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# AN UPDATED REVIEW OF HINGULESHWARA RASA – A HERBO-MINERAL FORMULATION

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# ABSTRACT

The oldest surviving healing system is the Ayurvedic system. Rasashastra is a branch of Ayurveda that is considered a therapeutic utilization of metallic-mineral substances for treating various diseases. There are several famous classical formulations successfully practised in Ayurveda for treating disease, but there is a lack of data regarding their proper pharmacokinetics & pharmacodynamics. One of the widely practised Ayurvedic formulations is *Hinguleshwara Rasa. Hinguleshwara Rasa* is a known herbo-mineral *Kharaliya Rasayana* formulation. Different classical references of *Hinguleshwara Rasa* are created with different compositions. The present study is focused on compiling all available literature regarding the pharmacological actions and properties of in-vivo, invitro, and clinical studies done on *Hinguleshwara Rasa*. Keywords: Hinguleshwara Rasa, Kharaliya Rasayana, In-vivo, In-vitro, Clinical study

#### INTRODUCTION

Kharaliya Rasayana is produced in Khalwa Yantra without Agni Samskara. As per various classical references, Hinguleshwara rasa is one such Kharaliya Rasayana effective in Vataja Jwara. Hinguleshwara Rasa, as the name suggests, contains Hingula, the main ingredient of the formulation, along with Pippali and Vatsanabha. Various classical references to Hinguleshwara Rasa are found in Bhaishajya Ratnavali, Rasa Tarangini, etc. The present paper highlights the information about the Hinguleshwara Rasa.

#### <u>Hinguleshwara Rasa</u>

In Bhaishajya Ratnavali, Hinguleshwara Rasa is quoted. Generally, Hinguleshwara Rasa, a herbomineral formulation, is prepared as per reference of Bhaishajya Ratnavali, which consists of Shuddha Hingula, Shuddha Vatsnabha and Pippali

Churna. All three dravyas are made into fine powder and triturated with Jala till the homogenous consistency of Vati is accomplished. Then, the Vati of Gunjaardha (1/2 Ratti = 62.5 mg) dose is formed<sup>[1]</sup>. It is indicated especially for Vataja Jwara, which means it shows antipyretic activity. In Rasa Tarangini, Hinguleshwara Rasa is indicated in Amavata, Navajwara, Jirnajwara, Savirama jwara and Vataja Jwara<sup>[2]</sup>. Hinguleshwara Rasa is described in Rasa Ratna Samucchaya as Brihat Jwarankusha Rasa. Through assessment of different Rasashastra texts, total no. of three ingredients i.e Shuddha Hingula, Shuddha Vatsanabha Å Pippali were analysed in Hinguleshwara Rasa. Hingula is the principal ingredient in all the references. This reference is mainly taken for research work because of its effectiveness and low dose.

Table 1: Ingredients, Anupana, Dose of *Hinguleshwara Rasa* as per Classical texts.

Sl.No	Ingredients	Anupana/ Sahapana	Matra	Bhavana with Duration
B.R <sup>[1]</sup>	1)Shuddha Hingula-1Pala 2) Shuddha Vatsanabha-1Pala 3)Pippali-1Pala	Madhu	½ Gunja	-
B.B.R(1) <sup>[3]</sup>	1) Shuddha Hingula-1 Tola 2) Shuddha Gandhaka-Tola 3)Tamra Bhasma-2Masha	Madhu,Dhanya kwa- tha, Jeeraka kwatha	2 Gunja	Salmali satwa bhavitha/ 1 yama
B.B.R(2) <sup>[3]</sup>	<ol> <li>Shuddha Hingula-1Pala</li> <li>Shuddha Jayaphala-3Pala</li> <li>Shuddha Parada-1Pala</li> </ol>	Mishari	1 Gunja	Dantimula kwatha/ dinardha
B.B.R(3) <sup>[3]</sup>	1) Shuddha Hingula-1Pala 2) Shuddha Vatsanabha-1Pala 3) Pippali-1Pala	Sheetala jala	Mulika beeja	-
B.R.R.S <sup>[4]</sup>	1) Shuddha Hingula-1Pala 2) Shuddha Vatsanabha-1Pala 3) Pippali-1Pala	Madhu	2 Gunja	-

