

RESEARCH WORKS DONE ON RASASINDURA (SUBLIMATED MERCURIAL PREPARATION) - A CRITICAL REVIEW

Biswajyoti Patgiri¹, Rohit Gokarn²

1. Associate Professor, Dept. of Rasashastra and Bhaishajya Kalpana Including Drug Research, I.P.G.T.&R.A., Gujarat Ayurved University, Jamnagar, Gujarat, India.
2. Ph.D. Scholar, Dept. of Rasashastra and Bhaishajya Kalpana Including Drug Research, I.P.G.T.&R.A., Gujarat Ayurved University, Jamnagar, Gujarat, India.

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Abstract

Rasasindura (RS) sublimated mercurial preparation often used in diseases like Madhumeha (Diabetes mellitus), Rajayakma (Tuberculosis), Pandu (Anaemia), Sthoulya (Obesity), Mandagni (Impaired digestive fire) etc. Mercurial preparations are constantly targeted due to lack of documentation and published works. Till date several research works have been carried out at institutional level on RS. Aim of the present work is to compile such research works done on RS in Department of Rasashastra and Bhaishajya Kalpana, Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar. Various pharmaceutical experiments revealed yield of RS ranging from 11.70% to 92.52% and was prepared in 6 hrs to 168 hrs. RS is HgS Hexagonal cinnabar with percentage of Mercury ranging from 82-85%. Safety of RS was established through acute and sub-chronic toxicity studies. Efficacy of RS was studied in diseases like Shukra kshaya (Infertility), Shwasa (Bronchial Asthma), Madhumeha (Diabetes mellitus), Kshudra kushta (Skin diseases), shwitra (leucoderma), Hypertention etc. In all the studies encouraging results were reported with decrease in signs and symptoms. Augmenting effect of RS was established by clinical studies.

Key words: Ayurveda; Rasasindura; Sublimated mercurial preparation; I.P.G.T & R.A.

***Address for correspondence:**

Dr. Biswajyoti Patgiri, M.D., Ph.D.

Associate Professor,

Dept. of Rasashastra and Bhaishajya Kalpana Including Drug Research,

Institute for Post Graduate Teaching & Research in Ayurveda,

Gujarat Ayurved University,

Jamnagar, Gujarat, India – 361 008

E-mail: patgiri06@yahoo.co.in

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INTRODUCTION

Ayurveda, a life science has contributed healthy lifestyle to humanity. Medicaments practiced in Ayurveda include herbal and herbo-mineral single and compound formulations.^[1] Combination of minerals with herbs have not only enhanced the properties of these drugs but also played a vital role in reducing toxicity. Several claims in present day have alarmed one to prove the safety of these medicaments. Use of Mercury in Indian system of Medicine has been specially targeted as it is toxic when used in its native form.^[2] Although these medicaments based on Traditional Knowledge are being used since ages, one cannot claim the safety of these medicaments without documented data. Lot of works have been carried out on these lines but only few of them are published and available for citation. For globalization and acceptance of these drugs, it is of great importance to make research works available to everyone so as to highlight the pros and cons of medicine. Reviewing previous work will definitely allow one to know regarding several factors associated with the drug discovery, like rectification of errors in earlier studies and developing better study design. Rasasindura (RS) a sublimated mercurial preparation is widely used by practitioners with different adjuvant and also in various compound formulations. RS is prepared by a unique process called as kupipakwa rasasyana. There have been more than 24 works carried out all over India on RS where as 13 works has been carried out in Institute for Post Graduate Teaching & Research in Ayurveda, Gujarat Ayurved University (IPGT&RA), Jamnagar alone.^[3] Present study comprises summaries of the works on RS carried out in IPGT & RA.

MATERIALS & METHODS

Works carried-out in the Department of Rasashastra & Bhaishajya Kalpana including Drug Research, IPGT & RA, Jamnagar in MD and M.Pharma during 1964 - 2011 were

compiled and screened to evaluate RS on Pharmaceutical, Analytical, Pharmacological and Clinical basis.

