ORIGINAL ARTICLE

Standard manufacturing procedure of *Malla Sindura*

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ABSTRACT

Background: *Malla Sindura* (MS) is one of the *Kupipakwa Rasayanas* prepared by a unique pharmaceutical process in *Valuka Yantra*, a specialized graduated heating system. In recent time, an electric muffle furnace is specialized and designed for *Kupipakwa Rasayan*. It is one such medicament indicated mainly in diseases such as *Shwasa*, *Kasa* (respiratory disorders), and is thought to be an effective drug in combating *Vedana* and *Vataroga hara* property. **Aim:** The aim of this study is to establish the standard manufacturing process for MS. **Objectives:** (1) To achieve good quality product, (2) to establish the quality control parameter. **Design:** Pharmaceutical standardization. **Materials and Methods:** Extracted murury **(***Hingulottha Parad)* and purified sulfur **(***Shodhita Gandhaka)* are mixed to make fine lusterless black powder (*Nischand Kajjai*); it was mixed with purified arsenic trioxide (*Shudh Somal*) and titurated for 6 h. After proper mixing, sufficient quantity of *Aloe vera* juice (*Kumari Swarasa*) was added for *Bhavana* and ground into a fine powder. The powder thus formed was filled in the *Kupi* and processed in an electrical muffle furnace for 48 h at graded heating (*Mridu*, *Madhyam,* and *Tivra*). On cooling, the product was collected formed the neck of the *Kupi*. Organoleptic and physicochemical parameters of MS were analyzed and tabulated. **Conclusion:** MS is a *Kanthasta Kupipakva Rasayana*. It requires *Mṛidu* (<250°C) and *Madhyamagni* (250-450°C) for 40 and 8 h of *Tivraagni* each to prepare MS with 52.10% yield with following parameters mentioned in Ayurvedic Pharmacopeia of India.

Key words: *Kupipakva Rasayana*, *Malla Sindura*, *Rasaushadhies*, standardization

INTRODUCTION

Rasashastra, a branch of Ayurveda deals, with pharmacotherapeutic aspects of metals and minerals.[1] Metals are well known and used for therapeutic purpose since from ancient time. The pharmaceutical processing techniques and their internal use remained same for a long time without much changes and progress. Since 8th to 9th century A.D. the popularity of *Rasashastra* had taken place in the field of Ayurveda. It is a branch of Ayurveda explaining pharmaceutical aspects of the conversion of metals and minerals into therapeutically potent drugs. The idea behind a combination of organic and metallic substances is to obtain quick therapeutic action using lesser dosage.[2] Many new pharmaceutical processing techniques along with equipment and drugs were evolved and developed which have revolutionized Ayurvedic pharmaceutical technology to such an extent that metals could be converted to such a form which is considered to most suitable for its internal use. The converted form of metals is less toxic, highly absorbable, and therapeutically very effective. There have been questions raised about quality, standardization and often about the safety of Ayurvedic medicines in recent past.[3] Formulation prepared in a glass bottle and by subjecting into a gradually raised temperature in a specific heating device like furnace, is known as *Kūpīpakva Rasāyana,*[4] *Makaradhvaja*,[5] *Rasasindhūra*,[6] *Svarṇa Vaṅga*,[7] *Samīrapannaga Rasa*,[8] and *Malla Sindhura*[9] (MS) are few therapeutically potent and widely used formulations prepared by this method. As *Rasoushadhies*

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which accomplish quickly desired effects in smaller doses.[10] Standardization of *Rasaushadhis* can be defined with the number of processes, involved in the production of a drug. The standard protocols are mentioned in the literature.[11] The selection of the processes for the preparation of MS was done on the basis of the specific process mentioned in classical texts. While reviewing *Rasashastra* texts, various reference of MS preparation are found with variation in their ingredient and temperature pattern. However, each reference has its own importance of therapeutic efficacy. Considering this fact present study was planned to develop the standard manufacturing procedure of MS prepared having less ingredients and high-temperature duration.[12]