R.K <sup>[5]</sup>	1) Shuddha Hingula-1Pala	Madhu	2 Gunja	-
	2) Shuddha Vatsanabha-1Pala			
	3) Pippali-1Pala			
R.T <sup>[6]</sup>	1) Shuddha Hingula-1Pala	-	<sup>1</sup> /2 Ratti	-
	2) Shuddha Vatsanabha-1Pala		(sardha	
	3) Pippali-1Pala		yava)	
R.R.S <sup>[7]</sup>	1) Shuddha Hingula- 2Pala	Mishari	1 Gunja	Danti kwatha/
	2) Shuddha Jayaphala-3Pala			dinardha
	3) Shuddha Parada-1Pala			
R.M <sup>[8]</sup>	1) Shuddha Hingula- 1Pala	Madhu	2 Gunja	-
	2) Shuddha Jayaphala-Pala			
	3) Shuddha Parada-1Pala			
A.F.I-Part2 <sup>[9]</sup>	1) Shuddha Hingula- 1Pala	Madhu	½ Gunja	Jala
	2) Shuddha Jayaphala-Pala	Mandoshna jala		
	3) Shuddha Parada-1Pala			

Note: B.R-Bhaishajya Ratnavali, B.B.R-Bharat Bhaishajya Ratnakar, R.K-Rasa Kamadhenu, R.T-Rasa Tarangini, R.R.S-Rasa Ratna Samucchaya, R.M-Rasa Manjari, A.F.I.-The Ayurvedic Formulary of India.

#### **DRUG REVIEW**

#### The Rasa Panchaka of Hinguleshwara Rasa is annotated as follows:

Table 1: Rasa Panchaka (Ayurvedic Pharmacology) of contents of Hinguleshwara Rasa<sup>[10]</sup>

Drugs	Rasa	Guna	Virya	Vipaka	Doshaghnata	Karma
Cinnabar	Tikta,	Laghu,	Ushna	Katu	Tridoshahara	Jwaraghna,
(Hgs)	Kashaya,	Ruksha,				Vishahara
	Katu	Tikshna				
Vatsnabha	Madhura	Laghu,	Ushna	Madhura	Vatakaphahara	Jwarahara,
(Aconitum		Ruksha,				Jangama
ferox Wall ex)		Tikshna,				Vishahara
		Vyavayi,				
		Vikasi				
Pipali	Katu	Laghu,	Ushna	Madhura	Vatakaphahara	Deepana,
(Piper longum		Snigdha,				Pachana,
Linn).		Ushna				Vrushya,
						Rasayana

#### Table 2: Rasa Panchaka (Ayurvedic Pharmacology) of Hinguleshwara Rasa<sup>[11]</sup>

Rasa Panchaka	Rasa	Guna	Virya	Vipaka	Doshaghnata	Karma
Hinguleshwara Rasa	Katu,	Tikshna	Ushna	Katu	Tridoshahara	Jwaraghna,
	Tikta					Pachana,
						Rasayana

Drug	Part used	Phytoconstituents	Pharmacological action
Hingula	-	-	Antimicrobial activity <sup>[11]</sup>
(Red sulphide of mercury)			
Vatsanabha	Root	Indaconitine,	Antipyretic,
(Aconitum ferox Wall ex)		Chasmanine,	Analgesic,
		Chasmaconitine	Sedative
Pippali	Fruit	Piperine,	Anti-inflammatory,
(Piper longum Linn.)		Piplartine,	Antibacterial,
		Piperundecalidine	Antimalarial,
			Immunostimulatory

#### Table 3: Chemical constitution and Pharmacological actions of *Hinguleshwara Rasa*<sup>[12][13]</sup>

*Hingula*(Cinnabar): *Hingula* is a red sulphide of mercury. It contains about 14 % of sulphur and 86% of mercury. *Hingula* owns *Jwarahara*, *Pachan* property.<sup>[14]</sup>

Aconitum chasmanthum Stapf. Ex Holmes. (Fam. Ranunculaceae)Rasatarangini describes the Antipyretic, Appetizer, Digestive, & Anti rheumatic properties of *Vatsanabha*.<sup>[15]</sup> Drugs with the Yogavahi property can adopt the qualities of the substances with which they are combined without losing their unique properties. As a result, such drugs can be used in different formulations to enhance the activity of those formulations. Bhavaprakasha and Rasatarangini mention Vatsanabha as Yogavahi, i.e., bioenhancer. If we want any formulation to react quickly in an emergency, at least one medication with Vyavayi should be added.<sup>[16]</sup>

