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"ARSENIC-CONTAINING KUPIPAKWA RASAYANA: INSIGHTS INTO TOXICITY, THERAPEUTIC USES, AND PHARMACOKINETICS (ADME)"

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ABSTRACT:

Introduction: Arsenic-containing *Kupipakwa Rasayana* such as Shila Sindoor, Malla Sindoor, Tal sindoor, and Sameer Pannaga Rasa, prepared from As_2S_2, As_2S_3 and As_2O_3, are traditionally valued for therapeutic efficacy.

Methods: Modern analyses (XRD, SEM, ICP-MS) and comparative toxicology studies were reviewed along with ADME data and clinical observations.

Results: Purification and *Kupipakwa* processing convert arsenic minerals into stable nano-sulfide complexes with reduced toxicity. As_2S_2 and As_2S_3 exhibit markedly lower toxicity and bioavailability than As_2O_3 due to poor gastrointestinal absorption. ADME studies show minimal systemic absorption, slow methylation and gradual urinary elimination. Nano-structured sulfides enable controlled micro-absorption and sustained therapeutic action.

Discussion: Integration of Rasashastra principles with modern evidence suggests that well-processed Kupipakwa Rasayana possess a favorable safety profile and offer benefits in inflammatory and respiratory conditions when given in classical micro-doses.

KEYWORDS: Kupipakwa Rasayana, arsenic, Shila Sindoor Malla Sindoor, Sameer Pannaga Rasa.

INTRODUCTION:

Rasashastra, the specialised pharmaceutical branch of Ayurveda, describes the transformation of metals and minerals through *Shodhana*, *Marana*, and *Kupipaka* to make them therapeutically safe and potent [1]. Arsenic-based Kupipakwa Rasayana such as Shila Sindoor, Malla Sindoor, and Sameer Pannaga Rasa are considered fast-acting and *yogavahi*, traditionally used in chronic systemic disorders [1]. Classical arsenic minerals including Haratala (As_2S_3), Manahshila (As_2S_2) and Gauripashana (As_2O_3) undergo major physicochemical modification during Kupipaka, resulting in the formation of stable arsenic sulphide complexes that reduce inherent toxicity [1,4]. Modern analytical studies using SEM, XRD, FTIR, EDS and ICP-MS confirm that properly processed Kupipakwa Rasayana contain nano- to micro-crystalline arsenic sulfide particles, mainly α-As_4S_4 and As_2S_3, with reduced solubility and bioavailability compared to raw arsenic compounds [5,6]. ADME research further demonstrates that arsenic sulfides have low aqueous solubility, minimal gastrointestinal absorption, slow hepatic methylation, and gradual urinary/biliary excretion, leading to comparatively reduced toxicity [7,8]. Toxicity studies on formulations like Sameer Pannaga Rasa report no significant subacute or chronic toxicity when prepared according to classical pharmaceutical procedures [2,3]. These findings support classical Ayurvedic claims regarding the safety of Kupipakwa Rasayana when properly purified and processed. Therapeutically, these formulations are used in Sannipata Jwara, Apasmara, Unmada, Sandhivata, and Vata-Kapha disorders and exhibit anti-inflammatory, immunomodulatory, neuroprotective, and Rasayana effects [1,9].

Despite their benefits, proper Shodhana, controlled heating, particle-size standardisation, accurate dosing and clinical supervision are essential because improperly processed arsenicals may retain toxicity [4,10]. Therefore, understanding the toxicity, ADME behaviour, and therapeutic relevance of arsenic-based Kupipakwa Rasayana through classical and modern scientific correlation is crucial for ensuring safe clinical practice [1–10].

AIMS AND OBJECTIVE:

1. To explore the historical background and classical Rasashastra principles related to Kupipakwa Rasayana, with special reference to arsenic-based kupipakwa preparations.

2. To analyze modern scientific evidence on the toxicity, nano-transformation, and physicochemical changes occurring in arsenic-containing Kupipakwa Rasayana.
3. To assess contemporary ADME (Absorption, Distribution, Metabolism, Excretion) and therapeutic findings to understand the safety and clinical relevance of these formulations.