Rasoushadhis are novel molecules for combating the various diseases. Among them *Kupipakva Rasayanas* are well known to be potent because of the specific pharmaceutical process, excellent clinical result, long-lasting potency, and safety even on prolonged use. MS is prepared by the combination of *Shudh Somal* (As_2O_3), *Pārada* (mercury), and *Gandhaka* (sulfur) in the ratio 1:2:2 and processing done by *Kupipakva* method in electrical muffle furnace (EMF). MS as the name denotes itself that, it is a type of *Sindura Kalpana* which is one such *Sa-agni, Sa-gandha, Bahir-dhooma, Kanthasta, Kupipakva Rasayana*, having *Sindura* color (vermilion). It is named due to the *Malla (Somal)* as a one of the main ingredients. MS is having mainly *Vataroga hara* property and is thought to be an effective drug in combating *Vedana*.[11]

A total of two formulations are found described by the name of MS *Vati*[13] and *Khanjarika Rasa*,[13] and two types of instruments are used for its preparation, i.e., *Valuka Yantra* and *Khalwa Yantra* in classical literature. Most of the classical books using *Rasa Karpura* is one of the ingredients of MS, but here attempt have been taken to prepare MS without *Rasa Karpura* as per reference of *Rasatantrasara* and *Shidhprayogsangrha*, due to easy and convenient preparation method along with the economy. Here, *Somal*, *Parada,* and *Gandhaka* are used in 1:2:2 ratio, but in different *Rasa* classics it is described that the amount of *Rasa Karpura* is one of the major ingredients taken in the same proportion.

There is an ever increasing concern pertaining to safety aspects of metals and mineral in developed countries; hence, there is a crying need to produce "standardized formulations." Drugs from traditional medicine many a time do not qualify meet this requirement because the methods of validation, quality control, and manufacturing process are not in accordance with globally accepted methodologies. Therefore, the need of an hour is to subject metallomineral formulations to rigorous modern scientific testing and develop standards to maintain quality.

Aim and Objective

To develop the standard manufacturing process for MS prepared by using EMF.

MATERIALS AND METHODS

All the ingredient such as *Hingula*, *Gandhaka,* and *Somal* were collected from the Pharmacy, Gujarat Ayurved University, Jamnagar. *Kumari*, *Nimbu*, etc. were taken from the local garden and local market of Jamnagar respectively and processed through prescribed methods as per the classical reference. The whole process has been divided into the following unit operative procedure.

Shodhana of Raw Materials

Shodhana of *Somal*[14]

In classics, it is mentioned that *Somal* (AS_2O_3) is one of the most toxic materials classified under *Sadharana Rasa Varga*. It is also mentioned in the schedule E1 of Drug and cosmetic act 1945. The *Shodhan* of *Somal* is done as per classic, Rastarangini, 11/137. The weighted quantity of cow milk was taken in *Dola Yantra* for *Swedan*. *Somal* was wrapped in cotton cloth and make a *Pottali*. This *Pottali* was tie up in *Dola Yantra* and boiled for 3 h continuously. Milk was added in *Dola Yantra* and whenever it required [Table 1].

Shodhana of Gandhaka[15]

Weighed quantity of *Goghrita* was taken in a vessel, and *Ashuddha Gandhaka Churna* was added to it. The heat was continued till complete melting and poured in vessel containing pre-heated *Godugdha*, through cotton cloth. Then it was thoroughly washed with hot water. This procedure was repeated 3 times. A solid mass with some granular part of *Gandhaka* was taken out of the vessel and then washed with hot water. The same procedure was repeated for each time, and fresh milk and *Ghrita* was taken every time. After drying, it was powdered, weighed, and kept in a glass jar [Table 2].

Hingulottha Parada Nirmana[16]

Shodhana of *Hingula* was done by giving *Bhavana* of lemon juice 3 times.[17] After that, it was washed, dried and stored. The required amount of *Parada* was extracted from *Hingula* by *Nada Yantra* method. Fine powder of *Shudha Hingula* was wrapped in cotton cloth (equal weight of *Hingula*) and burnt under the pot. Thus, due to heat, the sulfur part of *Hingula* burns and leaves the *Parada*, which gets evaporated as vapor and is collected on the inner side of the pot. *Parada* was collected by rubbing with cloth and then washing with hot water and filtering through four folders of cloth. This *Parada* was used to prepare MS [Tables 3-5].