Aconite is alleged to be a marked antipyretic, with temperature reduction due to various causes 1. The depressing action of the drug upon all muscle tissue; 2. This causes dilatation of the cutaneous blood vessels due to the peripheral action of aconite; 3. The slowing of the circulation reduces the metabolism.<sup>[17]</sup> *Piper longum Linn.* (Fam.-Piperaceae): It is Piperine is the main active constituent in the Piper longum Lin. Piperine is an alkaloid found naturally in plants belonging to the Piperaceae family, such as Piper nigrum L.(black pepper) and Piper longum L.(long pepper). It possesses antipyretic, anti-inflammatory, and analgesic properties. [18] The LD<sub>50</sub> value of piperine in mice was 750-800 mg/kg.

Piperaceae family, such as Piper nigrum  $L.\Box$  (black pepper) and Piper

[5] longum L.  $\Box$  (long pepper).

#### Pharmaceutical and Analytical Study of *Hinguleshwara rasa*<sup>[19]</sup>

*Hinguleshwara Rasa* contains marker integral Glycosides, Alkaloids, Steroids, Terpenoids, and Reducing sugar. **Table 4: Pharmaceutical and Analytical Study of** *Hinguleshwara Rasa* 

Physico-chemical Analysis	Value
Loss on drying	4.02%
Total Ash Value	7.82%
Water Soluble Extractive	18.2%
Alcohol Soluble Extractive	16.81%
рН	8.82%
Appearance	Slightly crimsons red
Odour	Strong
Taste	Bitter
Moisture Content	1.3%
Acid Insoluble Ash	0.16%

Mercury Content	22.56%
Sulphur Content	18.39%
Average Diameter	0.250 cm
Average Length	0.674 cm
Average Weight	119mg
Friability	2.2
Hardness	<1Kg/cm <sup>2</sup>
Disintegration Time	5 min

# **Evaluation of Hinguleshwara Rasa by ICP AES Elemental Qualitative Analysis for Standardiza-**<u>tion<sup>[20]</sup></u>

ICP AES elemental qualitative analysis is used for precious metal estimation at low levels and heavy metal estimation at sub-ppm levels & in pharmaceutical industries. In Shuddha Hingula (purified Cinnabar), we found elements like Chromium (Cr), Sodium (Na), and Tungsten (W), but these elements were not present in a sample of unpurified raw Hingula. In the sample of Shuddha (purified) and Ashuddha (un-purified) Vatsanabha, we did not find any significant element in this test. In a sample of Hinguleshwara rasa, we have not found elements which are present in Shuddha Hingula & Shuddha Vatsanabha like Chromium (Cr), Gallium (Ga), Molybdenum (Mo), Nickel (Ni), Lead (Pb), Tungsten (W). While preparing any formulation, we concluded that some elemental changes occurred after purification and trituration. No significant peculiar element was found in *Hinguleshwara Rasa*.

# <u>Clinical indications of *Hinguleshwara Rasa:* an experiential and scientific view<sup>[21]</sup></u>

Rasaaushadhi preparation destroys the infection as well as increases the immunity in the patients. *Hinguleshwara Rasa* is a preparation commonly given for various types of fevers and respiratory infections. It contains major ingredients like *Shuddha Hingula* and *Shuddha Vatsanabha*; Pippali is *Dipana, Pachana, Amahara* and *Rasayana* in action. *Hingula* is *also rejuvenating, antibacterial, immunomodulatory, anti-infective, bactericidal, and anthelminthic*, but Hinguleshwara Rasa is fruitful in allergies, respiratory infection, and pyrexia. After the administration of *Hinguleshwara Rasa,* less adverse drug reactions are observed. It has shown desired actions when given with specific adjuvants in specific diseases.

