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Ayurveda Perspective Of Drug- Drug Interactions – A Review Vivek¹, Suneha²

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ABSTRACT: -

Drug safety is a fundamental concept in medical practice. Ayurveda is a holistic approach of medicine which has elaborated the causes and methods of drug-induced consequences along with preventive measures in classical texts. The aim of Ayurveda is to prevent normal health and curing the diseased one. Present literature review was conducted from the various compilation of Ayurveda and electronic database with search terms of 'Vyapad', 'Viruddha', 'Ahita', 'herb-herb interaction', 'Asatmya', 'Prakritiviruddha' etc. Ayurveda texts have mentioned various causes for Adverse Drug Reaction which seems to be not much different than those explained in modern such as, excessive effects, drug interaction, drug intolerance in susceptible patients, and drug allergy. The word ADR may not be found in Ayurvedic literature but the concepts and safety issues are vibrant throughout the texts of Ayurveda.

The various concepts of drug interactions in Ayurveda sound similar to that of modern pharmacovigilance.

Keywords: Drug, Herb, *Viruddha*, *Ahita*, *Asatmya*



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INTRODUCTION

Drug interaction is one of the important issues related to drug safety that needs to be considered while prescribing any drug. Any drug may have harmful effects and may react adversely with other drugs/ food/ biological and other compounds which result in loss of therapeutic efficacy and resulting with some complications. The Ayurveda system also gives importance to the safety of drugs intake. The old ethical and traditional system of medicines utilizes various therapeutic procedures, Ayurvedic formulations, and herbs for the management of different diseases. The majority of Herbal Medicine is harmless in small doses ^[1]. The interactions between herbs or dietary supplements and drugs require attention, especially for the elderly, frail, or those taking multiple medications for chronic diseases ^[2].

A drug interaction is defined as measurable (modification in magnitude or duration) of the action of one drug caused by prior or concomitant administration of another substance (including prescription and non-prescription drugs, food, beverage, supplement or alcohol). Some of the issues that arise today about various interactions of herbs and drugs may have already been

encountered in earlier times when herbs were combined with each other. As Ayurveda is the only medical science, that gives importance on prevention from a disease and maintenance of health rather than treating any disease ^[3].

A decrease in drug dosage by integrity of an interaction could make the drug ineffective; mild increase in drug dosage could make it reach levels that produce side effects. The mechanism of drug plays an important role, how it acts either its herb or drug as the consequences of drug interactions are harmful such as life threatening, detritions of patient's status and can cause minor effects. The drug whose activity is affected by these interactions is called an *object drug* and the agent which precipitates such an interaction is referred as *precipitant*.

MATERIAL & METHODS

Literary search: Classical books of Ayurveda which includes *Charaka Samhita*, *Sushruta Samhita*, etc. and published journal articles, Internet exploration on terms like terms 'Vyapad', 'Viruddha', 'Ahita', 'herb-herb interaction', 'Asatmya', 'Prakritiviruddha' and 'Doshala' Classical

Table No.-1 Mechanism of Drug Interactions

PHARMACOKINETICS	PHARMACODYNAMICS	
1. Absorption 2. Distribution 3. Metabolism 4. Excretion	DIRECT 1. Antagonism 2. Synergism	INDIRECT

PHARMACOKINETICS

These interactions alter the concentration of the object drug at its site of action and consequently the intensity of response by affecting its absorption, distribution, metabolism or

excretion.

Drug interaction may also be due to-

1. Active transport
2. Change in PGP (Phosoglycoprotein)

Absorption

Absorption of an orally administered drug can be affected by other concurrently ingested drugs. This is mostly due to formation of insoluble and poorly absorbed complexes in the gut lumen.

Distribution

Distribution is those where distribution pattern of the object drug is altered. These interactions occur primarily due to displacement of one drug from its binding sites on plasma proteins by another drug. Drugs highly bound to plasma proteins that have a relatively small volume of distribution

Alteration of Distribution can be done by –

- i. Displacement from protein binding sites
- ii. Some disease states

Metabolism

Certain drugs reduce or enhance the rate of metabolism of other drug.

Alteration in metabolism by –

1. Enzyme induction (Metabolic effect ↑ Drug extent ↓)
2. Enzyme inhibition (Metabolic effect ↓ Drug extent ↑)

Enzymes involve in metabolism –

- a. Cytochrome- P450
- b. Cytochrome- 3A4

Excretion

It is defined as those where excretion pattern of the object drug is altered.

Major mechanism of Excretion interactions are –

1. Alteration of urinary pH
2. Alteration of Active Transport
3. Change in Active renal tubular secretion
4. Change in renal blood flow
5. Forced Diuresis

PHARMACODYNAMICS

Pharmacodynamic interactions are defined as those in which the activity of the object drug at its site of action is altered by the precipitant.

This may result in an enhanced response, an

attenuated response or an abnormal response.

Such interactions may be - direct or indirect.