Preparation of *Kajjali* of MS[11]

An equal amount of *Hingullotha Parad* and *Shuddha Gandhaka* was taken in in *Khalvayantra* and tituration (*Mardana)* was done for 24 h till fine, soft, lusterless (*Nishchandra*) *Kajjali* was formed. It was mixed with ¼th

Table 1: Result showing the *Shodhana* of the *Malla*

Batch No.	*Ashuddha Malla (Somal)* (g)	Temperature range (°C)	Duration of Swedan (h)	Yield of *Shuddha Malla (Somal)* (g)	Weight loss (g)	% loss of *Malla (Somal)* after *Shodhana*
I	250	70-90	3	219	31	12.4
II	250	70-90	3	220	30	12
III	252	70-90	3	222	30	11.9
Average	250.6	70-90	3	220.3	30.3	12.1

Table 2: Result showing the *Gandhaka Shodhana*

Batch No.	*Ashuddha Gandhaka* (g)	Temperature range (°C)	Duration of melting (min)	Yield of *Shuddha Gandhaka* (g)	Weight loss (g)	% loss of *Gandhaka* after *Shodhana* for 3 times
I	1000	118-120	5.3	987	16	1.6
II	1000	119-121	4.9	983	17	1.7
III	1000	119-121	5.0	982	18	1.8
Average	1000	118-121	5.06	984	17	1.7

Table 3: Result showing the *Nimbu Swaras* extraction

Batch No.	Name	Weight of *Nimbu* (g)	Weight of *Nimbu Swaras* (ml)
I	Raw *Nimbu*	200	90
II	Raw *Nimbu*	200	110
III	Raw *Nimbu*	300	160
Average		233.3	120

Table 4: Result showing the *Shodhan* of *Hingula*

Batch code	*Ashuddha Hingula* (g)	*Nimbu Swarasa* (ml)	Duration of *Mardana* (h)	Weight of *Hingula* after *Shodhana* (g)	% Gain
HS 1	500	80	3	503	0.6
HS 2	500	80	3	507	1.4
HS 3	500	80	3	506	1.2
Average	500	80	3	505	1.06

Table 5: Result showing the *Parad* extraction

Batch code	Weight of *Hingula* (g)	Weight of cotton cloth (g)	Weight of obtained *Parad* (g)	Percentage of obtained *Parad*
HP 1	500	500	359	71.8
HP 2	500	500	368	73.6
HP 3	500	500	372	74.4
Average	500	500	367	73.26

part of *Shudha Somal,* and tituration (*Mardana*) was done for 6 h until the uniform homogeneous mixture was formed. *Aloe vera* juice (*Kumari Swarasa*) used as a *Bhavana Dravya* for levgation of *Kajjali* in an adequate amount to wet the *Kajjali* (*Rasapankavat*)[18] semisolid and *Mardana* was carried out for 3 h, till the homogeneous, soft mass was formed and then it was dried in sunlight and it was taken one-fourth of the total amount of *Kajjali* as it was found to be sufficient to wet the total material [Table 6].

Preparation of MS Apparatus

Mortar and pestles, *Kanchakupi*, *Multani Mitti*, cloth, *Loha Shalakas*-2, kerosene oil, matchbox, thread, enamel tray, glass container, cork, copper coin, torch, knife; electric muffle furnace: Outer length: 40 cm, breadth: 40 cm, height: 50 cm, inner hearth length: 15 cm, breadth: 15 cm, depth: 30 cm, *Kanchakupi*: Amber-colored beer bottle, capacity: 625 ml, total height: 28 cm, cylindrical part:

