Research Article

Study of Polymorphic Configuration of Mercury Sulphide in *Rasasindoora*, an Ayurvedic drug

Shriram S. Savrikar, Unmeshi Sabnis, Mukund Sabnis

Jeevanrekha Analytical Services, Chhatrapati Sambhajinagar, Maharashtra, India 431001

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Abstract

Allotropes and polymorphic forms of chemical ingredients significantly affect the absorption, solubility, dissolution and bioavailability of the drugs determining their efficacy. Ayurvedic drugs are no exception to this phenomenon. The present paper deals with the polymorphic forms of Mercury Sulphide (HgS) found in *Rasasindoora*, an Ayurvedic drug abundantly used by Ayurvedic practitioners for its multifaceted therapeutic utility. Chemically *Rasasindoora* is a sulphide of Mercury (HgS). Ten samples of *Rasasindoora* were procured and analysed in this study for detection of polymorphs of Mercury sulphide (HgS) using X Ray diffraction (XRD) analysis. The study concludes that polymorphic composition of *Rasasindoora* varies from sample to sample. Polymorphs of Mercury sulphide Cinnabar (α-HgS) and Hyper-cinnabar (γ HgS) having hexagonal crystals and Metacinnabar (β-HgS) with cubic crystals were detected in *Rasasindoora*. Apart from this variation, wide variation in the crystalline and amorphous content in the samples of *Rasasindoora* was also observed. These variations appear principally due to the absence of standard manufacturing procedures of *Rasasindoora*. Absence of uniformity in multiple batches of Ayurvedic drugs was observed in past studies as well. The present study brings forth the subject as a major issue which needs to be addressed for quality control of Ayurvedic drugs.

Keywords: *Rasasindoora*, Polymorphs, Cinnabar, Metacinnabar, Hypercinnabar, X Ray Diffraction

Introduction

Allotropes and polymorphs are the physical forms of a solid chemical substance. The term Allotropy applies only to chemical elements, whereas, Polymorphism is the ability of a chemical compound (e.g., a drug substance) to exist in two or more different crystal structures. The term 'Polymorphism' originates from the Greek word, 'Polus' means many and 'Morph' refers to shape. Polymorphism means an ability to exist in many shapes. In terms of chemistry, it is the ability of a substance to exist as two or more crystalline phases that have different arrangements or conformations of the molecules in the crystal lattice (Byrn, 1982; Desiraju, 1987; Haleblian and Crone, 1969; Haleblian, 1975). Polymorphism can potentially be found in any crystalline material including polymers, minerals, metals and is related to allotropy which refers to elemental solids. Polymorphism is relevant to the fields of pharmaceuticals, agrochemicals, pigments and explosives. The complete morphology of a material is described by polymorphism and other variables such as crystal habit, amorphous or crystallographic defects. Polymorphism is an ability of a chemical element or a compound to exist as two or more crystalline phases. These phases have different molecular arrangements in the solid state but are identical in chemical composition. In some cases, the difference in molecular arrangement may not be restricted to packing and orientation of molecules, whereas, sometimes the molecular confirmation may differ although the packing is similar. In such cases, if two crystals just differ in terms of the adopted molecular confirmations, they are said to be polymorphic (Pevelen, and Tranter, 2016; Koppenaal, 2017). Allotropes and polymorphic forms of elements and compounds are known to significantly affect the solubility, absorption, dissolution and bioavailability of drugs (Raza et al, 2014). Ayurvedic drugs are not an exception to this phenomenon. Rasaushadhi a class of Ayurvedic drugs is principally prepared from Mercury and Sulphur. Metals gold, silver,

Address for Corresponding Author:
Shriram S. Savrikar,
Jeevanrekha Analytical Services, Chhatrapati Sambhajinagar,
Maharashtra, India 431001
E-mail: sssavrikar@gmail.com