RESULTS & OBSERVATION

RS in Tamaka Swasa (Bronchial Asthma)

In initial study carried out on RS in 1974, three batches of Samaguna RS were prepared with time duration of 32 hrs with an average yield of 55.6%. Samaguna RS was given bhavana with equal amount of Arkapatri Swarasa (leaf juice of *Calotropis procera* Linn.) and dried to form the compound. It was administered to 14 patients of Tamaka shwasa (Bronchial asthma) at a dose of 250-500 mg/day for 28 days. Encouraging results were obtained wherein 64.78% people got completely cured and 21.43% of subjects had symptomatic relief.^[4]

RS in Swasa (Asthma)

A study conducted in 1977-78 was a continuation study where three treatment groups selected for treatment were Arkadala Choorna (leaf powder of *Calotropis procera* Linn.)-250 mg, Arkadala Choorna 87.5 mg with 12.5 mg Kajjali and Arkadala Choorna 87.5 mg with 12.5 mg RS for 7 days of duration in 20 subjects. Results showed that Arkadala Choorna alone caused some side effects like nausea, vomiting, giddiness, etc. but with Kajjali and RS it did not cause any untoward effect. Study concluded that Arkadala choorna along with RS showed better results compared to other groups.^[5]

Pharmaceutical standardization of RS

Extensive study on the pharmaceutical aspect of RS with different proportion of Sulphur was carried out in 1985. All the samples were prepared in AIHORE yantra which is the easiest method of preparation of RS. Temperature was recorded by thermometer. Samaguna, Dwiguna, Triguna, Chaturguna,

Panchaguna, Shadguna, Sardhasamaguna, Sapadasamaguna, Ardhaguna, Tritiyamsha, Chaturthamsha and Shadamsha RS with 57.17%, 27.57, 21.64%, 18.54%, 15.40%, 11.70%, 41.75%, 46.46%, 78.64, 81.15%, 86.28 and 92.52% yield respectively. Duration of flame increased according to increased quantity of Sulphur.^[6]

RS in Male Infertility

Study conducted in 1986 includes four preparations of RS with 49.2% of product yield. Six Patients with male infertility were treated with 250mg of RS in first group, six patients were given 2 g of Atmagupta Beeja Choorna (Seed powder of *Mucuna pruriens* Linn.) in second and seven patients were subjected for combined treatment of both in the third group. Increase in motility and sperm count was observed in first and third group where as no difference was seen in second group. The difference found in first and third group were not statistically significant as the number of patients in each group was very small to conclude.^[7]

RS in Skin manifestation

Comparative Study of RS with special reference to its preparation time and its clinical efficacy in Kshudra Kushthas was carried out in 1986. Samaguna RS of six hours duration and 168 hours duration were prepared. Four practical in each method was prepared to develop standard manufacturing procedure. 52.57% of yield was obtained in six hours and 53.33% in 168 hours preparation. Ointment was prepared with 500 ml of Sikta taila and 50 g of RS. In Clinical study, six patients of Group 1 received RS 250 mg of RS (6 hrs) internally with milk and Malahara (ointment) for external application for a duration of 30 days and six patients of Group 2 received RS 250 mg of RS (168 hrs) internally with milk and Malahara for external application for a duration of 30 days. Study concluded that both the groups showed

significant results in Pama (Scabies), Dadru (Fungal infection) and Vicharchika (Eczema). RS prepared by 168 hrs showed better results in comparison to the other group, however the number of patients were very less to derive a definite conclusion.^[8]

Pharmaceutical study of RS

An attempt was made to prepare Shadguna RS (RS prepared by 1:6 proportion of Mercury and Sulphur) by two different methods and evaluate its aphrodisiac effect in 1986. First method was to prepare RS in 7 days i.e. in 168hrs, ten such preparations were done with an average of 13.4% yield, in second method, Samaguna RS (RS prepared by 1:1 proportion of Mercury and Sulphur) was prepared and then mercury was separated by sublimation and once again equal Sulphur was added and Kajjali was prepared followed by preparing RS in 168hrs; likewise five more times the procedure was repeated to obtain Shadguna RS, following this method it yielded 6.4% final product. In Clinical study ten patients received 250mg capsule Of RS BD with milk for 50 days. Marked improvement was observed in signs and symptoms like insomnia, loss of appetite, weakness, night falls etc. Significant results were also seen in increased sperm motility; however increase in sperm count was not statistically significant.^[9]