Table 6: Result showing the preparation of MS *Kajjali*

Batch No.	*Hingulottha Parad* (g)	*Shodhita Gandhak* (g)	*Kajjali* (g)	Weight of *Shudh Somal* (g)	*Kumari Swarasa* (ml)	*Kajjali* (g)	% Loss
Batch 1	400	400	780	200	330	992	1.53
Batch 2	400	400	783	200	310	992	1.14
Batch 3	520	520	1017	260	410	1266	0.86
Total	1320	1320	2580	660	1050	3250	3.53

MS: *Malla Sindura*

Height: 14 cm; circumference: 24.5 cm; diameter of the bottom: 6.5 cm, conical part: Height: 14 cm; diameter of the mouth: 2 cm, weight: Before *Kapadamitti*: 450 g; after *Kapadamitti*: 590 g.

Procedure

The preparation of MS[11] was divided into three stages namely, preoperative (*Purvakarma*), operative (*Pradhankarma*), post-operative (*Paschatkarma*) stages. MS was subjected to various organoleptic and physicochemical analysis such as texture, color, teats, odor, pH,[19] ash value,[20] loss on drying,[21] percentage of mercury,[22] and percentage of free sulfur.[23]

Purvakarma

Cotton cloth was cut into small pieces and smeared on the glass bottle with the help of *Multani Mitti*. This process was repeated 10 times after complete sun drying to each step. This 10 layered smeared *Kach Kupi* was filled prepared *Kajjali* and placed in EMF [Figure 1].

Pradhanakarma

Preparation of MS was carried out in EMF by providing *Kramagini*, i.e., controlled intermittent and gradually increasing temperature that is, 18 h of mild (140-250°C) and 22 h of moderate temperature (250-450°C) [Graph 1]. Accumulated *Somal* and *Gandhaka* at the neck of the bottle were cleared using a red hot iron rod. After observation of the confirmative tests like coin test [Figure 3] complete cessation of *Gandhaka* and *Somal* fumes, the mouth of the *Kupi* was corked and the temperature was gradually increased to around 50°C up to 630°C and was maintained for 3 h to facilitate the complete formation of the compound. After cooling, the bottle was removed and thus MS was prepared in six batches of 400 g of *Kajjali* in each.

Paschatkarma

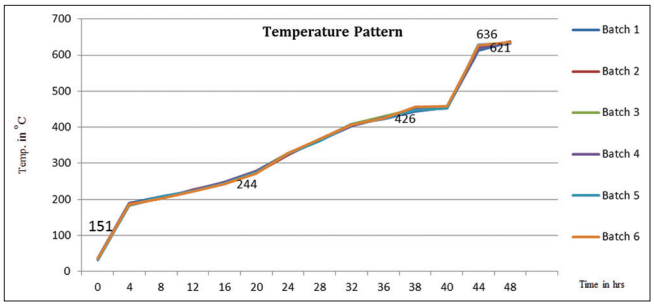
After allowing the *Kupi* to naturally cool, layers of wrapped cloth were carefully scraped, and the bottle was broken in specific manner. The product formed at the neck of *Kupi* was carefully collected and weighed. Apart from the product, some residue was also obtained in each batch [Figures 5 and 6].

Figure 1: Fumes during Jarana

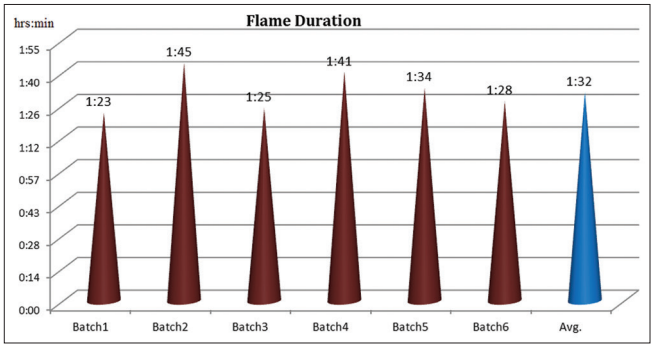
Figure 2: Flame during Jarana

OBSERVATIONS AND RESULTS

Different stages during the process such as *Gandhaka* and *Somal* fuming, melting of *Kajjali*, flaming (Figure 2), confirmative test for completion of product formation such as flame disappearance (Graph 2), *Sita Salaka* test, were observed and recorded [Table 7]. *Sita Salaka* test was taken using an iron spoke measuring 30 cm in length and 0.2 cm in diameter. This test was taken at 480°C temperature after 40 h of heating. *Sita Salaka* was slowly inserted up to 20 cm in the bottle and then slowly withdrawn. Adhesion of white particles on the lower part of *Salaka* indicated the proper formation