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copper, iron, lead, tin and zinc, and minerals like cinnabar, mica, red ochre and many other; are also used abundantly in Ayurvedic drugs. All these inorganic materials are collected in their natural form and then processed vigorously to produce therapeutically safe and effective drug formulations. The ingredients of Rasaushadhi, Bhasma and other Ayurvedic drug formulations produced from inorganic materials can be an element or a compound. These elements and compounds undergo multiple structural changes during the pharmaceutical processing. Pharmaceutical processing techniques practiced by Ayurvedic individual and corporate manufacturers are not much standardized. Mechanization and automation although appear currently used by Ayurvedic pharma industry in large scale production, manual processing also prevails and plays a significant role in many steps during processing. As a result, product uniformity is profoundly marked by its absence in marketed Ayurvedic drugs. This is more so in case of mineral, metal and herbo-mineral/metal Ayurvedic drug formulations. Physico-chemical nature, form and composition of these drug formulations are observed varied widely from batch to batch of the same manufacturer and product to product bearing the same name of drug produced from different manufacturers. Sometimes although chemical composition is same, allotropic and polymorphic composition of their ingredients appears different. These drug formulations are observed to contain one or more allotropic or polymorphic forms of the individual source chemical substance. Being known to affect the pharmaceutical characteristics and hence the therapeutic efficacy of a drug formulation, there is a dire need to study the allotropic and polymorphic forms of elements and compounds in Ayurvedic drug formulations.

Sulphur (S) as an element and Mercury (Hg) principally in the form of Mercury sulphide (HgS), are abundantly used in Ayurvedic drug formulations named Rasaushadhi. Naturally occurring or synthetically prepared red cinnabar and Kajjali, the Metacinnabar produced by mechanical grinding of Mercury and Sulphur together; are used in preparation of Rasaushadhi class of Ayurvedic drugs. Mercury sulphide exists in four polymorphic modifications: α-HgS with a trigonal structure, β-HgS with a cubic structure, ϒ-HgS with a hexagonal structure, and δ-HgS, which exists at a pressure of 13 GPa and has a cubic structure (Stadnik Vitalii et al., 2023). Red cinnabar (α-HgS) a stable from and the less common black metacinnabar (β-HgS) are primary crystalline forms of Mercury sulphide (HgS) found under normal conditions. Two more forms, Hyper-cinnabar- ϒ-HgS (hexagonal) and high-pressure form δ-HgS (cubic) have also been observed.

Sulphur and Mercury sulphide are pretreated with multiple organic materials like plant juices, milk, ghee and inorganic material like slaked lime during pharmaceutical processing to produce Rasaushadhi. These processing involve vigorous processes like wet grinding, heating, melting, quenching and physical washing. Different allotropes and polymorphs of Sulphur and Mercury sulphide are likely to be formed during their pharmaceutical processing. Rasasindoora is a most popular mercurial formulation widely used by Ayurvedic practitioners in the treatment of respiratory disorders, skin diseases and wide range of other chronic diseases (Sadanand Sharma, 2004).

Rasasindoora belongs to a class of Mercurial Ayurvedic drug formulations known as Kupipakva Rasa, being prepared in a Kupi, a glass bottle. These Mercurial formulations are also referred as Sindoora kalpa. Preparation of Sindoora kalpa involves intensive heating of the source materials in a specially designed long neck narrow mouthed closed glass bottle for prolonged hours extending from 36 to 48 hours.

The procedure produces a product named Rasasindoora, chemically a red sulphide of mercury (α-HgS) as reported by earlier workers (Biswas and Bellare, 2022). However, in addition to sulphide of mercury (α-HgS), other polymorphs Metacinnabar (β-HgS) and Hypercinnabar (ϒ-HgS) are also likely to be present in Rasasindoora. Moreover, although not expected, in addition to Mercury sulphide (HgS), Rasasindoora may contain varying amounts of free Sulphur (S) as well (Sawant and Savrikar, 2022). Stoichiometrically the molar ratio of Mercury (Hg) and Sulphur (S) in Mercury sulphide is 1:1. Thus a pure, stoichiometric sample of HgS contains approximately 86.2% Mercury and 13.8% Sulphur in terms of mass percentage.

Variations in polymorphic composition of Mercury sulphide (HgS) and presence or absence of free mass of Sulphur (S) in *Rasasindoora* may result due to absence of appropriate standard manufacturing practices. Such variations in polymorphic and allotropic forms of compounds and elements are known to affect the absorption, bioavailability and hence the therapeutic effect of the drug in reference. Considering the significance of the subject, the present study is undertaken. The present study is aimed at detection of polymorphic composition of Mercury sulphide in *Rasasindoora*. In addition, free mass of Sulphur if any, was also calculated on the basis of stoichiometric proportion of Mercury and Sulphur in HgS with the help of total percentage of Mercury and Sulphur using XRF analysis.