Different Cause Of Adverse Drug Reaction According To Ayurveda

1. Drug interaction (*Virudha Dravya Prayoga*)
2. Iatrogenic (*Vaidya Kruti*)
3. Over dose (*Atimatradravaya Prayoga*)
4. Administration of unwholesome drugs (*Ahitatama Dravyas*)
5. Administration of medicine in diverse pathological stages (*Avasthanusar Dravya Prayoga*)
6. Therapeutic procedural complications (*Panchkarma Vyapad*)
7. Improper use of *Rasaushadhi*

Possible Drug Interactions

1. Drug- drug interactions
2. Drug- herb interactions
3. Herb-Herb interaction
4. Herb-Food interaction
5. Herb-animal origin drug interaction
6. Disease related interaction

1. Herb-Drug Interactions

Ayurveda being the most popular alternative medicine in India, people are using Ayurvedic drugs simultaneously with allopathic drugs to treat same symptom or any other symptom. This creates an increasing chance for interactions between these drugs i.e. Herbal drugs and Allopathic drugs. Herbal Medicines affect Pharmacokinetic as well as Pharmacodynamic properties of standard drugs and thus cause herb-drug interactions. Drugs usually contain single chemical structure, while almost all herbal products contain mixture of pharmacologically active ingredients.

Herb –drug interactions are more common and occur more frequently than drug- drug interactions.

Table No.- 2 Herb-Drug Interaction and their result ^[4]

S.No.	Herb+ Drug example	Result
1.	<i>Ashwagandha</i> + Digoxin	Interfere with Thyroid Hormone
2.	<i>Bala</i> + Caffeine	Reduces potency of anti hypertensive drugs
3.	Ephedrine + Steroids	Toxicity
4.	Garlic + Lisinopril	Severe effect with anti coagulant drugs
5.	<i>Guggulu</i> + Diltiazem/ Propranolol	Reduce absorption
6.	<i>Yashti madhu</i> + anti hypertensive drugs	Decreased Efficacy
7.	<i>Yashti madhu</i> + Iron	Decreased absorption
8.	Pepper + NSAIDs	Enhance level
9.	Ginger + Warfarin	Bleeding
10.	Ginkgo + Warfarin	Decreases platelet aggregation resulting bleeding
11.	Ginkgo + Nifidine	
12.	Ginkgo + Aspirin	
13.	St. John's Wort (SJW) + Cyclosporin	Cyclosporin will be more metabolised resulting excretion

2. Herb-Herb Interaction

- *Piper betel* is contraindicated while taking *Garcinia Morella*
- *Basella alba* along with *Sesamum indicum* ^{[5],[6]}

3. Herb-Food Interaction

- Combination of *Payasa* (milk preparation) and *Mantha* (gruel) is contraindicated
- Wine with steamed grains
- Radish with milk ^{[5],[7]}

4. Herb-Animal Origin Drug Interaction

- *Kapot mamsa* (meat of pigeon) + *Sarshapa taila* (*Brassica alba*).
- *Shukar mamsa* (Pork) + *Narikel Taila* (oil of *Coccus nucifera*)
- Equal quantity of *madhu*, *Ghrita*
This has been proved to produce toxic effect by combination ^{[5],[7]}

5. Disease Related Interaction

Haritaki (*Terminalia chebula*) contraindicated in pregnancy, malnourished, anorexia after bloodletting ^[8]

Possible Interactions according to Ayurveda

Ayurveda describe various terms such as- *Viruddha* (Incompatibility), *Apathya*, *Asatamya* and *Ahittam* which are somewhere correlated to drug interactions.

❖ Incompatibility (*Virrudha*)

Incompatibility occurs as a result of mixing of two or more “Antagonistic substances” and an undesirable product is formed which may affect the safety, efficacy and appearance of the pharmaceutical preparation.

Table No. -3 Incompatibilities ^[9]

S.No.	Incompatibility	Example		
1.	<i>Viruddha</i>	<i>Takra Siddha Kampillaka</i> (<i>Mallotus Philippensis</i>)		
		Equal Amount Honey and <i>Ghruta</i>		
		Equal Amount of Honey and <i>Antriksha Jala</i>		
		Equal Amount Honey and <i>Pushkara Beeja</i>		
		Honey + <i>Ushna Jala Anupana</i>		
		<i>Bhallataka + Ushnodaka</i>		
2.	<i>Guna Viruddha</i>	<ul style="list-style-type: none"> • Fish + <i>Payasa- Rakta Dushti, Dosha Dhatu Mala Srotas Avrodhak</i> • <i>Gramya Anupaudak Pishitani + Madhu, Tila, Guda, Payo, Masha, Mulak, Bis, Rudh Dhanya – Badhirya, Andhya, Vepathu, Jaadya, Mookta, Maran</i> • <i>Sarshapa Taila Bhrishta Poshkar, Rohinik Shaak, Kapot + Madhu, Paya – Shonit Abhishyand, Dhamni Pravichya, Apasmara, Shankhak, Galaganda, Rohini, Maran</i> • <i>Mulak, Lashuna, Sursa + Paya – Kushtha</i> • <i>Madhu, Paya + Jatushaak, Pakwa Nikuch – Maran; Bala, Varna, Teja, Veerya Aprodha; Shandhya</i> • <i>Pakva Nikuch + Masha Soup, Guda, Sarpi – Dhatu Virodhik</i> 		
		3.	<i>Samyog Virrudha</i>	• <i>Padmotrika Shaak, Sharkara, Mairaiya, Madhu (Sehupyoga) – Vata Kopyati</i>
				• <i>Payasa + Manthan Anupana – Kapha Kopyati</i>
				• <i>Ushna Madhu – Marak</i>
				• <i>Ushna Aartasya + Madhu Sevan – Maran</i>
		4.	<i>Sanskar Virrudha</i>	<i>Sarshapa Taila Bhrisha Haridrak – Pitta Kopyati</i>

