WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 13, 866-879. Research Article ISSN 2277–7105

EVALUATION OF ANTI-HISTAMINIC ACTIVITY OF RASA GUTIKA IN GUINEA PIGS

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Article Received on 26 May 2026,
Article Revised on 15 June 2026,
Article Published on 01 July 2026,
https://doi.org/10.5281/zenodo.21030031

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How to cite this Article: Dr. Swetha Y.*[1], Dr. Shivasharanappa[2], Dr. Surekha S. Medikeri[3] (2026). Evaluation Of Anti-Histaminic Activity Of Rasa Gutika In Guinea Pigs. World Journal of Pharmaceutical Research, 15(13), 866–879.

ABSTRACT

Bronchial asthma is a common allergic respiratory disorder that poses a significant global health challenge. *Rasa Gutika*, a herbo-mineral formulation described in Ayurvedic literature for the management of *Shwasa Roga* (respiratory disorders), was evaluated for its antihistaminic activity and potential therapeutic role in allergic bronchial asthma. The study was carried out in 2 experimental phases. The 1st phase involved the assessment of antihistaminic activity using a histamine-induced bronchospasm in guinea pigs. The 2nd phase evaluated the effect of the formulation on histamine-induced smooth muscle contraction using an isolated guinea pig tracheal chain preparation. In the histamine-induced bronchospasm, administration of *Rasa Gutika* produced a significant delay in the onset of pre-convulsive time compared to the control group. The maximum protective effect was observed at 30 min, which was sustained up to 180 min, followed by a gradual decline at 240 and 300 min, although the response remained statistically significant. The combination of *Rasa Gutika* with *Anupana* (Kantakari Kashaya and Pippali Churna) demonstrated better protective activity than *Rasa Gutika* administered alone. In the isolated guinea pig tracheal chain preparation, *Rasa Gutika* significantly inhibited histamine-induced smooth muscle contraction. The formulation

administered along with *Anupana* exhibited a better relaxant effect when compared to the formulation alone.The findings of the study indicate that *Rasa Gutika* possesses significant antihistaminic activity and may provide therapeutic benefits in allergic conditions such as bronchial asthma. Furthermore, the use of *Anupana* enhanced the pharmacological efficacy of the formulation.

KEYWORDS: Rasa Gutika, Bronchial Asthma, Antihistaminic Activity, Allergic Disorders, Anupana, Histamine-Induced Bronchospasm, Guinea Pig Tracheal Chain Preparation.

INTRODUCTION

Rasashastra is a specialized branch of Ayurveda that deals with the therapeutic application of metals, minerals, and herbal substances for the management of diseases and promotion of longevity. Among the various substances used in Rasashastra, Parada (mercury) occupies a prominent position due to its unique medicinal properties. Classical texts describe properly purified and processed Parada as a potent therapeutic agent. Mercurial formulations are generally administered in small doses, exhibit a broad spectrum of therapeutic activities, and are known for their rapid assimilation in the body.[1]

Rasa formulations described in the classical literature are broadly categorized into four types: Kharaliya Rasayana, Pottali Rasayana, Parpati Rasayana, and Kupipakva Rasayana. Kharaliya Rasayana is a type of moorchita yoga, in which the process of moorchana imparts specific therapeutic qualities to the formulation. In this preparation, mercury is triturated with other ingredients in a khalva yantra to obtain the desired medicinal product.[2]

Kharaliya Rasayana is considered the most widely practiced among the four types of Rasayana preparations, namely Parpati, Pottali, Kupipakwa Rasayana, and Kharaliya Rasayana, due to its broad therapeutic applications, popularity, and ease of preparation. These formulations are prepared through extensive bhavana and mardana processes. Trituration refers to the process of reducing a drug into fine particles by grinding it in a mortar and pestle, either manually or mechanically. This process not only decreases the particle size of the drug but also promotes intimate mixing of the ingredients. Further, trituration with suitable liquid media facilitates physicochemical changes within the material, enhancing the therapeutic efficacy and bioavailability of the formulation.

