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LITERATURE REVIEW OF *SHILASINDURA* WITH SPECIAL REFERENCE TO CLASSICAL AND CURRENT RESEARCH UPDATES

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ABSTRACT

Shilasindura is a *Kupipakva Rasayana* formulation containing arsenic (Arsenic disulphide-*Manshila*), widely utilized in the management of critical diseases such as *Shwasa* (respiratory disorders), *Kasa* (cough), and *Kushta* (skin ailments) in the contemporary era. According to Ayurvedic pharmaceutical principles, *Shilasindura* is classified as *Sagandha* (contains sulphur), *Sagni* (includes heating), and *Kanthastha Kupipakva Rasayana* (final product accumulates at the neck of the glass bottle). *Shodhit Manshila* (purified arsenic sulfide) serves as a key ingredient in this formulation. The present study constitutes a comprehensive review of *Shilasindura*, meticulously compiled from various classical *Rasa* texts and research articles published across diverse journals, sourced through academic databases. This investigation has systematically documented references to *Shilasindura* across nine classical Rasa texts and five research publications dedicated to this subject. Furthermore, the study presents detailed insights into *Shilasindura's* pharmaceutical processing, analytical evaluation, safety profile, and therapeutic efficacy based on available literature and research findings.

KEYWORDS: *Shilasindura, Kupipakva, Manshila, Ayurveda.*

INTRODUCTION

Rasashastra, a specialized branch of *Ayurvedic* science, focuses on pharmaceutical processes involving mercury, metals, and minerals, combined with various herbal substances. *Rasaushadhi*, or herbo-metallic medicinal preparations, demonstrates exceptional therapeutic efficacy even in minimal doses due to its enhanced potency. *Rasashastra*, the branch of

Ayurvedic science focused on herbo-metallic preparations, encompasses four primary formulations: *Kupipakva Rasayana* (herbo-metallic medicines developed using a glass bottle in a sand bath with a gradual temperature increase), *Khalvi Rasayana* (herbo-metallic medicines prepared using a mortar and pestle), *Pottali* (a compact form of herbo-metallic formulations fried in liquid sulphur), and *Parpati* (a thin, brittle herbo-metallic preparation).[1]

Among these formulations, *Kupipakva Rasayana* stands out as a distinctive pharmaceutical preparation due to its specialized heating process. Mercury (*Parada***)** serves as a primary ingredient, either alone or in combination with sulphur. The formulation is developed in a uniquely designed glass container known as *Kachkupi* (a glass bottle coated with seven layers of mud-smeared cloth) and processed using *Valukayantra* (a traditional sand bath) or an Electrical Muffle Furnace (a modern alternative) under a controlled, gradually increasing temperature pattern. *Shilasindura* is one of the significant formulations within the *Kupipakva Rasayana* category.

Manshila (realgar) is an arsenic compound utilized in the treatment of *Kasa* (cough), *Shwasa* (asthma), *Kandu* (itching), *Jwara* (fever), and *Vishavikara* (symptoms resulting from poisoning). *Manshila* is used after processing called as purification in *Ayurveda* pharmaceuticals. All ingredients utilized in the preparation of *Kupipakva Rasayana* must undergo the *Shodhana* (purification) process, a crucial procedure that transforms toxic minerals into non-toxic therapeutic compounds.[2]

Shilasindura, introduced in the early 20th century. It is a herbo-metallic formulation developed using the *Kupipakva Rasayana* method, (which involves gradual heating in a glass bottle placed in a sand bath). It is classified as *Sagandha* (containing sulphur), *Sagni* (requiring heating), and *Kanthastha* (where the final product accumulates at the neck of the *Kachkupi*). The preparation begins with equal proportions of *Shuddha Parada* (Purified mercury), *Shuddha Gandhak* (Purified sulphur), and *Shuddha Manshila* (Purified realgar), which are thoroughly triturated to create a homogeneous *Kajjali*, serving as the base material for *Shilasindura.*

Shilasindura exhibits rapid action due to its *Vyavayi* (Quick absorption) and *Vikasi* (facilitates the loosening and relaxation of affected bodily tissues) properties. It is utilized in the treatment of various ailments, including *Kasa* (cough), *Shwasa* (asthma), *Sannipataja Vikara*

(diseases caused by the combined imbalance of *Vata, Pitta, and Kapha*), and *Kushta* (skin disorders). Additionally, it demonstrates *Rasayana* (rejuvenating) properties, contributing to rejuvenation and overall well-being.[3]

Here an attempt is made to review the *Shilasindura* under different aspect like pharmaceutical, therapeutic and safety.