Disease	Adjuvant Medicine
1. Acute bronchitis	Vasakarishta
2. Bronchiectasis	Shwasakuthara Rasa/Pushkara Mulasava/Soma Choorna.
3. Chronic bronchitis	Dashamoola Katutraya Kashaya / Vasakarishta
4.Chronic bronchial asthma	Shwasakuthara Rasa/ Pushkaramoolasava / Soma Choorna
5. Cor pulmonale	Prabhakara Vati / Arjunarishta / Vasakarishta
6. Deviated nasal septum	Laghu Sootha Shekhara Vati / Roudra rasa /
	Pushkaramoolasava.
7. Emphysema	Poornachandrodaya Rasa/Talisadi Choorna/Vasakarishta
8.Galashotha	Vranapahari Rasa/Pippalyasava
9. Jeerna Jwara	Arogyavardhini Vati/Amritarishta
10. Laryngitis	Sheetamshu Rasa/Pippalyasava
11. Nava Jwara	Amruthothara Kashaya/Amritarishta
12. Nasal polyps	Roudra rasa /Sheetamshu Rasa/Dashamoolarishta
13. Pratishyaya	Naradiya Lakshmivilasa Rasa/Pushkaramoolasava

#### Amayika Prayoga

14. Pinasa	Naradiya Lakshmivilasa Rasa/Pushkaramoolasava			
15. Pharyngitis	Sheetamshu Rasa/Pippalyasava			
16. Pulmonary Kochs	Anti Kochs Treatment/Pushkaramoolasava			
17. Purana Jwara	Godanti Bhasma/Mahasudarshana Kashaya			
18. Rheumatoid arthritis	Simhanada Guggulu/Maharasnadi Kashaya/Kshara Basti			
19. SLE	Hemagarbha Pottali/ Maharasnadi Kashaya/ Pippalyasava			
20. Tracheitis	Sheetamshu Rasa/Somasava			
21. Udara Krimi	Krimimudgara Rasa/Vidangarishta			
22. Vishama Jwara	Sudarshana Ghana Vati/Puta Pakwa Vishamajwarantaka lauha/Saptaparna			
	Kashaya			

#### Evaluation of the antibacterial activity of Hinguleshwara rasa<sup>[22]</sup>

*Hinguleshwara Rasa* was tested against pathogenic bacteria strains Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Salmonella typhi and Pseudomonas aeruginosa for the antibacterial activity which causes the infection in the human body—to study antibacterial action in a vitro well diffusion method used. *Hinguleshwara Rasa* was trailed with bacteria at different concentrations.

Bacteria	12.5%	10.0% Concentration	5.0% Concentration	
	Concentration			
Streptococcus aureus	Moderate sensitive	Highly sensitive	Insensitive	
Streptococcus pyogenes	Highly sensitive	Highly sensitive	Highly sensitive	
Escherichia coli	Moderate sensitive	Less sensitive	Less sensitive	
Salmonella typhi	Highly sensitive	Highly sensitive	Highly sensitive	
Pseudomonas aeruginosa	Highly sensitive	Highly sensitive	Highly sensitive	

Hinguleshwara Rasa was highly potent against Streptococcus pyogenes, Salmonella typhi, and Pseudomonas aeruginosa.

#### Mode of Action of Hinguleshwara Rasa<sup>[10]</sup>

In biomedical science, Fever occurs due to an imbalance of body temperature, which is controlled by the hypothalamus. This temperature regulation is affected by Pyrogens, which can increase the thermostat, causing a rise in body temperature. When these pyrogens flow through the hypothalamus, they bind to specific receptors in the hypothalamus, which is why body temperature increases, finally producing fever.

Jwara is caused by Ama, which is formed by Mithyahara-Vihara. Hinguleshwara Rasa has Tikshna, Ruksha, and Ushna properties, which will enter into the Srotas and directly work on the hypothalamus to control the body temperature and decrease the fever. Ama is considered the main reason for Jwara; the Deepan and Pachana guna of these Dravyas help complete Ama Pachana and relieve the Sroto-Avarodha. In such a manner, it cures the Jwara. One should also have a better knowledge of which organ & how the medicine will work for the good line of treatment. In *Jwara Roga*, one such unique formulation with minimal ingredients that has proven useful is *Hinguleshwara Rasa*.

#### Effect of *Hinguleshwara Rasa* in *Jwara*<sup>[23]</sup>

Jwara- At the time of birth and death it is present. It afflicts the body, the senses and the mind. The certain symptoms of Jwara are an increase in the temperature of the body, anorexia, excessive thirst, malaise, body ache with heaviness, and pain in the cardiac region. *Vatsanabha* have active principles like aconitin, pseudoaconitine, these acts as inflammatory, analgesic, diaphoretic. These properties reduce phlegm, inflammation, and fever. It increases the absorption and smooth transportation of the drug into the cell membrane. Pippali contains active principle Piperine, which acts as an immuno-modulator & antiinflammatory.