Graph 1: Comparison of temperature pattern of all six batches of *Malla Sindur*



Graph 2: Flame duration during preparation of *Malla Sindura*

Figure 3: Coin test

of MS. MS collected from the top of the *Kupi* from all the batches were weighed and calculated for the percentage of absolute and relative yield [Table 8]. MS was subjected to various organoleptic and physicochemical analysis result obtained is depicted in Tables 9 and 10.

DISCUSSION

MS is a *Kanthastha Kupipakva Rasayana* (a preparation in which product is obtained at the neck of glass bottle). For the preparation of *Kupipakwa rasayan*, preparation of *Kajjali*, time duration, and heating pattern are the most important factors to obtain maximum quantity of yield and to increase the efficacy of the product without any untoward effect. As per classical texts, the *Kramagi*[24] heating pattern should be

Figure 4: Breaking of *Kupi*

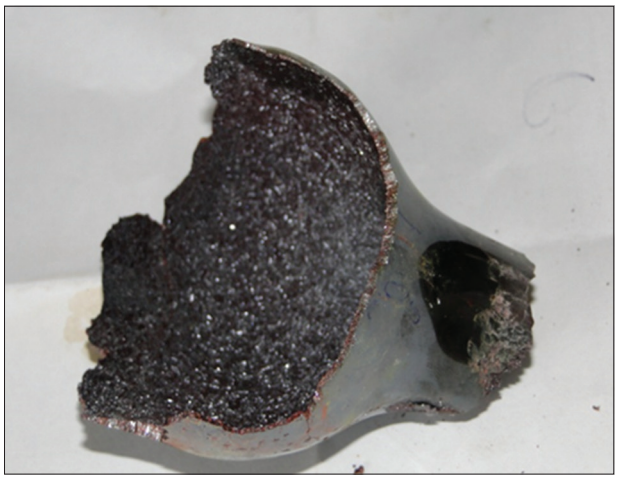


Figure 5: *Malla Sindura*

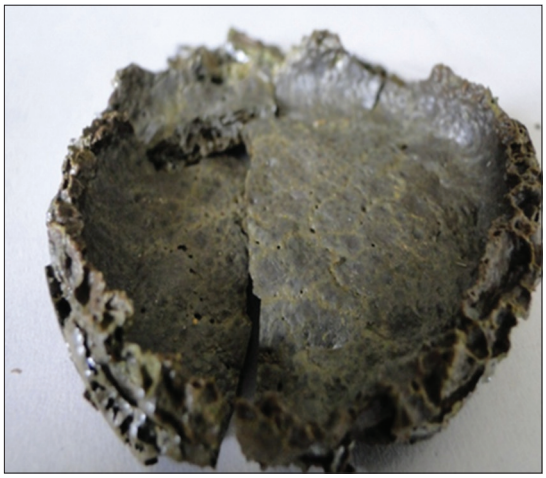


Figure 6: Residue of *Malla Sindura*

provided during processing of any *Kupipakwa Rasayana*. It means temperature pattern should be an increasing order but intermediate heating process. In can be divided into three stages, i.e., *Mridu*, *Madhya* and *Tivraagni*. Here, *Mriduagni* indicates the melting stage of *Kajjali*, *Madhyamagni* indicates the boiling stage of *Kajjali* and *Tivraagni* means

