



Review of *Rasashastra* from the Perspective of Adverse Drug Reactions

Author: Sima A. Kurule¹

Co Authors: Lata A Rathod² and Nirmala R Sonawane³

¹Rasashastra and B.K. Dept., YCAMC, Aurangabad, Maharashtra, India

²Swasthavritta Dept. C.S.M.S.S. Ayurved College, Aurangabad, Maharashtra, India

³Panchakarma Dept, Parul institute of Ayurved, Gujarat, India

ABSTRACT

Pharmacovigilance is the need of hour to keep an eye on the adverse drug reactions induced by all systems of medicine. A Drug or formulation produces adverse events if it is not procured, produced, and used as per the classical guidelines. Various classical preparations along with some proprietary formulations were manufactured by the developed pharmaceutical industries which have brought many challenges about safe use of Ayurvedic Medicines especially metallic preparations and herbo-mineral drugs of *Ayurveda* are always in doubt regarding safety and toxicity. *Rasashastra* is the alchemy of traditional Indian system of medicine which deals with the preparation of therapeutic products by using metals, minerals, animal products and toxic substances. *Rasaushadhis* were known to cure illnesses in a short time period, very small dosage, and also easily palatable. Being the pharmaceutical branch *Rasashastra* literature is full of standard methods to prepare various medicines, and it also mentioned adverse drug events occurred due to inaccuracy in the procedures accepted. In this review article an attempt was made to throw some light on origins of those adverse drug reactions mentioned in literature.

Key Words *Rasaushadhi, Adverse drug reaction*

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INTRODUCTION

Medicine or Drug is the one amongst four basic factors of the *Ayurvedic* treatment¹. The *Ayurvedic Materia Medica* mentions resources of plant, animal, metal, and mineral origin² which are suggested to be used in numerous pathologies. Considering the resources, *Ayurvedic* formulations are mainly -1) Herbal 2) Mineral / metallic and 3) Herbo-mineral combination. Herbo-mineral, metallic and mineral drugs are

called as *rasaushadhi*. *Rasushadhis* are palatable, highly effective in minute doses in a very short time, builds popularity and occupied a significant place in *Ayurvedic* therapeutics³. They are being routinely prescribed in different parts of the India for hundreds of years but globally a serious question was raised about the safety of *Ayurvedic* preparations because it contains various heavy metals like mercury, lead, and also some poisonous substances like aconite.



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Any untoward effect caused because of a drug, aside from expected beneficial action is named as adverse reaction⁴. A drug or formulation produces adverse events if it is not obtained, manufactured, and prescribed as per the classical guidelines. Some therapeutic factors which can also contribute to a rise within the chances of ADR of *Ayurvedic* medicines like the irrational use of medicines without precision in diagnosis, disease variant, stages of the disease, and specific prototype of the person.

In earlier period *Rasavaidyas* or *Ayurvedic* Physicians were used to prepare medicines for their patients themselves but now days increased industrialization in *Ayurveda* manufacturing brought many challenges regarding drug safety. Good manufacturing practices are essential to produce quality genuine medicines. The Drug and Cosmetic Rule 1945 also in its Schedule T

explains G.M.P. for *Ayurveda* Drugs which clearly target on the Safe Basic control measures and procedures that need to be administered to produce a product that meets specifications and is safe to consume.

Rasashastra, an important branch of *Ayurveda* entirely uses various metals and minerals in therapeutics. It deals with types, characteristics, processing techniques, properties, and therapeutic uses of metals, minerals & poisonous herbs. Ancient *Ayurvedic* scholars were very much aware of the toxic nature of raw material used and keeping within the mind they have described ‘*Aushadh sevan janya vikar*’ in their classics elaborately, which reflect their concern about the adverse effect of *Ayurvedic* drugs. There are some guidelines given by the *Rasacharya* to minimize adverse drug reactions and increase the safety of *Rasaushadhi* during their preparation and use.

