



TIME OF DRUG ADMINISTRATION IN AYURVEDA: CHRONOTHERAPY

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ABSTRACT

Ayurveda is ancient machine of Indian medicine. So many principles are located here regarding to deal with sicknesses. Time of drug administration (*Aushadha Sevan Kaala*) is one in all them. The very last aim of *Chikitsa* is to reap equilibrium in *Doshas* and *Dhatu samya*, that's best by using given proper *Aushadhi* (Drug) in right time. Effectiveness of the drug administered depends on the time it's far taken. *Aushadha Kala* being a good deal flexible can be followed in line with the need of a person for purchasing preferred effects. Chronotherapy includes changing the timing of medication management to enhance the general manager of a sickness and to reduce remedy facet-outcomes and is an emerging concept inside the area of therapeutics. In various *Ayurvedic* texts, *Acharyas* had defined *Aushadha Sevana Kalas* in step with the biological clock for accomplishing the equilibrium between the *Doshas* and *Dhatus* which in the long run ends in *swasthya* (exact health).

Keywords: *Aushadha Sevan Kaala*, *Doshas*, *Dhatusamya*, Chronotherapy

INTRODUCTION

Chronotherapeutic, or chronotherapy, is the synchronization of medication with the biological rhythms of

disease activity and symptom intensity.^[1] Chronotherapy is an method that fulfils the criteria of drug

transport at a particular time as according to the pathophysiological want of the disorder, to enhance patient compliance. Chronotherapeutic is an emerging approach inside the treatment of various biological issues. Circadian rhythms are the crucial factor inside the biological cycle through which the drug dosing have to be matched with the rhythms of the illnesses for a success treatment of the contamination or the disease

The effectiveness of many drugs varies depending on the dosage administration time associated with 24 hours biological rhythm under the control of circadian clock. [2] *Ayurveda* has already been defined the variation in physiology and patho-physiological elements together with healing interventions and manner according to circadian rhythm for the maximum effectiveness and to limit the side results e.g. Disorders due to *Vata*, *Pitta* and *Kapha Dosha* get aggravated during rainy, autumn and winter season respectively, [3] seasonal *Panchakarma* during aggravation of *doshas*, [4] etc.

In *Ayurveda*, all physiological and pathological phenomenon depend upon delicate balance of *doshas* and to exactly adjust *doshic* biological clocks modifications are made inside the form of *dinacharya* and *ritucharya*. The idea of *ritucharya* implies dietetics, habits and behavioural adjustments to seasonal modifications. *Ritucharya* pursuits at fitness upkeep in all seasons via a balanced country of *doshas* i.e. *Doshas samya*. A balanced (and nicely adjusted) eating regimen is the conditions for maintaining the most excellent state of *doshas*.

Time specific administration of drugs outcomes in top-rated pharmacological utility of the drug. *Bheshaja sevana kala* a classical idea is currently studied as chronotherapy within the current science gaining its importance in clinical practice.

Acharya Vagbhata mentioned that- “*Kalo bhaishajya yoga kr*” [5] means for every action in the Universe is bound with the causative association of *kala* and hence *Aushadha* employed in a proper *Kaala* will result in expected *kaarya*.

Thus, to get the desired effect of the treatment consideration of that particular time for administration of

medicine is valuable. Synchronizing the drug therapies with body rhythms will indeed improve the result of treatment and that is studied presently under “chronotherapeutics”. [6]

Aim

- To explore and re-evaluate the various *Ayurvedic* concepts and principles related to time of drug administration (*Ausadh sevana kaala*) in *Ayurveda*.
- To explore the relationship between *Kaala* and *Ausadh sevana kaala*.
- To explore the clinical approach for time of drug administration in *Ayurveda*.

Materials & Methods

Materials related to *Ausadh, kaala, Ausadh sevana kaala*, Chronotherapeutics, Chronotherapy and other related topics have been collected. The main *Ayurvedic* texts used in this study are *Charak Samhita, Sushruta Samhita, Ashtang Samgraha, Ashtang Hridaya*, and *Sharangdhar Samhita* etc. We have also referred to the modern books and searched various websites to collect information on the relevant topics.

