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Rasasindura: An Integrative Review of Its Preparation Properties and Pharmacological Actions

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ABSTRACT:
A clear understanding of the conceptual foundations of Rasashastra is essential for examining the various dimensions of drug design and development. Rasasindura (RS) stands out as an important formulation, widely employed in clinical practice with different anupāna. In this study, references to the drug were gathered from major classical works and examined with the aim of outlining its developmental phases. Twenty-two Ayurvedic treatises, beginning with Rasahridayatantra of the 10th century and extending up to Rasatarangini compiled in the 20th century, were scanned for descriptions of RS. In addition, published research and institutional reports were consulted to integrate contemporary findings.
The review shows that authors of Rasashastra from the 10th–12th centuries were already proficient in methods such as Gandhaka jarana and associated processes. Across the surveyed literature, thirty-nine distinct procedures for preparing RS were documented, differing in the proportion of Parada and Gandhaka (ranging from 1:¼ up to 1:6), the type of Bhavana dravya, mode of heating, and duration of preparation. The prescribed heating time varies considerably across texts, extending from about half a day to nearly a week, depending on the amount of sulfur incorporated. Recent studies have introduced modified pharmaceutical approaches and analytical tools that help in better understanding and characterizing RS. Toxicological evaluations further indicate that the formulation is safe when administered within therapeutic limits.

KEYWORDS: Rasasindura, Kupipāka, Kajjali, Pharmaceutical standardization, Ayurvedic herbo-mineral medicine.

INTRODUCTION

Rasaśāstra, the classical branch of Ayurveda dealing with metals and minerals, has described many preparations that act quickly, require very small doses, and remain stable for long periods.(1,2) Among these are the Kupipāka Rasāyana formulations, which are produced through the process of Pārada Mūrchanā, a method believed to impart specific therapeutic qualities to mercury. Rasasindura (RS) is one

of the well-known preparations of this group. It is obtained by preparing Kajjali, a smooth, black powder formed by triturating purified mercury and sulphur with certain herbal media, and then heating this mixture in a specially designed furnace for a fixed duration. Classical literature mentions several variations of RS depending on the proportion of sulphur used, from the Chaturāmśa(3) type (¼ part sulphur) to the Ṣaḍguṇa Balijarita(4) form (six times the amount of sulphur). Texts also describe that mercury processed through the Gandhaka Jaraṇa technique becomes more potent and develops enhanced medicinal qualities(5). The degree of sulphur incorporation and the nature of heating (Agni) are considered to influence its therapeutic strength(6). Nearly forty references to RS are spread across traditional Rasaśāstra treatises. Reviewing these descriptions helps in understanding the formulation thoroughly and in selecting the most appropriate method for pharmaceutical preparation and standardization. Recent research on RS was also examined to refine and expand the conceptual understanding of the drug.

METHODS

Twenty two classics starting from Rasahridayatantra (10th AD) to Rasatarangini (20th AD) were reviewed for relevant references of Rasasindura (RS), Rasabhasma and Gandhaka Jarana etc. In addition, few recent researches on RS have also been reviewed to provide updates on the formulation.

10th Century AD

A formulation similar to RS prepared in Loha Samputa (Parada Bhasma) has been mentioned for the first time in Rasahridayatantra of 10th AD (7). Valuka Yantra is mentioned for the first time in this text.(8)

12th Century AD

Rasarnava, a text of 12th AD, mentions different types of 'Gandhaka Jarana'(9,10) and processes of Parada Marana (11). Rakta varna Parada Bhasma consisting of Parada, Gandhaka and Makshika Satva is mentioned in this later text, but, the term RS or its method of preparation are not found in this text.

Another text of the same period, Rasendra Chudamani has mentioned about Kajjali,(12) Pisti of Gandhaka and Parada(13) and Valuka Yantra(14). But, information on RS is not available.