Table 1 *Rasadravya grahyagrahyatva* (characters and variety of authentic raw material)

Name of <i>rasadravya</i>	<i>Grahya lakshana</i>	<i>Grahya prakar</i> (Acceptable variety)
<i>Abhraka</i>	Black colour, Sigdha, Heavy, Pruthudala ,	<i>Krishna Vajrabhraka</i>
<i>Makshika</i>	Bright golden colour with blue ting, heavy, angle less	<i>Suvarnamakshika</i>
<i>Vimala</i>	Heavy, Shiny, Hexagonal	<i>Hemavimal</i>
<i>Shilajatu</i>	-----	<i>Karpurganghi Shilajeet</i>
<i>Rasak</i>	Without lamellae	<i>Karvellak</i>
<i>Gandhak</i>	<i>Shukapicchavat</i> -Greenish Yellow, Hard, Smooth	<i>Amalasar</i>
<i>Gairik</i>	Deep red Colour ,Soft ,Smooth	<i>Suvarnagairik</i>
<i>Hartala</i>	Golden colour, <i>Guru, Snigdha, Tanupatra</i> , Bright	<i>Patra</i>
<i>Manshila</i>	Red colour with yellow tinge, heavy	<i>Shyamangi</i>
<i>Kapardika</i>	Oval shape ,large edges, yellow tinge, possess nodule on its back,	----
<i>Hingul</i>	Coral red colour , possess white shiny lines	<i>Hamsapada</i>
<i>Suvarna</i>	Red colour on heating, White on cutting, yellow while rubbing on touch stone, shining, bright, heavy, soft, smooth	<i>Khanija</i>
<i>Rajat</i>	White like moon while heating-cutting and running on touch stone, bright, heavy	<i>Khanija</i>
<i>Tamra / Copper</i>	Smooth ,red, heavy, malleable	<i>Nepalaka</i>
<i>Vang / Tin</i>	White like silver, soft, smooth, heavy, melt rapidly	<i>Khuraka</i>
<i>Naag / Lead</i>	Black, heavy, soft, rapidly melt, smells putrid.	-----
<i>Yashada</i>	Heavy, soft, bright, quick melting	-----
<i>Vatsanabh</i>	Bulky, Heavy, smooth, newly harvested, not contaminated	-----



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MATERIALS AND METHODS

A) Selection of raw material:

The raw material used to prepare medicine should be authentic and prescribed quality⁵.

Rasashastra literature mentioned differing kinds of metals and minerals along with the preferred varieties (*Grahyadravya*) as shown in table no.1.

If the chosen material variety is different from the approved variety mentioned within the texts then the prepared medicines are of deprived quality and it would be harmful to the individuals.

B) Shodhan / purification process:

Metals, minerals, *vishadravya* are considered to be toxic on consumption but while using it as an ingredient in *rasaushadhis*, these materials should pass through a unique pharmaceutical process called *shodhan* or purification⁶. It was indicated to diminish the toxic properties of *rasadravya*. Various processes like *nirvaap*, *dhalan*, *swedan*, *bhavana*, etc with the particular medium on *rasadravya* results in the elimination of unwanted doshas⁷. If any substance was administered further without purification then the prepared medicine may lead in serious adverse events as shown in table no.2.

