.75
Na	2.87	1.87
Sn	49.25	3.85
Zn	16.24	96.31

ICP-OES analysis of the two samplesVPX1and VPX2 was represented in the Table 1**.** Although both the samples contained similar elements, their percentage amount was different. The sample VPX1 was found to contain more amount of Tin and Calcium than in VPX2 while the amount of the Zinc content reversed in both the samples. Fig.2a &2b depicted the thermograms of the samples VPX1 and VPX2 respectively. In the thermogram of VPX1 there was no weight loss upto 200°C which clearly indicates the absence of moisture and any other solvent in the sample. This observation was also confirmed by the FTIR spectra. There was a negligible

Indian Journal of Science and Technology Vol. 4 No. 12 (Dec 2011) ISSN: 0974- 6846

Fig. 2. Thermogravimetric analysis of Vanga parpam samples VPX 1(a) and VPX 2(b)

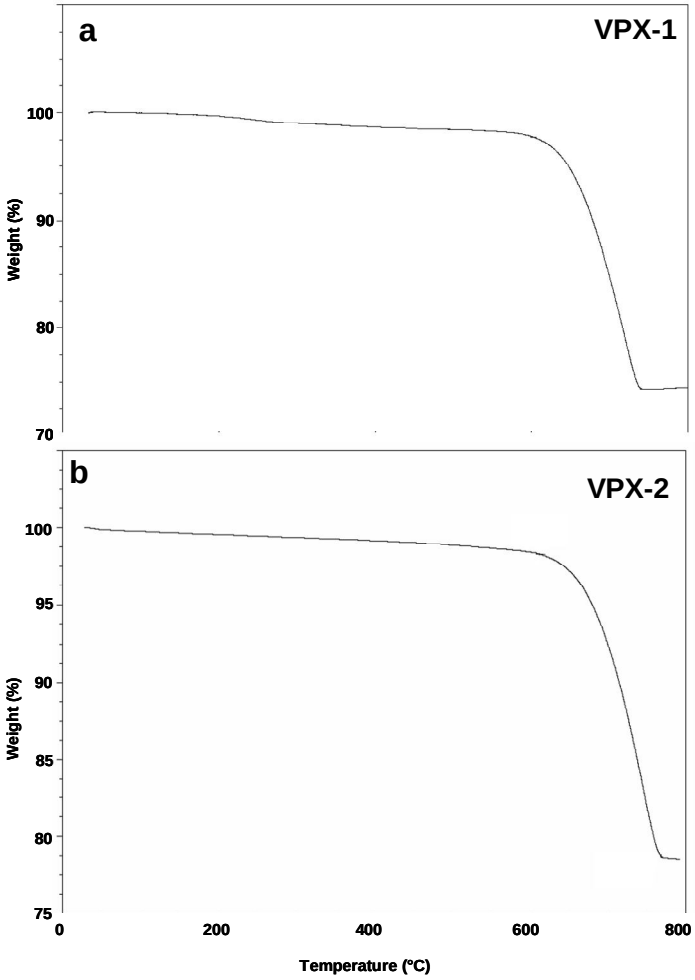
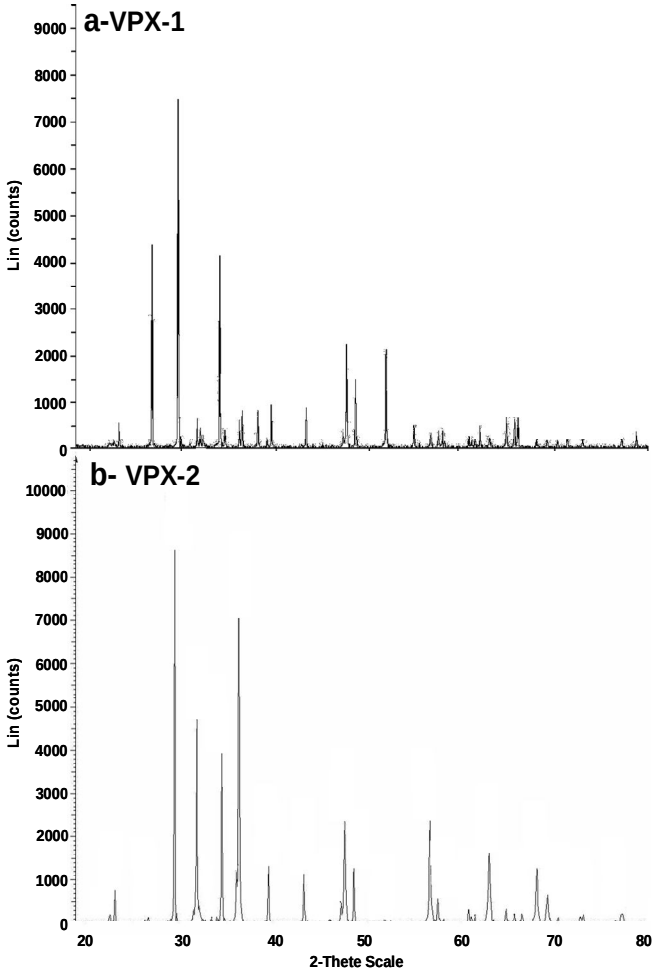