METHODOLOGY

This review is based on an integrative analysis of classical Ayurvedic literature and modern scientific research related to arsenic-containing Kupipakwa Rasayana. Classical information was collected from authoritative Rasashastra texts, including *Rasa Tarangini, Rasaratna Samuccaya,* and *Ayurveda Prakasha*, focusing on pharmaceutical methods, therapeutic indications and historical descriptions of Kupipakwa formulations. Modern scientific evidence was sourced from peer-reviewed journals indexed in PubMed, ScienceDirect, NCBI-PMC, ResearchGate and other academic databases.

Data from classical sources and modern research findings were organized and analyzed thematically under:

(1) Classical pharmaceutical principles,
(2) Arsenic-based Kupipakwa formulations,
(3) Toxicological evaluation,
(4) Nano-structural transformations, and
(5) Pharmacokinetic (ADME) behavior.

The aim was to synthesize traditional knowledge with contemporary scientific evidence to provide a comprehensive and balanced overview of the therapeutic potential and safety profile of arsenic-containing Kupipakwa Rasayana.

CLASSIFICATION OF ARSENIC-CONTAINING KUPIPAKWA RASAYANA:

S.NO	References	Ingredients	Indication	Dose
1.	Rasa Chandanshu	Parada Gandhaka Hartala Mall	Sannipata, Unmada, Sandhivata, Kaphaja roga	1–2 Ratti
2.	Rasa Chandanshu	Parada Gandhaka Abhraka bhasma Tankana Vatsanabha Trikatu churna	Mahavata, Murcha, Vatvyadhi adhikar etc.	1–2 Ratti

3.	A.G.D.S,[12] A.F.I, Rasatantrasara evam siddhaprayoga samgraha	Parada Gandhaka Hartala Manashila Malla	Sannipata Roga, Kaphonmada, Kaphajasandhibandha, Jwara, Shwasa, Kasa	½–1 Ratti
4.	Vaidya Chintamani	Parada Gandhaka Haratala Swarnamakshika Loha Haritaki Trikatu Tulasi Mula Karkatasringi Vatsanabha Tankana	Vatavyadhi	1–2 Ratti
5.	Vaidya Rahasyama	Parada Gandhaka Abhraka bhasma Tankana Vatsanabha Trikatu churna	Mahavata, Murcha, Vatvyadhi adhikar etc.	1 Ratti

SAMEERA PANNAGA RASA[11]

MALLA SINDOOR[12]

S.no	References	Ingredients	Indication	Dose
1.	Rasayana sangraha and Siddha bhaisajya manimala	Suddha parada Rasakarpura Malla/Somala Suddha Gandhaka	Kasa, Swasa, Gulma Grahani, Kshaya Apasmara	1 Ratti
2.	Rasayana sara sangraha sannipataja vyadhi adhyaya	1st references Sweta, Rakta, Peeta, Krishna variety of Somal , Shudha Gandhaka, Shudha parada, Bhavana Dravya - Nimbu swarasa 2nd Reference- Shudha	Visuchika, Sannipataja/ Tridoshaja vyadhis Tridoshaja vyadhis	1 Ratti

		Manashila, Shudha Haratala, Black variety of Malla, Shudha Parada, Shudha Gandhaka Bhavana Dravya - Arka Ksheera		
3.	Rasayana Sara Sangraha Sarva Roga Adhyaya	Shuddha Malla, Bhubukshita Parada, Shuddha Gandhaka Bhavana Dravya - Snuhi ksheera Arka ksheera	Ama rogas	1 Ratti
4.	Rasayosagar	1st reference Parad Rasakapur Safed somal Suddha Gandhaka Bhavana Dravya - Nimbu swarasa (upto 3 days) 2nd reference Sweta, Rakta, Peeta, Krishna variety of Somal, Shudha parada, Shudha Gandhaka, 3rd reference Shuddha Malla, Bhubukshita Parada, Shuddha	Sannipataja vyadhi, Swasa, Kasa,Vatavikar Sannipataja/Tridoshaja Vyadhis, Haija (cholera) Tridoshaja vyadhis	1 Ratti 1 Ratti 1 Ratti