Asthma is a chronic respiratory disorder characterized by recurrent episodes of wheezing,

breathlessness, chest tightness, and coughing. The term *asthma* is derived from a Greek word meaning "panting" or "laboured breathing." It is one of the major non-communicable diseases (NCDs) affecting individuals of all age groups and is the most common chronic illness among children. The condition is primarily caused by inflammation and narrowing of the airways, leading to airflow obstruction and the manifestation of respiratory symptoms such as cough, wheezing, dyspnea, and chest tightness. The Global Asthma Network estimates 35 million Indians have asthma.[3] The Global Burden of Disease (GBD) 1990-2019 estimated 34.3 million Indians with asthma, which is 13.09% of the global burden. It is also reported that 13.2 asthma deaths per thousand in India.[4]

The severity and frequency of asthma symptoms may vary among individuals and can fluctuate over time. In *Ayurveda*, asthma can be correlated with *shwasa roga*, a condition resulting from the vitiation of *prana vayu* due to various internal and external etiological factors. The aggravated *vata dosha*, associated with *kapha dosha*, causes obstruction in the respiratory channels. As a result, the normal movement of *prana vayu* is disturbed, leading to abnormal directional movement and the manifestation of *shwasa roga*, characterized by difficulty in breathing and other respiratory symptoms.[5]

Kajjali is one of the most important examples of *sagandha murchana* in *Rasashastra*. It is prepared by triturating *Parada* (mercury) with *Gandhaka* (sulphur) and other ingredients without the addition of any liquid medium until a fine, smooth, black powder is obtained. The resulting product resembles *Kajjala* (collyrium) used for application to the eyes, and hence is known as *Kajjali*.[6]

Kajjali possesses several important therapeutic properties. It is described as *vrishya* (aphrodisiac), *doshatrayapaha* (alleviating all the three doshas—vata, pitta, and kapha), and *sarvamayahara* (effective in the management of a wide range of diseases).[7]

These properties make *Kajjali* a valuable component in various *Ayurvedic* formulations. The *yogavahi* property of *Kajjali* enhances its ability to carry and deliver associated drugs effectively to the target tissues, facilitating deeper penetration and better accessibility to sites that may otherwise be difficult to reach. When *Kajjali* is combined with other therapeutic substances, it potentiates their pharmacological activity, enabling effective therapeutic outcomes even at lower doses. This synergistic action not only improves the bioavailability of the incorporated drugs but also enhances their overall therapeutic efficacy.

Rasa Gutika is *Sagandha, Niragni murcchana*, explained in the *Kasa chikitsa* of *Rasendra Sara Sangraha*. It is prepared by triturating *kajjali* (prepared from *Hingulotha Parada* and *Gandhaka*) in the ratio 1:2 along with *Pippali, Haritaki, Vibhitaki, Amalaki* and *Bharangi,* given *bhavana* with *Babbula Kashaya* for 21 times and then *madhu* is added to prepare *vati*.[8]

METHODLOGY

Preparation of test drug: *Rasa Gutika* was prepared in Dept of Rasashastra and Bhaishajya Kalpana, GAMC, Bengaluru as per the reference of *Rasendra Sara Sangraha*. *Kajjali* which is present in *Rasa Gutika* was prepared from *Hingulottha Shuddha parada*, *Shuddha Gandhaka*. Other herbal drugs include *Pippali, Haritaki, Vibhitaki, Amalaki, Bharangi*. All these are mixed with *kajjali* and given *bhavana* with *babbula kashaya* for 21 times in *khalva yantra* then *madhu* it added to it to prepare *vatis.*

Experimental animals: Adult healthy Guinea pigs of either sex weighing about 250-400 were peocured from Acharya B.M.Reddy college of Pharmacy, Bengaluru. They were fed and housed as per OECD guidelines. The animals were randomly selected and kept in their cages for 5 days prior to dosing to allow for acclimatization to the laboratory conditions. Animal protocol was obtained from Institutional Animal Ethical Committee (IAEC) with reference no: IAEC/ABMRCP/2025-26/43. The experimental study was carried out in Acharya B.M. Reddy College of Pharmacy, Bengaluru, Karnataka.

