

Sheeta Jala as *Anupana* in *Ichhabhedi Rasa*: A *Dravyaguna* Hypothesis on *Agni*-Mediated Modulation of *Jayapala*'s Purgative Action

Anu Prabha^{1*}, Harikrishnan S²

¹Professor and Head, Department of Dravyaguna Vijnana, SAM College of Ayurvedic Sciences and Hospital, SAM Global University, Raisen, Madhya Pradesh 464551, India

²Department of Kayachikitsa, SAM College of Ayurvedic Science and Hospital, SAM Global University, Raisen, Madhya Pradesh 464551, India

*Corresponding Author: Prof. (Dr.) Anu Prabha | Email: dr.anuprabha@gmail.com | ORCID iD: <https://orcid.org/0009-0008-2617-6625>

Dr. Harikrishnan S | Email: drhari2337@gmail.com | ORCID iD: <https://orcid.org/0009-0007-8609-0906>

ABSTRACT

Background: *Ichhabhedi Rasa* is a classical *Kharaliya Rasayoga* of *Rasashastra*, used as a *Tikshna Virechaka* in *Udara Roga*, *Gulma*, *Jwara* and other conditions of vitiated *Kapha* and *Pitta*. Across its twenty-four documented varieties, it is administered with *Sheeta Jala* as *Anupana*, and purgation continues only for as long as cold water is taken, ceasing on ingestion of warm liquids such as tea. This observation is recorded descriptively only in trade and patient-facing literature rather than in peer-reviewed sources; a recent review has termed the cold water *Anupana* non-intuitive without offering a mechanistic account.

Objective: To establish which single ingredient of *Ichhabhedi Rasa* is pharmacologically prominent, and to propose a testable biochemical rationale for its *Sheeta Jala Anupana* beyond the classical *Virya-Viparyaya* principle.

Methods: A conceptual and literary review of classical *Rasashastra* texts and contemporary pharmacological literature on *Ichhabhedi Rasa* and its constituent *Dravyas*, with particular attention to *Croton tiglium* L. (*Jayapala*) phytochemistry.

Findings: *Shuddha Jayapala* (purified seeds of *Croton tiglium* L.) is the only ingredient that independently carries *Rechana Karma*; the remaining ingredients function as *Yogavahi* carriers (*Shuddha Parada*, *Shuddha Gandhaka*), *Dipana* supports (*Shunthi*, *Maricha*) or a moderating antidote (*Shuddha Tankana*). All six principal ingredients of *Ichhabhedi Rasa* are recorded as *Ushna* in *Virya* across the compendia consulted. *Jayapala*'s purgative principle, phorbol esters of the phorbol-12-myristate-13-acetate (PMA) type, is a substrate for tissue carboxylesterases that hydrolyse it to the less active phorbol, a temperature- and transit-time-dependent process.

Hypothesis/Conclusion: *Ushna Guna*, being *Agni-Vardhaka* and associated with accelerated gastric emptying, is proposed to hasten this hydrolytic inactivation, explaining the abrupt cessation of purgation observed with warm liquids. *Sheeta Guna*, being *Agni-Mandakara* and associated with delayed gastric emptying, is proposed to slow the same hydrolysis and sustain *Jayapala*'s local irritant action on the intestinal mucosa for as long as cold water continues to be given. The hypothesis is divided into two separately testable components, and the experiments needed to confirm or refute each are specified.

Keywords: *Ichhabhedi Rasa*; *Jayapala*; *Sheeta Jala Anupana*; *Virya-Viparyaya*; Phorbol Ester Hydrolysis

How to cite this article: Anu Prabha. *Sheeta Jala* as *Anupana* in *Ichhabhedi Rasa*: A *Dravyaguna* Hypothesis on *Agni*-Mediated Modulation of *Jayapala*'s Purgative Action. *Int J Drug Deliv Technol*. 2026;16(84s):272-280. DOI: 10.25258/ijddt.16.84s.31.

Article Type: Hypothesis/Perspective Article.

Source of support: XX

Conflict of interest: XX

1. INTRODUCTION

Virechana, one of the five procedures of *Panchakarma*, achieves elimination of vitiated *Doshas*, principally *Pitta* and *Kapha*, through the *Adhomarga*.¹

Ichhabhedi Rasa is a *Kharaliya Rasa Kalpana* chiefly employed as a *Rechana Yoga*. The name is explained in the classical tradition as denoting that *Rechana* follows administration of *Yoga* with *Chulluka Jala* and *Sita*, the word *Ichha* referring to the physician's or patient's ability to induce purgation at will through control of the *Anupana*. Twenty-four varieties of *Ichhabhedi Rasa* are documented across six classical texts, *Bhaishajya Ratnavali*, *Rasa Tarangini*, *Rasa Ratna Samuchchaya*, *Rasayoga Sagara*, *Rasendra Chintamani* and *Rasendra Sara Sangraha*, differing in ingredient proportion, method of preparation, *Bhavana Dravya*, *Anupana*, dose and indication.²

A recurring feature across these varieties is the near-universal prescription of cold water, variously termed *Sheeta Jala*, *Sheetala Jala* or *Chulluka Jala*, as the vehicle of administration; this rests directly on the classical verses themselves (Section 4.3). Standard pharmacopoeial and

clinical descriptions of the marketed preparation likewise state that the medicine is administered with cold water and that purgation continues only until cold water is taken. The further observation, that substitution of cold water with a warm beverage such as tea brings the purgative action to an abrupt halt, is repeated in patient-facing pharmacovigilance literature and clinical commentary rather than in the classical verses.³ This observation is treated here as the motivating clinical premise, since it is widely and consistently repeated in practitioner commentary; the purpose of this article is to propose a mechanism that would explain it.

A 2026 conceptual review has described the use of *Sheeta Jala* as *Anupana* as non-intuitive yet crucial for controlling the rate of absorption and localising the purgative effect,⁴ without situating this within the formal *Rasa-Guna-Virya-Vipaka-Prabhava* analysis that *Dravyaguna Vijnana* applies to every *Anupana*, without examining why *Shuddha Jayapala* should be regarded as the functionally defining constituent, and without proposing a testable biochemical mechanism. This article

addresses these three gaps and proposes a hypothesis that has not previously appeared in the literature reviewed.