Table 2 Toxic effects due to use of *Ashuddha dravya* for medicine preparation

Name of <i>Rasadravya</i>	Toxic effects caused by <i>ashuddha dravya</i>
<i>Abhraka</i>	<i>Hrud-parshvapida, Shotha, Pandu, Kushtha roga, Agnimandhya, Guru. Vata-kaphavardhaka</i>
<i>Vaikrant</i>	<i>Kilasa, Kushtha, Daaha, Parshvapida&pandu.</i>
<i>Makshik</i>	<i>Netravikara, Mandagni, Kushtha, Halimaka.</i>
<i>Shilajatu</i>	<i>Daaha, murccha, Bhrama, Raktapitta, Agnimandya</i>
<i>Tuttha</i>	<i>Vaanti, Bhraanti</i>
<i>Kharpara</i>	<i>Vaanti, Bhraanti</i>
<i>Gandhaka</i>	<i>Kushtha, Taapa, Bhrama, Pittajavikara, Roopasukha-virya-balahara.</i>
<i>Hartala</i>	<i>Daaha, kshobha, kampa, toda, raktavikara, kushtha, vaatakaphaja roga karaka, mrityukaraka.</i>
<i>Manahshila</i>	<i>Ashmari, mutrakruchcha, mandagni, malabaddhata.</i>
<i>Hingula</i>	<i>Andhata, kshaya, klama, bhrama, moha, prameha.</i>
<i>Swarna</i>	<i>Sukha-virya-balanaashaka, rogakaraka.</i>
<i>Rajata</i>	<i>Aayu-sukha-balahara, santaapa, malabaddhata, rogakaraka, angasaada.</i>
<i>Taamra</i>	<i>Vaanti, moorchcha, bhrama, utklesha, kushtha, daaha, moha.(ashtadosha)</i>
<i>Lauha</i>	<i>Aayu-bala-kantinashaka, hridpida, shaitihilya, rogakaraka</i>
<i>Vanga</i>	<i>Kantihara, kushtha, kilasa, gulma, prameha, kshya, paandu, shotha, shleshma-jwara, bhagandara, shukraashmari, raktavikara.</i>
<i>Naaga</i>	<i>Kantihara, kushtha, sandhivedana, pakshaghata, gulma, prameha, aanaha, shotha, bhagandara, agnimandhya, anshashotha, udarashula, kshya.</i>
<i>Yashada</i>	<i>Gulma, prameha, kshaya, kushtha.</i>
<i>Vatsanabha</i>	<i>Daaha, murccha, hrudgati avarodha, mrutyu.</i>

C) Drug manufacturing process:

Rasaushadhis although named after mercury '*rasa*' or '*parada*', can be classified into two distinct groups mercurial and non-mercurials. *Murcchana* is the process to induce assured therapeutic properties in *parad* with a certain process while *marana* or incineration is the methodology where

metals and minerals get converted to bodily assimilable ash.

1) *Murcchana*⁸:

It is the process in which mercury with or without sulfur is converted into a suitable compound, which could be used internally for curing diseases even without reduced to ashes. Basic types of



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murcchana are described in table no.3. Long-term use of *sagandha murcchana* was permissible, itself suggest the safety of a selected formulation. *Rasaushadhies* prepared by *parada* without *gandhaka* i.e. *nirgandha murcchana* should not be

used for several days; its use was restricted till the disease condition cured. If such formulations were continued further then it may produce adverse events.

Table 3 Types of *Murcchana*

Type of <i>Murcchana</i>	Example	Duration of therapy
<i>Sagandha murcchana</i>	<i>Kajjali, rasantoor, rasaparpati</i>	Can be used as long term therapy
<i>Nirgandha murcchana</i>	<i>Mugdharasa, rasapushpa, rasakarpoor</i>	Limited use till the disease cured.

2) *Marana / Incineration:*

Incineration is the process in which *rasadravya* with the help of *maraka dravya* and herbs are

reduced to ashes by *puta*. It yields an assimilable product called *bhasma* which will not create any harm to the human body.

Table 4 Methods of *Dhatu maran*

<i>Bhasma</i>	<i>Maraka dravya</i>	<i>Bhasma quality</i>
I	<i>Parad / mercurial compound</i>	<i>Uttam bhasma</i> (superior quality)
II	Herbs	<i>Madhyam</i> (medium quality)
III	<i>Gandhak / sulphur</i>	<i>Kanishtha</i> (inferior quality)
IV	<i>Ari loha</i>	<i>Durgunprada</i> (non acceptable for internal use)

Table 5 *Puta* required for various drugs

Name of <i>rasadravya</i>	Type of <i>puta</i>
<i>Suvarna , rajat , naag , vang , mukta , praval</i>	<i>Kukkutaputa</i>
<i>Louha , tamra , abhraka , shankh</i>	<i>Mahaputa , Gajaputa</i>
<i>Makshika</i>	<i>Varah puta</i>
<i>Hartala, somal</i>	<i>Bhandputa</i>

