Review Article

Present trends of researches in Rasashastra emphasizing safety of certain metallic preparations - A brief review

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Abstract:

Safety and efficacy of metallic preparations has always been a concern. There has been timely wakeup calls by various incomplete researches. Although constant efforts have been undertaken by research scholars in various institutes but these were not highlighted due to lack of awareness regarding publications. This is a sensuous endeavor to bring those attempts in front of scientific community. Toxicity of various metallic preparations like *Naga Bhasma, Tamra Bhasma* etc and some commonly used *Kupipakwa* preparations that include *Sameerapannaga Rasa, Rasamanikya, Rasakarpura* and *Rasasindhura* has been studied to evaluate safety and were found to be safe for clinical use at therapeutic dose.

Key words: Toxicity, metalic preparations, *Bhasma, Kupipakwa*

Introduction:

The pharmaceutical section of *Ayurvedic* system of medicine recognizes three major sources of medicine, those of herbal origin (e.g. herbs), metal / mineral origin (e.g. salts, metals like gold, copper, silver), and animal origin (e.g. milk, honey etc). *Kashthaushadhis* and *Rasaushadhis* are two main groups of medicines, the former is devoid of any metals/minerals and is purely herbal product and can be considered as safest of medicines, and later consist of metals and minerals in the form of *Bhasma*. In recent past, concerns have been raised on the quality and safety issues of Ayurvedic preparations using *Bhasma*[1]. Safety and efficacy are the major factors for drug designing. Safety of a drug is defined as quality of being risk free, although no drug in the world is risk free, i.e. in appropriate dose and form even poison can be nectar[2]. "Heavy metals" are chemical elements with a specific gravity at least 5 times or more the specific gravity of water[3]. There are about 60 heavy metals, however very few of them possess significant toxicity[4]. Concern of containing heavy metals in Ayurvedic drugs is an issue, which is to be solved by establishing safety data on the same. With this background, a number of studies have been carried-out at IPGT & RA. Initially Institutional guidelines were followed, later updated study protocols like CCRAS and AYUSH guidelines were adopted for toxicity studies. Here an attempt has been made to review the trends of research in present scenario on safety and toxicity of various metallic preparations like *Naga Bhasma, Tamra Bhasma* etc and some commonly used *Kupipakwa* preparations that include *Sameerapannaga Rasa, Rasamanikya, Rasakarpura* and *Rasasindhura*.

Materials & Methods:

The works carried out on *Rasa Sindhura*[5], *Rasa Karpura*[6], *Rasa Manikya*[7], *Sameera*

Pannaga Rasa[8], *Naga Bhasma*[9], *Tamra Bhasma*[10,11] have been reviewed.

Observation & Result:

Rasasindura, a mercurial drug prepared by method of *Kupipakwa Rasayana. T*oxicity of *Samaguna Balijarita Rasasindura* and *Shadguna Balijarita Rasasindura* has been attempted. This study involves the repeated administration of drug over long term period (40days) in doses corresponding to the therapeutical doses in human beings i.e. 22.5 mg/kg in rats. The study concludes that both *Samaguna* and *Sadaguna Balijarita Rasasindura* have no toxic effects.

Rasakarpura is *Kupipakwa Rasayana* containing mercury as an ingredient. Study was aimed to assess toxicity profile of *Rasakarpura* and *Rasakarpura Drava*. This shows LD_{50} dose is much higher than 20.28-mg/kg doses. This Study concludes that, no mortality was observed in Swiss albino mice receiving both test drugs up to 40 times higher dose than the Therapeutic Equivalent Dose TED (0.50 mg/kg).

Chronic toxicity study shows that both *Rasakarpura* and Mercuric chloride have steep dose response curve with regards to toxicity. Increasing the dose by fivefold resulted in 100 percent mortality. The point to be noted here that on acute single dose administration the animals tolerated fairly high dose that is TED X 20 where as chronic administration lead to drastic decrease the level of dose tolerated.

In Dermal toxicity, human clinical trial dose has been applied on rat skin and dermal toxicity has been observed. In rats, results shows that both the drugs could be absorbed into systemic circulation and mercuric chloride may produce moderate degree of toxicity. In rabbits, result shows that there is marked reduction in spermatogenesis, which the only serious effect observed with the test drugs.