		Gandhaka		
5.	Rasatantra sara and Siddha prayoga sangraha	Shuddha parada, Shuddha Gandhaka, Shuddha somal		1 Ratti
6.	AFI Part - 1 Second edition (Siddhabhaisajyamanimala, adhyaya 5:37)	Rasa (parad)- Suddha Rasavidhu (parad)- Rasakarpura Bali (Gandhka)- Suddha- Malla –suddha	Tamaka Svasa (bronchial asthma), Vata kaphaja roga, Phiranga roga (syphilis)	½–1 Ratti

SHILA SINDOOR

Sr. No.	**Texts**	**Ingredients**	**Indication**	**Dose**
1	Rasayogasagara, Volume-II, Shakaradirasa/431-433[13]	Parada Gandhaka Manahshila	Kushtha	1–2 Ratti
2	Rasayogasagara, Volume-II, Shakaradirasa/434-436[13]	Shadguna gandhaka jarit Parada Gandhaka Manahshila	According to disease	1 Ratti
3	Rasayogasagara, Volume-II, Shakaradirasa/437-441[13]	Swarnagrass yukta parada Gandhaka Manahshila	Kasa,swasa, kaphapardhan Vyadhi	1/2 – 1 Ratti
4	Rasayogasagara, Volume-II, Shakaradirasa/442[13]	Parada Manahshila Bhavana Dravya Dhatur pushpa swarasa	Yogvahi, rasayan	1–2 Ratti
5	Rasayogasagara, Volume-II, Shakaradirasa/443-448[13]	Parada Gandhaka Manahshila Vatsanabha Haratala Makshik Bhavana Dravya - Vat-shringa & Hanspadi swarasa	Samast sanipattaj rog, samast jwara	1–2 Ratti
6	Rasamritam: Malla Vijnaniyam 4/14-15[14]	Parada Gandhaka Manahshila	hwasa, KaphaVatagadahara	1-Ratti

		Bhavana Dravya - Kumari Swarasa		
7	Ayurveda Saar Samgrah[15]	Parada Gandhaka Manahshila Bhavana Dravya - Kumari Swarasa	Kapha and Vataja Kasa, Kandu, Kshaya, Aruchi, Medoghna.	1-2 Ratti
8	Rasa Tantra Saar Evam Siddha Prayog Samgrah[16]	Parada Gandhaka Manahshila Bhavana Dravya - Kumari Swarasa	Shwasa, Kasa, Mada, Visarpa, Kanhtamala, Ratktadushti	2- Ratti
9	Ayurvediya Aushadhi Gundharm Shastra[17]	Parada Gandhaka Manahshila Bhavana Dravya - Kumari Swarasa	Shwasa, Kasa, Mada, Visarpa, Kanhtamala, Ratktadushti	2- Ratti

TAL SINDOOR

S.no	References	Ingredients	Indication	Dose
1.	Rastantrasaar & siddhapryog sangrha[18]	Suddha parada Suddha Gandhaka Suddha hartal	Kasa, Swasa, vaat rakta, kushtha	1-2 Ratti
2.	Rasyogsagar[19]	1st reference- Shudha hingul, Shudha Gandhaka, Shudha hartal, Bhavana Dravya - kumari Swarasa, palash pushpa	Kushtha, atisaar, vaatrog, apchi	3 Ratti
		2nd Reference- Shudha Parada, Shudha Gandhaka, Shudha hartal, Shudha tankan Bhavana Dravya - naagwalli, ark mool, adrak, chitrak mool, triphla, rason, naagwalli	Kushtha, udar rog, pancha gulma	3 Ratti
		3rd Reference- Shudha Parada, Shudha Gandhaka, Shudha hartal, Shudha somal Bhavana Dravya - kumari Swarasa, tulsi	Vaat – kaphaj vyadhi	1 Ratti