Fig. 3. Powder XRD analysis of Vanga parpam samples of VPX 1(a) and VPX 2(b)



weight loss of 2.3% just above 200° C. A major weight loss about 24% was observed at 601°C which could be ascribed to decomposition of carbonate. Hence TGA analysis confirmed the absence of moisture, presence of low percentage of about 24% of carbonate (in the form of Calcium carbonate) and the rest 76% mainly due to other metallic oxides. In the sample VPX2 there was a negligible loss of weight below 100 ˚C which was more clearly shown by the DSC and this observation was supported by FTIR spectra.

Powder X Ray Diffraction (PXRD) was used to fingerprint a particular crystalline phase or mixture of phases. In fact it is a very important tool in the pharmaceutical industry for checking the presence of polymorphism, solubility and bioavailability in oral drugs. The intense sharp diffraction peaks in both the samples clearly confirmed the presence of high crystallinity. The PXRD patterns of VPX1 are presented in Fig.3a. In order to identify different phases that were coexisting as per the EDX results, Joint Committee on Powder Diffraction Standards (JCPDS) files were consulted. The JCPDS numbers 89102 indicated that the peaks at 2θ values of 32, 34, 36, 47.5, 56.5, 64, 64.5˚ correspond to that of ZnO phase. Hence the presence of ZnO phase was established. The peaks at 2Θ values of 26.6 , 34, 39, 51.8, 54.8, 57.9, 61.9, 64.8˚ were close to those reported for the standard tetragonal -rutile phase of tin(IV) oxide - JCPDS card 411445 (Shek & Lai,1997; Abello *et al*., 1998; Klug & Alexander, 1998; Min & Choi, 2004) . The peaks at 2Θ values 35, 32 and 52 were due to SnO. The presence of $CaCO_3$ was also evident from the characteristic peak at 2Θ values of 29˚ and 36˚. The PXRD patterns of the sample VPX2 are presented in Fig.3b. The Diffraction patterns of the sample showed peaks at 2θ values 26.6, 34, 39, 51.8, 57.9, 61.9, 64.8˚ which were close to those reported for the standard tin(IV)oxide of tetragonal - rutile phase diffraction peaks JCPDS card 411445. There were no peaks at 2θ values 25, 52 which indicates the absence of SnO phase. The presence of $CaCO_3$ phase was also evident from the intense peak at 2θ value of 29˚,

Indian Journal of Science and Technology Vol. 4 No. 12 (Dec 2011) ISSN: 0974- 6846

Fig. 4. SEM analysis of Vanga parpam samples VPX 1(a) and VPX 2(b)

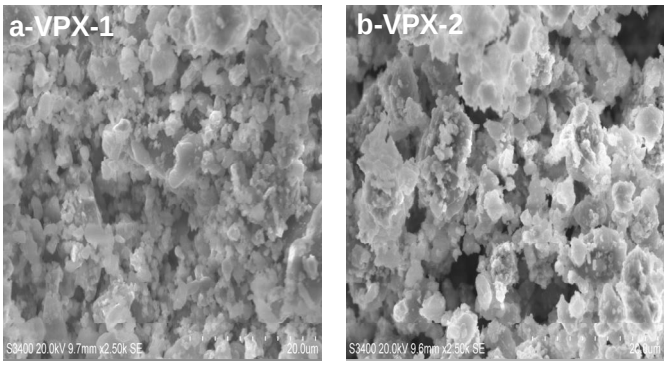


Fig.4 illustrates SEM images of both the samples which showed the presence of agglomeration of the particles which may be due to repeated calcinations during processing. There was a distinctive difference in the surface morphology due to the variation in the constitution of the samples. They also correlated well with the particle size distribution of nano and submicro sized particles. Table II depicts the EDX analysis data for the samples. EDX provided useful information on the distribution and the chemical form of the elements constituting the sample (Arvelakis & Frandsen, 2005). The elemental composition of sample VPX1 and VPX2 by EDX is presented in Table 2.