RS in Anti diabetic compound

Effect of Madhumeha hara yoga (Anti diabetic compound) with RS was studied in 1986. Samaguna RS was prepared by Ashtasamskarita Parada, adapting 6 hrs of time duration, average yield of preparations was 43.12%. Clinical study was done by prescribing tikta and ushna veerya dravyas alone and along with RS. Clinical study comprised of three groups of 6patients each, Group1included Herbal drugs where as Group 2 and 3 along with different proportion of RS. Herbal Ingredients used and proportion of RS used in second and third group was not

mentioned clearly in the study. Study concluded that, in Group 1, 50% patients got relieved of signs and symptoms where as in group 2 & 3, 75% and 80% patients got relieved of signs and symptoms of Madhumeha.^[10]

RS as Aphrodisiac

Augmenting effect of RS was screened in 1989. Samaguna RS was prepared in three batches with 12hrs of preparation with yield of 48.8%. Vrushya Yoga (Aphrodisiac compound) was prepared by 75 different ingredients of Herbal and Mineral origin in one group and along with RS in other group. Treatment duration was for 30days with milk as anupana (adjuvant). Group 2 showed significant results in libido, increased sperm count in patients of oligozospermia and increased motility of sperms. Study concluded that RS has augmenting effect to enhance property of Vrushya Yoga.^[11]

RS as oral contraceptive

Experimental Study of oral contraceptive with special reference to augmenting property of RS was studied in 1990. Two batches of Samaguna RS were prepared by 11hrs with an yield of 17.5%. Compound A containing Vidanga (*Embelia ribes* Burm.f.), Pippali (*Piper longum* Linn.), Palasha beeja (seed of *Butea monosperma* Lam.), Tankana (Borax), Shuddha Haratala (Arsenic trisulphide) and Compound B which was made with addition of RS to the above drugs were screened for Anti-fertility activity,^[12] vaginal cornification, vaginal opening, ovarian weight gain test on isolated rats, to rule out toxic effect. Results revealed that compound possess anti-implantation activity irrespective of dose, they also possess weak oestrogenic activity, but no anti ovulatory and oxytocic activity was evident. Both compounds did not produce any toxic effect on uterus and liver. On comparison of results, augmenting effect of RS was not significant.^[13]

RS in Hypertension

Study of hypotensive formula alone and along with RS was studied in 1990. Three batches of samaguna RS was prepared with average yield of 44.23%, time taken for preparation was 7.18 hrs on an average. Hypotensive formula (A) was prepared with following ingredients i.e Tamra Bhasma (incinerated Copper), Abhraka Bhasma (incinerated Mica), Swarnamakshika Bhasma (incinerated copper pyrite), Shuddha Gandhaka (purified Sulphur), Shweta Chandana (*Santalum album* Linn.), Guduchi Satva (extract of *Tenospora cordifolia* Wild.), Sariva (*Hemidesmus indicus* Linn.), Mallika (*Jasminum officinale* Linn.), Parpataka (*Oldenlandia corymbosa* Linn.), Arjuna (*Terminalia arjuna* Roxb.), Ushira (*Vetiveria zizanioides* Linn.) and Brahmi (*Bacopa monnieri* Linn.) each one part and Sarpagandha Ghana (extract of *Rauwolfia serpentina* Linn.) four parts. Thus formed mixture was given bhavana (Levigation) with Musta (*Cyperus rotundus* Linn.), Shatavari (*Asparagus racemosus* Wild.), Murva (*Maerua oblongifolia* Forsk.), Parpataka (*Oldenlandia corymbosa* Linn.), Draksha (*Vitis vinifera* Linn.), Durva (*Cynodon dactylon* Linn.), Dadima (*Punica granatum* Linn.), Ketaki (*Pandanus tectorius* Parkinson.), Sahadevi (*Vernonia cinerea* Less.) and Kumari (*Aloe vera* L.) QS. Hypotensive formula (B) was prepared by adding 5% RS to the above mixture. Group A was given in 1.5 g dose twice a day and Group-B, 1 g twice a day with water for 6 weeks. Relief in Cardinal signs and symptoms of hypertention was 85.55% in Group B where as 67.64% in Group A. In both group A & B, systolic BP was lowered to highly significant level at weekly assessment as well as final results. Hence augmenting effect of RS is evident.^[14]