AIM

To review *Shilasindura* formulation using ancient *Ayurvedic* literature and latest published research literature.

MATERIALS AND METHODS

The references for *Shilasindura* will be examined across various *Rasashastra* texts, which focus on herbo-metallic formulations. These texts include *Rasamruta (RA), Kupipakva Rasa Nirmana Vidnyana (KRNV), Rasayoga Sagar (RYS), Rasayanasara (RS), Sachitra Rasashastra (SR), Bhartiya Rasashastra (BR), Rasendra Sambhava (RS), Rasa Tantra Saara (RTS),* and *Ayurveda Saara Sangraha (ASS)*.

Published research studies on *Shilasindura* were reviewed using various search engines and research databases, including *PubMed, Google Scholar*, and the *Ayush Research Portal*. The search was conducted using keywords such as *"Kupipakva Kalpana," "Safety Study on Shilasindura,"* and *"Pharmaceutical Study on Shilasindura."*

RESULTS

Shilasindura was mentioned in the total 9 *Rasa* classical literatures, (Table 1). Total 5 research articles were published on the *Shilasindura*, (Table 3).

Need of *Shilasindura* Preparation

Purified realgar (*Shodhit Manshila*) is beneficial in the management of fever caused by infections (*Bhuta Upadrava*), cough (*Kasa*), asthma (*Shwasa*), tuberculosis (*Kshaya*), fever-reducing treatment (*Jwarahara*), and skin disorders (*Kushta*). Additionally, it functions as a rejuvenating agent (*Rasayana*).[4] *Kajjali* (a homogenous mixture of purified mercury and purified sulphur), possesses broad-spectrum therapeutic properties. It is known for its efficacy in treating various ailments (*Sarvarognashaka*), enhancing spermatogenesis (*Vrushya*), and balancing the three *doshas—Vata, Pitta*, and *Kapha* (*Tridoshashamak*). As a result,

Shilasindura becomes a highly potent formulation, significantly improving its effectiveness in the treatment of numerous diseases.

Common Method of Preparation

To prepare *Shilasindura*, purified mercury (*Shuddha Parada*) and purified sulphur (*Shuddha Gandhak*) are taken in a mortar and pestle (*Khalva yantra*) and triturated together. This process of trituration leads to the formation of a homogenous mixture that gradually turns black, known as *Kajjali*. Over time, *Kajjali* acquires *Nishchandratva*, characterized by the absence of shiny particles of free mercury. Subsequently, purified realgar (*Shuddha Manshila*) in powdered form is added to the *Kajjali*, and the mixture undergoes further trituration until it achieves homogeneity. This blended substance is then levigated using the juice of *Aloe vera* [L.] Burm.f. (*Ghritkumari Swarasa*).

After levigation, the *Kajjali* is placed into a glass bottle (*Kachkupi*), which is coated with seven layers of mud-smeared cloth. The sealed bottle is then subjected to a specific heating pattern (*Kramagni)* in an Electric Muffle Furnace (EMF) until the formation of *Shilasindura* is achieved.

Dose and *Anupana* (Adjuvant): A human dose of *Shilasindura* is ½ to *2 Ratti* (62.5 -250 mg) per day and the *Anupana* is *Madhu* (honey).

Table 1: Details of each reference for preparation of *Shilasindura*.

Ref.	**Ingredients**	***Bhavana Dravya* (levigating drug)**	**Paka kala (heating duration)**	**Indications**	**Dose and *Anupana*** (carrier)
RS[5] (1st) (*Rasayanasara*)	*Sh.Parada* (Purified mercury)-1 part, *Sh. Gandhak* (purified sulphur)-2 part, *Sh.Manshila* (Purified realgar)-1 part	-	4 Days	*Kushtadi Vikara* (Skin disorders, etc)	-
RS[6] (2nd)	*Sh.Parada*-1part, *Sh.Gandhak*-1part, *Sh.Manshila*-1part.	-	-	*Anek rognashak.* (multiple disorders)	-
RS[7] (3rd)	*Sh.Parada*-1part, *Sh.Gandhak*-1part, *Sh.Manshila*-1part.	-	4 *Prahara* (12 hours)	*Raktastha doshnashak* (Blood disorders)	1-4 *Chawal ki matra* (wt. of rice) (0.020-

