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## Synergism and Antagonism in Ayurvedic Formulations

Anusha Rao M.R.<sup>1\*</sup>, Govinda Sharma K.<sup>2</sup> and Nisha Kumari P.R.<sup>3</sup>

<sup>1</sup>Department of Rasashastra Bhaishajya Kalpana, S.D.M College of Ayurveda and Hospital, Hassan, Karnataka, India

<sup>2</sup>Department of Rasashastra Bhaishajya Kalpana, S.D.M College of Ayurveda and Hospital, Hassan Karnataka, India

<sup>3</sup>Department of Rasashastra Bhaishajya Kalpana, B.G Garaiya Ayurvedic College, Gujarat, India

### ABSTRACT

Rasashastra and Bhaishajya Kalpana encompasses a wide variety of *Kalpanas*. The method of preparation and mode of administration vary vastly amongst them. These variations need to be analysed to get the maximum benefit from each formulation. Synergism and antagonism are two pharmacodynamic terms understood under the purview of *Samanya vishesha siddhanta*. The facilitation of a pharmacological response by the concomitant use of two or more drugs is called “Synergism”. This co-operation usually results in a total effect greater than the sum of their independent actions. The phenomenon of opposing actions of two drugs on the same physiological systems is termed as “Antagonism”. To understand synergism and antagonism in Ayurvedic formulations, some formulations are analysed, each containing a few ingredients, to see the factors where these are evident. In the context of choosing raw materials, *Shodhana* method / Processing of drugs specific to the formulation, method of preparation, adjuvants used / Media in which the raw drugs are suspended/dissolved, use of *Visha Dravyas*, and the method of administration- *Kala, Matra* ; synergism and antagonism were observed at various stages.

To conclude, it was observed that instances of synergism and antagonism were observed at each stage of a formulation, whether amongst the ingredients, or against the site of action of the medicine which elucidates the role of these pharmacodynamic terms in understanding Ayurvedic formulations. Researches done under this light would further help in understanding the concept and mode of action of Ayurvedic formulations.

### KEYWORDS

*Ayurveda, Synergism, Antagonism, Samanya vishesha*



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## INTRODUCTION

The word “drug” is defined as a substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient. Pharmacodynamics is the quantitative study of the biological and therapeutic effects of drugs. Such studies also elucidate the mechanism of action of a drug and may correlate the drug actions with its chemical nature<sup>1</sup>.

Various factors modify the effect of drugs; Synergism and Antagonism are two among them. The facilitation of a pharmacological response by the concomitant use of two or more drugs is called “Synergism”. This co-operation usually results in a total effect greater than the sum of their independent actions. The phenomenon of opposing actions of two drugs on the same physiological systems is termed as “Antagonism”<sup>2</sup>.

Synergism and antagonism can be understood under the purview of “*Samanya Vishesh Sidhanta*” in Ayurveda<sup>3</sup>. Formulations contain multiple drugs, combined in specific proportions and methods, and are administered in a particular way, to yield maximum benefit. In this article, an attempt has been made, to understand the synergistic and

antagonistic relationships among the various ingredients of Ayurvedic formulations.

However, the study has been restricted to simple formulations containing a few ingredients serving as a method to analyse which can be extrapolated to other formulations as well.

## MATERIALS AND METHODS

Literatures of print and electronic media were used as a source of information to collect data about formulations which could help in understanding synergism and antagonism through Ayurveda. Journals and research articles available online were also included for reference. A few formulations containing 3 to 5 ingredients were chosen to understand the concept under each factor.

## DISCUSSION

These formulations have several components; each playing a particular role in its specificity towards mode of action. These factors are:

- The Raw drugs/Ingredients
- *Shodhana* - Purification/ Processing of drugs specific to the formulation
- Method of Preparation
- Adjuvants used / Media in which the raw drugs are suspended/dissolved

- Use of Visha Dravyas
- Method of administration- Anupana, Kala, Matra

#### **Raw drugs / Ingredients used:**

Ingredients in formulations are usually collected and chosen to act synergistically or antagonistically among themselves and also on their target Dosha / Dhatu / Mala.

For example - *Panchakola phanta* consists of five drugs I.e. Pippali (*Piper longum* fruit) , Pippalimoola (*Piper longum* root), Chavya (*Piper chaba*), Chitraka (*Plumbago zeylanica*), Nagara (*Zingiberiae officinale*)<sup>4</sup>.

The properties of these five drugs are *teekshna*, *ushna*, *deepana*, *pachana*, *kaphavatanut* and the action expected from this particular formulation is similar. Individual drugs act synergistically amongst themselves to give an additive effect upon *kapha* and *vata* and also help in removing *ama* from the body.

The components of a formulation need not be only synergistic, some drugs may have opposing properties as well and still be a part of the same formulation. For instance, in the formulation *Lashuna Ksheerapaka*<sup>5</sup>, processing of *lashuna* (*Allium sativum*) is done in milk, which acts antagonistically to its *teekshna* property.