Table 7: Observations during preparation of MS

Time (h)	Set temperature (°C)	1st batch temperature recorded (°C)	2nd batch temperature recorded (°C)	3rd batch temperature recorded (°C)	4th batch temperature recorded (°C)	5th batch temperature recorded (°C)	6th batch temperature recorded (°C)	Observations
1	140	37	36	33	35	32	36	
2	160	164	166	164	163	168	162	Light white fumes
4	180	189	188	183	185	184	187	*Kajjali* started melting
6	190	197	194	198	193	197	192	Light yellow fumes
8	200	208	203	205	204	208	203	Light yellow fumes
10	210	218	215	217	214	216	212	*Gandhaka* collected at the neck color
12	220	224	227	223	225	224	221	Melting of *Kajjali* was confirmed by inserting *sheeta shalaka*
14	230	236	236	237	232	235	238	Complete melting of *Kajjali* reflecting light
16	240	243	246	244	248	245	243	Light fumes
18	250	257	259	254	256	257	252	Thick yellow fumes
20	270	277	274	278	278	275	272	*Kajjali* seen reddish from torch.
22	290	296	299	293	294	297	293	Thick fumes with reddish reflection of bottom
22	300	308	306	306	305	309	307	Thick fumes
24	320	324	323	329	326	327	328	*Kajjali* solidied
26	340	348	346	348	345	348	346	Yellow fumes of *Gandhaka*
28	360	365	367	364	364	362	367	Hot *Shalaka* used to clean *Gandhaka*
30	380	385	389	385	388	382	387	Yellowish white fumes of *Gandhaka* and *Somal*
32	400	409	407	408	403	406	407	Hot *Shalaka* done 4-6 times in this duration to clear the *Gandhaka*
36	420	422	428	429	426	424	425	Yellow fumes of *Gandhaka*
40	450	455	453	458	457	453	458	Honey coumb appearance seen, bottom appeared red
44	530	537	531	528	529	532	536	Flame started 3-4 inch in length *Sheeta Shalaka*, coin test was taken, corcking
48	630	635	637	636	632	634	636	Furnace turned off

MS: *Malla Sindura*

Table 8: Results showing the formation of MS

Batch	Weight of *Kajjali*	Weight of MS	Residue	% Yield
MS 1	400	187.2	91	46.8
MS 2	400	172	89	43
MS 3	400	231.4	80.8	57.85
MS 4	400	190.6	56.8	47.65
MS 5	400	234.1	79	58.52
MS 6	400	236.5	81.3	59.12
Average	400	208.7	79.65	52.1

MS: *Malla Sindura*

Table 9: Results of organoleptic tests

Parameter	Character of MS
Texture	Compact
Color (after trituration)	Reddish pink
Taste	Teastless
Smell	Indistict

MS: *Malla Sindura*

Table 10: Results of physiochemical tests

Parameter	Batch I	Batch II	Batch III	Average
pH	7.1	7.3	7.2	7.2
Ash value	9.24	9.29	9.25	9.26
Loss on drying	0.33	0.34	0.35	0.34
Percentage of mercury	61.12	59.97	60.8	60.63
Percentage of free sulfur	7.29	7.14	7.32	7.25

immense heating, which takes place a confirmative test of the final product. One such effort had been done by Prajapati *et al*.,[25-27] who has given the temperature range for the particulars of *Agni*, such as - *Mriduagni* 140-200°C (18 h), *Madhyamagni* 200-450°C (22 h), *Tivraagni* 450-630°C (8 h). This standardization was done in an electric muffle furnace for the preparation of MS in the ratio of 1:2:2. However, for the present study, for the preparation of the MS, 48 h of heat patterns was designed, this heating pattern was modified from as per mentioned in classics. In the most of the classical text, *Rasa Karpura* is one of the main ingredients of MS and using the same proportion of *Parada*. It was observed that there is an increase in the heating duration for the *Jarana*. Here, an attempt was made to prepare the MS without using the *Rasa Karpura* as per reference mentioned in RTS and SPS. It have been made to prepare MS without *Rasa Karpura* (to reduce ingredient, toxicity, and cost) while maintaining its therapeutic efficacy. The heating process was carried out in a *Kramagni* pattern, i.e., increasing order but intermediate heating. This *Kramagni* was slightly modified as per classics because it was not possible to provide continuous heat after *Mukhikaran* to such a long duration. Hence, duration of *Mriduagni* and *Madhyamagni* was increased, and the duration of *Tivraagni* was slightly shortened. Heat was gradually increased over a period as per the schedule, i.e., 18 h *Mandagni* (140-250°C), 22 h *Madhyamagni* (250-450°C), 8 h *Tivraagni* (450-600-630°C). Therefore, the duration of *Mriduagni* and *Madhyamagni* period was increased and decreasing the duration of *Tivraagni*.