DISCUSSION

Vitality of Kaala

Ayurveda has given great importance to the *kaala* (time) for the *swastha* (healthy) as well as the *roga* (disease). From the basic *dina charya* (daily regimen), *ritu charya* (seasonal regimen), *dosha kala* (time of each dosa), *avasthapaka* (stages of digestion) *kaala*, *dhathu poshana* (process of nourishment) *kaala*, the process of ageing (*Jara*), *samprapti* (pathogenesis) in a disease to its *Chikitsa* (treatment), all the factors depends on time e.g.

- *Kaala* as a *Nidana* for *roga* [7]
- *Kalaja* and *Akalaja vyadhi* [8]
- *Kala* in *Sadhyasadyata* (prognosis) [9]
- Importance of *kala* in *Arishta* (bad prognosis) [10]
- Importance of *kala* in *Chikitsa* [11]
- Importance of *kala* in collection of drugs [12]
- *Aushadha sevana kala* [13]

It has already been mentioned in the classics that while treating a disease success can be achieved only when there is proper combination of *Desha* (region), *Kaala* (time), *Pramana* (dosage), *Satmya* (whole-

someness), *Asatmya* (unwholesomeness), *Pathya* (useful), and *Apathya* (harmful)^[14] among these, *Kaala* acquires second position, which shows the importance

of *Kaala* in *Chikitsa*. As per Ayurvedic texts *Kaala* means:

1. **Shad Aveksha Kaala** (Six observatory aspects of time) –^[15]

Table 1: *Shad Aveksha Kaala*

<i>Dina</i> (Different parts of the day)	<i>Rogi</i> (Patient)
<i>Aushadha</i> (Drugs)	<i>Vyadhi</i> (Disease)
<i>Jeerna Laxana</i> (stage of the digestion of the food)	<i>Ritu</i> (nature of the season)

2. **Dasha Bhesaja Kaala** (Ten types of times for the administration of medicine) ^[16,17]

Table 2: Relation between different time phase -*doshas*- digestion stage

Relation Between Different Time Phase - <i>Doshas</i> - Digestion Stage				
1	<i>Doshas</i>	<i>Vaata</i>	<i>Pitta</i>	<i>Kapha</i>
2	Vaya (Age)	Old Age	Young Age	Childhood
3	Day	2pm-6pm	10am-2pm	6am-10am
4	Night	2am-6am	10pm-2am	6pm-10am
5	Digestion stage	<i>Pakvavastha</i> (End stage)	<i>Vidagdhavastha</i> (Middle stage)	<i>Amavastha</i> (Initial stage)

Table 3: Relation between different season/ *kaala* and *bala* (immunity)

Relation Between Different Season/ <i>Kaala</i> And <i>Bala</i> (Immunity)				
1	<i>Kala</i>	<i>Hina Bala</i> (Debility)	<i>Madhyabala</i> (Medium Strength)	<i>Srestha Bala</i> (Maximum Strength)
2	<i>Adanakala</i>	<i>Grisma</i>	<i>Vasanta</i>	<i>Sisira</i>
3	<i>Visarga Kala</i>	<i>Varsa</i>	<i>Sharada</i>	<i>Hemanta</i>

The three bodily humors (*Vaata-Pitta-Kapha*), *Agni* status (power of digestion and metabolism) and *Bala* (Immunity) follow the biological clock along with the environmental cues and predominance of this organic entity range in different seasons. Any trade inside the normal seasonal property will desynchronize these rhythm upshots in manifestation of diseases. *Ayurveda* classics have well defined the variation in presentation of disorders in accordance with day, night, seasons and mealtime to get the maximum effectiveness of drug. Similarly for the selection of a proper drug, not only the strength of disease and patient, age, constitution (*Prakriti*), psychological issue (*Satva*), digestive capacity (*Agni*), accustoms of patient (*Satmya*), involved *Dosha* and *Dushya* were taken into consideration however also the time of administration of drug has also been pondered over.