Another formulation, *Shadangapaniya*<sup>6</sup> as explained in *Sharangadhara Samhita*,

contains six drugs namely; *Musta*(*Cyperus rotundus*), *Parpata*(*Fumaria parviflora*), *Usheera*(*Vetivera zizanoides*), *Chandana*(*Santalum album*), *Udeechya*(*Pavonia odorata*) and *Nagara*(*Zingiberiae officinale*) used in *Jwara*. All the drugs in this formulation are *Laghu*, *Ruksha* and they act antagonistically to the *Ama* present in the body during *Jwara* thus aiding in the treatment of the same.

The synergism and antagonism amongst ingredients is clearly noted here and can be understood in almost all formulations. It gives an insight as to why specifically a formulation consists of particular ingredients. The concept of *Pratinidhi dravya*<sup>7</sup> wherein substitutes for drugs have been explained, also suggests that alternatives used should possess similar qualities as that of the originally intended ingredient.

#### **2. Shodhana**

Most formulations contain a few or more ingredients which require specific processing techniques before they are added along with the other ingredients. This pre-processing is usually done for ingredients which cannot be used directly owing to their toxic nature / some active components which can only be made available after this particular processing.

For example - *Kamadugha Rasa*<sup>8</sup> is a formulation which consists of three ingredients namely; *Swarna gairika* (Red ochre), *Abhraka bhasma*, and *Guduchi satwa* (*Tinospora cordifolia*).

*Shodhana* of *gairika* is done by *bharjana* (frying) with a sufficient quantity of ghee or triturating it with cow's milk which removes its *doshas* and makes it more *pittahara*. *Abhraka bhasma* undergoes a special procedure called "*Amritikarana*" which makes the *bhasma* more assimilable and this procedure also involves *bharjana* of the *bhasma* with a specific quantity of ghee. Both these pre procedures for ingredients aid in the *pittaharana* karma of the formulation as a whole by acting antagonistically against the *ushna* and *teekshna* properties of *pitta*. The ingredients thus, are synergistic in their action against *pitta*.

*Gandhaka*<sup>9</sup> (Sulphur) is extensively used in *Rasashastra*. It needs to undergo the process of *Shodhana* to remove impurities and reduce its *teekshnata*. *Shodhana* is performed by liquefying powdered *Gandhaka* in ghee and passing it through a cloth into a media of milk. The *Pittahara* properties of milk and ghee reduce the side effects caused by *ushna teekshna Guna* of *Gandhaka* and also help in the removal of impurities.

### 3. Method of preparation

The method of preparation is specific to each formulation. These methods usually are synergistic to the actions expected from the formulation.

For example - *Hima*<sup>10</sup> is one among the *panchavidha kashaya kalpana*. The word meaning of "*hima*" is cold and so is the action expected out of it. Acharya Sharangadhara, in the context of *hima* preparation, explains that the drug should be kept for *nisha-usha*(*nishoshitam*) i.e overnight. The *sheeta guna* of *raatrikala* acts synergistically to the action expected to of the formulation. *Hima* is usually given to reduce *pitta* by virtue of its *sheeta guna* and the method of preparation enhances its property.

*Shatadhouta ghrita*<sup>11</sup> is a unique formulation. It is widely used in cases of *Visarpa* and *Dagdha* where the need to pacify *ushnata* is a priority. The action of washing the same *ghrita* hundred times increases the *Sheeta Guna* synergistically and potentiates its cooling action.

### 4. Adjuvants used/ media in which drugs are dissolved/ suspended

Apart from the main ingredients of a formulation, a few drugs are used as *prakshepaka dravyas* / *Bhavana dravyas* / media for preparation of the formulation. These are chosen specifically to ensure maximum bio availability of the other

ingredients and to get the best action perceivable.

For example - *Trikatu choorna* is the most commonly used prakshepaka dravya in most *avalehas*. *Avaleha* is relatively heavier for digestion and the addition of *trikatu* improves bioavailability and also ensures easy digestion by *Agni deepana*. The properties of *trikatu* are antagonistic to the *guru* and *manda* properties of *avaleha* which help in easier digestion.

*Gandhaka rasayana* is a popular formulation used in *kushtha*. *Gandhaka*, after purification is subjected to several *bhavanas* with different media like *godugdha* (cows milk), *twak* (*Cinnamomum zeylanica*) *kwatha*, *ela* (*Elattaria cardamomum*) *hima* etc. The *Bhavana dravyas* are selected to usually reduce the pittakara property of *gandhaka* and aid its *rasayana* property at the same time.

*Takrarishtha* is another formulation widely used in the condition of *grahani*. *Takra* (buttermilk) is the media for preparation of this formulation and the other drugs are added to *takra* and fermented. The action of *takra* on *grahani* has been established and using it as the media makes it even better<sup>12</sup>.