					0.080 gm.) with *Navneeta* (butter)
SR[8] (*Sachitra Rasashastra*)	*Sh.Parada*-8 *Tola*, *Sh.Gandhak*-8 *Tola*, *Sh.Manshila*-8*Tola* .	*Kumari Swarasa* (*Aloe vera* [L.] Burm.f.)	2 days	*Kasa* (cough), *Shwasa* (asthma), *Visham Jwara* (fever due to infection)	½-1 *ratti* (62.5 mg—125 mg) With *Madhu* (honey)+ *Ghrit* (cow ghee)
BR[9] (*Bhartiya Rasashastra*)	*Sh.Parada*-8 *Tola*, *Sh.Gandhak*-8 *Tola*, *Sh.Manshila*-8 *Tola*.	*Kumari Swarasa* (*Aloe vera* [L.] Burm.f.)	*Yamshoda shak*. (48 hours)	*Kapha-Vata gadahara* (disease due to *Kapha* and *Vata doshas*)	--
RYS[10] (1st)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	--	4 days	*Samastha Kushta* (all skin disorders), *SheetpurvakJwara* (fever with chills).	1-2 *ratti* (125 mg - 250 mg).
RYS[11] (2nd)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	--	4 days	*Bhavana Dravyanusar rognashak* (cures diseases as per levigating drug)	1 *ratti* (125 mg).
RYS[12] (3rd)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	--	4 *Prahara* (12 hours)	*Kasa* (cough)-*Shwasadi* (Asthma) *kapha Pradhan rognashak*	½-1 *ratti* (62.5 mg - 125 mg), with *Navneeta* (butter)
RYS[13] (4th)	*Sh.Parada*-1 part, *Sh.Manshila*-1 part	*Dhatturapushpa Swarasa* (*Datura stramonium* [L.]) *8 bhavana* (levigation)	4 *Ahoratra* (96 hours)	*Yogvahi* (carrier), *Rasayana* (rejuvenation).	1-2 *ratti* (125 mg-250 mg)
RYS[14] (5th)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1 part, *Sh.Makshik*-1 part, *Sh.Hartala*-1 part, *Sh.Vatsanabha*-1 part	*Vatashrunga* (*Ficus benghalensis* [L.])-*1 bhavana* (levigation), *Hansapadi*	12 *Prahara* (36 hours)	*Samastha Sannipata* (all disorders caused by all three *Doshas*), *samastha Jwara* (all types of fever).	½-1 *ratti* (62.5 mg-125 mg). with *Ardraka swarasa* (*Zingiber*

		(*Adiantum lunulatum* [L.])-*3 bhavana* (levigation).			*officinale* [L.]), *Panchakol kwath* (decoction of *Piper longum* [L.], *Piper retrofractum* [L.], *Plumbago zeylanica* [L.] and ~*Zingiber officinale* [L.])
KRN [15](1st) (*Kupipakva Rasa Nirmana Vidnyana*)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	-	4 days	*VishamJwara* (fever caused due to infection)	1 *ratti* (125 mg)
KRNV[16] (2nd)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	--	4 *Prahara* (12 hours)	*Raktasthadoshhara* (blood disorders)	1 *ratti* (125 mg).
KRNV[17] (3rd)	*Sh.Parada*-1 part, *Sh.Manshila*-1 Part	*Dhatturapushpa swarasa* (*Dhatura stramonium* [L.]) *8 bhavana* (levigation).	4 *Ahoratra*. (96 hours)	*Yogvahi* (carrier), *Rasayana* (rejuvenation).	1 *ratti* (125 mg).
KRNV[18] (4th)	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part, *Sh.Makshik*-1 part, *Sh.Hartala*-1 part, *Sh.Vatsanabha*-1 part	*Vatashrunga* (*Ficus benghalensis* [L.]) *-1 bhavana* (levigation), *Hansapadi* (*Adiantum lunulatum* [L.])-3 *bhavana* (levigation).	12 *Prahara* (36 hours)	*Sannipataroga* (all disorders caused by all three *Doshas*), *Samastha Jwara* (all types of fever).	1 *ratti* (125 mg). *Ardraka swarasa (Zingiber officinale* [L.]).
RTS[19] (*Rasa Tantra Saara*)	*Sh.Parada*-10 *Tola*, *Sh.Gandhak*10 *Tola*, *Sh.Manshila*5 *Tola*	*Kumari swarasa* (*Aloe vera* [L.] Burm.f.)	2 Days	*Shwasa* (asthma), *Kasa* (cough), *Visarpa* (herpes zoster), *Raktavikara* (blood disorders).	1-2 *ratti* (125mg-250 mg). with *Madhu* (honey).
ASS[20]	*Sh.Parada*-10 *Tola*,	*Kumari*	2 Days	*Sheetpurvak Jwara*	1-2 *ratti*