Table 6 *Bhasma pariksha* of *rasadravya*

<i>Bhasma pariksha</i>	Name of <i>Rasadravya</i>
<i>Nischandra</i>	<i>Abhraka</i>
<i>Avaami, Amlapariksha</i>	<i>Suvarnamakshik , Tuttha, Tamra,</i>
<i>Nirdhoom</i>	<i>Hartal, Manashila, Somal</i>
<i>Apunarbhav, Niruttha</i>	For All <i>Dahatubhasma</i>
<i>Varitar, Rekhapurna , Niswadatvam</i>	Common tests for all <i>Bhasma</i>

i) *Maraka draya:* Ancient Scholars of *rasashastra* explained four conducts⁹ of *dhatu marana* /metal incineration according to the *maraka dravya* used in the process as shown in table no.4. Administration of *bhasmas* prepared with *arilohas* was not suggested as it has the tendency to harm. *Rasoushadhi* manufactured with such *bhasma* as an ingredient may cause adverse events to the end-users.

ii) *Application of puta:* Temperature required for the preparation of *bhasma* was although the temperature employed in the *maran* that is *puta*. It helps in making the metals and minerals acquire better therapeutic values and also in removing or reducing their toxic properties to such an extent that they will not produce any harmful effects on body tissue when used for therapeutic purposes¹⁰. The type and number of *puta* were variable as it



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depends upon the material and purpose¹¹. Types of *puta* required for *rasadravya* are explained in table no.5. If adequate type and number of *puta* were not given then the *bhasma* was said to be ‘*apakwa*’ and possibly will produce adverse effects¹².

iii) *Bhasma pariksha*¹³:

The processed sample of *bhasma* must be tested on the basis of specific parameters given in classical texts, organoleptic parameters like colour, texture, etc, physicochemical parameters- *niruttha*, *amlapariksha*, *apunarbhav* etc. Specific

bhasma pariksha was essentially indicated for some *rasadravya* as per table no.6 with added common parameters.

iv) *Amrutikaran*¹⁴: It is an important process found described in the context of *abhraka*, *louha* & *tamra marana*. It had been indicated to eliminate leftover *doshas* of *bhasma* and to make them suitable for therapeutic uses. If these *bhasmas* were used without *amrutikarana* then it will cause adverse effects due to the residual *doshas*.

Table 7 *Apathya* during *rasaushadhi sevankaal*

Name of <i>Rasadravya</i>	<i>Apathya</i>
<i>Parad</i>	<i>Kakarashataka</i>
<i>Abhraka bhasma</i>	<i>Kareer, karvellaka, kshara, vruntaka, Oil</i>
<i>Louha bhasma</i>	<i>Kushmand, Til taila, mash, rajika, madhya, amlarasadravya</i>

Table 8 Remedies to cure adverse effects caused due to *rasaushadhi sevan* (*Vikarshanti Upaya*)

Name of <i>Rasadravya</i>	<i>Vikarshanti upaya</i>
<i>Ashuddha Parad</i> /Mercury	<i>Kakamachi swaras</i>
<i>Amurcchit parad</i>	<i>Kushmandadi Gana, shuddha gandhanka + cow's milk</i>
<i>Abhraka</i>	<i>Atasibeej powder with water</i>
<i>Makshik</i>	<i>Kulattha kwath, daadim tvak kwath</i>
<i>Rasak</i>	<i>Cow's urine</i>
<i>Gandhaka</i>	<i>Cow's milk+ cow's ghee + sugar</i>
<i>Hartal</i>	<i>Kushmand swarasa + sugar + cumin seeds</i>
<i>Manshila</i>	<i>Cow's Milk + honey</i>
<i>Naag</i>	<i>Shuddha gandhanka + cow's milk</i>

Table 9 Contraindications of *vishdravyayukta rasaushadhi*.