Ten samples of *Rasasindoora* prepared by different research scholars using the standard method of preparation described in the Ayurvedic classics, were subjected to XRD

Analysis in this study, specifically for detection of types of polymorphs of Mercury sulphide (HgS) present in them. X-Ray diffraction is usually used to detect the chemical compounds present in a sample. The technique gives information of the chemical composition, polymorphic form of the detected compound or element, allotropic form of the free element, and the shape of the crystals of the detected free element or compound. In addition, total percentage of Mercury and Sulphur was also detected using XRF analysis. On the basis of these values the percentage of free mass of Sulphur in the samples was calculated using stoichiometric calculations. However, the present work is principally related to study of polyforms of Mercury sulphide (HgS) in *Rasasindoora*, the drug in this reference using XRD analysis in this study.

Materials and Methods

Ten samples of *Rasasindoora* were procured and analysed in this study using XRD analysis. These samples were prepared by different research scholars using standard method used to prepare Ayurvedic mercurial drugs belonging to the class *Kupipakva Rasayana*, as described in Ayurvedic classics (Sharma, 2004). Some minor variations in plants used to process Mercury and Sulphur to produce the intermediates are observed. However, the proportion of the only ingredients Mercury and Sulphur (1:1) and the principal process of digestion of *Kajjali*, the basic intermediate to produce the final product *Rasasindoora* in all the samples, doesn't differ. Considering this uniformity, the standard classical method of preparation of *Kupipkava Rasayana* is described below.

Classical method of preparation of *Rasasindoora* (Sharma, 2004)

Mercury and Sulphur pre-processed using prescribed method, are mixed together in equal measures, in required amounts and then subjected to grinding in a stone mortar to produce a product named *Kajjali*. The *Kajjali* so produced is then filled in a specially designed narrow mouth long neck glass bottle wrapped with seven layers of mud smeared muslin cloth. The seven layers of the mud smeared muslin cloth are wrapped around the glass bottle one after another leaving the neck unwrapped, allowing each layer to dry completely. The *Kajjali* filled glass bottle is then buried neck deep in a sand bath. Thus, the readied sand bath is subjected to intensive heating by putting it on a charcoal burning traditional stove. The heating temperature is increased gradually. The temperature changes are monitored by using pyrometer. As the heating intensifies and the temperature starts rising the material in the bottle starts burning, producing blue coloured fumes from the mouth of the bottle. The process is also accompanied by accumulation of Sulphur at the neck of the bottle, which is cleared repeatedly by inserting an iron rod till the fumes gradually stop emerging from the bottle and the material at the bottom of the bottle appears red hot. The mouth of the bottle is then closed with a cork and sealed appropriately as soon as the emergence of fumes stops. Heating of the bottle is then continued further for two more hours facilitating collection of the product in the neck of the bottle. Thereafter the heating is stopped by removing the burning charcoal and allowing the bottle placed sand bath to cool of its own. The cooled bottle is then taken out of the sand bath. It is broken carefully in the middle in half to separate the product collected part of the bottle from its bottom. The product collected in the neck part of the bottle is then taken out and stored for further use.

X Ray Diffraction (XRD) analysis

X-ray powder diffraction (XRD) analysis is primarily used for phase identification of a crystalline or amorphous material. Identification of the crystallographic structure and chemical composition of the sample can be done by analysis of the X-ray diffractogram of the sample. Terra-II portable X-ray Diffraction analyser was used for XRD analysis of the samples in the present study. The X Ray diffraction analyser used in this study is equipped with sample loading cells to be fitted in a carrier. The carrier fitted with the sample loaded cells is inserted in a chamber designed for it. The sample powder to be loaded in the sample cells needs to have particles about 50 micro-meters in size. Although 2 g powder is required for the analysis, the test can be performed with as little as 20 mg powder.

The test procedure is initiated with insertion of the sample carrier fitted with pre-loaded sample cells in the designed chamber of the analyser. The analyser is then connected to the computer equipped with SwiftMin software designed for analysis of diffractogram. With the starting of the computer and opening the software, a dialogue box appears on the screen. The information of the sample as required needs to be filled in the dialogue box in related fields. Appropriate mode and necessary exposures are then selected and the analysis is started. A graph line starts appearing on the screen as the test progresses. A diffractogram is obtained at the completion of the analysis. The diffractogram so obtained is then downloaded. The downloaded diffractogram is then analysed further by X Powder software using PDF2 database. Peaks in the diffractogram related to specific chemical compounds, are then identified at the end of analysis with the help of the database.

The end result gives information of percent proportion of the crystalline and amorphous content of the sample. Further information about polymorphic and allotropic forms with chemical composition and crystal shape of the

detected substances is also obtained. The same is noted and recorded for further analysis and study.