(*Ayurveda Saara Sangraha*)	*Sh.Gandhak*10 *Tola*, *Sh.Manshila*5 *Tola*	*swarasa* (*Aloe vera* [L.] Burm.f.)		(fever with chills), *Raktavikara* (blood disorders).	(125mg-250 mg). with *Madhu* (honey).
RA[21] (*Rasamruta)*	*Sh.Parada*-2 pala, *Sh.Gandhak*-2 Pala, *Sh.Manshila*-2 pala	*Kumari swarasa* (*Aloe vera* [L.] Burm.f.)	2 Days	*Kapha-Vata gadapaha* (diseases caused by *Kapha* and *Vata Doshas*)	-
RS[22] (*Rasendra Sambhava)*	*Sh.Parada*-1 part, *Sh.Gandhak*-1 part, *Sh.Manshila*-1part	*Vataksheer* (*Ficus benghalensis*[L.]), *Arkaksheer* (*Calotropis gigantea* [L.]), *Snuhiksheer* (*Euphorbia neriifolia* [L.]).	-	*Kasa* (cough), *Shwasa* (asthma), *Jwara* (fever), *Kandu* (itching), *Vishapaha* (disease caused due to poison).	-

Table 2: *Bhavana Dravya* (levigating drug) used in the preparation of *Shilasindura*.

Name of *Bhavana Dravya* (levigating drug)	Number of times used
Kumari Swarasa (*Aloe vera* [L.] Burm.f.)	6
Dhattura Pushpa Swarasa (*Datura stramonium* [L.])	2
Vatashrunga (*Ficus benghalensis* [L.]), *Hansapadi* (*Adiantum lunulatum* [L.])	2
Arkaksheer (*Calotropis gigantea* [L.]), *vataksheer* (*Ficus benghalensis* [L.]), *Snuhiksheer* (*Euphorbia neriifolia* [L.])	1

Table 3: Published research articles regarding *Shilasindura.*

Reference	Methodology Adopted	Result
1.Dasari Srilakshmi. Title: *Shilasindura :* An antimicrobial agent.[23]	1.Preparation of *Shilasindura.* 2.Antimicrobial activity by Gradient Plate Technique and Kirby Bauer Method.	The antimicrobial activity of *Shilasindura* has been validated against Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus mutans, and Candida albicans. This efficacy has been demonstrated through both the Gradient Plate Technique and the Kirby-Bauer Method.
2.Dasari Srilakshmi. Title: In-Vivo Toxicity Evaluation of *Shilasindura.*[24]	1.Preparation of *Shilasindura.* 2.Acute toxicity study.	The study conducted on albino rats revealed no significant physical alterations indicative of gross pathological changes. The analyzed values of blood and serum parameters remained within normal limits. A