2. AIM AND OBJECTIVES

The present review examines the classical and contemporary basis for the use of *Sheeta Jala* as *Anupana* in *Icchabhedi Rasa*, with particular attention to the role of *Jayapala*, through the following objectives:

- (1) To review the *Dravyaguna* properties of *Jala*, particularly *Sheeta Jala*.
- (2) To tabulate the *Rasa-Guna-Virya-Vipaka* of the principal ingredients of *Icchabhedi Rasa* and establish their predominant *Ushna-Teekshna* character.
- (3) To establish, qualitatively and based on modern pharmacological evidence, why *Shuddha Jayapala* should be regarded as the pharmacologically defining ingredient of *Icchabhedi Rasa*.
- (4) To apply the principle of *Virya-Viparyaya* in explaining why *Sheeta Jala*, and not *Ushna Jala*, is prescribed as *Anupana*.
- (5) To propose and substantiate a specific biochemical hypothesis linking *Anupana* temperature to the duration of *Virechana*, distinguishing directly evidenced components from original extrapolations.

3. MATERIALS AND METHODS

This is a conceptual and literary review. Classical sources consulted include *Rasa Tarangini* (English translation by Angadi)⁵, *Bhaishajya Ratnavali* (edited by Mishra and Shastri)⁶, *Rasendra Chintamani* (Hindi translation by Mishra)⁷, *Rasa Ratna Samuchchaya* (edited by Shastri)⁸, *Rasendra Sara Sangraha* (English translation by Satpute)⁹, *Rasayoga Sagara* (translation by Sharma)¹⁰, *Bhavaprakasha* (edited by Misra and Misra)¹¹ and *Sushruta Samhita, Sutrasthana* (Hindi commentary by Shastri)¹², along with *Dravyaguna Vijnana* by Lucas¹³ and the Ayurvedic Formulary of India.¹⁵

Contemporary pharmacological and phytochemical sources were retrieved through PubMed, PubMed Central, ScienceDirect and Google Scholar, last searched on 13 September 2026, combining the terms *Icchabhedi Rasa*, *Jayapala*, *Croton tiglium*, phorbol ester hydrolysis, carboxylesterase phorbol, cold water gastric emptying and cold stress gastrointestinal motility. Titles and abstracts were screened for relevance to *Icchabhedi Rasa* pharmacology, *Croton tiglium* phytochemistry, phorbol ester metabolism, and thermal or cold stress modulation of gastrointestinal motility. No peer-reviewed clinical report of the observation that warm liquids abruptly terminate *Icchabhedi Rasa*-induced purgation was located; the only identified source for this observation is trade and patient-facing literature (Reference 3).

Verse-level citation is given only where the specific verse or chapter number is available in the primary or translated edition consulted, namely the *Bhaishajya Ratnavali* verse on *Sheeta Jala Anupana* (Chapter 40, Verses 65-66) and the *Rasa Tarangini* verse on classification (24th *Taranga*, Verse 320-322), and the *Sushruta Samhita* definition of *Sheeta* and *Ushna Guna* (*Sutrasthana* 46/415). For *Rasendra Chintamani*, *Rasa Ratna Samuchchaya*, *Rasendra Sara Sangraha*, *Rasayoga Sagara* and *Bhavaprakasha*, only the relevant chapter or section is identified. Pharmacological and biochemical claims regarding phorbol esters, their hydrolysis, and gastric motility are drawn directly from the primary research articles cited. The hypothesis advanced in Section 4.7 is an original synthesis that draws on the cited sources but is not stated or tested in any of them individually.

This article is a conceptual synthesis and hypothesis paper, not a systematic review; no pre-registered search string or formal screening process was applied, and PRISMA reporting guidance does not apply. The classical textual data in Table 1 are drawn from standard *Dravyaguna* compendia and *Nighantu* sources. A quantitative, variety-by-variety comparison of ingredient proportions and *Anupana* across all twenty-four classical varieties would require direct, verse-by-verse consultation of every primary edition and is proposed as future work (Section 7). Reference 3, cited for the observation that purgation ceases abruptly on warm liquids, is trade literature rather than peer-reviewed clinical documentation; it is included because the observation is widely repeated in *Rasashastra* practice and pharmacovigilance commentary.

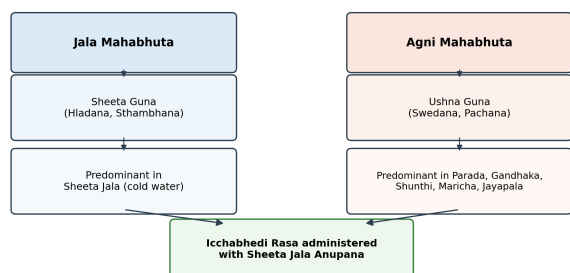
4. REVIEW AND DISCUSSION

4.1 Classical Definition of *Sheeta* and *Ushna Guna*

Among the *Gurvadi Gunas*, *Sheeta* and *Ushna* are the most influential, being closely associated with *Virya* itself.¹³ *Sheeta* is attributed to the predominance of *Jala Mahabhuta*, *Ushna* to *Agni Mahabhuta*. *Hemadri* defines *Sheeta* as the property responsible for *Sthambhana*, while *Sushruta* describes it as *Hladana*, *Sthambhana*, and as subduing *Moorchha*, *Trit*, *Sweda* and *Daha*. *Ushna*, the opposite property, is described by *Hemadri* as productive of *Swedana*, and by *Sushruta* as enhancing *Pachana*. *Bhavaprakasha* follows the same definitional line as *Sushruta*.^{11,12,14}

With respect to *Dosha*, *Sheeta Guna* increases *Kapha* toward its *Chaya* stage, aggravates *Vata*, and pacifies *Pitta*; *Ushna Guna* acts oppositely, aggravating *Pitta*, controlling *Vata*, and liquefying accumulated *Kapha*.^{13,14} This complementary relationship forms the conceptual basis for the present analysis.