Table 2. EDX Analysis Vanga Parpam samples (VPX-1 and VPX-2)

Element	VPX1 (Atom %)	VPX2 (Atom %)
C	7.97	3.07
N	0.00	0.00
O	32.01	4.77
Na	0.70	23.00
Ca	41.98	26.01
Cu	0.95	1.04
Zn	3.27	36.07
Sn	14.13	1.24
Si	1.07	1.05

The maximum Sn content in the standard Tin oxide was 78% while that in the VPX1 drug sample was 14.33% which was equivalent to 18.37 % SnO_2 as per the stoichiometry (Fig.5). The remaining major element was stoichiometric excess oxygen due to repeated calcinations *i.e*., procedure followed in the preparation of this drug sample. The elemental composition of sample VPX2 as shown by EDX indicates that the atom percentage of Tin in the drug sample was 1.24% which was equivalent to 1.58 % SnO_2 as per the stoichiometry which was very much less compared to that in VPX1. Presence of elements like C, Ca, Si, Fe, Na, Zn as evidenced from EDX studies, which would have been introduced during trituration with the plant juices help in enhancing the biological activity of the drug (Kumar *et al.*, 2006). The bar graph depicted the major variation in the constitution of the two samples.

Tin based herbal drug samples contain Tin oxide with the rutile structure as the basic constituent. The oxidation state of Tin was found to be IV along with Calcium and Zinc whose oxidation state being II. The presence of elements like Cu, Fe, Na which are added during trituration add therapeutic efficacy to the drug *Viz*:- Zinc as a constituent of many enzymes in the human body, Calcium and Iron for a healthy metabolism, Sodium and Potassium for maintaining fluid balance in the body.

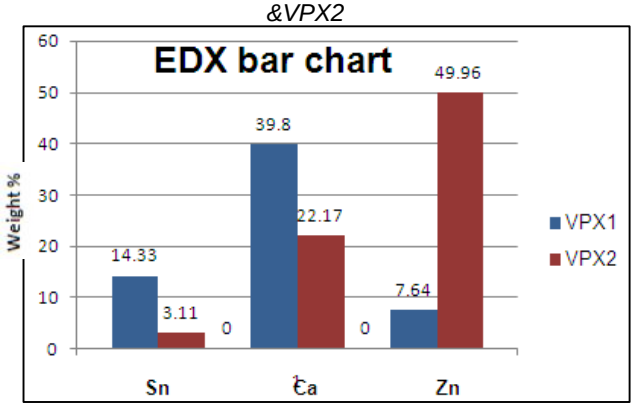
Both the commercial samples were prepared by following the protocol given by the Siddha Pharmacopeia But there was no information on the nature of the process followed. The divergent results ot their analysis suggests the following possibilities, *viz*;- incompleteness of the procedure (in this case incomplete calcinations), variation in the nature of the raw material and herbal extracts added during the processing. The variations in the constitution of the two samples also suggest that the therapeutic goal of the two brands of the same formulation may not be same as the Active Pharmaceutical Ingredient (API) in them may be different and hence the pharmacological properties would also be different. There was no toxic elemental contamination in both the samples. However the percentage concentration levels of the elements fall well within the safe limits recommended of WHO (Anonymous, 1992).

Both brands showed a good percentage of nanosized particles and there is wide distribution of size required for adsorption and absorption of the drug. The varying sizes (nano and sub micro size) of the particles of the samples suggest the possibility of adsorption and absorption of the particles for maximum bioavailability of the drug under therapeutic conditions (Kapoor, 2010).

Conclusion

By using analytical techniques it was made possible to compare the bulk and surface property of the two commercial brands of the tin based herbal drug *Vanga parpam* which is widely used for curing Urino genital infection. Even though the two drug samples are marketed under the name *Vanga Parpam* (tin based drug), the percentage of tin was found to be lesser than that of Calcium or Zinc present in both the samples and this indicated that the two drug samples differed in their

Fig.5. EDX analysis of vanga parpam samples VPX1 &VPX2



Indian Journal of Science and Technology Vol. 4 No. 12 (Dec 2011) ISSN: 0974- 6846

active pharmaceutical ingredient. The results of the study strongly advocate the need for strict adherence to the formulary principles of Traditional medicine so as to avoid quality control failures during mass manufacturing activities. The quality assurance of such medicines can be achieved only through good manufacturing practice, regulatory control, research and physic-chemical fingerprinting with reference to authentic drug formulations.

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