13th Century AD

1. Thirty one procedures of Parada marana methods have been mentioned in Ananda Kanda of 13th AD. Out of these, only two procedures involve with Kachakupi and Valuka Yantra (15,16). Product with Sindura or Rakta Varna is mentioned thrice, though they are prepared with the help of Yantras, other than Valuka yantra(17–19).
2. Rasa Prakasha Sudhakara, another text of the same period mentioned three preparations with different names and similar colours and manufacturing procedure of RS viz. Udayabhaskara Rasa(20) and Rasa Bhasma.(21,22)
3. Rasayana Khanda of Rasa Ratnakara from the same period elaborates eleven methods of Parada Bhasma. In this text a type of Rakta Varna (red colour) Parada Bhasma preparation has also been mentioned(23). But as it contains Makshika Satva it is not considered as RS.
4. Rasa Ratna Samucchaya of the same period describes on Valuka Yantra and Kachakupi(24), but information on RS is missing. Eight Parada Bhasma methods of unspecified colour are described. The composition of one formulation is found to be similar to RS,(25)which has been described as RS by the commentators(26).
5. One reference of RS in the context of Parada murcchana has been mentioned by author(27).

15th Century AD

1. Rasa Chintamani explained nineteen methods of Rasa Bhasma, out of which three formulationsresembling RS(28–30). One formulation (Kamadevarasa) has been mentioned in the context of therapeutics that is similar to RS(31).
2. Rasa Sanketa Kalika mentions a few preparations resembling RS with different names like two types of Haragauri Rasa(32,33) and Kamadevarasa(34) etc.
3. Rasendra Chintamani emphasized on Gandhaka Jarana and its importance. The term Rasa Sindura has been mentioned for the first time in this text, there are two reference of Sindura Pakas (35,36).

16th Century AD

1. One reference of Rasa Sinudra has been described in Bhava Prakasha(37).
2. Three preparations of Rasa sindura have been mentioned in Rasendra Sara Sangraha(38).
3. One preparation of Rasa sindura with the 2 name of Nayanananda Sindura (39) is available in Rasa Kaumudi.
4. One reference is available in Rasa Kamadhenu (Haragouri rasa), which is the same version as available in Rasa Sanketa Kalika of 15th Century AD

17th Century AD

Four references of RS are available in Ayurveda Prakasha(40–43). Need of Tapta shalaka in clearing the blocked mouth of Kachakupi is emphasized in this text(44).

18th Century AD

Many preparations of RS(45) have been mentioned in Yoga Ratnakara, most of them are the compilations from the earlier classics.

20th Century AD

1. Rasendra purana of 1916 mentions three methods of RS with varying proportions of Sulfur (Samaguna, Dviguna and Shadguna)(46–48).
2. Rasa Yoga Sagara (1927-1930) a comprehensive compilation of Rasa yogas mention ten preparations of RS(49). Author has not contributed anything special to his credit expect compilation.
3. Kupipakva Rasa Nirmana Vignana (1950), another compilatory text, mentions five types of RS(50).
4. Bhasma Vignana (1950) mentions 54 preparations under the heading of Parada Bhasma, out of these 17 preparations resembles RS
5. Rasa Tarangini refers seven preparations of Gandhaka Jarita RS(51–57). Various proportions of mercury and sulfur (starting from 1:1/2 to 1:6 i.e. from Ardhaguna to Shadguna Gandhaka have been prescribed to attain different therapeutic attributes.

All the above references have been reviewed (Table 1) and observed that Sulfur different proportions are the integral part in RS. Based on these varying proportions, the formulations are categorized in (Table 2). The duration of heat to be applied to RS also found to be varying. (Table 3) shows the variations on the same. Properties of RS according the amount of sulfur used also elaborated in classics(58–62) (Table 4). Dose of RS has been mentioned as per age(63,64) (Table 5).

RS is shadrasa yukta, ushana in veerya, madhura in vipaka and has got guru, snigdha, vajeekara and Sarvarogahara properties(65). RS is advocated to be administered along with specified Anupanas(66). A brief on the same in (Table 6).