Time of drug administration (*Ausadh sevana kaala*)

Acharya Charaka has mentioned that proper drug administration includes appropriate dosage and timing; and that confirms the success of the treatment.

“*Matra kalasraya yuktib, Sighiryauktou Pratisthita*” (C.S.Su 2/16)

Likewise, *Vagbhata* while stressing the importance of *kala-ausadha sambandha* (time – drug relationship) says that time potentiates efficiency of drugs - moreover a drug used at inappropriate time is not going to be beneficial.

“*Nahyapraprati ta kalamousadham Yougikam bhavati*” (A.S. Su 23/12)

As per various ancient scholars, *Aushadha Sevana Kala* (time) have been classified as below:

Charaka – 10 Sushruta – 10 Ashtanga Hrudya – 10 Ashtanga Sangraha – 11, Sharangdhara – 05

Table 4: *Ausadh sevan kaala* as per different authors [18,19,20,21,22]

Charaka - chi. 30	Ashtanga Hrudaya - Su.13	Ashtanga Sangraha - Su. 23	Sushruta Uttara 64	Sharangadhara – Purva 2
<i>Pratah Niranna</i>	<i>Abhakta</i>	<i>Abhakta</i>	<i>Abhakta</i>	<i>Suryodayajatah</i>
<i>Bhuktadau</i>	<i>Pragbhakta</i>	<i>Pragbhakta</i>	<i>Pragbhakta</i>	<i>Divasabhojane</i> a) <i>BhojanaPurva</i> b) <i>Sagrasa</i> c) <i>BhojanaMadhya</i> d) <i>BhojanaPashchat</i>
<i>Bhuktamadhye</i>	<i>Madhyabhakta</i>	<i>Madhyabhakta</i>	<i>Madhyabhakta</i>	<i>Sayambhojane</i> a) <i>Grasantare/Grase</i> b) <i>Bhojanapashchat</i>
<i>Bhuktapaschat after lunch (pratah)</i>	<i>pashchadbhakta</i>	<i>Adhobhakta</i>	<i>Adhobhakta</i>	<i>Nishi</i>
<i>Bhuktapaschat after dinner (sayam)</i>	<i>Nishi</i>	<i>Antarabhakta</i>	<i>Antarabhakta</i>	
<i>Muhurmuhu</i>	<i>Muhurmuhu</i>	<i>Muhurmuhu</i>	<i>Muhurmuhu</i>	
<i>Samudga</i>	<i>Samudga</i>	<i>Samudga</i>	<i>Samudga</i>	
<i>Bhaktasanyukta</i>	<i>Sabhakta</i>	<i>Samabhakta</i>	<i>Sabhakta</i>	
<i>Sagrasa</i>	<i>Sagrasa</i>	<i>Sagrasa</i>	<i>Grasa</i>	
<i>Grasantara</i>	<i>Grasantara</i>	<i>Grasantara</i>	<i>Grasantara</i>	
		<i>Nishi</i>		

Description and clinical indications of *Ausadh Sevan Kaala*

a) *Abhakta /Niranna (empty stomach):*

- Administration of *Aushadh* alone in empty stomach
- No interaction with food

Probable mode of action- As drug administered in empty stomach so that it directly interacts with *agni*. As in *abhakta kaala* stomach is devoid of *kapha* thus the *agni* digests the drug completely and one gets the maximum benefits.

Indications-

- Patients having good status of *Agni*
- In case of *Balwan Rogi* with *Balavan Vyadhi*.
- Used as *Rasayana*.
- In case of *Kaphaja* disorders etc.