		thorough evaluation of hepatic and renal functions showed no observable changes in these tissues upon microscopic examination. Therefore, the drug *Shilasindura* is considered safe for administration at a dose of 250 mg, equivalent to 2 *Ratti*.
3.Dr. Dasari Srilakshmi and Dr. Prasanna Lakshmi. Title: An Analogous Study Of Pharmaceutico-Analytical Aspects Of *Talsindura* And *Shilasindura*.[25]	1.Pharmaceutical Study: Preparation of *Shilasindura.* 2.Analytical Study: Physicochemical analysis of *Shilasindura.* Chemical analysis of *Shilasindura.* Solubility test of *Shilasindura.* Estimation of microbial contamination of *Shilasindura.* Assay of mercury, sulphur and arsenic of *Shilasindura.*	1.Physicochemical analysis of *Shilasindura* showed moisture content-0.48, acid insoluble ash-68.11, total ash-1.64, alcohol soluble extract-19.94, water soluble extract-9.92 and loss on drying at 105^0 C-0.48. 2.Chemical analysis of *Shilasindura* showed solubility in Con. HCl as partially soluble, in Glacial Acetic Acid as sparingly soluble and in Honey as soluble, in Distilled water as partially soluble, in Chloroform as soluble, in CCl_4 as soluble, in Isopropyle alcohol as soluble, in Petroleum ether as partially soluble, in Glycerin as partially soluble, in Benzene as soluble, in Aceton as soluble, in CH_3OH as soluble, in Methylenedichloride as soluble, in Ether as partially soluble. 3.Microbial contamination study showed Total Bacterial Count (CFU/gm) as 3900, Total Fungal Count (CFU/gm) as 40. E.Coli, Salmonella, P. aeruginosa and S. aureus were absent. 4.Assay of mercury, arsenic, combined sulphur and free sulphur of *Shilasindura* showed 59.11%, 13.86%, com, 19.75% and 4.70%.
4.Challa Srinivas Reddy. Title:Toxicokinetics and Tissue distribution studies of mercury in *Ayurvedic* preparation-*Shila sindura.*[26]	1. Toxicokinetic Studies. Male Wister albino rats were grouped into 3 groups of 6 animals each. Doses were set as 50 mg/kg (low dose), 300 mg/kg (medium dose) and 1000 mg/kg (High dose).	1. Above investigations conclude that low single dose or even low repeated dose of mercury could be safe and may not lead to accumulation in the tissues especially in kidney. 2. The administration of medium doses requires careful and stringent monitoring to ensure safety. 3. High single doses and high repeated doses have demonstrated highly deleterious effects, with further administration potentially leading to severe nephrotoxicity.

5.Dr. Sanjay Kumar Title: Pharmaceutical Standardization of *Shilasindura*:An *Ayurvedic* Herbo-Mineral Formulation.[27]	1 .Preparation of 3 batches of *Shilasindura.* 2.Organoleptic Tests of *Shila-sindura.* 3.Physico-chemical Tests of *Shilasindura* like – XRD, ICP-MS, Acid insoluble etc.	Weight of the *Shilasindura* were 34.3%, 53.09% and 49.40% in 1st, 2nd and 3rd batch respectively. The organoleptic evaluation revealed a brick-red color, a tasteless profile, an absence of odor, and a compact texture. Maximum temperature given was around 690-700^{O}C. 25 hours duration was preferred for proper formation of compound. The X-ray diffraction (XRD) analysis revealed sharp peaks indicating that the major compound present is Mercuric Sulphide (HgS), exhibiting 100% intensity at a 2-theta value of 26.6814, with an amorphous shape and structure. The elemental composition of *Shilasindura* was determined to be primarily HgS, along with trace amounts of As_2S_2. The study identified 21.80% Mercury, 6.23% Sulphur, and 14.34% Arsenic. Additionally, the particle size of *Shilasindura* was found to range between 652.9 nm and 941.2 nm. Acid insoluble Ash value was below limit of Quantification.

Table 4: Therapeutic efficacy of *Kajjali* (homogenous mixture of purified mercury and purified sulphur) and *Manshila* (realgar).

Reference	**Therapeutic efficacy of *Kajjali* (homogenous mixture of purified mercury and purified sulphur)**	**Therapeutic efficacy of *Shuddha Manshila* (purified realgar)**
Rasaratna Samucchaya (RRS)	---	*Sarva Rasayanaagra* (supreme in all rejuvenating drugs), *Tikta* (bitter), *Katu* (pungent), *Ushna* (hot), *Kapha-Vata nashak* (useful in diseases caused due to *Kapha* and *Vata Doshas*), *Bhootabadhahara* (useful in diseases caused by bacteria), *Vishanashak* (useful in diseases caused by poison), *Agnimandyahara* (cures weakened digestive fire), *Kanduhara* (cure itching) , *Kasahara* (useful in cough),*Kshayanashak* (useful in tuberculosis).[28]

Rasatarangini (RT)	*Sarva Aamayahara* (useful in all diseases), *Vrushya* (increase spermatogenesis), *Tridoshahara* (used in diseases caused by all three *Doshas* together).[29]	*Katu* (pungent), *Tikta* (bitter), *Snigdha* (soft), *Ushna* (hot), *Lekhana* (scraping), *Guru* (heavy to digest), *Kasa-Shwasahara* (useful in cough and asthma), *Bhootaupdrava nashini* (useful in diseases caused by bacteria), *Agnimandyahara* (cures weakened digestive fire), *Kshayahara* (useful in tuberculosis), *Aanahahara* (useful in abdominal distension due obstruction of passage of urine or stool), *Kanduhara* (useful in itching), *Rasayani* (shows rejuvenating property), *Jwarahara* (useful in fever), *Varnya* (improves complexion), *Vishanashak* (useful in diseases caused due to poison).[30]

DISCUSSION

The references for *Shilasindura* were examined in classical *Rasa Shastra* texts, with the majority of them adhering to the same formulation guidelines outlined in *Rasayanasara* for its preparation.