RS in treatment of Leucoderma

Augmenting effect of RS with special reference to Svitraghna Yoga (SY) was

studied in 1990. Samaguna RS was prepared in two batches with 51.5% yeild. Shvitraghna yoga 1 was prepared by combination of following drugs Aragwadha (*Cassia fistula* Linn.), Amalaki (*Emblica officinalis* Gaertn.), Bakuchi (*Psoralea corylifolia* L.), Bhringaraja (*Eclipta alba* L.), Bhallataka (*Semecarpus anacardium* L.), Chitraka (*Plumbago zeylanica* L.), Chakramarda (*Cassia tora* L.), Guggulu (*Commiphora wightii* Arn.), Haritaki (*Terminalia chebula* Retz.), Haridra (*Curcuma longa* L.), Kakodumbara (*Ficus hispida* L.), Khadira (*Acacia catechu* L.), Katuki (*Picrorhiza kurroa* Pk.), Mareecha (*Piper nigrum* L.), Nimba (*Azadirachta indica* A. Juss.), Pippali, Shunthi (*Zingiber officinale* Roscoe.), Vibhitaki (*Terminalia bellirica* Roxb.), Vidanga. Shvitraghna yoga 2 was prepared by combining RS to Shvitraghna yoga 1. Shvitraghna hara taila was prepared by using above herbal drugs and given for ext application. SY 2 showed statistically significant results compared to the 1st group. Thus it can be said that RS is having Augmenting effect.^[15]

Toxicity and Bronchodilating study of RS

Toxicity and Bronchodilating effect of RS was studied in 2002. Samaguna and Shadguna Balijarita Rasasindura were prepared in 24 hours duration. The temperature was gradually increased after every 8 hour as follows; Mridu Agni (room temperature – 200°C), Madhyam Agni (200-450 °C) and Tikshan Agni (450-650 C). Yield of 50% observed in Samaguna RS where as 13.65% yield was obtained in Shadguna RS. Further Samaguna and Shadguna RS samples were subjected for Bhavana with Vasa Swarasa (Leaf juice of *Adhatoda vasica* L.). In Pharmacological study test drugs were subjected for the chronic toxicity study in 40 days duration, in Charles Foster albino rats, administering the dose of 22.5 mg/kg body weight. Also the 4 test drug samples Samaguna RS, Shadguna RS, Vasa Bhavita Samaguna RS and Vasa Bhavita Shadguna RS were assessed for their

bronchodilating effect in the isolated guinea pig tracheal spirals. The study concludes that both Samaguna and Sadaguna Balijarita RS have little or no toxic effects. The tissue responses to drug and its modifying effect on the histamine induced contractile response in guinea pig were studied. Shadguna RS and Samaguna RS samples without Vasa Bhavana did not affect histamine induced contraction whereas Vasa Bhavita Samaguna RS and Vasa Bhavita Shadguna RS showed mild and moderate anti-spasmodic effect. Study concluded that, Shadguna Balijarita RS difficult to prepare pharmaceutically and as its qualities are nearly similar to Samaguna Balijarita RS in terms of efficacy and safety.^[16]

Analytical profile of Samaguna and Shadguna Balijarita RS

Pharmaceutico-Analytical profiles of Samaguna and Shadguna Balijarita RS was studied in 2004. Three batches of Samaguna RS of 6 hrs duration gave an average yield of 45.37%, whereas Shadguna RS 6hrs average yield was 12.36%. In Samaguna RS 24hrs, 48.14% yield was observed and Shadguna RS 24 hrs yielded 11.78%. Samaguna RS 7days gave 44.63% and Shadguna RS 12.41% yield. Analytical study revealed 82-85% of mercury detected in RS by volumetric method. X-ray diffraction studies showed the presence of Metacinnabar HgS in cubic form in Kajjali where as in Samaguna RS prepared in 6 & 24 hrs was found to be synthetic Cinnabar in Hexagonal form and Samaguna RS prepared in 7days and all the batches of Shadguna RS i.e 6 hrs, 24 hrs and 7 days was in Natural cinnabar form HgS with Hexagonal crystal structure.^[17]