Thesis works & Published articles: Pharmaceutical standardization, Analytical profiles, evaluating safety and toxicity data, and clinical efficacies in Tamaka Shwasa, Vrana, Shwitra, Kshudra Kushta, Hypertension, Male sexual problems were attempted in these studies (67).

Table 1: Collected references of RS

S.No	Name	Reference	Composition	Bhavana Dravya	Duration & Type of Paka	Colour	Remarks
1	Parada Bhasma	RHT 14/2-6	P-1, G-1/4	Niyamaka Gana	Tivragni	Raktabha	Putapaka
2	Udaya Bhaskara Rasa	RPS 3/10-11	P-1, G-1	Nimbu Swarasa	Tikshnagni, 3days	Kamala Varna	Kupipaka
3	Rasa Bhasma	RPS 3/15-18	P-1, G-1	-	Tushgni, 12 yama	Rakta varna	Talastha
4	Rasa Manikya	RPS 3/19-22	P-4, G-4, Na-1	Kumari Swarasa	2days	Kamala Varna	Karmavipakaja Roganashaka
5	Rasasindura	RRS / Preparation added by Dr. Kulkarni	P-1, G-1	Nyagrodha ankura Swarasa	Mandagni, 4 yama	Tarunaditya Sannibha	Commentry on Parada Bhasma Prakarana
6	Parada Murchana	RP 43	P- 5, G-1.25, N-1/10, S-1/5	-	4days	Sindura tulya	
7	Parada Murchana	RP 43	P- 5, G-5, N-1/10, S-1/5	-	4days	Sindura tulya	
8	Parada Murchana	RP 43	P- 5, G-2.5, N-1/10, S-1/5	-	4days	Sindura tulya	
9	Rasa Bhasma	Ra.Chi1/5-11	P-1, G-1	-	12hrs	Padmaraga	Repeat process for 7 times
10	Rasa Bhasma	Ra.Chi 1/85-92	P-1, G-1, N-1	Nagarjuni Swarasa, Kakamachi Swarasa	8prahara	Balarka Sannibha	
11	Rasa Parpatika	Ra.Chi 1/93-95	P-1, G-1, N-1	-	8prahara	Raktaparpatika Samam	
12	Kamadeva Rasa	Ra.Chi 7/88-96	P-1, G-2	Bhahupali swarasa	Mandagni, 4prahara	Daradena Samam	Cork with Tankana
13	Haragouri	RSK 4/90-	P-3, G-1,	Unmatta	Kramagni,		

	Rasa-1	92	N-1/10	swarasa	12 yama		
14	Haragouri Rasa-2	RSK 4/93	P-1, G-1	Sarpakshi swarasa	Kramagni, 12 prahara		
15	Madana Kamadeva Rasa	RSK 4/99	P-1, G-1	Karpasa Rasa	Kramgni, 12prahara		
16	Sindura Paka	R.Chi 2/13	P-1, G-1	-	Kramagni	Sindura dyuti	-
17	Rasa Sindura	R.Chi 2/14	H-1, G-1	-	Kramagni	-	-
18	Sindura Rasa	BP 7/191-95	P-1, G-1/2	-	Kramagni, 8prahara	Darada Samam	-
19	Sindura Rasa	BP 7/191-95	P-1, G-1/4	-	Kramagni, 8prahara	Darada Samam	-
20	Rasa Sindura	RSS 1/66-68	P-10, G-30, Na-1	-	Kramagni, 3days	Bandhuka Pushpa Varna	Antardhuma
21	Rasa Sindura	RSS 1/69-71	P-1, G-1	Vatankura swarasa	Mandagni, 4prahara	Tarunaditya Varna	
22	RasaSindura	RSS 1/72-76	P-1, G-1, N-1, GD-1	Nimbu swarasa	Kramagni, 12 prahara	-	-
23	Nayananandа Sindura	RK 3/36-37	P-1, G-1	Mulika swarasa, Rakta mandala Dhattura swarasa	Mandagni, 12hrs	-	-
24	Rasa Sindura	AP 1/397	P-20, G-20, N-1/40, S-1/20	-	Kramagni, 3days	Arunabha	
25	Rasaraja Rasa Sindura	AP 1/398	P-1, G-1,N-1/4	-	Kramagni, 12 prahara	Kumkum Pinjaram	
26	Rasa Sindura	AP 1/401-403	P-3tola, G-3tola, N-1masha		Kramagni, 3days	-	
27	Rasa Sindura	AP 1/426-427	P-1, G-1/2		Kramagni, 4prahara	Sindura sadrasha	
28	Rasa Sindura	AP 1/426-427	P-1, G-1/4		Kramagni, 4prahara	Sindura sadrasha	