Pharmaceutical Constituents

Kajjali and *Manshila* are the key ingredients used in the preparation of *Shilasindura*. Their usage together enhances the properties of *Shilasindura* as compared when used individually. The properties of both *Kajjali* and *Manshila* are illustrated in Table no. 4.

Kajjali (homogenous mixture of purified mercury and purified sulphur) is the primary ingredient of *Shilasindura*, while *Manshila* (realgar) is another crucial component that distinguishes the *Kupipakva* formulation from others. However, the proportion of *Shodhit Manshila* (purified realgar) varies across different references, ranging from half the quantity (in two formulations) to equal parts (in 16 formulations) relative to the other ingredients, as indicated in Table no. 1.

The formulation of *Shilasindura* described in *Rasatantrasara*, *Siddhaprayoga Sangraha*, and *Ayurveda Saara Sangraha* shares similarities, indicating a comparable approach to its preparation. Likewise, the *Shilasindura* mentioned in *Rasayogsagara* and *Kupipakva Rasa Nirmana Vidnyana* exhibit resemblance, suggesting a parallel methodology in their composition.

In the 1st method described in *Rasayanasara* and the 3rd method outlined in *Rasayogsagar, Suvarna Grasita Parada* (a formulation in which purified mercury is meticulously triturated with purified gold to achieve a homogeneous mixture) is utilized.

Makshik (chalcopyrite), *Hartala* (orpiment), and *Vatsanabha* (*Aconitum ferox* [L.]) are referenced in the preparation of *Shilasindura* as per the 5th method described in *Rasayogsagar* and the 4th method outlined in *Kupipakva Rasa Nirmana Vidnyana*. These substances may be beneficial in addressing *Sannipata vikaras* (which are disorders arising from the simultaneous imbalance of all three *Doshas*)

Manshila (realgar) is the primary ingredient in all the mentioned references, although its proportion varies, ranging from half a part to an equal proportion of the ingredients. The preparation method of *Shilasindura* is modified in the second procedures described in *Rasayansara* and *Rasayogsagar*. Initially, *Shadgunabalijarita Chandrodaya* (purified mercury triturated with six times the quantity of purified sulphur) is prepared using the *Kupipakva* method (a technique for preparing herbo-metallic medicines by gradual heating in a glass bottle immersed in a sand bath). This process involves purified mercury (*Shuddha Parada*) and purified sulphur (*Shuddha Gandhak*). Subsequently, an equal proportion of purified sulphur (*Shuddha Gandhak*) and purified realgar *(Shuddha Manshila*) is incorporated into the previously prepared *Chandrodaya (Sindura*) and triturated to create a homogenous *Kajjali*. From this *Kajjali, Shilachandrodaya* is prepared using the *Kupipakva* method.

In *Rasayogsagara* and *Kupipakva Rasa Nirmana Vidnyana*, there exists a method where *Gandhak* (sulphur) is not mentioned as an ingredient. Instead, only *Shuddha Parada* (purified mercury) and *Shuddha Manshila* (purified realgar) are utilized in equal proportions. The sulphur present in *Manshila* (realgar) may contribute to forming a physical bond, resulting in a uniform mixture. In *Rasayana*sara and *Rasayogsagara Shilasindura* is named as *Shilachandrodaya* Rasa.

Bhavana Dravya* (levigating drug) used in the preparation of *Shilasindura

The total number of times *Bhavana Dravyas* that were used is depicted in Table no. 2.

Bhavana is a levigation method in which a recommended drug in the form of juice or decoction is used for trituration with the aim of particle size reduction. As per *Rasayansara* and *Rasayogsagar's* 1st, 2nd and 3rd method, *Bhavana Dravya* was not mentioned for the preparation of *Shilasindura*. In *Bhartiya Rasa Shastra*, *Rasatantrasara*, *Ayurveda Saara*

Sangraha and *Rasamruta*, *Kumari Swarasa* (*Aloe vera* [L.] Burm.f.) was mentioned as a *Bhavana Dravya*. According to *Bhavprakash*, *Kumari* (*Aloe vera* [L.] Burm.f.) exhibits several therapeutic properties, including: *Bhedana* (penetrative ability), *Rasayana* (rejuvenating property), *Vrushya* (enhances spermatogenesis), *Visha nashana* (beneficial in conditions caused by toxins or poisons), *Granthi nashana* (reduction of abnormal muscular growth), *Rakta* (blood disorder) and *Twakaroga nashana* (useful in skin disorders) properties.

