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REGULATORY SYSTEMS OF INDIA CONTROLLING RESIDUAL LIMIT OF HEAVY METALS IN ASU DRUGS

Shilpa Gawande Kolarkar[1]* and Tushar Khairnar [2]

[1]P.G. Scholar, Department of Agadtantra, College of Ayurved and Research Centre, Nigdi, Pune.

[2]Professor, Department of Agadtantra, College of Ayurved and Research Centre, Nigdi, Pune.

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***Corresponding Author**
Dr. Shilpa Gawande Kolarkar
P.G. Scholar, Department of Agadtantra, College of Ayurved and Research Centre, Nigdi, Pune.

ABSTRACT

Ayurveda is an ancient science of medicine. In number of Ayurveda Sidha Unani Herbo-mineral formulations whether generic or branded, metals are purposefully used to enhance the efficacy of these formulations. Many times, only *Bhasmas* are also used as a single medicine or in combination with other herbal powders used by many Ayurveda practitioners. These metals are used after purification process called as *Shodhana* of the respective metal powders with certain plant extracts or decoctions or Ghrit or Madhu and heating them to a certain temperature to get rid of impurities as mentioned in Ayurveda literatures. ***Objective:-*** There are many regulators in India, controlling the manufacturing standards of these drugs which have defined the permissible residual limit for heavy metals that every Ayurveda practitioner should be aware of. Patients with prolonged use of these drugs may suffer with chronic toxicity of either liver or kidneys or both. *Methodology* by going through various declarations done by these regulators, appendices provided and literatures published by Government of India or Ayush, we have tried to enlighten this aspect of regulatory system and permissible residual amount stated for heavy metals by the Indian regulatory system. *Conclusion (Results and interpretation)* Though creating awareness regarding these heavy metal residual permissible limits, regulation system among ASU drug manufacturers, Ayurveda practitioners and pharmacokinetics of these formulations when consumed in prescribed dosage with limited time duration, controlling over the counter (OTC) sale without prescription of these drugs are many challenges before ASU manufacturers and Ayurveda practitioners.

KEYWORDS: *Bhasmas*, Herbo-mineral formulations, permissible residual-amount of heavy metals, regulators.

INTRODUCTION

Agadtantra is a branch of Ayurveda which deals with various organic and metallic poisons which are classified as *Dhatu* under *Sthavar visha*.[1] This branch explains specific physical characteristics of various metals categorized under *visha*, *Upavisha* which are used in preparation of medicines. *Vishaktata* or toxic effects of these metals if used in impurified form internally or externally is explained in the form of signs and symptoms caused.

These metals after purification are used in the *raskalpas* that is Herbo-mineral medicinal formulations of Ayurveda which are being used since thousands of years for treating various diseased conditions which are found to be effective in curing many diseases.[2] There are misconceptions regarding the poisoning of these metal contents of medicines.[3] There is also lack of awareness regarding the permissible residual limits of the heavy metals in ASU drugs. Combining this misconception and unawareness gives rise to the need of revised measures for standardization and regulation of ASU drugs.

Regulatory control for ASU drugs

In India, there are several laws dealing with drugs for which monographs with quality standards and certain other requirements are prescribed. These monographs should be interpreted subject to the restrictions imposed by these laws wherever they are applicable.[4]

1. **GMP** (Good manufacturing practices) enforced 7th March 2003. Watches for the quality of raw material and the manufacturing set up including the machineries and personnel management protocols such as maintenance of machines, equipment and timely training sessions for personnel involved in manufacturing of the drugs or the formulations. Manufacturing of ASU drugs is Governed by 1. Rule 151 - 155 B - Manufacture and regulate licensing of ASU herbal medicines. 2. Rule 156 – 160 – Conditions of Licensing. 3. Rule 160 A – 160 J – Approval of testing laboratory and regulate testing and quality control.[5]

GMP for ASU drugs mentions **schedule E** which contains only the list of poisonous herbs and metals name but there are no methods for determining metal amount in the manufactured drugs even in the quality control methods.[6]

2. **API** (Ayurveda Pharmacopeia of India) There are some tests for determining the heavy metal residual limits, which are merely chemical tests. These tests are supposed to be done for metal limit detection. According to the depth of the stain obtained after the chemical reaction between the test drug and chemical agent given; the amount of heavy metal in milligrams is determined. This is the amount of metal contained in that 1ml solution of the test drug. These 'limit tests' are for following heavy Metals-As (Arsenic), Fe(iron), Pb (Lead).[7]

Permissible limits of heavy metals as per API

1. Lead 10 ppm
2. Arsenic 3 ppm
3. Cadmium 0.3 ppm
4. Mercury 1 ppm

3. **IP:** (Indian Pharmacopeia) 2007 VOL 1[8] - Has given chemical tests to identify the limit of Arsenic, iron, mercury etc. These are applicable for modern pharmaceuticals drugs. The permissible limits for heavy metals in plant species present due to phytoaccumulation as per Indian Pharmacopoeia 2007 guidelines are given.
4. **Drugs and Cosmetic Act**, **1940:** Controls FSSI which has prescribed maximum permissible metal contaminants of the food stuff. Many times, ASU preparations are sold under category of food supplements, where these limits should be taken into consideration. ASU medicines are covered under the act by inserting chapter IV-A, came into force February 1983.[9]
5. **Poisons Act, 1919**- controls possession and sale of lead, arsenic, oxides of mercury, zinc chlorides. This law is applicable for industrial storage and pharmacies who are licensed for keeping these poisons.[10]

MATERIAL AND METHODS

The revised appendices related to the regulations controlling the heavy metal residual limits for metals and its content in the herbo- mineral drug formulations_and_various declarations done by GMP, API, IP, drug and cosmetic act 1945, Poison act 1919 of Government of India and Ayush were read thoroughly and studied.