Contraindications-

- In case of Children, Pregnancy, Female patients
- In *Doshakshaya* and *Dhatukshaya*

b) *Pragbhakta/ Bhuktadau (before meals)*

- Administration of *Ausadh* just before the intake of food

- *Ausadh* intake should be immediately followed by food (*Hemadri*)
- The *Ausadh* directly acts on the *Amashaya* and the vitiated *Doshas* [23]

Probable mode of action- As drug is used just before the food, So, its first interaction is with *agni*, leads to quick metabolism and also there is less chance of any toxic effects of drug as food follows the drug. Food also reduces the expulsion of drug, so can be used in debilitated patients. *Apana Vayu* is in active state during this *kaala* so it's a right time of drug administration for *Apana Vayu vikriti*.

Indications-

- Disorders of *Apanavayu*
- Diseases of lower body parts
- Obesity/ Fat disorders etc.

c) *Madhyabhakta (in between meals)*

- *Ausadh* is administered in between the meal.
- As per *Chakrapani* and *Indu*, half of the food is taken initially, followed by *Ausadh* administration, and again followed by remaining food.

- *Acharya Sushruta* explained that due to *Avisaari Bhaava* (not spread) of *Aushadha*, it acts on *Madhya Deha Rogas* [24]

Probable mode of action- In this case *ausadh* is taken in between the meals so it is covered by both upper and lower ends and cannot spread so act locally for *sthanika doshas*. During this period *Samana vaayu* is stimulated that enhances the *paka* of *ausadh*.

Indications-

- Vitiating of *Samanavayu* -*Mandagni* -*Paittika* disorders
- *Koshthagatavyadhi*- *Shula*-*Gulma*-*Grahani*

d) Pashchadbhakta/ Adhobhakta (after lunch and dinner)

- *Ausadh* is administered after meals (after lunch & dinner).
- *Hemadri* & *Indu*- *Ausadh* is to be administered immediately after meals

Probable mode of action- In this *kaala ausadh* is administered after meals i.e., after lunch & dinner. After lunch, there is stimulation of *Vyana Vayu* and after dinner of *Udana Vayu*, So, they could be used in the respective disorders. As the site of *vyaana vayu* is considered to be *hrudaya* (heart). *Acharyas* have stated that as every flower bloom in the morning every-day similarly every morning heart also blooms, activating *vyaana vayu* in it. Thus, the medicine administered in the morning will reach *hrudaya* and will act properly on *vyana vaayu*. The activity of *vyana vaayu* reduces in the night. The activities of *vyana* are then taken over by *udana vaayu*, thus the administration of *ausadh* after dinner helps to cure the diseases related with *udana vata*.

Indications-

- Disorders related with *Vyana vayu*- *Udana vayu*
- e) Muhurmuhu (frequently administered)**
- *Aushadha* is administered frequently regardless of *Bhukta* or *Abuktavastha*
 - *Bhukta* and *Abhuktavastha* are chosen according to the power of patient

Probable mode of action- In order to get immediate relief, the *Ausadh* is given frequently, and that maintained its plasma concentration and make it more bio-available. The *Kala* provides an opportunity to admin-

ister higher therapeutic dose of *ausadha* to pacify the aggravated *Doshas*.

Indications-

- Preferred during acute conditions
- *Pranavaha-Udakavaha* -*Annavaastrogotata* disorders

f) Antarbhakta (after digestion of meal in noon)

- The administration of *ausadha* in between two meals is considered as *Antarabhakta*
- *Ausadh* is to be taken in the afternoon and after digestion of medicine, again food is to be given to the patient in the evening
- As per *Indu*²⁵, first *Antara Bhakta* is during day, and the next one is 1 *Yaama* after evening food. This is equivalent to *Nishi*.

Probable mode of action- Due to *madhyanha* i.e. *Pittakala*, *Agni* is in a stimulated condition. So, *ausadha* is properly metabolized and produces desired effect.