In the 4th method described in *Rasayogsagar* and the 3rd method outlined in *Kupipakva Rasa Nirmana Vidnyana, Dhatturapushpa Swarasa (Datura stramonium* [L.]) is mentioned as the *Bhavana Dravya* (levigating agent). This may be attributed to the fact that *Dhattura pushpa* (*Datura stramonium* [L.]) also possesses *Twakaroga nashana* (properties beneficial in managing skin disorders). It may amplify the *Kushtahara* (Skin disorder healing) property of *Shilasindura*. In the 5th method described in *Rasayogsagar* and the 4th method outlined in *Kupipakva Rasa Nirmana Vidnyana, Vatashrunga (Ficus benghalensis* [L.]) and *Hansapadi* (*Adiantum lunulatum* [L.]) are utilized as *Bhavana Dravyas* (levigating agents). The *Raktadoshnashak* (blood disorder-alleviating) property of *Shilasindura* may be enhanced.

In *Rasendra sambhava*, *Vataksheer (Ficus benghalensis* [L.]), *Arkaksheer (Calotropis gigantea* [L.]), and *Snuhiksheer (Euphorbia neriifolia* [L.]) are utilized as *Bhavana Dravya* (levigating agents), likely due to their inherent properties, including *Ushna* (hot potency), *Teekshna* (quick-acting nature), *Kaphaghna* (effectiveness against diseases caused by *Kapha Dosha*), *Kasa-Shwasahara* (usefulness in managing cough and asthma), *Jwarahara* (beneficial in fever), and *Kandughna* (relieving itching).

It has been observed that all *Kupipakva Rasayanas* (herbo-metallic medicines prepared using a glass bottle in a sand bath with a gradual rise in temperature) contain numerous essential elements along with certain major compounds, enhancing their therapeutic potency. Additionally, *Bhavana Dravyas* (levigating agents) may contribute to the presence of these trace elements.

Heating pattern and duration of heating of *Shilasindura*

Kupipakva preparation having unique heating pattern called as *Kramagni* starting with mild to moderate and raised up to high heating temperature. Total duration of heating is twenty four -hour heating pattern commonly recommended in various texts for the preparation of *Shilasindura*. *Rasayogasagar* and *Rasayansar* suggest a heating duration of 12 hours (four

Prahara), whereas *Rasayogasagar*'s first, second, and fourth methods, along with the first and third methods of *Kupipakva Rasa Nirmana Vidnyana,* advocate a heating duration of four days (96 hours).

A controlled increase in temperature is applied to the *Valukayantra* (sand bath) during the preparation of *Shilasindura.* The commonly followed temperature pattern includes *Mrudu Agni* (mild heat) at 150–250°C, *Madhyam Agni* (medium heat) at 250–600°C, and *Teevra Agni* (strong heat) at 600–750°C. Sulphur begins to melt at 112.8°C, causing free sulphur to volatilize, which may react with oxygen and convert into its oxide form. At moderate temperatures (350–600°C), the *Kajjali* (homogeneous mixture of all the constituents used to prepare *Shilasindura*) undergoes boiling, leading to the dissociation of mercury. Dissociated mercury can form bonds with arsenic and sulphur, resulting in the final product known as *Shilasindura*. At high temperatures (600–750°C), the product undergoes sublimation.

Shilasindura Color

Ancient scholars described the color of *Shilasindura* as brownish red (*Sindura Varniya*). The color varies based on the chemical composition formed during the sublimation of the final product. Advanced analytical tools, such as X-ray diffraction, can be utilized to detect and confirm the compounds formed during the preparation of *Shilasindura.*