Name of Drug	Individuals	Disease condition
Formulations of <i>vatsanabha</i>	Children, elderly, pregnancy	<i>Heart disease</i>
Formulations of <i>ahiphen</i>	Children, elderly, pregnancy	<i>Diabetes, kidney disease, productive cough</i>
Formulations of <i>jaypala</i>	Children, elderly, pregnancy	<i>Piles, bowel disease, diarrhea, rectal prolapse</i>

D) Drug administration (Sevanvidhi):

1) *Matra/Dose*: *Rasaushadhis* are more popular than herbal medicines because of their minute

dosage. All the *rasaushadhis* mentioned in the classical texts are described with their individual therapeutic doses best suited for the individuals.



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Consumption of remedy in *alpamatra* /reduced dose, or *atimatra* /overdose can lead to toxic or untoward effects.

2) Duration: Long-term consumption of certain drugs can produce complications eg: *arogyavardhini* is one of the popular *rasaushadhi* effectively used in many disease conditions but its use should be limited for one *mandala* period, after that, it may produce adverse effects. A *mandala* is a period of nearly 40 days in which time the human system completes one physiological cycle. Likewise, inadequate action of the drugs may be noticed if not administered for a prescribed period.

3) Sahapana and anupana¹⁵: *Rasaushadhi*'s were advised to be administered with specified *anupana* and *sahapana* or vehicle, which helps in proper assimilation and absorption of the medicine. An ordinary medicine with appropriate *anupana* can yield extraordinary outcomes. It also helps in controlling the untoward effects of the prescribed drug.

4) Pathya-apathya: *Pathya* literally means anything it may be *ahara* and *vihara* which is not harmful to one's physiological state, in contrast, the *apathyas* are considered to be harmful to our body channels. The concept of *pathya-apathya* is important during the consumption of *rasaushadhi* as it may alter the pharmacokinetics of the drug. *Apathya ahara-vihara* may induce the failure of treatment which in turn leads to unintended drug reactions. *Apathya ahara* while consumption of certain *rasaushadhi* mentioned in ancient scripture is enlisted in table no.8.

5) Contraindications¹⁶: *Vishdravyas* are natural poisons but in *rasashastra* they are used as an ingredient in manufacturing *rasaushadhi* only after proper purification. Such formulations were contraindicated in some patients and certain disease conditions as shown in table no.9. Care must be taken while prescribing such cautious products otherwise it may leads to adverse drug reaction.

E) Remedies for Adverse drug reactions:

If any undesired events were noticed due to faulty processing, improper administration, or non-compliance of code of conduct, treatment procedures for such complications have also been prescribed as per table no.8

DISCUSSION

Ayurveda the traditional system of healing is gaining prime importance and becomes popular globally. World Health Organization in 2004 proposed guidelines of the safety monitoring of herbal medicines. To respond the same AYUSH decided to implement Pharmacovigilance programme to keep watch on the adverse drug reactions caused by the ASU drugs. Before that all users believed that the *Ayurvedic* formulations are harmless, without side effects but these all are evidenced as myths. Our ancient scholars are very well known about the possible adverse events, ample pieces of evidence available in the classics clearly reflect that the pioneers of *rasashastra* were well aware of the toxicity or untoward effects that can occur with the improper usage of metals



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or minerals. They have documented evidences of raw material authentication, standard operating procedures like *shodhana*, *marana*, *murcchana*, *amrutikaran* to convert inorganic material into therapeutic active compounds. Quality control parameters of the finished goods and user guide (*matra*, *anupan*, *kaal*, *pathya-apathya*) were also described deeply to avoid every chance adverse reaction. By chance any adverse reaction exists due to any reason than to overcome such casualties therapeutic remedies were also enlisted.

CONCLUSION

Rasaushadhi can cause adverse effect if it is not manufactured as per the classical guidelines. GMP is very much essential to prepare quality genuine medicines, which will be safe to consume. Unauthentic or Adulterated raw material, improper processing, lack of quality control and faulty administration, drug interactions are some possible reasons of ADR. Ancient *rasacharyas* were well versed with the, pharmacokinetics and pharmacodynamics of metallic preparations. Detailed literal awareness is necessary while practicing to curtail the occurrence of adverse effects.



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