*Mantha kalpana*<sup>13</sup> is a unique formulation which is prepared by the action of *manthana* i .e. churning. Various drugs

like *Kharjura* (*Phoenix dactilyfera*) are used to make *mantha*. *Mantha*, when administered with *amla*, *guda* or *sneha*, helps in conditions of *Mutrakrichra* and *Udavarta* and administered with *sharkara*, *ikshurasa* or *draksha* (*Vitis vinifera*) helps in alleviating disorders of pitta and so on. The role of adjuvant is thus understood that the type of adjuvant changes the action of the formulation on the body. The adjuvant may act synergistically or antagonistically with the ingredients of the formulation and give a new effect. The adjuvant used, or the media in which drugs are suspended or dissolved are usually chosen to act synergistically or antagonistically with the properties of the ingredients, based on the action required.

##### 5. Use of visha dravyas

In several formulations, *visha dravyas* are used. These drugs are poisonous in nature and therefore are subjected to preprocessing before being added to the formulation but, sometimes, another ingredient may be added which may act as a chelating agent for the poison<sup>14</sup> which reduces harmful effects of the poison, if any are still remnant after the preprocessing.

For example- *Anandabhairava rasa*<sup>15</sup> is a frequently used formulation which contains *Vatsanabha* (*Aconitum ferox*) as one among the ingredients. *Vatsanabha*

undergoes *shodhana* before being added by the use of *gomutra* or such *dravyas*. Still, the formulation contains *tankana* (borax) which is known to antagonistically act against *vatsanabha* and reduce the side effects of poison if still remnant.

*Sanjivani Vati*<sup>16</sup> as explained in *Sharangadhara Samhita*, contains *Vidanga*(*Embelica ribes*), *Nagara*(*Zingiber officinale*), *Krishna*(*Piper longum*), *Pathya*(*Terminalia chebula*), *Amalaki*(*Embilica officinalis*), *Vibhitaki*(*Terminalia bellarica*), *Vacha*(*Adathoda vasica*), *Guduchi*(*Tinospora cordifolia*), *Bhallataka*(*Semecarpus anacardium*), *Vatsanabha*(*Aconitum ferox*). As per the reference, one *Vati* is to be administered in *Aama*, *ajirna* and *gulma*, two in *visoochika*, three in *sarpa dasta*. This reiterates the concept of *sthavara visha* acting antagonistically to *jangama visha*. *Vatsanabha* and *Bhallataka* are *sthavara visha* which act antagonistically to the *sthavara sarpa visha*.

## 6. Method of administration

The method of administration of a given medicine is specific to the patient and condition. The same medicine given at different times and in different dosage may have a range of effects.

For example - The time of administration of medicine is very specific in treatment.

*Aushadha kala* has been explained in many texts of Ayurveda but the rule is strictly followed when administering *vamana virechana aushadhi*. Medicine to induce *vamana* is to be administered in *kapha kala* and that of *virechana* should be in *pitta kala*. Usually these medicines by virtue of their properties, help in removal of the *utklishta dosha* and when done in the specific *dosha kala*, it becomes even more effective.

*Rasayana aushadhi* follows its separate and different mode of administration. Several *rasayanas* are specifically explained to be given in increasing dosages over a period of time only to be tapered and gradually stopped. This may act in synergistically improving the action by promoting a cumulative effect. This can be understood in the context of *vardhamana pippali rasayana*<sup>17</sup> explained in *Charaka Samhita*.

*Hingwashtaka Churna*<sup>18</sup> contains *Trikatu* (*Piper longum*, *Piper nigrum*, *Zingiber officinale*), *Ajamoda* (*Trachyspermum ammi*), *Saindhava*, *Jeeraka* (*Cuminum cyminum*), *Krishna jeer aka* (*Carum carvi*), *Hingu* (*Ferula narthex*) and is to be specifically administered with *ghrita* along with the first bolus of food. This method of administration acts synergistically to its expected action on *Apana vata* being the

specific *oushadha kala* and enhances its action.

The method of administration, in terms of dose, adjuvant or timing has a synergistic or antagonistic action on expected action of the medicine.

## CONCLUSION

The instances of synergism and antagonism can be observed in every single formulation, and at all levels; right from the ingredients to their processing and the way in which the final product is administered.

These terms are understood in the context of Ayurvedic formulations in the context of choosing raw materials, *Shodhana* method / processing of drugs specific to the formulation, method of preparation, adjuvants used / media in which the raw drugs are suspended/dissolved, use of *Visha Dravyas*, and the method of administration- *Kala, Matra*.

Many studies have been conducted on the difference in action when different techniques are used during the processing stage of a formulation or the adjuvants used while administering. However, these studies if conducted in the light of understanding the synergistic and antagonistic relationships among the ingredients, the processing media and the

adjuvants would be further interesting and can bring out new possibilities and venues for research.



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