❖ **Apathya**

The *Aahar-Vihar* which is not beneficial and nutritional to body and doesn't give happiness to mind is known as *Apathya* as explained by *Aacharya Charaka* [10]

Example-

- *Rasa Karpura Gutika + Amla Dravya, Ushna Dravya, Guda*
- *Parada Rasayana Sevan + Madya, Kushmand, Kulath, Karkotaka, Kapitha*
- *Gandhaka + Kshara, Amla, Lavana*
- *Abhraka + Karira, Karvellaka, Amlakola, Taila*
- *Suvarna Bhasma + Bilwa Phala*
- *Loha + Lakucha, Badara, Jambeer. Chanaka, Karvellaka*
- *Hartala + Lavana, Amla, Katu*
- *Shilajatu + Guru, Vidahi, Kulatha, Kakmachi, Kapota*

❖ **Asatmaya**

- Materials against nature, substances which are not tolerated by the individual or any diet that is causing disease or unhealthy for a person.
- *Asatmaya* is what is not tolerated by the body. This intolerance is projected in many forms-
 - i. Vomiting, nausea, giddiness, watering of mouth.
 - ii. Gastric irritation
 - iii. Skin rashes, photosensitivity, exfoliation of the skin, visual disturbances.
 - iv. Burning and scalding of urine.
- Few examples are death, abdomen pain, loss of lustre, chest pain, intoxicating and GI bleeding by administration of *Apakva Lohabhasma* [11]

❖ **Ahitkara**

Unwholesome (*Ahitatama*) drugs are not suitable for therapeutic purpose, and administration of such drugs may induce the failure of treatment which intern leading to unintended drug event. Many a times tangent property of drug i.e. by utilizing analogous property of drugs with diseases lead to ADRs by aggravating the

original conditions as in blood vitiating (*Rakta doshaka*) property of *Tamarindus indica* [12] and *Sapindus mangifera* [13]; asthenia, blister producing capacity of *Semicarpus anacardium* [14] are few examples of such ADRs.

The *Ahara* which makes the *Samadhatu Vishama* and to already *Vishama Dhatu* causes more vitiation is known as *Ahitkara Aahara*.

Example- *Yavaka, Masha, Varshanadeya, Aushar, Sarshap Shaak, Gau Mamsa, Mriga Mamsa, Kaankapot, Bheko, Chilcham, Aavik, Aaviksheer, Kusumbh Sneha, Mahishi Vasa, Kumbhir, Kakmudag, Chatak, Hasti Meda, Aaluk, Nikuch, Faanit.*

DISCUSSION

Possible Mode of Action

The theories of Ayurvedic principles are suggestive of improper reaction or interactions or side effects between the substrates, resulting in the production of metabolites that are known as *Ama* in Ayurvedic terminology and causing *Abhishyandi* (blockage in body channels), like in the digestive area of the GIT or *Mahasrota*, or affecting *Rakta* i.e., after metabolism vitiating circulation and congesting the normal functioning in the respective *Dhatuvaha Srota* or histological to cytological level where *Ama* is reached. The primary cause of interaction is the basic antagonism in terms of Ayurveda, known as *Virya*, which is the potential of action of a substance, the concomitant use of *Sheeta* and *Ushna Virya* often leads to such interaction instantly. There are various other ways of antagonism by way of *Matra* (dose), *Samskara* (preparation), *Samyoga* (combination), *Prakriti* (body constitution), *Desha* (place), *Kaala* (environmental factors), etc. all may lead to make the chemical change in the state of *Virya*,

resulting in the above mechanism.

To acquire optimum therapeutic effect and prevent side effects of drug substances Ayurveda gives importance to

- *Aushadha sevan Kaala* (time of drug administration)
- *Anupana* (drug adjuvant)
- *Pathya- Apathya* (diet regimen)

Ayurveda emphasized towards safe treatment and cure disease through its root cause without initiating another disease.

CONCLUSION

Base for *Viruddha* is different due to *Agni, Saara, Samhana, Prakriti, Ritu, Dosha*, etc. Hence *Viruddha* is *Aniyata*. Limited examples are mentioned in *Samhitas* and understanding these examples with the help of Pharmacology, gives clue about the drug interactions and base for *Viruddhatva*.

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