XRF analysis

Vanta handheld X Ray Fluorescence (XRF) Analyzer was used for detection of Mercury and Sulphur in the samples of *Rasasindoora* in this study. XRF analyser used in this study is a dispersive X-ray fluorescence spectrophotometer used to identify and analyse the elements from Magnesium to Uranium (Mg to U) present in a test sample. The powdered sample under test is filled in a sleeved sample cup. It is spread evenly to form a flat surface on the top side of the cup. The powder filled open end of the cup is then closed by attaching a thin mylar film. The X-ray emitting opening of the Vanta XRF analyser is then positioned directly over the flattened surface of the film covered sample filled cup. The test is initiated after setting the time of exposure and analysis is started. The results of analysis are displayed on the screen immediately after the completion of the test.

Results

Ten samples of *Rasasindoora* were analysed in this study. Cinnabar (α-HgS) was detected in eight samples. Whereas, Metacinnabar (β-HgS) and Hyper-cinnabar (HgS) were found respectively in two and three samples (Table 1). Percent mass of free Sulphur in the samples was calculated on the basis of total percent content of Mercury and Sulphur found in XRF analysis using stoichiometric proportion of Hg and Sulphur in Mercury sulphide (HgS) (Table 2).

Crystalline and amorphous content of the samples was detected during XRD analysis. The average crystalline and amorphous content of these samples was 72.1%+/-7.68 and 27.9%+/-7.68 respectively (Table 3).

Discussion

Three types of polymorphs of Mercury sulphide Cinnabar (α-HgS), Metacinnabar (β-HgS) and Hyper-cinnabar (ϒ-HgS) are found to exist in nature. However, among them α-HgS (cinnabar) red and β-HgS (metacinnabar) black in colour are the most commonly known. α-HgS (Cinnabar) has a trigonal or hexagonal crystal structure. Whereas β-HgS (Metacinnabar) has a cubic crystal structure (Kassem et al., 2016).

Rasasindoora is an Ayurvedic mercurial medicinal formulation. An intermediate product named '*Kajjali*' produced by grinding Mercury and Sulphur together, usually in equal proportions, is used as a base material for preparing *Rasasindoora*. Prior to grinding Mercury and Sulphur, to produce *Kajajli*, both are pre-processed as per methods described in Ayurvedic classical texts. Kajjali, so produced is black in colour. It is observed to contain Metacinnabar (β-HgS), a black sulphide of mercury. Chemically one atom of mercury (Hg - atomic mass 200.59 u) is bonded with one atom of Sulphur (S- atomic mass 32.65 u) to produce 232.65 u of mass of HgS. Thus, Mercury (Hg) contributes 86.2% and Sulphur (S) 13.8% of

Table 1. Polymorphic and Allotropic forms of ingredients found in *Rasasindoora*

S. No.	Sample code	Mercury Sulphide (HgS)	
		Polymorph	Crystal shape
1	RKRS-292	Cinnabar (α HgS)	Hexagonal
		Metacinnabar (β HgS)	Cubic
2	RKRS-293	Cinnabar (α HgS)	Hexagonal
3	RKRS-304	Hypercinnabar (ϒ Hg S)	Hexagonal
4	RKRS-314	Cinnabar (α HgS)	Hexagonal
5	SHRS-429	Cinnabar (α HgS)	Hexagonal
6	YRRS-505	Hypercinnabar (ϒ Hg S)	Hexagonal
7	AHRS 533	Cinnabar (α HgS)	Hexagonal
8	AHRS-534	Cinnabar (α HgS)	Hexagonal
		Hypercinnabar (ϒ HgS)	Hexagonal
9	AHRS-536	Cinnabar (α HgS)	Hexagonal
		Metacinnabar (β HgS)	Cubic
10	AVRS-540	Cinnabar (α HgS)	Hexagonal
		Metacinnabar (β HgS)	Cubic

Table 2. Percentage of Mercury and Sulphur in *Rasasindoora* observed in XRF analysis

