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Toxicovigilance : A prerequisite to drug safety surveillance in Ayurveda

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ABSTRACT

Toxicovigilance is the active process of identifying and evaluating the toxic risks existing in a community and evaluating the measures to reduce or eliminate them. Although the technical term "toxicovigilance" does not feature in Ayurvedic texts, its essence is highlighted in *Agada Tantra*. *Agada Tantra* has comprehensive approach on toxic effects of *Visha Dravyas* (toxic substances) and its management. Through toxicovigilance; not merely there is scope for Ayurveda to find solution for toxicity issues, besides there is extensive scope for screening and regulating Ayurvedic formulations containing poisonous drugs of herbal/metal/mineral origin. In fact, study of poisonous drugs and ADR monitoring is an essential aspect in toxicological departments. It is the need of the hour to employ the Ayurvedic discipline of toxicology to explore the challenges that Ayurveda is facing today with regard to drug safety. A comprehensive study of all potential exposure associated with Ayurvedic medicaments, risk assessment, prevention and management can be the primary footstep in this direction. At this point, vigilance of toxic drugs is to be done by considering the guidelines on collection, pharmaceutical processing, indications, contraindications, dosage and antidotes as mentioned in Ayurvedic classics. Thus, data of toxicovigilance can be effectively applied in monitoring drug safety in Ayurveda.

Key words: Toxicovigilance, *Visha Dravyas*, Adverse Drug Reactions.

INTRODUCTION

The concept of toxicovigilance encompasses the active detection, validation and follow-up of clinical adverse events related to toxic exposures in human beings.^[1] *Agada Tantra*, a branch of *Ashtanga Ayurveda*, deals with toxic effects of *Visha Dravyas* (toxic substances) and their impact on health. Science

of Ayurveda emphasizes the usage of *Visha Dravyas* (toxic substances) of herbal/metallic/mineral origin as medicine after *Shodhana* (purification/detoxification process). Charaka explains "even a strong poison can become an excellent medicine if administered properly; on the other hand, even the most useful drug can act as a poison if handled carelessly".^[2] Hence dose differentiates a drug from poison. The pharmacology concepts and drug safety issues are vigorous all through the literatures of Ayurveda, but absolute methods to estimate drug safety is not pursued.

Improvement of patient safety is gaining momentum world wide, so the subject of drug safety has become vital in the present scenario. The detection, assessment and prevention of adverse events and all other problems related to medicines are considered under pharmacovigilance. As adverse drug reactions (ADR) reports under pharmacovigilance raises high

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concern towards formulations containing toxic medicinal plants, metals and minerals; an attempt towards drug safety needs to be started with screening and regulating Ayurvedic formulations containing poisonous drugs. In fact, study of poisonous drugs and adverse drug reactions (ADR) monitoring is crucial in toxicological department. Due to numerous formulations and also due to diversity in drug choice, it is extremely difficult to ascertain fixed safety standards for herbal preparations. The classical references about poisonous compounds are scattered and there is difference of opinion about pharmaceutical processing, indications and dosage of these drugs. Detailed study of toxic drugs i.e. toxicovigilance from Ayurveda point of view will be a basic requirement towards drug safety. This will guide towards the prominent areas of research and thereby helpful in establishing the standards. Accordingly an attempt is made to review the Ayurveda manuscripts regarding the therapeutic utilization of toxic drugs in Ayurveda and to appraise application of toxicovigilance in monitoring drug safety.