Panchamahabhuta Basis of *Sheeta* and *Ushna Guna*



RESEARCH PAPER

Figure 1. *Panchamahabhuta* basis of *Sheeta* and *Ushna Guna* and their representation in *Ichhabhedi Rasa* and its *Anupana*.

4.2 Rasadi Panchaka of the Principal Ingredients of Ichhabhedi Rasa

The ingredients common to the majority of the twenty-four classical varieties of *Ichhabhedi Rasa* are *Shuddha Parada* (purified mercury), *Shuddha Gandhaka* (purified sulphur), *Shuddha Tankana* (purified borax), *Shunthi* (*Zingiber officinale* Roscoe), *Maricha* (*Piper nigrum* L.). Table 1. *Rasadi Panchaka* of the principal ingredients of *Ichhabhedi Rasa* and of *Jala/Sheeta Jala*, compiled from standard *Dravyaguna* compendia and classical *Nighantu* sources. All six principal ingredients are recorded as *Ushna* in *Virya* across these sources. The *Vyavayi* and

Sl. No.	Dravya	Rasa	Guna	Virya	Vipaka	Karma
1	<i>Shuddha Parada</i>	<i>Shadrasa</i>	<i>Snigdha, Sara, Guru</i>	<i>Ushna</i>	<i>Madhura</i>	<i>Tridoshashamana, Rasayana</i>
2	<i>Shuddha Gandhaka</i>	<i>Katu, Tikta, Kashaya</i>	<i>Sara</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kapha-Vatahara, Dipana</i>
3	<i>Shuddha Tankana</i>	<i>Katu</i>	<i>Ruksha, Tikshna, Sara</i>	<i>Ushna</i>	<i>Katu</i>	<i>Vatanashaka, Kaphavishleshaka</i>
4	<i>Shunthi</i> (<i>Zingiber officinale</i> Roscoe)	<i>Katu</i>	<i>Laghu, Snigdha</i>	<i>Ushna</i>	<i>Katu</i>	<i>Vata-Kaphaghna, Dipana, Bhedana</i>

Note on Table 1: *Rasa* and *Vipaka* values for each *Dravya* are traced to a single primary compendium rather than pooled across sources. *Shuddha Gandhaka* is recorded here as *Katu, Tikta, Kashaya* in *Rasa* and *Katu* in *Vipaka*. Every principal ingredient of *Ichhabhedi Rasa* is *Ushna* in *Virya*. *Shuddha Parada's* *Yogavahi Guna* allows it to carry the potency of associated *Dravyas* regardless of its own *Virya*, so its *Ushna Virya* reinforces the pharmacological logic of the formulation. *Shuddha Tankana, Shunthi, Maricha* and *Shuddha Jayapala* additionally possess *Tikshna* or *Sara Guna*, denoting sharp, penetrating and quickly spreading action. *Shuddha Jayapala* carries two further *Gunas* not shared by the other ingredients: *Vyavayi*, the property by which a substance pervades the entire body and manifests its

and *Shuddha Jayapala* (purified seeds of *Croton tiglium* L.). Table 1 summarises the *Rasa, Guna, Virya, Vipaka* and predominant action of these *Dravyas*, compiled from standard *Dravyaguna* compendia and *Nighantu* sources, together with *Jala* and *Sheeta Jala* as described in *Bhavaprakasha*.^{11,13,15}

Vikasi Guna of *Shuddha Jayapala* follow the *Dashavidha Visha Guna* description of *Upavisha Dravyas* in *Charaka Samhita* (*Chikitsasthana* 23) and *Sushruta Samhita* (*Kalpasthana*).

Sl. No.	Dravya	Rasa	Guna	Virya	Vipaka	Karma
5	<i>Maricha</i> (<i>Piper nigrum</i> L.)	<i>Katu</i>	<i>Laghu, Tikshna</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kapha-Vataghna, Dipana</i>
6	<i>Shuddha Jayapala</i> (<i>Croton tiglium</i> L.)	<i>Katu</i>	<i>Guru, Ruksha, Tikshna, Vyavayi, Vikasi</i>	<i>Ushna</i>	<i>Katu</i>	<i>Vata-Kaphaghna, Rechana</i>
7	<i>Jala</i>	<i>Ayukta Rasa</i>	<i>Laghu</i>	<i>Sheeta</i>	<i>Madhura</i>	<i>Tridoshashana, Pachana, Pathya</i>
8	<i>Sheeta Jala</i>	<i>Madhura</i>	<i>Laghu, Sheetana</i>	<i>Sheeta</i>	<i>Madhura</i>	<i>Pittashamaka, Dahaprashamana, Raktashodhaka</i>

following the *Gandhaka Varga* of *Rasa Tarangini*; readers consulting compendia that additionally record a *Madhura* component of *Rasa* should note this variance across sources.

effect before it is itself digested, and *Vikasi*, the property of causing looseness at the level of the *Dhatu*s and joints. Drawn from the *Dashavidha Visha Guna* description of *Upavisha Dravyas* under which *Jayapala* is classified, these *Gunas* predict an onset of action fast enough, and a systemic reach wide enough, to be readily modulated by a change in *Anupana*, strengthening the case, developed in Section 4.4, that *Jayapala* is the constituent whose action the *Anupana* chiefly regulates. This uniformly *Ushna-Teekshna* character underlies the drastic *Rechana*

action of the formulation and is central to the rationale for its *Anupana*.

4.3 Classical Textual Basis for *Sheeta Jala* as *Anupana*

The prescription of cold water as *Anupana* is recorded directly in the classical verse describing the formulation, at *Bhaishajya Ratnavali*, *Udara Roga Adhikara*, Chapter 40, Verses 65-66.⁶ The verse instructs that the *Yoga*, prepared with *Shunthi*, *Maricha*, purified *Tankana* and *Gandhaka* together with *Jayapala*, is taken with a palmful (*Chulluka*) of water, and that purgation continues for as long as the patient tolerates it, cold water being drawn again and again until the desired evacuation is achieved. Comparable instructions recur in the general descriptions of *Rasendra Chintamani*⁷, *Rasa Ratna Samuchchaya*⁸, *Rasendra Sara Sangraha*⁹ and *Rasayoga Sagara*¹⁰, where *Anupana* is variously recorded as *Jala*, *Chulluka Jala* with *Sarkara*, *Sheetala Jala* or *Sheeta Jala*, depending on the specific variety and indication.