29	Rasa Sindura	YR 155/1-8	P-2, G-2, N-1/4	Nimbu swarasa	Kramagni, 8prahara	Sindura sadrusha	
30	Rasa Sindura	RaPu 3/157	P-5pala, G-5pala, N-8masha, S-1tola		Kramagni, 3days	Vahnibhi Rudravat Arunam	
31	Haragauri Rasa	RaPu 3/158-162	P-1, G-2	-	Kramagni, 27prahara	Hamsapada	
32	Shadguna Rasa Sindura	RaPu 163-168	H.P-1, G-6	-	Kramagni, 7days	Sindura colour	
33	Rasa Sindura	RT 6/168-176	P-1, G-1	3 Bhavanas each of Vatankura, Musali and Semala swarasa	Kramagni	Rakta Kamala Sadrusha	
34	Talastha Rasa Sindura	RT 6/177-182	P-1, G-1	-	Vanyopala agni	Shona Varna	Puta given in Adhasikata yantra
35	Ardha Gandhaka Jarita Rasa Sindura	RT 6/183-184	P-8, G-4, N-2	Lungamla swarasa	Kramagni	Hingulabha	
36	Samana Gandhaka Jarita Rasa Sindura	RT 6/185	P-1, G-1, N-1/4	Nimbu swarasa	Kramagni	Rakta varna	
37	Dwiguna Gandhaka Jarita Rasa Sindura	RT 6/186	P-1, G-2	Raktakarpasa pushpa swarasa	Kramagni, 1day	Rakta Kamalavat	
38	Triguna Gandhaka Jarita Rasa Sindura	RT 6/187-188	P-1, G-3	-	Kramagni, 1day	Rakta Kamalavat	
39	Shadguna Gandhaka Jarita Rasa Sindura	RT 6/189	P-1, G-6	Kumari swarasa	Kramagni, 7days	Sindura varna	

P-Parada, G-Gandhaka, Na-Naga, N- Navasadara, GD- Grahadhuma, RHT-Rasa Hridaya Tantra, RPS-Rasa Prakasha Sudhakara, RRS- Rasa Ratna Samucchaya, RP-Rasa Paddhati, RaChi- Rasa Chintamani,

RSK-Rasasanketakalika,RChi- Rasendra Chintamani, BP- Bhavaprakasha,RSS-Rasendra Sara Sangraha, RK-Rasa Kamadhenu, AP-Ayurved Prakash, YR- Yoga Ratnakara, RaPu- Resendra Purana, RT- Rasa Tarangini

Table 2: Variable proportions of Sulfur in RS

Hg:S	**1:1/4**	**1:1/3**	**1:1/2**	**1:1**	**1:2**	**1:3**	**1:6**	**Total**
No of references	04	01	04	23	03	02	02	**39**

RS- Rasasindura

Table 3: Duration of Heat

Duration of heat (hrs)	**12**	**24**	**36**	**48**	**72**	**81**	**96**	**168**	**Not mentioned**
No. of references	7	7	6	1	5	1	3	2	7