Dose of the standard and trial drugs

Based on various research publications available the dose of standard drug Chlorpheniramine maleate was fixed as 2mg/kg body weight of Guinea pigs.

Human dose of the trial drugs was converted to animal dose based on standard dose converting formula.[9]

Animal dose (mg/kg) = Human km / Animal km × HED (mg/kg)

Where, Human Km = 37; Animal Km (for guinea pigs) = 8

Dose of *Rasa Gutika* as mentioned in classics is 1 *masha*[10] (1 gm). Therefore, the animal dose by applying dose conversion factor was fixed as 80mg/kg.

Plain drug: 2mg of drug *Rasa Gutika* was made into suspension in 10 ml of distilled water. Each ml will contain 0.2mg of drug.

Drug with vehicle: 80mg/kg of drug + 2ml/kg of *kantakari kashaya* + 1g/kg of *pippali churna*

Each ml contains 80 mg of *Rasa Gutika*. Vehicle dose was approximated considering the approximate human dosage of vehicle.

ROUTE OF ADMINISTRATION

The drugs were administered through rabbit oral gavaging needle.

Vehicle: Group 3 was administed with *Rasa Gutika* with distilled water

Group 4 was administered with *Rasa Gutika* with *Kantakari kashaya* and *pippali churna* as *anupana.*

Study design

Study was conducted in 2 phases.

1st phase- Histamine induced bronchospasm in Guinea pigs.

2nd phase – Histamine induced contraction of smooth muscle by using isolated guinea pig tracheal chain preparation.

Phase 1

Table No. 1: showing grouping for Histamine induced bronchospasm in Guinea pigs

Groups	Particular treatment (n=3)
1.	Normal control
2.	Standard drug Chlorpheniramine maleate (2 mg/kg p.o.)
3.	Trial 1 *Rasa Gutika* (80mg/kg, p.o.)
4.	Trial 2 *Rasa Gutika* (80 mg/kg, p.o.) + *Kantakari kashaya* (2 ml/kg, p.o.) + *Pippali churna* (1 g/kg, p.o.)

PROCEDURE

Healthy guinea pigs were fasted overnight and randomly divided into four groups, with three animals in each group. Before administration of the test drugs, baseline pre-convulsion time (PCT) was recorded for all animals. Each guinea pig was placed individually in a histamine exposure chamber and subjected to 0.2% histamine aerosol. The time interval between the onset of histamine exposure and the appearance of convulsions was recorded as the pre-convulsion time. Immediately after the onset of convulsions, the animals were removed from the chamber and allowed to recover in fresh air.

After an interval of 24 hours, Group I served as the normal control, Group II received Chlorpheniramine Maleate, Group III received *Rasa Gutika* stock solution prepared in

distilled water, and Group IV received *Rasa Gutika* along with *Anupana*. The doses administered were as specified in Table 1.Following drug administration, the animals were exposed to 0.2% histamine aerosol at 30, 60, 120, 180, 240, and 300 minutes. The pre-convulsion time was recorded at each interval. The percentage protection offered by the treatments was calculated using the following formula.

Percentage Protection = $(1 - T_1/T_2) \times 100$

Where

T_1 = Mean pre-convulsion time before administration of the test drug

T_2 = Mean pre-convulsion time after administration of the test drug

The obtained data were subjected to appropriate statistical analysis for evaluation of significance.