RESULTS AND DISCUSSION

Challenges before global acceptance of ASU drug Industry and Ayurveda practitioners

1. Drug Safety and Standardization

To prove the safety of Herbo-mineral drugs by standardization of these drugs according to the metabolism of metal contents. Pharmacokinetics of the new drug and pre-existing generic entity is one of the regulatory requirements for an investigational new drug approval. However, for the majority of Herbo-mineral formulations used in the traditional or conventional medical practice, data on their disposition and biological fate in human are lacking. It is vital in the drug development process to understand the absorption, distribution, metabolism and excretion (ADME) of an active molecule from these formulations and how they interact with conventional drugs before their launch in the market in order to ensure the rational use of Herbo-mineral medicines. Pharmacokinetics in the Ayurvedic system are largely ignored due to the rigor, cost and time consumption of the drug development process.[11]

2. A stringent regulation

To restrict OTC sale of Herbo-mineral formulations to avoid self- medication is major need for Ayurveda practitioners and ASU drug manufacturers. Efforts are needed to establish and validate pharmaco-epidemiological evidence regarding safety and practice of Herbo-mineral medicines. Pharmacokinetic data of biomarkers contribute considerably to the scientific assessment of the various claims of Herbo-mineral products, which are increasingly marketed with curative claims worldwide.[8] Many Ayurvedic medicines are available as Over the Counter (OTC) medicines. However, it is not advisable to buy medicines without prescription. Ayurvedic medicines are prescribed in accordance with one's body constitution and the medicine for one individual may differ from the other. On the basis of ingredients, Ayurvedic medicines can be classified into three categories- Herbal, Mineral and Herbo-mineral. There should be stringent law stating that, consult your Ayurvedic physician regarding the medicine that has been prescribed to you. Take medicines under the supervision of a physician and only for the period as prescribed. Never self-medicate based on other people's experience.[12]

3. Quality check

Quality check of raw plants, raw metals, preparations and formulations is also a big challenging issue. There are many herbs which are controversial and some are very rare

which questions the authentication and standardization regarding contents and process of current ASU drug manufacturers. DNA based molecular marking is the most advanced technique should be used for quality control and standardization of medicinal plants.[13] Phytoaccumulation is one more challenge for ASU drugs. The permissible limits for heavy metals in plant species as per Indian Pharmacopoeia 2007 guidelines are given.[14]

CONCLUSIONS

There are regulatory systems controlling the residual heavy metal amount for ASU drugs. API (Ayurveda pharmacopeia of India) has stated about the tests which should be used for metal detection in ASU formulations. Even if, ASU drugs are sold under the category of food supplement, pharmaceuticals need to follow the limits of heavy metal content or contents under FSSI which works under Drugs and Cosmetic Act, 1940. In spite of this, many ASU formulations contains heavy metal or metals as a main ingredient which are necessary for the positive outcome in the patients. Hence, these permissible 'heavy metal residual limits' may not be possible to follow for ASU practitioners and ASU medicine manufacturers. The criteria for standardization of ASU formulations also should be revised according to standard books and literature for generic preparations. Also, stringent law for not allowing OTC (over the counter) sale of ASU formulations is desperately needed for the era.

REFERENCES

1. Susrutasamhita Ayurvedtattva-sandipika, Kaviraj AmbikaDatta Shastri, Chaukhambha Sanskrit sansthan, 2003; 1.
2. B Manish Et al, significance of rasakalpas in relevance with ayurvedic pharmacotherapeutics (Rasa shastra) in the management of male infertility, IAMJ, ISSN, 2320: 5091.
3. N Shrikanth et al, Myths and facts of Ayurvedic Bhasmas and Rasa kalpas: A producer consumer and end user oriented Pragmatic Approach, 2009.
4. Ayurvedic pharmacopeia of India Part 1 volume IX.
5. GMP, WHO guidelines for ASU drugs, chapter III.
6. API/Appendix-Vol-2-3-4.pdf
7. Ayurvedic Pharmacopoeia, partvolumeIX.pdf
8. Indian pharmacopoeia, 2007.
9. GMP, WHO guidelines for ASU drugs, chapter III.
10. Indian code.nic.in

11. Mishra Et al, Emerging Need of Pharmacokinetics in Demystification of Herbo-Mineral Compounds. International Journal of Ayurveda and Pharma Research, 2020; 8(6): 75-79.
12. Government of Dehli, Directorate of Ayush, FAQs.
13. Warude D Et al. Botanicals: Quality and Regulatory issues. Journal of Scientific & Industrial Research, 2005; 64: 83-92.
14. Indian journal of pharmacology, an official publication of Indian pharmacological society, 2011; 43(3).
15. IP (Indian Pharmacopoeia), 2007.