Sr No.	Sample	Total Hg and S detected in XRF		Mass of Sulphur calculated stoichiometrically[a]	
		Mercury %	Sulphur %	Sulphur % in HgS	Free Sulphur %
1	RKRS-292	74.59	21.62	11.95	9.67
2	RKRS-293	60.36	36.58	9.67	26.91
3	RKRS-304	74.82	22.04	11.99	10.05
4	RKRS-314	53.80	43.83	8.62	35.21
5	SHRS-429	63.29	29.41	10.14	19.27
6	YRRS-505	36.58	5.97	5.86	0.11
7	AHRS 533	66.17	20.11	10.60	9.51
8	AHRS-534	63.76	20.90	10.21	10.69
9	AHRS-536	64.71	20.27	10.37	9.9
10	AYRS-540	35.76	7.57	5.73	1.84

a, Stoichiometric composition of HgS – Hg 86.2% and S 13.8%

Table 3. Crystalline and Amorphous content in samples of *Rasasindoora*

S. No.	Sample	Crystalline content %	Amorphous content %
1	RKRS-292	86.9	13.1
2	RKRS-293	66.9	33.1
3	RKRS-304	76.2	23.8
4	RKRS-314	71	29
5	SHRS-429	72.4	27.6
6	YRRS-505	58	42
7	AHRS 533	81.4	18.6
8	AHRS-534	72.2	27.8
9	AHRS-536	69.8	30.2
10	AYRS-540	66.2	33.8
Average		72.1+/-7.68	27.9+/-7.68

the total mass of Mercury sulphide (HgS).

Kajjali, the base material of Rasasindoora is produced by grinding Mercury and Sulphur in equal measures as described earlier. As a result, Kajjali contains free Sulphur (S) in addition to Mercury sulphide (HgS). Mercury sulphide found in Kajjali black in colour is Metacinnabar (β-HgS). "Biswas and Bellare (2022) have found presence of β-cinnabar (52.32 wt %), orthorhombic sulphur (44.32 wt.%) and α-cinnabar (3.32 wt. %) in Kajjali by XRD analysis". Whereas, on the basis of matching of the XRD profile of Rasasindoora exactly with α-HgS in this study, it was inferred that Rasasindoora has a single crystalline α-HgS phase. However, out of the ten samples of Rasasindoora

Table 4. Temperature wise changes in *Kajjali* during preparation of *Rasasindoora*[a]

Temp°C	Phase of Cinnabar
318	Burning of *Kajjali* starts
325	Kajjali to *Rasasindoora* conversion
350	Evaporation of *Kajjali*
460	Complete decomposition of *Kajjali*

a, Biswas G and Bellare J (2022)

analysed in the present study, eight were found to contain Cinnabar (α-Hg S). Among these eight, four samples contained only Cinnabar (α-Hg S). In three samples RKRS-292, AHRS-533 and AVRS-540 Cinnabar (α-Hg S) was accompanied with Metacinnabar Cinnabar (β Hg S). In one sample (AHRS-534) in addition to Cinnabar (α-Hg S), Hypercinnabar (ϒ-HgS) was also found, whereas, two samples RKRS-304 and YRRS-505 were found to contain only Hypercinnabar (ϒ-HgS) (Table 1). This appears to be a result of variation in the heating of Kajjali, a mixture of Metacinnabar (β-HgS) and free Sulphur (S), during the preparation of Rasasindoora.

Observations in the present study and earlier studies indicate that prolonged intensive heating of black sulphide of mercury changes the polymorphic composition of Mercury sulphide (HgS) by converting Metacinnabar (β-HgS) to Cinnabar (α-HgS) and Hyper-cinnabar (ϒ-cinnabar). In this context, "Biswas and Bellare (2022) have reported that during the

Table 5. Temperature wise Phase transitions of Mercury Sulphide as reported in past studies

Temp. range °C	Phase transition temp. °C	Phase change
99.85 – 361.85	343	α HgS to β HgS [a]
193.85 – 248.85	253.85	X HgS (unknown phase)[b]
309.85 – 349.85	309.85 – 349.85	Pseudo-cubic to Cubic HgS [c]
469.85 – 480.85	474.85	Hyper-cinnabar γ HgS [b]
Upon cooling	343.85	β HgS to α HgS [c]

a, Dickson, F.W. & Tunell, G. (1959); b, A. M. T. Bell (2010); c, Ohmiya (1974)