4.4 Jayapala as the Pharmacologically Prominent Ingredient of *Icchabhedi Rasa*

Establishing which single ingredient of *Icchabhedi Rasa* is responsible for its defining action is necessary before the rationale of *Anupana* can be discussed, since an *Anupana* is classically selected to regulate the dominant *Dravya* of a *Yoga*. Two independent lines of evidence, one classical, the other pharmacological, converge on *Shuddha Jayapala*.

Standard *Dravyaguna* sources record that among the ingredients of *Icchabhedi Rasa*, *Shuddha Jayapala* alone possesses *Rechana Karma*. *Shuddha Parada* and *Shuddha Gandhaka* function through *Yogavahi Guna*, carrying associated drug into the *Srotas* rather than independently producing purgation. *Shunthi* and *Maricha* contribute *Dipana* and *Ushna* support, and *Shuddha Tankana* serves a moderating, near-antidotal role, pacifying the *Pichila* and *Sandra Guna* of *Kapha* and acting as a partial antidote to *Jayapala*.¹³ *Icchabhedi Rasa* is therefore best understood as a *Jayapala*-centred formulation in which every other ingredient carries, potentiates, supports or restrains the action of *Jayapala*, rather than as a formulation of co-equal purgative agents. This classical prominence is confirmed in the contemporary pharmacological literature. *Croton tiglium* L. seeds, bark and oil have a well-documented phytochemical and pharmacological profile, including antibacterial, anti-inflammatory and strongly purgative activity.¹⁶ *Croton tiglium* L. seeds are named as the

defining botanical ingredient of *Icchabhedi Rasa* and the related *Ashvakanchuki Rasa* in recent *Shodhana* research,¹⁷ and a 2026 conceptual review identifies purified *Croton tiglium* L. seed, together with *Kajjali*, as the two defining constituents, attributing its action to croton oil-driven acceleration of gastrointestinal motility.⁴ The active principles, principally phorbol esters of the phorbol-12-myristate-13-acetate type and crotonic acid, have been isolated and quantified from *Croton tiglium* L. seeds by high-performance liquid chromatography,^{18,19} and are absent from every other ingredient. *Jayapala* is thus both the classically designated *Rechaka Dravya* and the sole biochemically active purgative agent in the formulation; the remaining ingredients function as its carriers, potentiators or moderators. Any explanation of *Anupana* selection in *Icchabhedi Rasa* is therefore, at its core, an explanation of how *Anupana* interacts with *Jayapala*.

4.5 Virya-Viparyaya: The Rationale for *Sheeta*, and Not *Ushna Jala*

Dravyaguna Vijnana explains the action of two combined *Dravyas* based on their relative *Guna* and *Virya*.¹³ A substance of *Samana Guna* reinforces the primary drug's effect; a substance of *Viparyaya Guna* checks, moderates or directs it. *Icchabhedi Rasa* is entirely *Ushna* and *Teekshna* in composite potency, as shown in Table 1, so an equally *Ushna Anupana* would reinforce this without restraint, correlating with the observation that warm liquids intensify and then abruptly terminate purgation rather than sustaining it. *Sheeta Jala*, being *Viparyaya* to the formulation's *Ushna Virya*, acts as a counterbalancing vehicle: its *Sthambhana* tendency, described by *Hemadri* and *Sushruta*, moderates the otherwise unchecked *Ushna-Teekshna* action of the *Rasa Dravyas* and the *Rechana* action of *Jayapala*, converting an abrupt, potentially violent purgation into one that is controlled and sustained for as long as cold water continues to be taken.^{12,14}

The *Yogavahi Guna* of *Shuddha Parada* and *Shuddha Gandhaka*, the property by which they carry the formulation rapidly into the *Srotas*, is a further relevant classical principle. *Sheeta Jala*, acting through the opposite-potency principle upon this *Ushna-Teekshna* core, is proposed to restrict the distribution and rate of action of the *Yoga* to the *Annavaha* and *Pureeshavaha Srotas*, aligning with the view that *Sheeta Jala* restrains uptake of the drug's constituents and keeps its purgative effect confined largely to the gut.⁴

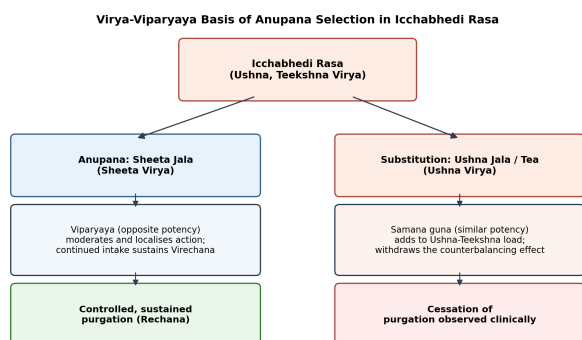


Figure 2. Proposed *Virya-Viparyaya* schema explaining the contrasting clinical outcome of *Sheeta Jala* versus *Ushna Jala* as *Anupana* with *Icchabhedi Rasa*.

4.6 Anupana Across the Classical Tradition

Rasashastra dosing logic classically varies *Anupana* with indication and with the relative proportion of *Ushna-Teekshna Dravyas* in a formulation. The verse describing the principal variety of *Icchabhedi Rasa*, at *Bhaishajya Ratnavali*, *Udara Roga Adhikara*, Chapter 40, Verses 65-66, records repeated *Chulluka Jala* as the *Anupana*, continued for as long as purgation is required. *Sheeta Jala*, *Sheetala Jala* and *Chulluka Jala* are recorded as the *Anupana* in the general descriptions of *Rasendra Chintamani*, *Rasa Ratna Samuchchaya*, *Rasendra Sara Sangraha* and *Rasayoga Sagara*, consistent with this verse. A systematic, variety-by-variety mapping of *Anupana* against *Jayapala* proportion across all twenty-four documented varieties would require direct, verse-by-verse consultation of each primary edition and is proposed as future work (Section 7).