Phase 2

Healthy guinea pigs of either sex weighing 250–400 g were sacrificed by cervical dislocation. The trachea was carefully dissected free from the surrounding tissues and immediately transferred to a Petri dish containing oxygenated Krebs solution. The trachea was cut into individual rings, which were tied together sequentially to form a tracheal chain.The prepared tracheal chain was mounted in a 20 mL organ bath containing Krebs physiological solution maintained at 37 ± 2°C. Throughout the experiment, the medium was continuously supplied with a carbogen gas mixture comprising 95% oxygen and 5% carbon dioxide to maintain optimal tissue viability. The composition of Krebs solution (g/L) was as follows: NaCl 5.9, KCl 0.35, $CaCl_2$ 0.28, $MgSO_4$ 0.11, $NaHCO_3$ 2.1, KH_2PO_4 0.16, and glucose 2.0. One end of the tracheal chain was attached to an S-shaped aerator tube, while the other end was connected to a force transducer.The tissue preparation was allowed to equilibrate for 45 minutes under a resting tension of 1.5 g. The contractile responses of the tracheal chain were recorded using a force transducer connected to a Biopac data acquisition system. A dose-response curve for histamine was obtained using graded molar concentrations to determine the concentration producing maximum contraction. After obtaining a maximal dose response curve of histamine, the tissue is washed and the trial drug *Rasa Gutika* stock solution .5ml was added and allowed it to remain for 10 minutes. Later the histamine was added (dose being fixed by the maximal response curve) and the change in curve was noted. Again, the tissue is washed, the organ bath is filled with Kreb's solution and the procedure is repeated for next dose of test drug. Procedure was repeated for all test drug stock solutions i.e. RG 0.5ml, RG 1ml, RG+V 0.5ml, RG+V 1ml. The height of contraction due to histamine after

addition of test drugs were measured and tabulated. The percentage reduction in the height was calculated.

After recording the maximum histamine response, the tissue was washed thoroughly with fresh Krebs solution. The test drug stock solution (0.5 mL) was then added to the organ bath and allowed to remain in contact with the tissue for 10 minutes. Subsequently, histamine at the predetermined concentration was added, and the change in contractile response was recorded. The tissue was again washed and re-equilibrated with fresh Krebs solution before testing the next sample. The same procedure was repeated for all test drug stock solutions.

OBSERVATION AND RESULTS

Phase 1: Table 2: Average values of Pre-convulsive dyspnoea time (PCT) in seconds.

Group	G-1 (Normal control)	G-2 (Standard)	G-3 (Rasa Gutika)	G-4 (Rasa Gutika + Kantakari kashaya + Pippali churna
30 min	22±1.15	106.67±2.03	155±1.73	159.67±1.45
60 min	20±1.15	133.33±2.73	146.67±2.40	155±1.73
120 min	24±1.15	153.67±1.20	157.33±1.20	163.33±2.40
180 min	22±1.5	156.67±2.03	163±2.08	165±1.73
240 min	24±1.5	71.67±2.03	37±1.15	30.33±0.88
300 min	23.3±1.76	56.67±1.86	37±0.58	28.33±1.15

Values are expressed as mean ±SEM;

Table No.3 Percentage protection in different groups at different interval of time.

	G1 Normal control	G2 Standard	G3 Rasa Gutika	G4 Rasa Gutika + Kantakari Kashaya + Pippali churna
30 min	0	79.3%	85.8%	86.22%
60 min	0	84.99%	86.36%	87.09%
120 min	0	84.51%	84.74%	85.30%
180 min	0	85.95%	86.50%	86.66%
240 min	0	66.5%	35.13%	20.87%
300 min	0	58.88%	37.02%	17.75%

Table No 4: Details of Contractile response of trachea in Trial 1.