DISCUSSION

Indian system of medicine has abundant references of mercurial compounds and RS is one among them. It is of great importance that one should understand the pharmaceutical

processing and judicious combination of different ingredients to make it safe and efficacious compound. In spotlight of current circumstances authors have tried to compile previous research works done on RS in IPGT to highlight pharmaceutical, Analytical, Pharmacological and Clinical findings.

Pharmaceutical

Initially AIHORE YANTRA was used to prepare RS where the bottle was wrapped with 7 layer of mud smeared cloth and kept directly over a coal chullika (burner) with specific diameter and length.^[6] Bottle used to be in direct contact with burning coal due to which many a time there was failure due to breakage. Temperature pattern was measured by thermometer which had limitations as after boiling stage inner temperature could not be taken. Outer temperature also was limited to the maximum capacity of the thermometer i.e 400°C hence the accuracy in ascertaining the changes at different temperature was not up to the mark. In later period RS was prepared in muffle furnace, where in controlled temperature pattern was adapted i.e Mridu Agni (room temperature – 200°C), Madhyam Agni (200-450°C) and Tikshan Agni (450-650°C). Electric muffle furnace was definitely easy for process standardization, especially temperature control was possible as desired in various stages.^{[16][17]}

Analytical

Detailed analytical study was carried out in all the research works however limitations of the time period in earlier works only physico-chemical tests were carried out with % of mercury in RS varying from 82-85%. In later period characterization of RS by XRD and revealed the presence of RS in HgS Hexagonal Natural cinnabar form in Shadguna RS and Synthetic Cinnabar form in Samaguna RS.^[17]

Pharmacology

Toxicity study of Samaguna and Shadguna RS has proved least toxic effect. Histopathology studies have shown mild to moderate changes in the liver in both the groups. Though Shadguna RS has shown better tolerability compared to Samaguna RS but the same is not significant enough to claim. No Bronchodilating effect was obtained without Bhavita RS, whereas Vasa Bhavita Samaguna RS showed mild and Vasa Bhavita Shadguna RS moderate anti-spasmodic effect.^[16]

Augmenting effect of RS had screened for Antifertility activity and toxic effect, the results revealed that compounds possess anti-implantation activity irrespective of dose, also possess weak oestrogenic activity, but no anti ovulatory and oxytocic activity was evident. Both compounds did not produce any toxic effect on uterus and liver. On comparison of results, augmenting effect of RS was not significant.^[13]

Clinical

Three studies on Shukra kshaya related to male sexual problems, two studies on Shwasa, a study each on Kshudra kushta, Shwitra, Madhumeha and Hypertention have been carried out. In all the studies, RS was administered with suitable adjuvant. The therapeutic dose was ranging in between 12.5mg to 250mg. No adverse Effects were reported in any of the clinical studies. No statistical significance could be drawn as the studies contained less number of cases.

CONCLUSION

Rasasindura is a sublimed mercurial preparation prepared by different proportion of sulphur. Kramagni maintenance is very essential for the pharmaceutical process of Kupi paka. Yield of RS in various experiments ranges from 11.70% to 92.52% and can be prepared in 6hrs to 168hrs. Analytically RS is HgS Hexagonal cinnabar with percentage of Mercury ranging from 82-85%.

Pharmacologically, safety of RS has been established through acute, sub-chronic toxicity studies. RS is proven to possess anti-implantation activity and anti-spasmodic properties in experimental rats. RS was administered along with various herbs and adjuvant, the dose ranging from 12.5-250 mg and the duration up to 30 days in diseases like Shukra kshaya, Shwasa, Madhumeha, Kshudra kushta, shwitra, Hypertention etc. In all the studies encouraging results were reported with decrease in signs and symptoms. Augmenting effect of RS was established by clinical studies. These results may be valuable for further studies in larger population.

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