4.7 Proposed Hypothesis: Agni-Mediated Modulation of Jayapala Phorbol Ester Stability

The chemistry of *Jayapala's* active principle offers a specific, testable explanation of the *Sheeta Jala* rationale beyond the *Virya-Viparyaya* reasoning of Section 4.5.

The purgative and irritant action of *Shuddha Jayapala* is attributable principally to phorbol esters of the phorbol-12-myristate-13-acetate (PMA) type and to crotonic acid, which act locally at the intestinal mucosa, activating protein kinase C and provoking fluid secretion, mucosal irritation and increased peristalsis, confirmed in isolated intestinal epithelial and colonic smooth muscle preparations.²⁰ This is a contact, local-irritant mechanism whose intensity and duration depend on how long an intact, active ester remains in contact with the gut wall rather than on systemic absorption. PMA is used here as the representative member of a wider family of tiglane phorbol diesters in *Croton tiglium* L. seed oil, for example 12-O-acetylphorbol-13-decanoate, and the hydrolytic argument developed below applies, in principle, to this broader ester family.

PMA-type phorbol esters are not chemically inert once inside the body. Independent biochemical studies demonstrated the metabolic conversion of this phorbol ester in mouse skin and liver microsomes,²¹ identified a carboxylesterase in mammalian liver that hydrolyses these phorbol diesters and showed that the tumour-promoting phorbol ester and regulatory diacylglycerols are substrates for this enzyme,²² and isolated a distinct ester hydrolase from murine liver specifically active on phorbol diesters.²³ A 2025 study on Thai traditional detoxification processing of *Croton tiglium* L. seeds demonstrated by HPLC that heat and aqueous processing measurably reduces PMA content, attributing this to hydrolysis of PMA to the less active phorbol, and noting that phorbol esters administered orally are subject to hydrolysis by esterases in the liver and intestine.¹⁸

Two further facts complete the proposed chain of reasoning. Enzymatic hydrolysis is, as a general principle of enzyme kinetics, temperature dependent, proceeding more slowly as temperature falls. Cold stimuli have been shown, in a controlled human study using the cold pressor test, a cutaneous, reflex-mediated stress response rather than direct cooling of an ingested bolus, to delay rather than hasten gastric emptying, through reduced antral and antropyloroduodenal motor activity,²⁴ a finding more directly paralleled by a rodent study in which intragastric cold water administration itself inhibited colonic

motility,²⁵ while *Ushna Guna* substances are classically *Pachana* and *Agni-Vardhaka*, hastening digestive transformation.¹²

Classical *Agni* is a broader digestive-transformative construct than gastric emptying rate alone; the two are treated here as a working correlate for the purposes of this hypothesis, not as strict equivalents, and this correlation itself remains to be tested.

This biochemical layer is intended to complement, not substitute for, the classical *Sthambhana*-based explanation of Section 4.5. The *Sthambhana* action of *Sheeta Guna* on peristalsis is, by itself, a sufficient classical account of prolonged intestinal transit, but it does not on its own explain why an intact purgative principle should require prolonged mucosal contact in order to remain effective. The present hypothesis specifies the pharmacodynamic consequence of that prolonged contact, namely preserved phorbol ester activity, and in doing so extends the classical account to a falsifiable molecular claim rather than restating it in modern vocabulary. Two sub-hypotheses separate the mechanism into components that can be tested independently.

H1 (temperature-dependent hydrolysis). The rate at which gut and hepatic esterases hydrolyse *Jayapala's* active PMA-type phorbol esters to the less active phorbol is temperature dependent, proceeding more slowly at lower tissue temperature.

This rests on enzyme-kinetic principles and the hepatic and dermal esterase evidence cited above (refs 21-23), extended to the intestinal mucosa. This extension is presently an assumption rather than a demonstrated finding: the cited carboxylesterase and ester-hydrolase evidence derives from rat and mouse liver, mouse skin and murine serum (refs 21-23), and no study identified in this review has directly measured carboxylesterase or ester-hydrolase activity against PMA-type phorbol esters in human or animal intestinal mucosal tissue. H1 should therefore be read as a cross-tissue extrapolation from hepatic and dermal esterase kinetics, pending direct intestinal confirmation (Section 7).

H2 (site-specific transit effect). The sustaining effect of *Sheeta Jala* requires that cold water repeatedly slow transit and lower luminal temperature specifically at the intestinal mucosal surface, not merely delay gastric emptying as a single event: a slower gastric emptying rate alone would postpone rather than sustain *Virechana*, the opposite of the clinical observation. H2 proposes that successive small volumes of *Sheeta Jala*, drawn again as instructed classically (Section 4.3), continually replenish a cooled luminal environment at the intestinal level, sustaining local hydrolytic slowing at the site of ongoing mucosal contact.

H1 is supported, at one remove, by hepatic and dermal esterase-kinetic evidence. H2 is not directly tested by either cited motility study, which examined gastric emptying²⁴ and colonic motility²⁵ as separate endpoints in separate species without measuring intestinal-segment-specific transit or luminal temperature alongside esterase activity. H2 is accordingly the more fragile component and the priority target for direct testing (Section 7).

Combining H1 and H2, *Sheeta Jala*, by lowering local luminal temperature and, through repeated small-volume administration, sustaining delayed transit at the intestinal

level, is proposed to slow hydrolysis of *Jayapala's* active phorbol esters by gut and hepatic esterases, preserving the drug in active form for longer mucosal contact and sustaining *Virechana* for as long as cold water is administered. *Ushna Jala*, by raising local temperature

and accelerating gastric emptying and digestive transformation, is proposed to accelerate this hydrolytic inactivation, depleting the active ester pool and producing the abrupt cessation of purgation observed clinically. Figure 3 represents this mechanism schematically.