The *Hingulottha Parada* was used because as per classical text; its properties are equal to those of *Astasamskarita Parada*.[28] The *Shudha Gandhaka* and *Hingulottha Parada* was taken iron *Khalwa Yantra,* and *Mardand* was started until the *Nischandratva,* and *Rekhapurnatva* tests of *Kajjali* were passed in 16 h, but 24 h trituration was done for the fineness. The weight of *Kajjali* was found to be decreased (3.53% on an average). After preparation of *Kajjali* one-fourth amount of *Somal* was added in *Khalwa Yantra* and *Mardanda* was done for 6 h to form homogeneous uniform *Kajjali*. The weight of *Kajjali* was found to be decreased (0.5% on an average). After *Bhavana* of *Kumari Swarasa*, the weight of *Kajjali* was found to increased (1.52% on an average) which may be due to the added solid contents of *Kumari Swarasa*. This *Kajjali* was filled in *Kanch Kuppi* and shifted to EMF. Initially, white fumes were observed followed by yellow fumes was due to sulfur. Rigorous and intermittent probing by hot iron rod should be carried out during this period to avoid choking of *Kupi* by *Gandhak*. At temperature 380-410°C profuse, thick white and yellow fumes were seen followed by choking at the neck, and there was flaming. Completion of the process can be judged by *Sita Salaka* test and coin test, whereby, its coating appears white on the coin when it put on the neck of *Kanch Kuppi*. *Kupi* should be broken [Figure 4] after cooling naturally as it plays an important role for proper crystallization of the final product.

It was observed during a trial and error study that the amount of *Gandhaka* is directly proportional to the burning period. Therefore, as per the classical notes, a specific temperature pattern was mentioned for the *Samguna Kajjali,* i.e., *Mriduagni*, *Madhyamagni,* and *Tivraagni* in an equal ratio. In this, *Gandhaka* was just in the melting stage in the *Mriduagni* while in the *Madhyamagni* stage, *Gandhaka* boils and burns and in the *Tivraagni* period, *Parada* with *Gandhaka* sublimes. Thus, the temperature required for the melting of *Gandhaka* and sublimation of the product is not dependent on the amount of *Gandhaka*. Taking note of this, the most of the chemical reaction occurred in *Mridu* and *Madhayamagni*. Hence, the period of *Mridu* and *Madhyamagni* was increased and period of *Trivagni* is shortened. The period of *Madhyamagni* was designed for a longer period as more chemical reaction, and compound formation was done in this period. *Jarana* of *Gandhaka* gets more period for the burning, which is the main aim. Here, an attempt was made to prepare the MS without *Rasa Karpura* with specific designed temperature pattern. For this, many trial and error studies were carried out to finalize the temperature pattern.

During this temperature, pattern of *Kupipaka*, *Kajjali* was completely melted after temperature increased from 450°C and flame of sulfur occurred at the neck of the *Kupi* after 41 h on an average, which was continued for 1.32 h.

Initially, the maximum temperature of *Tivraagni* is decided up to 600°C but at that temperature, the product does not sublime completely and the yield of the product is lesser. The maximum temperature of *Tivraagni* was increases up to 630°C for the proper sublimation of product which increases the yield and decreases the residue.

CONCLUSION

MS is a *Kanthasta Kupipakva Rasayana* and can be prepared by following 18 h of *Mrdu* and 22 h of *Madhyamagni* and 8 h of *Tivraagni* were used as modified from classics, with yield of average 52.1%.

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