Drug	Base	Height	Difference	Contraction	Inhibition
Histamine 0.2 ml	14.9951	16	0.2526		
0.5 ml RG+HT	14.2267	14	0.2434	39.12	60.88
0.5ml CPM+HT	14.1500	2	0.0672	10.80	89.20
0.5 ml RGV+HT	13.8136	6	0.0863	11.25	88.75

RG – Rasa Gutika, HT – Histamine, RGV- Rasa Gutika + Kantakari Kashaya and Pippali churna

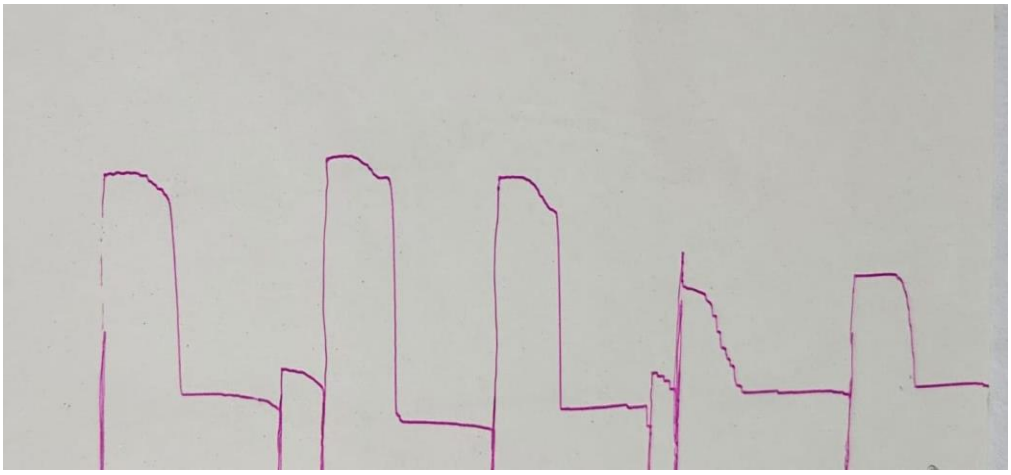

Fig 2: showing the contractile response of trachea in Trial 1.

Table no. 5: Details of Contractile response of trachea in Trial 2.

Drug	Base	Height	Difference	Contraction	Inhibition
Histamine 0.2 ml	14.1685	14.4404	0.2719		
0.5ml CPM+HT	11.2500	11.6900	0.4400	21.00	79.00
0.5ml RG+HT	13.8887	14.1817	0.2930	39.50	60.50
0.5ml RGV+HT	13.9483	14.0860	0.1377	18.25	81.75

RG – Rasa Gutika, HT – Histamine, RGV- Rasa Gutika + Kantakari Kashaya and Pippali churna

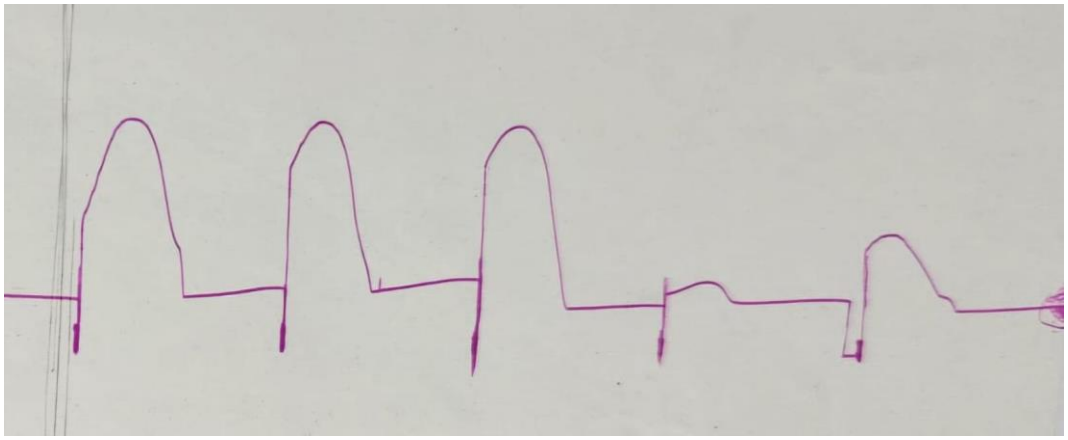

Fig 1: showing the contractile response of trachea in Trial 2.