Scope of poisonous substances in Ayurveda

Schedule-E(1) of Drugs & Cosmetic Act 1940 has enlisted 13 herbal, 1 animal origin and 7 mineral origin poisonous substances under ASU Systems of Medicine (2010 amendment).^[3] Therapeutic application of *Visha-Upavisha Dravyas* (toxic medicinal plants) is extensive in Ayurveda. Formulations containing *Visha-Upavisha Dravyas* (toxic medicinal plants) have broad clinical significance in present day to day practice. In order to ascertain the formulations containing *Visha-Upavisha Dravyas* (toxic medicinal plants); search of literature was carried out in authoritative books of Ayurveda mentioned in Schedule I of Drugs and Cosmetic act 1940.^[3] Vast number of formulations containing toxic medicinal plants (shown in Table 1) and application of these formulations in day today clinical practice (shown in Table 2) suggest about wide scope of *Visha-Upavisha Dravyas* (toxic medicinal plants) in Ayurvedic therapeutics. In addition, formulations containing metal/mineral origin substances are

innumerable and they have extremely broad scope in Ayurveda therapeutics.

Table 1: Showing the number of formulations containing *Visha-Upavisha Dravyas* (toxic medicinal plants) as one of the ingredient.

Drug name	Number of formulations in AFI ^[4]	Number of formulations in Bhaishajya Rathnavali ^[5]
<i>Vatsanabha</i> (<i>Aconitum ferox</i>)	38	130
<i>Kupeelu</i> (<i>Strychnous nuxvomica</i>)	05	17
<i>Ahiphena</i> (<i>Papavarum somniferum</i>)	06	22
<i>Jayapala</i> (<i>Croton tiglium</i>)	05	60
<i>Dhatura</i> (<i>Datura metal</i>)	17	44
<i>Bhanga</i> (<i>Cannabis sativa</i>)	11	13
<i>Gunja</i> (<i>Abrus precatorius</i>)	02	07
<i>Bhallataka</i> (<i>Semicarpus anacardium</i>)	15	45
<i>Arka</i> (<i>Calotropis procera</i>)	19	21
<i>Snuhi</i> (<i>Euphorbia nerilifolia</i>)	08	45
<i>Langali</i> (<i>Gloriosa superba</i>)	04	16
<i>Karaveera</i> (<i>Neerium indicum</i>)	04	14
AFI - Ayurvedic Formulary of India		

Table 2: Showing few important formulations of Visha-Upavisha Dravyas (toxic medicinal plants) that are frequently used in practice.

Drug name	Important formulations
Vatsanabha	Hinguleshwara Rasa (B.R) Tribhuvana Keerthi Rasa (Y.R) Agnitundi Vati (R.S.S) Anandabhairava Rasa (R.S.S) Maha Shankha Vati (B.R) Vishagarbha Thaila (Y.R)
Kupeelu	Agnitundi Vati (R.S.S) Vishamushti Vati (S.B.M.M) Lakshmi Vilasa Rasa (B.R) Visha Garbhathaila (B.R) Vishatinduka Thaila (B.R)
Ahiphena	Ahiphenasava (B.R) Grahani Kapata Rasa (B.R) Kaprura Rasa (B.R)
Jayapala	Ichhabhedhi Rasa (B.R.) Punarnavadi Mandoora (B.R) Draksha Asava (B.R) Dadimavaleha (Y.R)
Dhatura	Mahajwarankush Rasa (R.R.S) Lakshmivilas Rasa (B.R) Mahalakshamilas Rasa (B.R) Unmadagajankush (R.T) Kanakasava (B.R) Vishagarbha Thaila (Y.R) Maha Visha Garbha Thaila (Y.R)
Bhanga	Pushpadhanwa Rasa (B.R) Jatiphaladi Churna (Sha.Sam.)
Gunja	Gunjabhadra Rasa (R.T)