Table 4: Properties of RS according to the amount of Gandhaka

Proportion of sulfur	**Ra. Chi & AP**	**YR &AP**	**RT**
Samaguna	Suddhata sata gunorasahah	Rogaghna	Samanya gadanashanah
Dviguna	Sarvakushtahara	Rajayakshmajita	Maharogahara
Triguna	Sarva jadyata vinashanah	Kaminidarpa Nashanah	Pusatva Prakashnah
Chaturguna	Valipalita Nashanah	Tejasvi sarvasatrartha, Vishada	Mahotsaha, Medha-Smriti Vivardhana
Panchaguna	Kshaya nashanah	Siddha Bhavata	Gada Santapa Nashanah
Shadguna	Sarvarogahara	Mrityujit	Adbhuta Kriya krita

Table 5: Dose of RS

Age	**Dose**	
1 year	1/16 Rati	07.8mg
2 years	1/7 Rati	17.8mg
6 years	1/3 Rati	41.6mg
12 years	1/2 Rati	62.5mg
>12 years	1 Rati	125mg
	1-3 Rati	125-375mg

Table 6: Therapeutic uses and Anupana (Adjuvants)

S. No	**Diseases**	**Anupana**
1	Ajirna	Madhu & Musta Kwatha
2	Amavata	Guduchi, Shatavari, Pippali, Haritaki, Vacha and

		Shunthi Kwatha
3	Apasmara	Vacha Churna or Brahmi, Vacha, Shankha pushpi, Ela Kwatha
4	Arsha	Haritaki Kwatha
5	Aruchi	Matulunga Swarasa
6	Bhagandara	Triphala & Vidanga Kwatha
7	Dhatukshaya	Abhraka Bhasma or Swarna Bhasma
8	Garbhashaya Roga	Kakoli Churna & Narikela Taila
9	Gulma	Ajmoda Churna & Vida Lavana
10	Jirna Jwara	Guduchi, Parpataka Kwatha & Dhanyaka
11	Jwara	Jiraka, Pippali & Dhanyaka Kwatha
12	Kamla	Daruharidra Kwatha
13	Kaphaja Roga	Chitraka Moola, Sunthi, Maricha & Pippali
14	Kasa	Vasa Swarasa, Pippali & Madhu
15	Madatyaya	Hingu, Ajamoda, Shunthi, Dhanyaka and Souvarchala
16	Murccha	Pippali Churna & Madhu
17	Mutrakriccha	Sitopala, Sukshmela & Shilajatu equal with Dugdha
18	Nava Jwara	Tulasi , Ardraka Swarasa, Tambula Rasa
19	Pandu	Loha Bhasma
20	Parinama shoola	Yavakshara and Tankana
21	Pradara	Ashoka & Bala Kwatha
22	Prameha	Guduchi & Hridra Swarasa
23	Prameha (Atikalaja)	Vanga bhasma & Madhu
24	Pittaja Roga	Ela, Mishri & Karpur
25	Rajyakshma	Ghrita
26	Raktapitta	Draksha & Sita
27	Sannipatika Jwara	Nirgundi Swarasa
28	Shirashoola	Dashamoola Kwatha
29	Shotha	Punarnava Kwatha
30	Swasa	Vibhitaka & Vasa Swarasa
31	Swapna Meha	Jatiphala, Lavanga, Karpura, Ahiphena churna with Sitodaka
32	Unmada	Kushmanda Swarasa
33	Udara Shoola	Triphala Kwatha
34	Vajikarana	Shalmali moola, Mushli Churna, Vidarigana and Dugdha
35	Vamana	Brihat Ela Kwatha or Madhu
36	Varna	Brahati, Neeru, Guduchi and Sunthi Kwatha
37	Visphota	Chaturjata Churna and Guduchi, Nimba, Khadira, Indrayava Kwatha

Pharmacological Study of Rasasindura

1. Composition and Physicochemical Nature of Rasasindura (68)

- Rasasindura is primarily composed of α-mercuric sulfide (α-HgS, cinnabar form) with high purity (>99%).
- Preparative processes described in classical texts result in nano- to micron-sized particles (starting ~80 nm), a robust crystalline structure, and absence of soluble or organic mercury species which are associated with classical mercury toxicity.