Table no. 6: Details of Contractile response of trachea in Trial 3.

Drug	Base	Height	Difference	Contraction	Inhibition
Histamine 0.2	12.6676	12.9415	0.2739		
0.5ml CPM+HT	12.8500	13.1800	0.3300	14.50	85.50
0.5ml RG+HT	11.3483	12.0860	0.7377	24.50	75.50
0.5ml RGV +HT	11.4802	11.7755	0.2953	13.10	86.90

RG – Rasa Gutika, HT – Histamine, RGV- Rasa Gutika + Kantakari Kashaya and Pippali churna

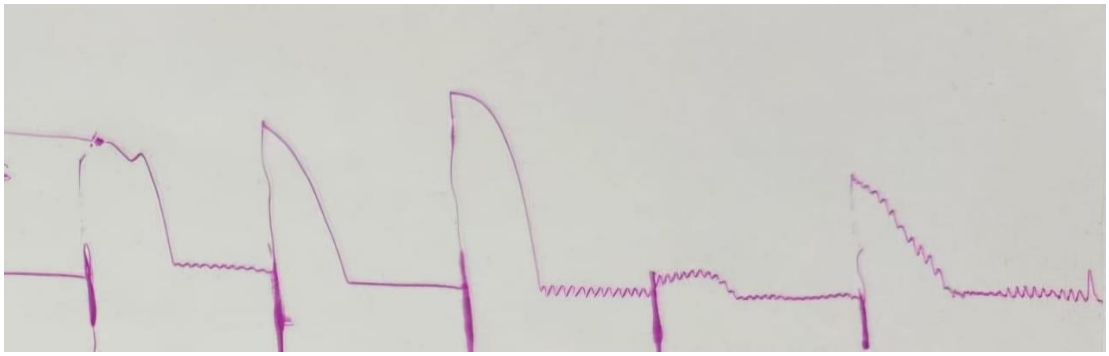

Fig 3: showing the contractile response of trachea in trial 3.

Table No. 7 showing results of Average % relaxation of Trachea

Sl.No.	Test Drug	Average % of inhibition of contraction
1.	Histamine stock solution 0.2ml	-
2.	CPM stock solution 0.5ml	85.55%
3.	Rasa Gutika stock solution 0.5ml	63.55 %
4.	Rasa Gutika + Vehicle 0.5ml	84.80 %

DISCUSSION

In the present study, the antihistaminic activity of *Rasa Gutika* and *Rasa Gutika* + vehicle was evaluated using two experimental models: histamine-induced bronchospasm in guinea pigs and histamine-induced contraction of isolated guinea pig tracheal chain preparation. These models were selected because the tracheal and bronchial smooth muscles exhibit close anatomical and physiological similarities and are highly sensitive to histamine. The guinea pig model is widely employed for assessing bronchodilator and antihistaminic activities due to its marked responsiveness to histamine-induced bronchoconstriction. Furthermore, the isolated tracheal chain preparation provides a reliable method fsor studying the direct effects of *Rasa Gutika* and *Rasa Gutika* + vehicle on airway smooth muscle contraction. The observed inhibition of histamine-induced bronchospasm and reduction in tracheal smooth muscle contraction indicate the potential antihistaminic activity of the *Rasa Gutika* and *Rasa Gutika* + vehicle. The average percentage inhibition of contraction observed in the tracheal chain preparation further supports its efficacy in counteracting histamine-mediated responses. The receptor pharmacology of guinea pigs closely resembles that of humans when compared to other commonly used laboratory animal species, making them a suitable experimental model for pharmacological studies involving respiratory disorders.

1. Efficacy of Rasa Gutika on histamine induced bronchospasm in guinea pig

A significant response was observed in all treatment groups, as evidenced by a marked increase in the pre-convulsive dyspnoea time (PCT), indicating a delay in the onset of histamine-induced bronchospasm.