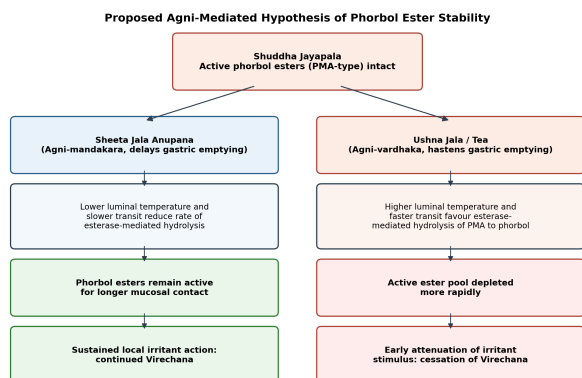


Figure 3. Proposed hypothesis linking *Anupana* temperature, gastric emptying rate, and enzymatic Illustrative thermal plausibility estimate. A representative *Chulluka* volume of 100-150 mL of water at approximately 10°C, warmed to a core or luminal temperature of 37°C, requires, using the specific heat capacity of water (4.184 J/g·°C), approximately 11-17 kJ per administration. Resting splanchnic blood flow is approximately 1500-1800 mL/min, corresponding to 25-30% of resting cardiac output.²⁸ A single such bolus would, on these figures, be buffered back toward core temperature within several minutes, considerably shorter than the duration over which sustained *Virechana* is clinically observed. This illustrates why the classical instruction to repeat cold water administration (Section 4.3) is mechanistically necessary to H2: a single bolus is unlikely to sustain a cooling effect for as long as *Virechana* continues, whereas repeated dosing could do so. Direct measurement of intraluminal temperature (Section 7) would replace this estimate.

This hypothesis refines, rather than departs from, the classical *Virya-Viparyaya* explanation of Section 4.5, proposing a specific biochemical pathway through which the *Sheeta-Ushna* opposition could operate molecularly. No study has yet measured phorbol ester hydrolysis under cold versus warm gastrointestinal conditions, nor has any study administered *Icchabhedi Rasa* with controlled *Anupana* temperature. Each component of this reasoning is independently documented, but the synthesis, and the H1/H2 division in particular, is original and requires experimental confirmation (Section 7).

4.8 Safety Considerations

Icchabhedi Rasa contains *Shuddha Parada* and *Shuddha Gandhaka* as *Kajjali*, together with *Shuddha Jayapala*, whose unpurified seed contains toxic phorbol esters and crotin. Classical contra-indications in *Rasa Tarangini* include administration to *Garbhini*, *Sootika*, *Bala*, *Vridhdha*, *Krishna* and *Ksheena*, and those with *Gudabhramsha* or *Baddhaguda*.⁵ *Rasayoga Sagara* additionally lists *Vata Roga*, general debility, childhood, old age and grief as conditions warranting caution.¹⁰ Classical dosing distinguishes *Matra* by *Vaya* and *Koshtha*, and micro-dosage of 125 to 250 mg, with defined disintegration and hardness parameters, is emphasised in

hydrolysis of *Jayapala* phorbol esters to the duration of *Virechana*.

pharmaceutical standardisation literature as essential to safe use.²⁷ *Croton tiglium* L. oil exerts a biphasic action on intestinal transit in animal models, low doses increasing and higher doses decreasing transit, underscoring the importance of precise micro-dosage²⁶. Correct classical purification (*Shodhana*) of both the mineral components, *Parada* and *Gandhaka*, and the botanical component, *Jayapala*,^{17,19} together with adherence to the classical *Anupana* and *Matra*, are inseparable components of this formulation's safety profile. If *Anupana* temperature modulates gastrointestinal transit time as proposed, it may also influence the dissolution and mucosal residence time of the co-administered *Kajjali* component, and hence its systemic mercury and sulphur absorption; this possibility is speculative and is proposed as a research question in Section 5. Self-medication without qualified supervision is not advisable.

4.9 Limitations of This Analysis

This analysis is subject to the following limitations, distinct from the research gaps identified in Section 5.

First, it is a conceptual and literary synthesis rather than a systematic review, and no pre-registered search protocol was applied to the contemporary pharmacological literature.

Second, a quantitative, variety-by-variety comparison of ingredient proportions and *Anupana* across all twenty-four documented classical varieties is not attempted; the argument for *Jayapala's* pharmacological prominence rests on qualitative classical *Karma* descriptions (Section 4.4) and modern pharmacological evidence.

Third, the central hypothesis links enzyme-kinetic evidence obtained in hepatic and dermal systems (H1) to gastrointestinal motility evidence obtained in separate studies that did not themselves measure esterase activity, and assumes, without direct evidence, both that intestinal rather than merely gastric transit is slowed (H2) and that a small, repeated volume of cold water can alter esterase kinetics, a claim supported here only by an illustrative estimate (Section 4.7).

Fourth, one source cited for the motivating clinical observation, Reference 3, is trade literature rather than peer-reviewed clinical documentation; a systematic

search of PubMed, PubMed Central, ScienceDirect and Google Scholar did not identify a peer-reviewed clinical report of this observation.

Fifth, this article proposes no new experimental, clinical or in vitro data of its own, and the central hypothesis remains untested pending the studies specified in Sections 5 and 7.

Sixth, the *Rasadi Panchaka* values in Table 1 are drawn from standard compendium sources rather than a single authoritative classical text.

Seventh, the thermal plausibility estimate in Section 4.7 is illustrative, based on standard physiological reference ranges rather than directly measured intraluminal temperature or flow data specific to this clinical scenario. These limitations do not diminish the value of the hypothesis as a specific, falsifiable proposal, but should be considered when assessing the strength of the evidence presented.

5. IDENTIFIED RESEARCH GAP

(1) No published work has analysed *Sheeta Jala* as *Anupana* in *Icchabhedi Rasa* through the formal *Rasa-Guna-Virya-Vipaka-Prabhava* framework applied to individual *Anupana Dravyas* in classical *Bhaishajya Kalpana*.