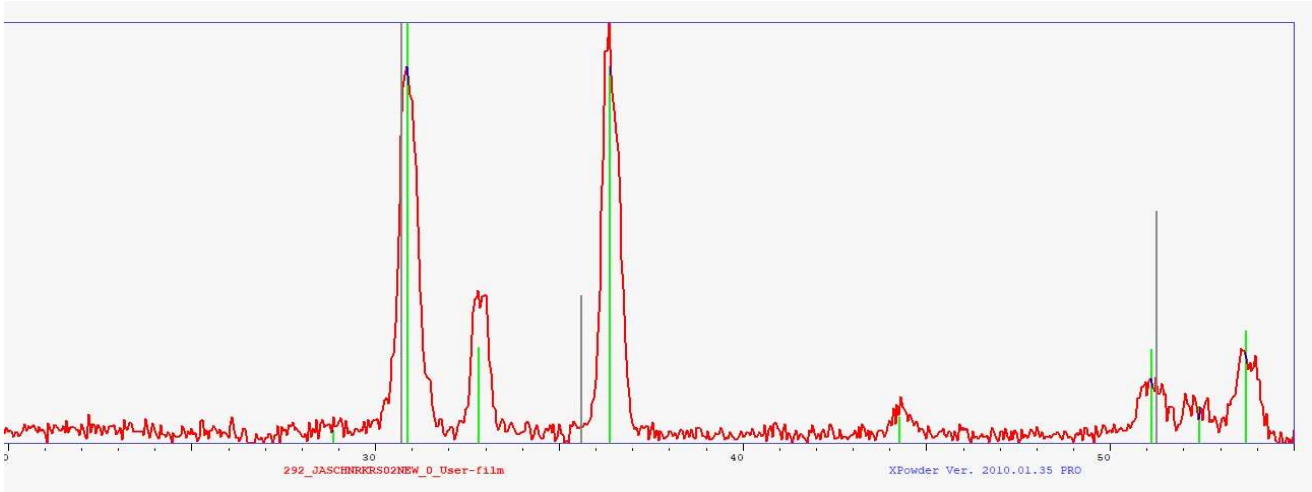

Figure 1. X Ray Diffractogram of *Rasasindoora* showing peaks of Cinnabar (green) and Metacinnabar (black) in sample RKRS-292

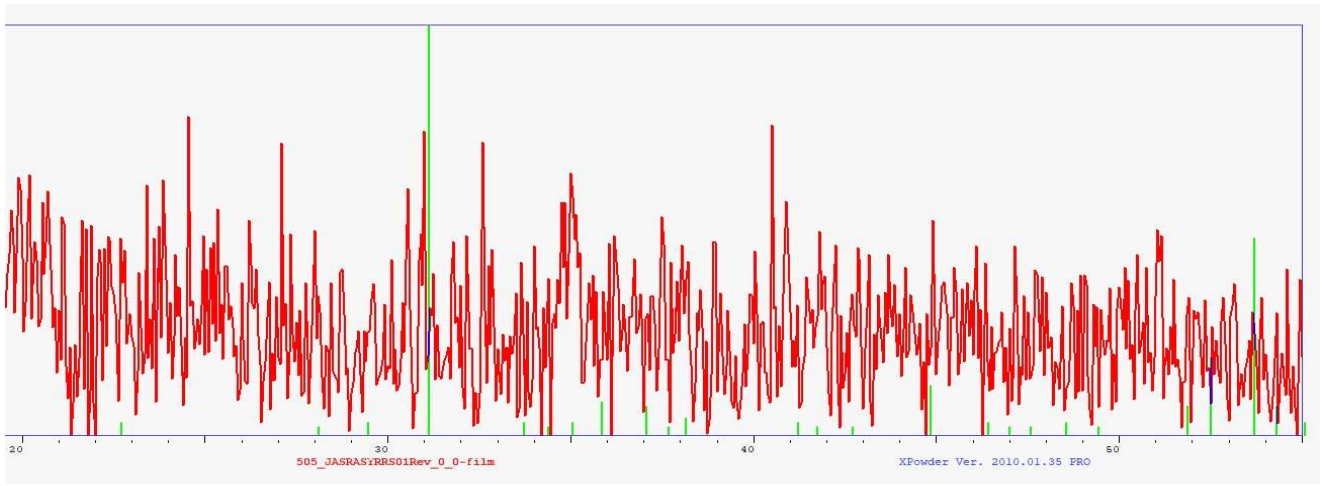

Figure 2. X Ray Diffractogram of *Rasasindoora* showing peaks of Hyper-cinnabar (green) in sample YRRS-505

preparation of Rasasindoora, Kajjali starts evaporating at (~350°C) and completely decomposes at around 460°C". On the basis of this observation, it was inferred that in the classical Ayurvedic method, Kajjali did not transform to Rasasindoora till the temperature reached at 325°C, whereas, in the sealed glass bottle the evaporation of Kajjali started only above 350°C after complete combustion of excess Sulphur. In this process, the evaporated product got sublimed at the neck of the glass bottle along with the phase transition from β-HgS to α-HgS(Biswas and Bellare, 2022).