The maximum protective effect of *Rasa Gutika* was observed at 30 minutes in both treatment groups. This early response may be related to the rapid absorption and pharmacological action of the formulation. The findings are consistent with the traditional Ayurvedic concept of *Rasoushadhis* being *Ashukari*, indicating a quick onset of therapeutic activity.

The *Rasa Gutika* with *Anupana* group demonstrated greater protective activity than the *Rasa Gutika* plain group at all observation intervals. The difference between the two groups was found to be statistically highly significant, suggesting that the co-administration of *Anupana* enhances the therapeutic efficacy of the formulation. These findings support the Ayurvedic concept that *Anupana* can potentiate the action of the principal drug and improve its overall effectiveness.

All treatment groups exhibited maximum protection at 30 minutes following administration. The protective effect was sustained up to 180 minutes and gradually declined thereafter. However, a significant level of protection persisted even at 240 and 300 minutes when compared with the control group. The duration of action observed in the study indicates that repeated administration at appropriate intervals may help maintain the therapeutic effect during acute episodes of bronchospasm.

2. Effect of Rasa Gutika on Histamine-Induced Contraction of Isolated Guinea Pig Tracheal Chain Preparation

In the present study, both *Rasa Gutika* (RG) and *Rasa Gutika* with *Anupana* (RGV) significantly inhibited histamine-induced contraction of the isolated guinea pig tracheal chain, indicating the antihistaminic potential of the formulation. The RGV group exhibited a greater percentage inhibition of contraction when compared to the RG plain group, suggesting an enhanced pharmacological effect in the presence of *Anupana*.

The isolated guinea pig tracheal chain is a well-established experimental model for evaluating the effects of drugs on respiratory smooth muscle[11]. This preparation is commonly used to assess the contractile and relaxant responses produced by various agonists and antagonists.

Spasmogenic agents such as histamine, acetylcholine, and barium chloride produce dose-dependent contractions of tracheal smooth muscle and are widely employed in pharmacological screening studies.

Guinea pig tracheal smooth muscle contains H_1, M_3, and β_2 receptors. Activation of H_1 and M_3 receptors results in bronchial smooth muscle contraction, whereas β_2 receptor stimulation produces bronchodilation. Histamine, released from mast cells and basophils during allergic reactions, induces bronchoconstriction, increases vascular permeability, and promotes mucus secretion. These effects contribute to airway hyperresponsiveness, a characteristic feature of bronchial asthma.

The significant inhibition of histamine-induced tracheal contraction observed in the present study suggests that *Rasa Gutika* possesses antihistaminic activity. The enhanced response seen with *Anupana* further indicates its role in improving the therapeutic efficacy of the formulation.

PROBABLE MODE OF ACTION

The present study was undertaken to evaluate the probable mode of action of *Rasa Gutika* with respect to its anti-histaminic activity. The therapeutic efficacy of the formulation may be attributed to its *Shwasa-hara* and *Rasayana* properties as described in Ayurvedic literature.

The pharmacological action of a compound formulation is generally influenced either by the predominant action of its major ingredients or by the synergistic interaction of all the constituent drugs. In the case of *Rasa Gutika*, both mineral and herbal components may collectively contribute towards its therapeutic efficacy in bronchial asthma.

Parada is one of the major ingredients of *Rasa Gutika*. Owing to its *Ushna Virya*, it may help in *Sroto-shodhana* and stimulation of *Agni* (*Deepana*). Its *Sara, Snigdha*, and *Guru* properties may assist in alleviating aggravated *Vata Dosha*, which plays a significant role in the pathogenesis of *Shwasa Roga*. By regulating Vata and clearing the respiratory channels, Parada may contribute to the reduction of respiratory distress.

Gandhaka is another important mineral constituent of the formulation. Its *Snigdha* and *Sara Gunas* along with *Madhura Rasa* may impart *Balya* action and support the pacification of *Vata Dosha*. In addition, its *Ushna Guna* and *Katu Vipaka* may facilitate *Sroto-shodhana*,

thereby helping in clearing obstruction within the respiratory passages and improving respiratory function.