Rasamanikya is preparation containing *Haratala (As_2S_3) as main ingredient prepared by Kupipakwa Rasayana. A*cute toxicity and chronic toxicity effect of the drug *Rasamanikya* were evaluated. There was no any significant change observed in ponderal and biochemical parameters in both drug treated group except mild to moderate fatty changes in liver were observed and no significant change in either cholesterol or blood sugar level was observed. Thus it is concluded that *Rasamanikya* is therapeutically safe.

Sameerapannag Rasa is a *Kupipakwa Rasayana* containing heavy metal contents such as *Parada (Hg), Somala (As_2O_3), Haratala (As_2S_3), Manashila (As_2S_2).* The study was aimed to evaluate the safety profile of *Sameera Pannaga Rasa*. The therapeutic dose (5.5 mg/kg) was chosen as starting dose and test drugs were administered in progressive dose levels with limit test was set at 2000mg/kg. In results of pharmacological study no any acute toxicity was observed on gross level of any of group and LD50 was ranging from 971.67 mg/kg - 2000 mg/kg.

Naga Bhasma with *heavy metal Constituent Naga (Pb)* was prepared by two different methods. Acute toxicity study showed no mortality in Charles Foster albino rats and in any of the four groups LD_{50} was more than 160 times higher to that of Therapeutic Equivalent Dose (TED) (12.5 mg/kg).

In Chronic toxicity study was carried out in Charles Foster albino rats at a dose level TED x 05. Mild Fatty Changes and Sinusoidal dilation was observed in liver in group I. Overall toxicity study shows that both the test drugs do not produce significant toxicity at the dose level studied.

Tamra Bhasma contains heavy metal Constituent like *Tamra (Cu)* and *Parada (Hg).* The study attempts to provide evidence about the safety of the drugs and to compare the toxic effect of *Tamra Bhasma* prepared by two different methods. The observed toxic effects were mild in intensity. It is possible that they may not become apparent at the doses equivalent to therapeutically used doses which are fivefold lower. This aspects needs to be considered.

Another work on *Tamra Bhasma* aims at studying, acute and chronic toxicity studies of *Tamra*

Bhasma prepared by three different media. Pharmacologically no any significant pathological affect of *Tamra Bhasma* was found in any of the parameters.

Discussion:

Rasasindura and *Rasakarpura* are mercurial preparations, showed mild anti spermatogenetic effect, suggestive of contradiction for long term use. However the studies were conducted by administering drug without adjuvant mentioned in classics, hence further study is required to confirm above remarks. *Tamra Bhasma* showed mild toxicity, but in clinical study it had shown a very good result in *Grahani*. Here regarding observed toxicity, further repetition of study is suggestive to withdraw definite conclusion. In the histopathological study of *Rasamanikya*, mild fatty changes were observed in liver, but were not significant enough to suggest hepato-toxicity. However to avoid risk, caution can be taken in treating patients with hepatic diseases. *Naga Bhasma* and *Sameera Pannag* showed no toxic effects.

Safety pharmacology is to investigate the effect of new chemical study for further studies, but in case of Ayurvedic drugs it's the other way. Reverse pharmacology[12] i.e. establishing safety data for clinically proven age old medicaments. All metals are present in the earth's crust and enter our bodies continuously at low levels. The studies mentioned above help to establish the fact that frequently used Ayurvedic metallic preparations which contain Lead, Mercury, Copper and Arsenic as ingredient are not only safe but also effective in treating various ailments. Here noteworthy point is that, use of these medicaments is with different adjuvant (*Sahapana* and *Anupana*) which reduces the risk of toxicity.

Use of metallic medicaments is age practice in Ayurveda. If the drug was causing major toxic effects, then it would have been reported and withdrawn from the system. But where there is a description of metallic preparations, our scriptures also make us aware of untoward effects of them (if not prepared properly) and also antidotes to counteract the situation. Efficacy of metallic drugs used in clinics and its wide utilization is self evident of the safety, but in current scenario establishing systematic data of safety gives scientific backup for existing facts.

Conclusion:

Thus the trends of research are changed as per the need of time and adopted for fruitful results. *Naga Bhasma, Sameerpannaga Rasa, Rasamanikya, Rasasindur, Rasakarpur* and *Tamra Bhasma* are safe for clinical use at therapeutic dose. Acute toxicity study of all the drugs has not produced any toxic effect, over 40-360 times of TED. These preparations are safe and never develop any untoward effects, when manufactured and administered by following specified classical guidelines.

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