Key Points:

- XRD confirmed Rasasindura's composition as pure α-HgS.
- The intermediate Kajjali (β-HgS) showed a smaller particle size (~30 nm) and higher cytotoxicity than final Rasasindura.
- Neither Rasasindura nor Kajjali contained toxic organic mercury, critical for reducing toxic risk.

2. Toxicological Profile & Safety Evaluation(68)

a) Cell Line & Zebrafish Studies

- **NIH3T3 fibroblast cells:** Rasasindura showed no significant cytotoxicity up to 75 ppm, whereas Kajjali became toxic above ~20 ppm — attributed to particle penetration differences.
- **Zebrafish larvae:** Even at extremely high concentrations (1000 ppm), no observable toxicity or morphological abnormalities were reported for either Rasasindura or Kajjali, indicating low acute toxicity in vivo models.

Implication: The Ayurvedic processing significantly alters HgS toxicokinetics compared to raw mercury compounds, making Rasasindura relatively safe at reasonable concentrations.

3. In Vivo Animal Pharmacology & Therapeutic Effects(69)

a) Wistar Rat & Mouse Studies

- Therapeutic and high doses were administered intragastrically in Wistar rats.
- No significant histopathological or biochemical abnormalities were seen in brain, liver, kidneys, or testes at therapeutic doses — even up to eight times the normal dose.
- High doses induced mild hyperactivity in some animals but no overt organ dysfunction.

Therapeutic Efficacy (Oligospermia Model):

- In mice with lead acetate-induced oligospermia, Rasasindura significantly increased sperm count and motility and reduced abnormalities.
- Gene expression analysis suggested activation of calcium channel genes (Catsper and Calpain) — a plausible mechanism for improved spermatogenesis.

4. Mechanistic Insights & Gene Modulation (69)

a) Gene Expression Profile

Microarray analyses showed that Rasasindura influenced expression of key gene groups linked to:

- Anti-inflammatory pathways
- Anti-obesity and anti-diabetic signatures
- Anti-cancer potential
- Immunomodulatory responses — e.g., beta-defensin expression indicating potential antimicrobial and immune enhancing activity
- Metallothionein-2 induction, a known metal detoxification protein — possibly protecting against Hg ion toxicity.

Interpretation: These molecular effects suggest that Rasasindura's pharmacological actions may extend beyond traditional indications, potentially influencing systemic metabolic pathways and immunity.

5. Comparative Toxicology with Other Mercury Forms (70)

a) Structural Stability & Toxicity Relevance

- Confirms Rasasindura consists of single-phase, defect-free α-HgS nanoparticles (~24 nm).
- Absence of elemental mercury (Hg^0) or organic mercury species means the toxic risk that is typical for mercury drugs is greatly reduced.
- The strong Hg–S covalent bond resists in vivo transformation to toxic mercury species — an important determinant of safety.

6. Protective and Adaptive Effects in Models

Although not a direct pharmacological end-point, one study using zebrafish suggests that pre-treatment with sparingly soluble HgS (as in Rasasindura) can induce adaptive, protective biochemical pathways that reduce the neurotoxicity of other mercury forms (e.g., $HgCl_2$), possibly through stress response and glutathione-related pathways.

DISCUSSION

A review of the available classical material shows that Rasashastra scholars from the 10th to 12th century AD were already familiar with Gandhaka Jaraṇa and related methods. The earliest preparation resembling Rasasindura—made using the Loha Samputa technique—appears in the Rasahridaya Tantra of the 10th century. This text also records the use of the Vāluka Yantra, and the author highlights that heating must continue until the entire samputa turns red-hot. The mention of Kācha Kupi (glass bottle apparatus) is found for the first time in Anandakanda. Interestingly, although the author knew about both Kācha Kupi and Vāluka Yantra, these were not applied for preparing Pārada Bhasma in that period. Their systematic use becomes evident only later in the Rasaprakāśa Sudhākara (13th century), where these devices are repeatedly employed, particularly in the preparation of Udaya Bhaskara Rasa.