Pippali, possesses *Deepana, Pachana, Rasayana, Anulomana, Shulaprashamana and Raktashodha* properties and is indicated in disorders such as *Kasa, Shwasa, Kustha, Prameha, Shleshmodara* and *Jeerna Jwara*.

Piperine, the principal alkaloid of *Pippali*, is responsible for its pungency and acts as a potent bioavailability enhancer. It improves the absorption and efficacy of various drugs by bioavailability[12]

Triphala, an important herbal component of *Rasa Gutika*, contains bioactive constituents such as tannins, gallic acid, ellagic acid, and chebulinic acid. These constituents have been reported to exhibit significant antioxidant and immunomodulatory properties.. The antioxidant properties of Triphala may help in reducing oxidative stress associated with bronchial asthma, while its immunomodulatory action may assist in regulating inflammatory and hypersensitivity responses involved in the disease process.

Bharangi is indicated in *Shwasa* and *Kasa* due to its *Kapha-Vatahara* and *Shothahara* properties. It helps remove accumulated *Kapha* from the respiratory tract, clears,reduces airway inflammation, and facilitates easier breathing.It possesses anti-inflammatory, anti-allergic, bronchodilator, expectorant, antioxidant, and immunomodulatory activities. These actions help reduce bronchial inflammation, promote mucus clearance, improve airflow, and relieve symptoms such as cough, wheezing, chest congestion, and dyspnea.

Babbula has *Kaphahara* and *Shothahara* properties. It helps soothe the respiratory passages, reduce airway inflammation, and minimize irritation responsible for persistent cough. It exhibits anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory activities. Hence, *Babbula* helps alleviate symptoms of bronchial asthma.

Kantakari

It is a well-known drug indicated in *Shwasa* and Kasa owing to its *Kapha-Vatahara*, *Shwasahara*, and Kasahara properties. *Kantakari* possesses bronchodilator, expectorant, anti-inflammatory, antiallergic, antioxidant, and antimicrobial activities. These actions help dilate the bronchi, promote the expulsion of mucus, reduce airway inflammation and hypersensitivity, and improve pulmonary function. Thus, *Kantakari* effectively relieves

symptoms such as cough, wheezing, chest congestion, and breathlessness associated with respiratory disorders.

Thus, this combined action of mineral and herbal constituents in *Rasa Gutika* may contribute synergistically towards its anti-histaminic, anti-inflammatory, antioxidant, and immunomodulatory activities.

CONCLUSION

In Phase I of the study, all treatment groups demonstrated a significant increase in pre-convulsive dyspnoea time (PCT), indicating protection against histamine-induced bronchospasm. The maximum protective effect was observed at 30 minutes following drug administration and was maintained up to 180 minutes. Although the protective effect gradually declined after 240 minutes, a statistically significant level of protection persisted even at 300 minutes when compared to the control group. The *Rasa Gutika* with *Anupana* (RGV) group exhibited significantly greater protection than the *Rasa Gutika* plain (RG) group at all observation intervals ($p < 0.001$), indicating the enhancing effect of *Anupana* on the therapeutic activity of the formulation.

In Phase II, both RG and RGV significantly inhibited histamine-induced contraction of isolated guinea pig tracheal chain preparations, demonstrating marked relaxant activity on respiratory smooth muscle. The RGV group showed greater inhibition of contraction compared to the RG group.

Based on the findings of both experimental phases, it can be concluded that *Rasa Gutika* possesses significant antihistaminic activity and may be beneficial in the management of allergic respiratory conditions such as bronchial asthma. The results further suggest that the administration of *Anupana* enhances the pharmacological efficacy of the formulation.

ACKNOWLEDGMENT

Principal and staff of GAMC, Bengaluru.

Staff and students of Acharya B.M.Reddy College of Pharmacy, Bengaluru.

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