In ayurveda, *Jwara* is caused by the weakness of *Jatharagni* and the formation of *Ama*. In the *Jwara*,

the dosha is "Vata", Dushya is "Rasa Dhatu", Adhishthana is "Amashaya", and Srotas are Swedavaha and Annavaha, Lakshana of Srotodushti is "Vimarga gamana or Sanga", and effect on Agni is "Agnimandhya". Hinguleshwara rasa contains three ingredients: Shuddha Hingula, Shuddha Vatsanabha, and Pippali. Hinguleshwara rasa contains Hingula, which acts on Jwara. Hingula has the property of Katu, Kashaya, Tikta Rasa, Ushna Virya, Laghu, Ruksha, Tikshna Guna, Katu Vipaka, Jwaraghna, Tridoshahara, Vishahara, it acts as Agnideepaka, reduces Ama dosha here with these properties. Vatsanabha reduces the fever with the help of Vyavayi and Vikasi Guna. Vatsanabha has the property of Ushna Guna, Yogavahi, Katu, Tikta, Kashaya Rasa, Katu Vipaka, Ushna Virya, Kapha-Vata Shamaka. It is act as Shoolahara, Jwarahara, Shwasahara, Kasahara Rasayana, Deepana, Pachana. The Vyavayi, Vikasi Guna, Tikshna and Ushna Veerya of Shuddha Vatsanabha pass through the Sukshma Srotas by Yogavahitwa and perform to Swedajanana which is Lakshana of Jwara Muktiawastha. Pippali has the properties of Katu Rasa, Laghu, Snigdha, Teekshna guna, Anushna Virya, Madhura Vipaka, and Kapha-Vata Shamaka. It causes Deepana, Pachana, Jwarahara, Rasayana, Kasahara, and Shwasahara to reduce Ama and act as Agnideepak. Hinguleshwara Rasa are Katu, Tikta Rasa, Laghu, Ruksha, Tikshna Guna, Ushna Virya, Katu Vipaka and act as Jwarahara, Deepana, Pachana, Tridoshahara, Amadoshahara. If we treat Mandagni, Jwara will also resolve. Hinguleshwara Rasa is Ushna, Tikshna and Sweda Janak, so it unblocks Srotas. So, Hinguleshwara Rasa is beneficial for the treatment of Jwara.

#### Role of *Bhavana* Process in the antipyretic effect of *Hinguleshwara Rasa*<sup>[24]</sup>

*Bhavana* is a kind of *Samskara* performed to modify the properties of the drug. *Hinguleshwara Rasa* is a formulation mentioned under *Jwaradhikara, which has Jwaraghna property that* is potentiated by giving *Bhavana* with *Nimbu Swarasa*. As per the experimental study, Bhavita Hinguleshwara Rasa has a long and sustained antipyretic activity profile compared to *Hinguleshwara Rasa* without *Bhavana*. Paracetamol provides only temporary symptomatic relief, whereas Hinguleshwara Rasa resolves the basic pathology of the Jwara through Ama Pachana and thus produces sustained results.

# <u>In-vitro anti-inflammatory and antioxidant activi-</u> <u>ties of *Hinguleshwara Rasa-based* herbomineral</u> <u>formulations<sup>[25]</sup></u>

In the first sample, Hinguleshwara Rasa (HR1) was prepared as per the methodology described in Rasatarangini using Shuddha Hingula (10 g), Shuddha Vatsanabha (10 g), and Pippali (10 g). In the second and third samples, Hinguleshwara Rasa was prepared by replacing Shuddha Hingula with Kajjali where Kajjali made from Hingulotha Parada and Shodhita Parada constitutes two varieties of Hinguleshwara Rasa, i.e. HR2 and HR3. In vitro, antioxidant activity was studied using 2,2-diphenyl-1-picrylhydrazyl, and the absorbance was recorded at 517 nm. For evaluating the in vitro anti-inflammatory studies, the inhibition of albumin denaturation technique was performed. The results showed that the formulation of Hinguleshwara Rasa has shown dose-dependent activity, which was observed in 100 g concentration. HR1, HR2, and HR3 showed 36.11, 17.22, and 16.11% radical scavenging activity. It could be concluded that the changes made in the formulations did not affect the in vitro anti-inflammatory and antioxidant effects of the herbomineral formulations.