Thermal behaviour of Cinnabar has been reported by Ballirano et al. (2013); Dickson and Tunell, (1959) in this context, have reported that transition of α-HgS to β-HgS takes place at 343°C, whereas fast conversion of metacinnabar (β-HgS) to Cinnabar (α-HgS) is observed below 343.85°C upon cooling (Dickson and Tunell, 1959). According to Ohmiya (1974) Cinnabar (α HgS) further converts to metacinnabar (β-HgS) at an impurity dependent

temperature, varying from 373 K (99.85°C) (HgS 99.97 wt.%) to 635 K (361.85°C) (HgS 99.999 wt.%). In this context, earlier researchers have reported that the temperature of the α-HgS to β-HgS polymorphic transformation is dependent on sulphur fugacity (Tauson and Abramovich, 1980; Tauson et al., 1986). In earlier studies the Cinnabar-Metacinnabar transition was observed at temperature of 607 K (333.85 °C). Besides a third form of HgS hyper-cinnabar is produced at a high temperature phase formed at 743 K (469.65°C) with an undefined hexagonal structure (Dickson and Tunell, 1959; Potter and Barnes, 1978). Hyper-cinnabar (γ HgS) was first reported by Mikolaechuk, A G & Dutchak (1965) at higher temperatures. Hyper-cinnabar (ϒ-HgS) is black in colour with purple cast, intimately associated with Metacinnabar (β-HgS). It is a high temperature phase of Mercury sulphide having hexagonal crystals, whereas, Cinnabar (α-HgS) is red in colour with hexagonal crystals.

"Bell et al. (2010) reported that the hyper-cinnabar formation temperature depends on stoichiometry but forms between 743 K (469.85°C) to 754K (480.85°C). Evidence for a partial phase transition to the high temperature hyper-cinnabar HgS structure was noted at 748 K (474.85°C)." A previously unknown phase (XHgS) was also observed produced by transformation of the initial Metacinnabar phase in a neoformed synthetic sample heated in a sealed Ti container in the temperature range 467 K (193.85°C to 522 K (248.85 °C) in this study. This phase disappeared at 527 K (253.85 °C). The proportion of cinnabar continued to increase up to 647 K (373.85°C). Both Metacinnabar (β-HgS) and Cinnabar (α-HgS) phases are retained on cooling. Interestingly in this study no phase transitions were observed for the natural Cinnabar sample (Bell et al., 2010).

In addition, "Potter and Barnes, (1978) suggested changes in stoichiometry are required in HgS transformations, further inhibiting them; the presence of trace elements in Metacinnabar (β HgS), likely to be incorporated in natural samples, can also greatly restrict transformation to Cinnabar (α-HgS)" (Boctor et al., 1987; Dini, 1995). The grain size alone has been shown to facilitate the Metacinnabar - Cinnabar transition (Tauson and Abramovich, 1985).

Kajjali, the base material used to prepare Rasasindoora is a mixture of Metacinnabar (β-HgS) and free elemental Sulphur (S). As a result, the phase transition between α, β and γ HgS during heating of Kajjali during preparation of Rasasindoora and its cooling is bound to be affected by the fugacity of Sulphur in accordance with the reports of Tauson and Abramovich, (1985) and Tauson et al. (1986) mentioned above. The temperature wise changes in Kajjali to produce Rasasindoora using classical process described in Ayurveda has been studied and reported by Biswas and Bellare (2022) mentioned in table 3.

Thermal behaviour of Cinnabar has also been studied by different research workers. Observations of these studies have been concisely presented in table 4 for the benefit of readers.

Three phases of Mercury sulphide Cinnabar (α-HgS), Metacinnabar (β-HgS) and Hyper-cinnabar (ϒ-HgS), detected in ten samples Rasasindoora analysed in the present study is the effect of temperature variations and presence of elemental impurities in the base material used in preparation of respective samples of Rasasindoora. The samples of Rasasindoora showing presence of Hyper-cinnabar (ϒ-HgS) appear to have been produced at a higher temperature as compared to other samples.

It has been recognized that crystal polymorphism is an important factor related to the physicochemical and biological properties of drug substances and formulations. Polymorphic and allotropic behaviour of active ingredients has a determining effect on the solubility, dissolution, bioavailability, processability and stability of the drug in reference. In this context, "(Raza et al., 2014; Kanaujia et al., 2015) submitted that allotropes and polymorphic forms of an elements and compounds are known to affect significantly the solubility, absorption, dissolution and bioavailability of drugs." However, among the polymorphic forms some are stable and some are metastable. In this context, it is universally accepted that the metastable form has higher solubility than the stable form.