	Gunja Thaila (B.R) Indraluptahara Lepa (Sha. Sam)
Bhallataka	Sanjivani Vati (A.F.I) Amrtabhallataka Ghrita (A.F.I.) Kutaja Avaleha (A.F.I) Prasarini Taila (A.F.I) Panchatikta Guggulu Gritha (B.R)
Arka	Arka Lavana (B.R.) Dhanvanthari Ghrita (Sa.Yo.) Marichadi Taila (Sha.Sam.) Pravala Panchamritham (Y.R)
Snuhi	Shankha Vati (B.R) Marichadi Taila (C.D) Shadbindu Taila (B.R)
Langali	Bolabaddha Rasa (R.R.S) Karanja Thaila (B.R.) Somarajee Thaila (B.R.)
Karaveera	Manikya Rasa (B.R) Mahamarichadi Thaila (Y.R.)
B.R - Bhaisajya Ratnavali; ^[5] R.T - Rasa Tarangini; ^[6] Sha.Sam - Sharangadhar Samhita; ^[7] Y.R. - Yoga Ratnakara; ^[8] R.R.S - Rasa Ratna Samucchaya; ^[9] S.Y - Sahasra Yoga; ^[10] C.D - Chakra Datta; ^[11] R.S.S. - Rasendra Sara Sangraha; ^[12] S.B.M.M - Siddha Bhaishajya Mani Mala. ^[13]	

Factors for appraisal of toxic drugs in Ayurveda

Ayurveda has emphasized on specific factors that are majorly responsible for the action of drugs. Consideration of factors such as collection and processing of raw materials, dosage and mode of administration, duration/course of drug administration, specific diet regimen is extremely crucial in administration of *Visha-Upavisha Dravyas* (toxic medicinal plants) because even a trivial variation may cause severe ADR's. Good agricultural and collection practices (GACP) to be stringently followed in case of toxic herbs collection. *Shodhana*

for each drug is unique and Ayurveda classics recommend diverse *Shodhana* methods for each poisonous compound. Standardization of processing technique and adoption of standardized guidelines in manufacturing the drugs is essential to avoid the ADR's. From pharmacological point of view during preparation of the medicines, if the raw drugs are not taken in the proper quantity then desired action on body may not be obtained or the formulation may show unwanted actions. Adverse drug reactions (ADR) are also results of improper dose of drugs and repeated/large doses. It is the dose by which *Visha* (poison) becomes *Amruta* (nectar) and *Ausadha* (medicine) becomes *Visha* (poison). Along with dosage, additive drug effect also needs to be considered while prescribing multiple formulations. Eliciting drug history in patients with pre-existing kidney or liver disorders may reduce magnitude of complications that may arise due to overdosing of formulations containing toxic ingredients. Specific *Anupana* (adjuvant) as explained in Ayurveda classics have definite role in drug efficacy and safety. *Jayapala* (*Croton tiglium*) being the best example to show its purgative effect enhanced and suppressed by intake of cold water and hot water respectively.^[14] References of drug specific diet and regimen explained in Ayurveda, enlightens us on the care adopted in the system to prevent ADRs. One such example being indication of *Ghrutha*, *Ksheera* and *Shashtika Shali* use during the administration of *Bhallathaka* (*Semicarpus anacardium*) owing to its extreme *Teekshna*, *Ushna Gunas*.^[15] Hence these factors are to be essentially considered by an individual physician and accordingly rational prescription of the drugs will accomplish safety. As a general rule most of the formulations containing metal/mineral drugs, have to be discontinued following a period of 45 days. Improving patient awareness on diet, regimen, and duration of drug administration will bring down common misconception amongst the community that all Ayurvedic medicines are always safe and absolutely devoid of side effects. There is reported evidence about overdose effect of *Mahashankha Vati*, an Ayurvedic medicine containing aconite,^[16] which was

consumed without the prescription. It clearly demonstrates lack of awareness in patient community about Ayurvedic medicines and ill effects of over the counter sale. Patient education on appropriate intake of medication also avoids the medication errors and thereby reduces the ADRs.

CONCLUSION

Drug safety is achievable by the three tiers such as detection, monitoring and prevention of adverse events. Toxicovigilance has a pivotal role in the preventive tier of drug safety. Creating comprehensive, unbiased and easily accessible information on poisonous drugs used in Ayurveda therapeutics can build awareness among Ayurvedic physicians, drug manufacturers and patients which is the need of the hour.

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