# Efficacy of Hinguleshwara Rasa in Amavata<sup>[26]</sup>

All ingredients of *Hinguleshwara Rasa* are *Ushna Virya*. This synergetic effect of the constituents of *Hinguleshwara Rasa* helps to pacify *Amavata* with its predominance of *Ushna virya*. It has promising results on the ailments of Jwara, Sotha, Agnidourbalya, Gaurav, Aruchi, School, and *Angamarda* in *Amavata*. It also cures *Sthabda Gatra* (stiffness of the body).

# In-vivo Histopathological Efficacy Study of *Hinguleshwara Rasa* and Indomethacin on FCAinduced Rheumatoid Arthritis in Paw Model of <u>Rats<sup>[27]</sup></u>

Rheumatoid arthritis resembles *Amavata* disease. The effect of *Hinguleshwara Rasa* on *Amavata* is mentioned in the text of *Rasatarangini* in Ayurveda. In this study, the investigation was made to catch pre-

ventive & curative changes in the rat paw of Freud's Complete Adjuvant induced RA model. Indomethacin was kept as standard control, and Hinguleshwara Rasa was used as a treatment. Histopathology studies help to know the changes that happen before and after in the paw of standard drug rats; this study reveals that compared to indomethacin, preventive and curative action are found in Hinguleshwara Rasa. It may help in the treatment of rheumatoid arthritis in humans. We concluded that Hinguleshwara Rasa showed better restoration of joint histopathological changes that occurred due to FCA damage in microscopic examination of tissue samples of the bones of rats. It proves that Hinguleshwara Rasa's efficacy on Amavata was better than that of indomethacin treatment.

# Analytical, Sub Acute Toxicity and In Vivo Efficacy Study of *Hinguleshwara Rasa* on *Amavata* [Rheumatoid Arthritis (RA)<sup>[28]</sup>

Hinguleshwara Rasa, which is prepared, and an analytical study was done through analysis of the sample. ICP AES qualitative analysis was done for some elements in the sample. This study helps to find elemental changes in the sample. The XRD report shows that the structure of Hingula was not changed in Ashuddha Raw Hingula, Shuddha Hingula, and Hinguleshwara Rasa. The peak of the Hingula was increased in Shuddha Hingula and Hinguleshwara Rasa. The intensity of the peak increased, but the atomic structure was not affected in all samples. FEG-SEM for images of the formulation. We produced images of Raw Hingula, Shuddha hingula, Ashuddha Vatsanabha, Shuddha Vatsnabha, Pippali, Hinguleshwara Rasa. HPTLC method was used to develop fingerprint patterns to precisely identify plant & mineral materials in their form. Regarding the subacute toxicity of Hinguleshwara Rasa, we obeyed OECD 407 guidelines. Histopathology reports of different Organs and Biochemical reports show that five times the therapeutic dose of Hinguleshwara Rasa i.e. 30 mg/kg was found may be safer in this repeated dose '28' days toxicity study. A 60 mg/kg dose was found to be mildly toxic in the male and female animals. In male animals, 240 mg/kg dose was mild to

moderately toxic. In female animals in '28' a day sub-acute toxicity study (Repeated single dose toxicity study), we found it is toxic. *In vivo* study of *Hinguleshwara Rasa* in rheumatoid arthritis shows that *Hinguleshwara Rasa* compared with indomethacin help to reduce swelling in FCA induced Rheumatoid Arthritis rat model in 14 days. Compared to indomethacin treated animals, In *Hinguleshwara Rasa* treated animals shows focal and minimal pathological changes, focal and minimal congestion of blood vascular tissue & normal histo-architecture in the rats of bones of tissue samples.

# CONCLUSION

*Hinguleshwara Rasa* is an eminent formulation for clinical practice in Ayurveda. Its contents are Shuddha Hingula, Shuddha Vatsanabha, and Pippali. The importance of Hinguleshwara Rasa has been described through various studies. Hinguleshwara Rasa is a Rasaaushadhi. In this modern era, it is required to evaluate the toxicity of drugs and their efficacy in treating diseases by doing different studies in the future.

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