The name Rasasindura in its present sense appears for the first time in Rasendra Chintamani (15th century A.D.), describing a formulation of mercury and sulphur prepared by the Kupipāka process. Several other formulations similar to Rasasindura are scattered across classical texts under different names—Udaya Bhaskara Rasa, Kāmadeva Rasa, Haragauri Rasa, Madan Kāmadeva Rasa, Sindura Pāka, and Nayanananda Sindura. All these essentially combine purified Pārada and Gandhaka and are processed in a glass bottle (Kachakupi) using the Vāluka Yantra heating system.

From this, it appears that the idea of producing a deep-red sulphide of mercury began around the 10th century AD. However, the successful development of the bright vermilion variety of Rasasindura through the Kupipāka technique seems to have been achieved only by the 13th century. Rasa Kāma Dhenu records that the kupi could be made from glass, clay, gold, iron, or silver. Later authorities such as Bhāva Prakāśa and Rasendra Sara Sangraha stressed the importance of coating the bottle with layers of clay-smeared cloth to strengthen it. Āyurveda Prakāśa additionally mentions the use of a heated iron rod (taptā śalākā) to clear the mouth of the kupi when it becomes blocked during heating. Rasataranginī offers a detailed explanation of the different proportions of sulphur used, ranging from Samaguṇa to Ṣaḍguṇa Balijārita preparations.

Subsequent Rasashastra scholars studied the Kupipāka procedure in depth and, based on cumulative experience, classified the heating pattern (kramāgni) into three distinct stages: Mṛdu Agni, Madhyama

Agni, and Tīvra Agni. These roughly correspond to temperature ranges of 30–250°C for Mṛdu, 250–450°C for Madhyama, and 450–650°C for Tīvra.(71)

The available experimental evidence indicates that classical Ayurvedic processing converts mercury into a stable, phase-pure α-HgS form in Rasasindura, thereby markedly reducing its inherent toxic potential. Comparative studies with Kajjali **(**β-HgS**)** highlight the importance of complete pharmaceutical processing, as Kajjali exhibits higher cytotoxicity while Rasasindura remains largely non-toxic in cell line, zebrafish, and rodent models even at supratherapeutic doses. The observed pharmacological efficacy, particularly in reproductive disorder models, is supported by gene expression changes involving calcium channel regulation, anti-inflammatory pathways, immunomodulation, and induction of detoxification proteins such as metallothionein. These findings provide a mechanistic basis for the traditional therapeutic claims of Rasasindura and explain its distinct toxicological behavior compared to other mercury compounds.

CONCLUSION

A close examination of the classical literature shows that the earliest versions of Kupipākva Rasāyana begin to appear from around the 10th century onwards. The texts do not always agree on the exact quantity of Gandhaka to be used or the total heating time required for preparing Rasasindura, and references mention durations that range anywhere from half a day to nearly a week. With time, progress in both pharmaceutical practice and analytical science has led to improved methods for preparing and identifying Rasasindura. Modern toxicity evaluations have further demonstrated that the formulation is safe when administered in the recommended therapeutic dose.

Rasasindura, when prepared according to classical Ayurvedic principles, represents a chemically stable and biologically compatible mercurial formulation with a favorable safety profile. The transformation of mercury into defect-free α-HgS, absence of toxic mercury species, and resistance to in vivo dissociation collectively account for its low toxicity. Experimental pharmacological and toxicological data support its therapeutic potential and safety within prescribed doses, challenging generalized perceptions of mercury toxicity. Overall, Rasasindura exemplifies the successful integration of traditional Ayurvedic pharmaceutics with modern pharmacological and molecular validation, warranting further clinical and translational research.

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