		4th Reference- Shudha hartal Chuna Bhavana Dravya – laal kapaas pushpa swaras 5th Reference- Shudha Parada, Shudha Gandhaka, Shudha hartal, Shudha Manahshila Shudha tankan Shudha navsadar 6th Reference- Shudha parad Shudha gandhak Shudha hartal	Pittaj jwara, hikka, chardi, kushtha Kasa, swasa, pancha gulma,aamvata Kushtha	1 Ratti 1 Ratti 1 Ratti

DISCUSSION

The evaluation of arsenic-containing Kupipakwa Rasayana reveals a remarkable intersection of classical Ayurvedic pharmaceutics and modern scientific understanding. Classical Rasashastra emphasizes that metals and minerals undergo profound transformation when subjected to Shodhana and Kupipakwa procedures. These traditional claims gain scientific support from contemporary analytical studies demonstrating nano-structural changes, formation of stable sulfide complexes and significant alterations in physicochemical behavior of arsenic minerals after processing. Such findings validate the Ayurvedic principle that appropriate pharmaceutical methods can convert inherently toxic substances into therapeutically acceptable forms.

A major point emerging from the literature is the distinct difference in toxicity between various arsenic species. Modern toxicology consistently shows that arsenic trioxide exhibits high solubility and rapid systemic absorption, leading to pronounced toxicity, whereas arsenic sulfides such as realgar (As_2S_2) and orpiment (As_2S_3) display poor gastrointestinal absorption and comparatively lower toxicity. These scientific observations align closely with Ayurvedic practices, which never recommend the use of unprocessed arsenic compounds but advocate rigorous purification and micro-dose administration.

Analytical studies on Kupipakwa preparations such as Shila Sindoor further strengthen the pharmacological rationale behind these formulations. Techniques like SEM and XRD reveal particle size reduction to the nano range, improved structural stability and altered bio-

interaction properties. This nano-transformation plausibly explains the classical descriptions of faster onset of action, improved potency and sustained therapeutic activity in Kupipakwa medicines.

Modern ADME findings provide another layer of evidence. Realgar-based formulations exhibit minimal systemic absorption, slow metabolic conversion and gradual excretion, which corresponds well with the long-standing Ayurvedic practice of prescribing these drugs in very small doses. The slow-release nature observed in nano-realgar studies provides a scientific explanation for the prolonged therapeutic effects traditionally attributed to Kupipakwa Rasayana.

Overall, the discussion highlights that the safety and efficacy of arsenic-based Ayurvedic formulations cannot be evaluated solely through the lens of raw arsenic toxicity. Rather, their traditional pharmaceutical transformations significantly alter their biological interactions, highlighting the need for integrative evaluation that considers both classical knowledge and modern scientific findings. The convergence of these two perspectives offers valuable insights into why certain Kupipakwa Rasayana have been clinically effective for centuries and how they can be rationally assessed in the present era.

CONCLUSION

Arsenic-containing Kupipakwa Rasayana represent a unique blend of classical pharmaceutical wisdom and modern scientific relevance. The Kupipakwa process, rooted deeply in Rasashastra, transforms raw arsenic minerals into stable, nano-structured sulfide complexes with markedly altered toxicity and pharmacokinetic behavior. Contemporary evidence supports classical claims by demonstrating reduced solubility, lower systemic absorption, and controlled metabolic conversion of arsenic sulfides when compared to arsenic trioxide. Moreover, analytical and ADME studies validate the traditional rationale for micro-dosing and highlight the potential therapeutic utility of these formulations when prepared according to established Ayurvedic procedures.

The convergence of ancient processing methods with modern toxicology underscores that the safety and efficacy of these preparations depend entirely on proper purification and precise pharmaceutical techniques. While further experimental research is needed to clarify their mechanisms of action and long-term safety, current evidence suggests that well-prepared Kupipakwa Rasayana possess a favorable benefit–risk profile. Thus, the integration of classical Rasashastra principles with modern scientific insights provides a balanced

foundation for understanding the relevance of arsenic-based Kupipakwa Rasayana in contemporary practice.

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