Therapeutic Indication

Shilasindura having *Kapha Vatahara* property. According to *Rasa tantra saara* and *Rasayansar* it is recommended in *Raktavikara* like *Kushta*, *Visarpa*. *Rasayogsar* mentioned that it can be administered in various disorders as per the levigation drugs. In *Rasa tantra saara* it is mentioned that it is useful in *Kasa* (cough), *Shwasa* (asthma). It is also prescribed for *Shitpurvak Jwara* (fever with chills) and *Visham Jwara* (fever caused due to infections), as according to *Kupipakva rasa nirmana vidnyana* and *Ayurved Saara Sangraha,* respectively. As per *Kupipakva Rasa Nirmana Vidnyana, Shilasindura* it is indicated for *Samasta sannipata* (all diseases caused due to imbalance of all three *Doshas*) and *Samasta jwara* (all kinds of fever) when *Hartala* (orpiment) and *Vatsanabha* (*Aconitum ferox* L.) are a part of the ingredient in. It is a *Kupipakva rasayana,* having rejuvenation and *Yogvahi* (carrier) properties.

Analytical Evaluation

According to the referenced study on *Shilasindura*, its composition was analyzed using X-ray diffraction (XRD), revealing a predominant concentration of mercury sulfide (HgS) along with trace amounts of arsenic sulfide (As_2S_2). A minimal quantity of arsenic, originating from *Manshila*, was also detected. The particle size of *Shilasindura* was found to range between 652.9 nm and 941.2 nm, indicating its potential for efficient assimilation within the body.

Safety of *Shilasindura*

An oral dose of *Shilasindura* at 22.5 mg/kg was administered for 14 days as part of an in-vivo acute toxicity study. The total clinical dose was calculated as 125 mg × 2 (a) × conversion factor (b) 0.018 = 4.5 mg (c)/per 200 g of rats, equivalent to 4.5 × 1000/200 = 22.5 mg/kg. The study revealed no gross pathological changes, including hepatic or renal pathology. Hence, *Shilasindura* is considered safe at a dosage of 22.5 mg/kg in rats, which corresponds to a 250 mg dose in adults.[27]

During a 28-day study examining the toxico kinetics and tissue distribution of mercury (*Parada*) in *Shilasindura*, doses of 50 mg/kg (low dose, below the therapeutic range), 300 mg/kg (medium dose, equivalent to the therapeutic range), and 1000 mg/kg (high dose, exceeding the therapeutic range) were administered. It was observed that the low dose of 50 mg/kg and the medium dose of 300 mg/kg did not lead to mercury accumulation in the kidney, as these dosages fall within the range recommended by the *Acharyas*. However, the high dose of 1000 mg/kg resulted in adverse effects, potentially leading to nephrotoxicity. It is important to note that this high dosage far exceeds the amounts prescribed for human use, and thus, administering *Shilasindura* at higher doses is not advisable.[29]

Antimicrobial study

A 100 mg dose of *Shilasindura* was administered and incubated for approximately 72 hours with various test organisms, including Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus mutans, and Candida albicans. The study demonstrated that *Shilasindura* was effective against all these organisms.[26]

The antimicrobial activity of *Shilasindura* was evaluated against Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus mutans, and Candida albicans, and its effectiveness was confirmed against all these organisms. Pseudomonas aeruginosa affects the lungs, urinary tract, skin, and blood; therefore, *Shilasindura* can be used as an effective

antibiotic in conditions such as *Shwasa* (asthma), *Kushta* (skin disorders), and *Raktavikara* (blood disorders). Escherichia coli is known to cause fever, making *Shilasindura* effective in *Jwara* (fever), as mentioned by the *Acharyas*. Staphylococcus aureus impacts the skin, blood, and lungs, suggesting that *Shilasindura* may be beneficial for *Kushta* (skin disorders) and *Shwasa* (asthma), in line with ancient recommendations. Finally, Candida albicans causes systemic infections that spread via the bloodstream, indicating that *Shilasindura* may be effective in *Raktavikara* (blood disorders), including conditions such as *Kushta* (skin disorders) and *Jwara* (fever).[26]

CONCLUSION

Shilasindura is a *Kupipakva* formulation composed of *Shuddha Parada* (purified mercury), *Shuddha Gandhak* (purified sulphur), and *Shuddha Manshila* (purified realgar). Most classical texts adhere to the reference from *Rasayanasara* for its preparation. *Kumari swarasa* (*Aloe vera* [L.] Burm.f.) is commonly employed as an herbal medium for levigation. The required temperature for the formulation process varies, ranging from 12 to 96 hours. *Shilasindura* has been found to be safe in both acute and subchronic toxicity studies when administered at a therapeutically equivalent dose. It exhibits significant antimicrobial activity against Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus mutans, and Candida albicans.

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