(2) No published work has established, through systematic quantitative comparison across the twenty-four classical varieties, that *Shuddha Jayapala* is the functionally defining ingredient of *Icchabhedi Rasa* around which the remaining *Dravyas* and the *Anupana* are organised; the present article establishes this qualitatively and from modern pharmacological evidence alone.

(3) No study has measured the rate of enzymatic hydrolysis of *Jayapala's* active phorbol esters under cold versus warm gastrointestinal conditions.

(4) No experimental study has administered *Icchabhedi Rasa*, or purified *Jayapala* alone, with controlled variation of *Anupana* temperature to test the *Agni*-mediated hydrolysis hypothesis, particularly the site-specific transit claim of H2.

(5) No dose-response or temperature-response clinical documentation correlates the volume or temperature of *Anupana* with the onset, intensity and cessation of *Virechana* produced by *Icchabhedi Rasa*.

(6) The influence of *Anupana* temperature on the dissolution, absorption or systemic exposure of the mercury- and sulphur-bearing *Kajjali* component is unexplored, representing an intersection of *Dravyaguna* and *Rasashastra Visha Vijnana*.

(7) No study has measured whether repeated small-volume cold water administration produces a luminal temperature depression at the intestinal mucosa of a magnitude and duration capable of altering esterase kinetics or distinguished the effect of *Anupana* temperature on gastric emptying from its effect on intestinal transit specifically, a distinction on which H2 depends.

6. CONCLUSION

Icchabhedi Rasa is best understood, on classical and modern pharmacological evidence, as a *Jayapala*-centred formulation in which *Shuddha Parada*, *Shuddha Gandhaka*, *Shunthi*, *Maricha* and *Shuddha Tankana* carry, potentiate or moderate the action of a single biochemically active purgative agent, purified *Croton tiglium* L. seed. The prescription of *Sheeta Jala* as its

Anupana is embedded in the classical verse describing the formulation and repeated across the classical descriptions of the formulation reviewed in this article, and the *Virya-Viparyaya* logic of *Dravyaguna Vijnana* offers a coherent classical explanation for pairing a *Sheeta* vehicle with an overall *Ushna-Teekshna Yoga*. This article proposes, as an original contribution, a biochemical hypothesis extending this classical reasoning to the molecular level, divided into two separately falsifiable components: that temperature-dependent esterase hydrolysis governs inactivation of *Jayapala's* active phorbol esters (H1), and that *Sheeta Jala*, through repeated administration, sustains this slowing at the intestinal level (H2), an inactivation accelerated, by contrast, by the faster gastric transit and enhanced *Agni* of warm *Anupana*. Each element of this hypothesis rests on documented literature; the synthesis is new and remains to be tested. It is offered as a precise, falsifiable proposal, structured so that its weaker component (H2) and stronger component (H1) can be tested and reported on separately.

7. FUTURE SCOPE

(1) In-vitro or ex-vivo assay of phorbol ester hydrolysis rate in gastric and intestinal homogenate incubated at cold, body and warm temperature, testing H1.

(2) A structured clinical observational study correlating *Anupana* temperature and volume with onset time, duration and severity of *Virechana* following standard *Matra* of *Icchabhedi Rasa*.

(3) Animal studies comparing purgative response and mucosal phorbol ester residence time following administration of purified *Jayapala* or *Icchabhedi Rasa* with cold water as against warm water.

(4) In-vitro dissolution and disintegration studies of *Icchabhedi Rasa* tablets in cold versus warm aqueous media, extending the analytical parameters reported by Mehkarkar et al.

(5) Systematic textual mapping of *Anupana* selection against *Jayapala* proportion across all twenty-four classical varieties of *Icchabhedi Rasa*, based on direct, verse-by-verse consultation of each primary edition.

(6) Direct intraluminal temperature measurement, at the gastric and intestinal mucosa separately, following administration of a standard *Chulluka* volume of cold water repeated at clinically realistic intervals, testing directly the illustrative estimate of Section 4.7 and whether gastric emptying and intestinal transit are affected differentially, thereby testing component H2.

(7) A dedicated study of *Anupana* temperature's effect on *Kajjali* dissolution and systemic mercury and sulphur exposure, addressing the safety question raised in Sections 4.8 and 5.

The seven proposals above correspond directly to the numbered gaps identified in Section 5, and are intended to be read as a single set of research priorities rather than two independent lists.

8. CONFLICT OF INTEREST

The authors declare no conflict of interest.

9. SOURCE OF FUNDING

None declared.

10. ETHICAL APPROVAL

Not applicable. This article is a conceptual and literary synthesis and did not involve human participants, human data, or animal experimentation. Authors should confirm

the specific ethical-disclosure requirements of the journal to which this manuscript is submitted.

11. AUTHOR CONTRIBUTIONS

AP and HS jointly conceived the central hypothesis. AP conducted the classical textual and Dravyaguna analysis and drafted the manuscript. HS conducted the contemporary pharmacological and phytochemical literature review and critically revised the manuscript for intellectual content. Both authors read and approved the final manuscript.