Indications-

- Disorders of *Vyana vayu*

g) Samudga (just before and after meal)

- *Ausadha* is administered at the time immediate before and after meals
- *Indu* and *Hemadri* specify that *ausadha* should be consumed immediately in relation to food

Probable mode of action- As *ausadha* is administered at the time immediate before and after meals so it acts on *Vyana*, *Apana* and *Udana Vayu*. *Samudga Kala* probably helps in the therapeutic activity of the *ausadha* in correcting the pathogenesis and establishing *Anulomana* of *Vata Dosa*.

Indications-

- Disorders related with *Vyana-Apana-Udanavayu*
- h) Sabhakta (mixed with food)**
- *Ausadha* is administered with food
 - According to *Indu*- *Ausadha* is processed or cooked along with food or it is given with food
 - *Kashyapa* mentions it to be *Bala* and *Agni Rakhshaka* [26]

Probable mode of action- As *ausadha* is taken by mixing or cooked along with food, so, when the food is digested and gets converted into *aahaara rasa*, the *ausadha* also gets digested and its extract comes with

aahara rasa. This medicated *aahara rasa* gets circulated in the body and helps to cure diseases all over the body.

Indications-

- *Arochaka, aruchi, sarvangasamshrita vyadhis* etc
- Useful in women, old, children, debilitated patients

i) Sagraasa (with each and every bite of food)

- *Ausadha* is given with each and every bite of food

Probable mode of action- As *ausadha* is given with each bite of food, enhances its absorption right from buccal mucosa and offers rapid onset of action. *Sagraasa kaala ausadh* stimulates the *Pranavayu*.

Indications-

- Specially indicated for *Leha, Churna, Vati Kalpana*
- *Prana vayu* disorders

j) Grasantare (in between two bites of food)

- Intake of *ausadh* between the bolus of food
- In *Ashtanga Hrudaya, Sarvanga Sundari Teeka* it is clearly mentioned that *Aushadhi* is administered between bolus of food but in *Ayurveda Rasayana Teeka* it is said as *Graasa Sampruktamaushadham* [27]

Probable mode of action- helps in correcting the *Gati* (activity) *Vikruti* of *Vata Dosha* by promoting *Anulomana of Vata Dosha*. The process of deglutination is supervised by *prana vaayu*. Thus, the medicine taken along with each bolus of food will come in contact with *prana* and will help to cure *prana* related diseases.

Indications-

- Disorders of *Prana Vayu*
- In *Hridya roga* [28]

k) Nisha (before sleep)

- *Ausadh* is administered after digestion of food consumed
- According to Indu, the exact *Nisa Kala* is the time after the evening meal has digested and 3 hours have passed.
- In *Shaarangadhara Samhita, Deepika Commentary*, it is mentioned that the timing of administration of medicine is 1 *Yaama* after evening meals. [29]

- *Chiraparinamana* (long lasting action) of the *Shamana Aushadhi* is achieved as no food intake occurs until the next morning. [30]

Probable mode of action-the *Nisa Kala*, in which there is *Kapha vrddhi* due to *Kala Prabhava* is an aid to the activity of *ausadha* used and *ausadha* admits elective affinity (*Gamitva*) towards the part, above the neck. Selective action of the *ausadha* towards the *urdhvajatrugata* parts because the *Adhara gati* of *ausadha* is prevented by food.

Indications-

- *Urdhvajatrugata* Disorders
- Indicated for *Vamana, Dhumapana*.

CONCLUSION

Acharya Charaka says that *Aushadha* given at appropriate *Kala* (time) is more efficacious than one given at inappropriate *Kala*. The effect of a drug depends on the dosage administration time. In *Ayurveda*, it has been mentioned that the predictable variations in bodily functions during a day, season and age alters the severity of disease symptoms, results of diagnostic tests and effects of drugs. The drug release in body and its specific action on specific *dosha* or disease conditions vary with the Circadian variation of *dosha* and disease symptoms. Chrono pharmacology and Chronotherapeutic has emerged an important area for research for medical fraternity as its correct knowledge helps doctors to treat patient more effectively. Hence the success of treatment always depends upon the time of drug administration.

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