The present study indicates that characterization of allotropic and polymorphic forms of solid drugs is necessary to ensure quality, safety and efficacy of the drugs. Methods like XRD and DSC can be effectively used to identify and manage these different forms.

Free Sulphur in Rasasindoora

It has been reported in earlier studies that although not expected, in addition to Mercury sulphide (HgS), Rasasindoora may contain free Sulphur (S) in varying amounts (Sawant and Savrikar, 2022). This happens due to absence of standard manufacturing practices. On this background the samples were analysed to detect proportionate percentage of Mercury and Sulphur using XRF analysis in the present study. As mentioned above Mercury and Sulphur are taken in equal measures of mass to prepare Rasasindoora, which is chemically a Mercury sulphide (HgS). The stoichiometric molar ratio of Mercury (Hg) and Sulphur (S) in Mercury sulphide is 1:1. Thus a pure, stoichiometric sample of HgS contains approximately 86.2% Mercury and 13.8% Sulphur in terms of mass percentage. On the basis of total percentage of Sulphur detected in the samples by XRF analysis, the percentage of free Sulphur in the samples of Rasasindoora was calculated

subtracting stoichiometric mass of Sulphur in HgS.

It is observed that in two samples YRRS-505 and AYRS-540 free Sulphur was found in negligible amounts, whereas, in remaining eight samples of Rasasindoora free sample content ranged from Min. 9.51 % to Max 35.21 %. Ideally, free Sulphur should not be present in the final product Rasasindoora. Presence of free Sulphur in Rasasindoora is an indication of incomplete process of burning Sulphur during digestion of Kajjali. Thus, only two samples YRRS-505 and AYRS-540 having negligible presence of free Sulphur appear to be products of complete process. The negligible presence of free Sulphur in these samples appears to be a result of adulteration due to mishandling during collection of the final product from the glass bottle.

Crystalline and Amorphous content of Rasasindoora

A drug must dissolve in the body fluids before it is absorbed. Therefore, a drug with higher dissolution rate will be absorbed more readily showing better bioavailability and better therapeutic activity. The amorphous form of Active Pharmaceutical Ingredient (API) has been observed to exhibit higher solubility as compared to the crystalline form (Tauson and Abramovich, 1985). It has been noticed that usually less stable or amorphous forms have higher solubility and faster dissolution as compared to the stable crystalline forms of the chemical ingredients. A wide variation in crystalline and amorphous content in the samples of Rasasindoora analysed in this study was observed. The amorphous content averaged 28.91%+/- 8.61 ranging between 13.1% in RKRS- 292 to 42% in YRRS-505 (Table 3).

Conclusion

Ten samples of Rasasindoora, a most popular classical Ayurvedic mercurial drug product prepared by different research workers, were analysed in this study for detection of polymorphic forms of Mercury sulphide along with percentage of crystalline and amorphous content in these samples using XRD analysis. Presence of free mass of Sulphur in the samples was also calculated using stoichiometric proportion of Hg and S in HgS, on the basis of total percentage of Mercury and Sulphur detected by XRF analysis. There was no uniformity in polymorphic structure of Mercury sulphide in the samples analysed in this study. Out of the ten samples of Rasasindoora analysed, eight were found to contain Cinnabar (α-HgS). Among them, four samples contained only Cinnabar (α-HgS), whereas, in three samples, Cinnabar (α-HgS) was accompanied by Metacinnabar (β-HgS). In one sample in addition to Cinnabar (α-HgS), Hypercinnabar (ϒ-HgS) was also found. Remaining two samples were found to contain only Hypercinnabar (ϒ-HgS) (Table 1). Free Sulphur was detected in significant amounts in eight samples indicating incomplete processing of the product. The proportion of crystalline and amorphous content also found varying widely. All these observations indicate that a wide variation exists in the polymorphic structure of Mercury sulphide in Rasasindoora used by the academicians, researchers and practitioners of Ayurveda. The crystalline and amorphous content also varies widely in this product. This is a result of batch-to-batch variations in quality of raw materials and temperature variations during the preparation of Rasasindoora. Such variation is bound to affect the pharmacokinetics of the drug affecting its therapeutic efficacy. On this background this study underlines the need of standardization of manufacturing procedures of Ayurvedic medicines.

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