REFERENCES

1. Agnivesha. Charaka Samhita [Hindi commentary by Shukla VD, Tripathi RD]. Varanasi: Chaukhambha Sanskrit Pratishthan; Sutrasthana, Chapter 15, Chikitsa Prabhritiya Adhyaya (classification of Panchakarma including Virechana).
2. Kamath N, Chavan RR, Gowda S. Icchabhedi Rasa: a herbo-mineral formulation review. *Int Ayurvedic Med J*. 2019.
3. Mohanty B, Gurav SS. Concept of Tikshna Virechana with application of Icchabhedi Rasa and fluid management in it. *Int J Ayurveda Herb Res*. 2026;4(1):1–7. doi: 10.54060/a2zjournals.ijahr.140.
4. Sarma SS. Rasa Tarangini [English translation by Angadi R]. Varanasi: Chaukhamba Surabharati Prakashan; 24th Taranga (Visopavishadi Vijnaniya), Verse 320–322, p.466.
5. Das G. Bhaishajya Ratnavali [edited by Mishra B, Shastri AD]. 18th ed. Varanasi: Chaukhambha Sanskrit Samsthana; Vol. 2, Chapter 40 (Udara Roga Adhikara), Verses 65–66.
6. Dhundhuknath. Rasendra Chintamani [Hindi translation by Mishra SN]. 1st ed. Varanasi: Chaukhamba Orientalia Publication; 2000. 9th Chapter (Udara Roga Adhikara).
7. Vagbhatacharya. Rasa Ratna Samuchchaya [edited by Shastri KA]. Udara Roga Adhikara / Uparasa Adhyaya (chapters describing varieties of Icchabhedi Rasa).
8. Bhatt GK. Rasendra Sara Sangraha [English translation by Satpute AD]. Varanasi: Chaukhamba Orientalia Publication; Udavarta Roga Adhikara Adhyaya (chapter describing the Brhat Icchabhedi Rasa variety).
9. Sharma HP. Rasayoga Sagara [Hindi translation]. Vol. 1. Varanasi: Krishnadas Academy; section describing the eighteen varieties of Icchabhedi Rasa.
10. Misra BS, Misra R, editors. Bhavaprakasha of Bhavamisra. 11th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2004. Poorvakhand, Vari Varga (chapter on the properties of water).
11. Sushruta. Sushruta Samhita, Sutrasthana [Hindi commentary by Shastri KA]. Varanasi: Chaukhambha Sanskrit Sansthan; Sutrasthana 46/415.
12. Lucas DS. Dravyaguna Vijnana. Vol. 2. Varanasi: Chaukhamba Visvabharati Prakashan; Detail Drugs, p.358–362, p.414–418; Non-Detail Drugs, p.654.
13. AyurSoln. Sheet x Ushna Guna [Internet]. Moodbidri: AyurSoln; 2021 [cited 2026 Sep 13]. Available from: <https://ayursoln.com/dravyaguna-ayurvedic-pharmacology/concepts-of-dravyaguna/basic-concepts-of-dravyaguna/concept-of-guna-property/gurvadi-guna/sheet-x-ushna-guna/>
14. Government of India. The Ayurvedic Formulary of India. Part I. 2nd ed. New Delhi: Department of AYUSH, Ministry of Health and Family Welfare; 2003. 20-Rasayoga, 20:5, p.258–259.
15. Zhang T, Liu Z, Sun X, Liu Z, Zhang L, Zhang Q, Peng W, Wu C. Botany, traditional uses, phytochemistry, pharmacological and toxicological effects of Croton tiglium Linn.: a comprehensive review. *J Pharm Pharmacol*. 2022;74(8):1061–1084. doi:10.1093/jpp/rgac040.
16. Jamadagni P, Ranade A, Bharsakale S, Chougule S, Jamadagni S, Pawar S, Prasad GP, Gaidhani S, Gurav A. Impact of Shodhana, an Ayurvedic purification process, on cytotoxicity and mutagenicity of Croton tiglium Linn. *J Ayurveda Integr Med*. 2023;14(2):100710. doi:10.1016/j.jaim.2023.100710.
17. Poowanna R, Pulbutr P, Kijjoa A, Nualkaew S. Purgative effect, acute toxicity, and quantification of phorbol-12-myristate-13-acetate and crotonic acid in Croton tiglium L. seeds before and after treatment by Thai traditional detoxification process. *Int J Mol Sci*. 2025;26(16):7714. doi:10.3390/ijms26167714.
18. Pal PK, Nandi MK, Singh NK. Detoxification of Croton tiglium L. seeds by Ayurvedic process of Shodhana. *Anc Sci Life*. 2014;33(3):157–161. doi:10.4103/0257-7941.144619.
19. Wang X, Lan M, Wu HP, Shi YQ, Lu J, Ding J, Wu KC, Jin JP, Fan DM. Direct effect of croton oil on intestinal epithelial cells and colonic smooth muscle cells. *World J Gastroenterol*. 2002;8(1):103–107. doi:10.3748/wjg.v8.i1.103.
20. Berry DL, Bracken WM, Fischer SM, Viaje A, Slaga TJ. Metabolic conversion of 12-O-tetradecanoylphorbol-13-acetate in adult and newborn mouse skin and mouse liver microsomes. *Cancer Res*. 1978;38(8):2301–2306.
21. Mentlein R. The tumor promoter 12-O-tetradecanoyl phorbol 13-acetate and regulatory diacylglycerols are substrates for the same carboxylesterase. *J Biol Chem*. 1986;261(17):7816–7818.
22. Shoyab M, Warren TC, Todaro GJ. Isolation and characterization of an ester hydrolase active on phorbol diesters from murine liver. *J Biol Chem*. 1981;256(23):12529–12534.
23. Fone DR, Horowitz M, Maddox A, Akkermans LM, Read NW, Dent J. Gastrointestinal motility during the delayed gastric emptying induced by cold stress. *Gastroenterology*. 1990;98(5):1155–1161.
24. Yang X, Xi TF, Li YX, Wang HH, Qin Y, Zhang JP, Cai WT, Huang MT, Shen JQ, Fan XM, Shi XZ, Xie DP. Oxytocin decreases colonic

- motility of cold water stressed rats via oxytocin receptors. *World J Gastroenterol.* 2014;20(31):10886–10894. doi: 10.3748/wjg.v20.i31.10886.
25. Mehkarkar D, Rathi B, Rajput DS, Wanjari A, Khan M. Pharmaceutical standardization of Icchabhedi Rasa: an Ayurvedic formulation. *Joinsymed.* 2018 Apr 6;6(1):10–13.
26. Wang X, Zhang F, Liu Z, Feng H, Yu ZB, Lu Y, Zhai H, Bai F, Shi Y, Lan M, Jin J, Fan D. Effects of essential oil from *Croton tiglium* L. on intestinal transit in mice. *J Ethnopharmacol.* 2008;117(1):102–107. doi: 10.1016/j.jep.2008.01.023.
27. Harper D, Chandler B. Splanchnic circulation. *BJA Educ.* 2016;16(2):66-71. doi:10.1093/bjaceaccp/mkv 017.